U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

AMERICAN RECOVERY and REINVESTMENT ACT OF 2009

CHALLENGE GRANT APPLICATIONS

Omnibus of Broad Challenge Areas and Specific Topics

APPLICATION SUBMISSION DATE

APRIL 27, 2009

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Funding Opportunity Announcements and Application Instructions are contained in separate files. Follow the links below to view these documents.

FUNDING OPPORTUNITY ANNOUNCEMENT

RECOVERY ACT LIMITED COMPETITION: NIH CHALLENGE GRANTS IN HEALTH AND SCIENCE RESEARCH (RC1) (RFA-OD-09-003)
(HTTP://GRANTS.NIH.GOV/GRANTS/GUIDE/RFA-FILES/RFA-OD-09-003.HTML)

APPLICATION INSTRUCTIONS

SF424 (R&R) APPLICATION INSTRUCTIONS AND ELECTRONIC SUBMISSION INFORMATION
(HTTP://GRANTS.NIH.GOV/GRANTS/FUNDING/424/INDEX.HTM)

NIH Challenge Grant Program

NIH has received new funds for Fiscal Years (FYs) 2009 and 2010 as part of the American Recovery and Reinvestment Act of 2009 (Recovery Act). NIH has designated at least $200 million for a new initiative called **NIH Challenge Grants in Health and Science Research** (see http://grants.nih.gov/grants/funding/challenge_award/), contingent upon the submission of a sufficient number of scientifically meritorious applications. In addition, Recovery Act funds allocated to NIH specifically for comparative effectiveness research (CER) may be available to support additional grants. Projects receiving these funds will need to meet this definition of CER: "a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Such a study may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy." Such research may include the development and use of clinical registries, clinical data networks, and other forms of electronic health data that can be used to generate or obtain outcomes data as they apply to CER.

This new program will support research on topic areas which address specific scientific and health research challenges in biomedical and behavioral research that would benefit from significant 2-year jumpstart funds. NIH Institute and Centers have selected specific Challenge Topics within each of the Challenge Areas. The research in these Challenge Areas should have a high impact in biomedical or behavioral science and/or public health.

As part of the Recovery Act, the NIH invites, through this limited competition, NIH Challenge Grant (RC1) applications from domestic (United States) institutions/organizations proposing novel research in areas that address specific knowledge gaps, scientific opportunities, new technologies, data generation, or research methods that would benefit from an influx of funds to quickly advance the area in significant ways. This program is designed to support research in scientific areas identified by the Institutes and Centers, as described in the Challenge Grant Request for Applications (RFA) (see http://grants.nih.gov/grants/guide/rfa-files/RFA-OD-09-003.html).

Challenge Areas

The NIH has identified a range of Challenge Areas that focus on specific knowledge gaps, scientific opportunities, new technologies, data generation, or research methods that would benefit from an influx of funds to quickly advance the area in significant ways. Within each broad Challenge Area (noted below) the NIH Institutes, Centers, and Offices have specified particular Challenge Topics that address their missions. Applicants to the Challenge Grants Program are invited to submit applications in any of the areas listed in this Omnibus Solicitation. Those topics marked with an asterisk have been designated as the Institute, Center or Office's highest priority; however, applicants may apply to any of the topics. Applicants are encouraged to contact the program staff listed within each of the topics.

This Omnibus Solicitation describes all the topics listed under these broad Challenge Areas:

(01) Behavior, Behavioral Change, and Prevention

(02) Bioethics

(03) Biomarker Discovery and Validation

(04) Clinical Research

(05) Comparative Effectiveness Research (CER)

(06) Enabling Technologies

(07) Enhancing Clinical Trials

(08) Genomics

(09) Health Disparities

(10) Information Technology for Processing Health Care Data

(11) Regenerative Medicine

(12) Science, Technology, Engineering and Mathematics Education (STEM)

(13) Smart Biomaterials – Theranostics

(14) Stem Cells

(15) Translational Science

As instructed in the RFA, applicants MUST specify both the broad Challenge Area (01-15) and the specific Challenge Topic that their research addresses.

NIH Institutes, Centers and Offices and Contact Information

INSTITUTES, CENTERS AND OFFICES	PROGRAM CONTACT
National Institute on Alcohol Abuse and Alcoholism (AA) http://www.niaaa.nih.gov	Dr. Trish Powell Phone: 301 443-5106 E-mail: ppowell@mail.nih.gov
National Institute on Aging (AG) http://www.nia.nih.gov	Dr. Kathie Reed Phone: 301-496-3121 E-mail: reedk@mail.nih.gov
National Institute of Allergy and Infectious Diseases (AI) http://www.niaid.nih.gov	Dr. Patricia Haggerty Phone: 301-451-2615 E-mail: haggertp@niaid.nih.gov
National Institute of Arthritis and Musculoskeletal and Skin Diseases (AR) http://www.niams.nih.gov	Dr. Robert Carter Phone: 301-496-4353 E-mail: carterrob@nih.gov
National Center for Complementary and Alternative Medicine (AT) http://www.nccam.nih.gov	Dr. Richard Nahin Phone: 301-496-7801 E-mail: nahinr@mail.nih.gov
National Cancer Institute (CA) http://www.cancer.gov	Dr. Dinah Singer Phone: 301-496-8636 E-mail: singerd@mail.nih.gov
National Institute on Drug Abuse (DA) http://www.nida.nih.gov	Dr. Christine Colvis Phone: 301-443-6480 E-mail: ccolvis@nida.nih.gov
National Institute on Deafness and Other Communication Disorders (DC) http://www.nidcd.nih.gov	Dr. Judith Cooper Phone: 301-496-5061 E-mail: cooperj@nidcd.nih.gov
National Institute of Dental and Craniofacial Research (DE) http://www.nidcr.nih.gov	Dr. Pamela McInnes Phone: 301-443-8618 E-mail: pmcinnes@nidcr.nih.gov
National Institute of Diabetes and Digestive and Kidney Diseases (DK) http://www.niddk.nih.gov	Dr. Brent Stanfield Phone: 301-594-8834 E-mail: stanfibr@niddk.nih.gov

INSTITUTES, CENTERS AND OFFICES	PROGRAM CONTACT
National Institute of Biomedical Imaging and Bioengineering (EB) http://www.nibib.nih.gov	Dr. William Heetderks Phone: 301-451-6771 E-mail: heetderw@mail.nih.gov
National Institute of Environmental Health Sciences (ES) http://www.niehs.nih.gov	Dr. Gwen Collman Phone: 919-541-4980 E-mail: Collman@niehs.nih.gov
National Eye Institute (EY) http://www.nei.nih.gov	Dr. Grace L. Shen Phone: 301-451-2020 E-mail: sheng@mail.nih.gov
National Institute of General Medical Sciences (GM) http://www.nigms.nih.gov	Dr. Judith H. Greenberg Phone: 301-594-0943 E-mail: greenbej@nigms.nih.gov
Eunice Kennedy Shriver National Institute of Child Health and Human Development (HD) http://www.nichd.nih.gov	Ms. Mona Rowe Phone: 301-496-1877 E-mail: rowem@mail.nih.gov
National Human Genome Research Institute (HG) http://www.genome.gov	Dr. Mark Guyer Phone: 301-496-7531 E-mail: Mark.Guyer@nih.gov
National Heart, Lung, and Blood Institute (HL) http://www.nhlbi.nih.gov	Dr. Carl Roth Phone: 301-496-6331 E-mail: rothc@nhlbi.nih.gov
National Library of Medicine (LM) http://www.nlm.nih.gov	Dr. Valerie Florance Phone: 301-594-4882 E-mail: florancev@mail.nih.gov
National Center on Minority Health and Health Disparities (MD) http://www.ncmhd.nih.gov	Dr. Nathaniel Stinson Phone: 301-402-1366 E-mail: Nathaniel.Stinson@nih.gov
National Institute of Mental Health (MH) http://www.nimh.nih.gov	Dr. Jean Noronha Phone: 301-443-3367 E-mail: jnoronha@mail.nih.gov
National Institute of Nursing Research (NR) http://www.nih.gov/ninr	Dr. Linda Weglicki Phone: 301-594-6908 E-mail: weglickils@mail.nih.gov
National Institute of Neurological Disorders and Stroke (NS) http://www.ninds.nih.gov	Dr. Robert Finkelstein Phone: 301-496-9248 E-mail: finkelsr@ninds.nih.gov

INSTITUTES, CENTERS AND OFFICES	PROGRAM CONTACT
Office On Science Policy OD (OSP) – Bioethics http://bioethics.od.nih.gov	Dr. Sarah Carr Phone: 301-435-6753 E-mail: carrs@mail.nih.gov
Office Of Behavioral And Social Sciences Research OD (OBSSR) http://obssr.od.nih.gov/index.aspx	Dr. Deborah Olster Phone: 301-402-1147 E-mail: olsterd@od.nih.gov
Office of Rare Disease Research OD (ORDR) http://rarediseases.info.nih.gov/ORDNews.aspx?PageID=10	Dr. Stephen C. Groft Phone: 301-402-4336 E-mail: grofts2@od.nih.gov
Office Of Research On Women's Health OD (ORWH) http://orwh.od.nih.gov	Dr. Lisa Begg Phone: 301/496-7853 E-mail: beggl@od.nih.gov
OD/OSC Common Fund	Dr. Brenda Weis Phone: 301-435-5840 E-mail: weis@mail.nih.gov
National Center for Research Resources (RR) http://www.ncrr.nih.gov	Dr. Louise Ramm Phone:301-435-0879 E-mail: ramml@mail.nih.gov
Fogarty International Center (FIC) (TW) http://www.fic.nih.gov	Dr. Joshua Rosenthal Phone: 301-496-1653 E-mail: joshua_rosenthal@nih.gov

CHALLENGE AREAS AND CHALLENGE TOPICS OF THE NIH CHALLENGE GRANT PROGRAM

Topics in the table below that are marked with an asterisk (*) have been designated as an Institute, Center or Office's highest priority; however, applicants may apply to **any** of the topics.

Broad Challenge Area	Specific Challenge Topic
(01) Behavior, Behavioral Change, and Prevention	**01-AA-101*** **Identifying Phenotypic Markers for Positive Behavior Change.** Identify reliable, robust intermediate phenotypic markers (using cognitive neuroscience and behavioral economics) that can be used to personalize approaches to support positive health behavior change in the near term. Examples include behavioral disinhibition, delay discounting, heart rate variability and implicit cognition. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-AA-102*** **Functional Roles of Neuroimmune Factors in Mediating Behavior.** Neuroimmune factors significantly impact both normal brain functions and a variety of neurological and behavioral disorders. Emerging data suggest that physiological functions of neuroimmune factors, such as cytokines and chemokines, are not restricted to mediating neuroinflammatory responses but may be considered as a new class of neurotransmitter, neuromodulator, or neurohormone in the brain. This paradigm shift offers a new framework to understand the roles of neuroimmune factors in a variety of behavioral conditions such as excessive drinking, anxiety, depression, etc. Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov **01-AA-103*** **Capturing Social Network Information for Groups at High Risk for Negative Health Behaviors.** Emerging evidence indicates that social networks influence health behaviors such as eating habits, alcohol consumption, and smoking. Research in this area is needed to enhance existing methodologies and/or devise novel methods that will capture social network information among groups at heightened risk for particular negative health behaviors. The ultimate public health goal is to use this information to influence behavioral choices and improve health outcomes. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-AA-104** **Computational Brain Modeling of Alcohol-Seeking and Drinking Behavior.** Alcohol use disorder is a complex disease involving a variety of neurotransmitter, neuromodulator, and neurohormonal systems and various intracellular networks. It is, most likely, that targeting a combination of sites within these systems and networks will be essential in developing effective medications. These systems and networks are part of neurocircuits responsible for different aspects of alcohol addiction, including craving, reward, protracted abstinence symptoms, impaired control, tolerance, inhibition, and executive function. Research is encouraged to develop system computer modeling of these neurocircuits as an important step forward in understanding alcohol seeking and drinking behavior and identifying multiple targets in the brain for the development of effective medications. Although creating a valid computer model of this kind of biological network requires an immense effort, the payoff would be enormous. Correctly predicting the linked effects of changes of various neurotransmitter and neuromodulator systems and intracellular networks within and across these neurocircuits will provide a solid foundation for treating problematic drinking. Contact: Dr. Mark

Broad Challenge Area	Specific Challenge Topic
	Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-AA-105 Mechanisms of Behavior Change.** This initiative will support research to better understand the mechanisms underlying the initiation and maintenance of behavior change among heavy drinkers, by modeling the relationship among neurophysiological, psychological and social factors involved (modeling across scale). This will lead in turn to new methods to support positive change, moving beyond interventions that consist primarily of education and persuasion. Research is needed on both treatment-seeking and community-dwelling populations, examining the mechanisms and processes involved in initiating change, including predictors of success or failure as well as processes that underlie maintenance of change or relapse. Research needs to explicitly examine mechanisms, and may use statistical modeling techniques such as structural equation modeling, but priority will be given to projects that experimentally manipulate potential mediators of change. Development of novel technologies, experimental approaches and mathematical modeling methods is also encouraged. Research projects that incorporate or integrate two or more disciplines of research or levels of analysis such as psychological, neurophysiological, or genomic are of particular interest. Consideration will also be given to exploratory or developmental projects that are expected to help refine hypotheses and generate pilot data. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **01-AA-106 Alcohol's Effect on Adolescent Brain Development.** Adolescence is a period of rapid brain growth and neural remodeling, particularly in the prefrontal cortex, an area which subserves "executive" functions such as cognitive flexibility, self-regulation and the evaluation of risk and reward. Two major developmental brain processes, myelination and synaptic pruning, continue to occur throughout adolescence. In addition to these structural changes, neurotransmitter systems undergo substantial modification. Concurrently, there is a significant escalation in drinking during the adolescent period. Of particular concern are the widespread occurrence of episodes of binge drinking and intoxication, and the association of adolescent alcohol exposure with later alcohol abuse and dependence. Research is encouraged to determine whether alcohol interferes with normal adolescent brain development at the cellular and molecular level, and, if so, how it affects patterns of brain connectivity, that may influence drinking behavior and the emergence of alcohol-related disorders. Contact: Dr. Ellen Witt, 301-443-6545, ewitt@mail.nih.gov **01-AA-107 Alcohol, Brain Development, and Adolescent Decision Making.** Alcohol remains the most commonly abused substance among adolescents. However, little is know about cognitive, emotional and social processes that may contribute to high rates of adolescent drinking and how alcohol use in turn may affect these processes. During adolescence, developing brain systems underlying cognitive, emotional, and social behaviors develop at different rates. This asynchronous maturation of intellectual and emotional skills and their underlying neural substrates may help explain age and individual differences in judgment, decision making, sensation seeking, and risk taking which make adolescents vulnerable to developing alcohol abuse and dependence. Research is needed to determine differences between adolescent and adult decision-making processes and reward-based learning as they relate to alcohol drinking behavior, and to determine the effects of adolescent drinking on the development of decision-making processes, reward-based learning and their underlying neural substrates. Contact: Dr. Ellen Witt, 301-443-6545, ewitt@mail.nih.gov **01-AA-108 Alcohol, Pubertal Hormones, and Sex Differences in Alcohol Abuse and Dependence.** Between the ages of 12 and 17, adolescent males and females have

Broad Challenge Area	Specific Challenge Topic
	similar patterns of alcohol use and similar prevalence of alcohol abuse and dependence. By late adolescence, however, sex specific patterns begin to emerge, with females exhibiting fewer drinking days in the past month, fewer episodes of heavy drinking, and lower prevalence of alcohol abuse and dependence relative to males. Substantial changes in brain biology, physiology, and architecture occur during the transitions from pre-adolescence through adolescence and into young adulthood. The hormonal changes of puberty also affect the developing brain and may help explain the disparate drinking trajectories of boys and girls. Recent evidence suggests that an increase in gonadal steroids and stress response hormones during puberty may influence the structural and functional remodeling of the brain. Thus, hormonal mechanisms, such as activation of reproductive hormones, stress responses, and their effects on brain developmental processes could explain the observed sex differences in alcohol drinking patterns during puberty. With brain development and puberty proceeding at the same time as rapid escalation in alcohol use, it is important to consider potential effects of alcohol on the interaction between pubertal hormone changes and adolescent neurodevelopmental processes and the implications of alcohol-induced changes in these processes on sex differences in future alcohol use and misuse. Two-year studies are needed to investigate the degree to which hormonal changes at puberty interact with neurodevelopmental processes to promote sex effects in alcohol use and misuse, and the effects of alcohol on these interactive processes. Contact: Dr. Ellen Witt, 301-443-6545, ewitt@mail.nih.gov **01-AA-109 Alcohol and Chronobiology.** Recent research has demonstrated the potent effect of clock genes, those involved in regulation of circadian rhythms, in addictive behavior. Mutant or variant alleles of clock genes can alter incentive salience and modify the vulnerability of risk for alcohol dependence. Conversely, environmental disruption can create acute, or in the case of fetal alcohol exposure, long term disruption of circadian function and stress. This in turn can enhance alcohol self administration. Such observations clearly implicate circadian function as a potential factor in alcohol dependence. Research that characterizes the consequences of clock gene knock-outs or knock-ins for alcohol consumption would aid in establishing the link between clock genes and risk for alcohol abuse. Contact: Dr. Lindsey Grandison, 301-443-0606, lgrandis@mail.nih.gov **01-AA-110 The Impact of Alcoholic Beverage Container Labels on Drinking-related Behaviors and Beliefs.** Unlike most consumable products, alcoholic beverage containers carry little or no information about ingredients, calories and serving sizes. Researchers and consumer groups have pushed the importance of labels for educating the public about serving sizes in order to help consumers avoid unwanted side effects, stay within the boundaries of moderate consumption and make healthy dietary choices. For instance, while a single serving of wine per day could convey benefits for cardiovascular health, two or more servings per day can increase the odds of breast cancer and other cancers. Some malt beverages contain as many calories as some chocolate bars. Presumably, such information would be of value to consumers and could influence their drinking habits and beverage choices. Despite the logical appeal of placing detailed labels on beverage containers, it remains unclear what, if any, impact such labels might have on alcohol-related attitudes, beliefs and behaviors. Further, it remains unclear what information should appear and where. Innovative developmental studies to determine the impact of alcoholic beverage container labels on drinking-related behaviors and beliefs are encouraged. Contact: Dr. Aaron White, 301-451-5943, whitea4@mail.nih.gov **01-AG-101 Advanced analyses for social network health data.** Many aspects of health and disease are now understood to take place in a rich social context, and the

Broad Challenge Area	Specific Challenge Topic
	analyses of the network structure of real (and virtual) communities promises many insights into the processes by which health-related beliefs, norms, and behavior patterns are transmitted. Although the mathematics of networks and the complex systems they imply have become increasingly more tractable, significant challenges remain in the design and implementation of analyses that are robust to data limitations or model mis-specification. Contact: Dr. John Haaga, 301-496-3131, HaagaJ@mail.nih.gov **01-AG-102 Neural mechanisms of behavioral change.** Studies aimed at elucidating the neural mechanisms underlying behavioral changes during aging or age-related diseases and disorders, including choice of food and nutrition or the amount of physical activities. Contact: Dr. Molly Wagster, 301-496-9350, WagsterM@mail.nih.gov **01-AG-103 Individual-based model of social behavior.** Development of a robust and well-characterized individual-based model of social behavior that includes the dynamics of social interactions and that matches observed patterns of behavior. Contact: Dr. Lis Nielsen, 301-402-4156, NielsenLi@mail.nih.gov **01-AG-104 Test default options to promote healthier behaviors.** Exploration by behavioral economists and clinicians to develop and test default options (e.g., placement of fresh fruit displays in stores, the location of parking spaces at the workplace) to promote healthier behaviors. Contact: Dr. John Phillips, 301-496-3138, PhillipJ@mail.nih.gov **01-AG-105 Measurement of culturally-shared mental phenomena.** Development of new tools for the measurement of: culturally-shared mental phenomena (e.g., representations, scripts, prejudices); mechanisms by which these phenomena are transferred and adapted across individuals, and the distribution and transmission of cultural phenomena within populations. Contact: Dr. Jonathan King, 301-402-4156, kingjo@mail.nih.gov **01-AG-106 Identifying phenotypic markers for positive behavior change.** Identify reliable, robust intermediate phenotypic markers (using cognitive neuroscience and behavioral economics) that can be used to personalize approaches to support positive health behavior change in the near term. Examples include behavioral disinhibition, delay discounting, heart rate variability and implicit cognition. Contact: Dr. Jonathan King, 301-402-4156, kingjo@mail.nih.gov **01-AG-107 Functional roles of neuroimmune factors in mediating behavior.** Emerging data suggest that physiological functions of neuroimmune factors, such as cytokines and chemokines, are not restricted to mediating neuroinflammatory responses but may be considered as a new class of neurotransmitter, neuromodulator, or neurohormone in the brain. This paradigm shift offers a new framework to understand the roles of neuroimmune factors in a variety of behavioral conditions such as excessive drinking, anxiety, depression, etc. Contact: Dr. Molly Wagster, 301-496-9350, WagsterM@mail.nih.gov **01-AG-108 Capturing social network information for groups at high risk for negative health behaviors.** Emerging evidence indicates that social networks influence health behaviors such as eating habits, alcohol consumption, and smoking. Research in this area is needed to enhance existing methodologies and/or devise novel methods that will capture social network information among groups at heightened risk for particular negative health behaviors. Contact: Dr. Jonathan King, 301-402-4156, kingjo@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
	01-AG-109 Development of behavioral and social interventions that reduce stigma and improve quality and accessibility of health care services in low resource settings. In the same manner that the effects of stigma magnify the personal and societal problems related to diseases and disorders (e.g., mental health conditions, addiction, HIV), preventing or mitigating stigma and its effects can profoundly improve the lives of individuals, their families and the larger society. There is a critical need to translate existing knowledge related to the causes and consequences of stigma into scalable pilot interventions that can measure stigma and prevent or mitigate its negative effects on health. Contact: Dr. Sid Stahl, 301-402-4156, StahlS@mail.nih.gov **01-AR-101 Integrating Behavioral And Biomedical Research Approaches In Arthritis And Musculoskeletal Diseases.** Behavioral and social factors are involved in numerous ways in the onset, course and outcomes of chronic diseases. These factors are central in the experience of symptoms (such as pain and fatigue), disease-related distress, ability to cope, disability and, to varying extents, the success of prevention and treatment approaches. Biopsychosocial research needs in rheumatic, musculoskeletal, and skin diseases include studies of biological mechanisms of psychosocial or behavioral processes related to disease progression, and genetic and environmental influences on behaviors relevant to disease onset. Integrated approaches would allow tailoring interventions based on disease phenotype, individual psychological or social characteristics, and provide evidence to translate knowledge into behavioral change such as adopting and adhering to treatment and preventive interventions. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **01-AR-102 Studies investigating variability in patient outcomes related to behavior.** Individuals differ tremendously in their response to clinical disease and symptoms. We seek studies to investigate the behavioral differences, sex differences, ethnic background, family environment, previous trauma, education, or combination of factors underlying the observed variability in outcomes in rheumatic, musculoskeletal and skin diseases. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **01-AR-103 Education As A Global Challenge**. Health outcomes are linked to both education and literacy. Disease education is currently targeted to affected populations by patient advocate groups. In the NIAMS mission areas, there is a paucity of disease and science education targeted to children and the general public as a whole through education, we have an opportunity to improve outcomes, feed the pipeline of underserved students entering research careers in NIAMS areas, educate the public on the purpose and results of NIAMS clinical trials, and reduce the stigma associated with disfiguring diseases which are plentiful in the NIAMS portfolio. One year awards of 100K to fund current science education programs in the USA are proposed. NIAMS would challenge existing education programs to integrate the NIAMS mission areas. We could encourage current NCRR Science Education Partnership Award (SEPA) recipients to apply. The SEPA programs are robust and these organizations have the potential to integrate our areas of interest into educational models that are developed or in the process of development. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **01-CA-101 Research to Inform FDA Regulation of Tobacco Products.** The "Family Smoking Prevention and Tobacco Control Act" includes numerous provisions for which timely research is needed to expand the evidence-base for implementation. Topic areas for research include but are not limited to: product and constituent standards

Broad Challenge Area	Specific Challenge Topic
	reporting and testing; product marketing and sales, including health related claims; product labeling and advertising; consumer perception studies; regulation of menthol; potential reduction of nicotine levels in tobacco products; extended use or additional indications of medications to treat nicotine dependence; and preventing youth's tobacco use. Proposals should specify the specific provision or provisions of the legislation the research will address and how the proposed research will inform FDA regulation of tobacco products. Contact: Dr. Cathy Backinger, 301-435-8638, cathy_backinger@nih.gov **01-CA-102 The Role of Nutrition in Cancer Biology.** Diet and nutrition have fundamental effects on health. The exact associations and mechanism involved are poorly understood. Example of topics include: Diet associated differences in the microbiome – how does that affect the composition of the microbiome, inflammation, immune repertoire; the effect of nutrition on adaptive and innate immunity; application of multiscale modeling to linking effects of nutrition from the molecular to cellular to organism to population studies. Contact: Dr. Barbara Spalholz, 301-496-7028, spalholb@mail.nih.gov **01-CA-103 The role of health behaviors in cancer prevention.** High priority domains of behavior change include tobacco use, diet, physical activity, sun exposure and adherence to recommended cancer screening. Behavior change studies among cancer survivors also are encouraged. In addition, interventions targeted to health care providers to improve the delivery of high quality cancer care are welcome. Contact: Dr. Linda Nebeling, 301-435-2841, nebelinl@mail.nih.gov **01-DA-101 New Tools for Social Neuroscience and Neurofeedback.** NIDA is soliciting research to validate existing measures and techniques, and to encourage the development, improvement and/or adaptation of technologies which, by the end of the funding period, will be verified field-deployable tools that can detect and deliver feedback with maximum precision and reliability. Building on currently available technologies, these tools will be effective and practical instruments for the early identification of children and adolescents with insufficient self-regulation and for incorporation into therapeutic programs facilitating the amelioration of these individuals' dysregulation. Contact: Dr. Elizabeth M. Ginexi, 301-402-1755, LGinexi@nida.nih.gov **01-DA-102 Individual-based model of social behavior.** Employ animal behavioral models to understand social behaviors as antecedents to, or vulnerability for, drug abuse and addiction; effects of drugs of abuse on social interactions; and the consequences of addiction on social behaviors. Includes studies of neurobiological substrates and environmental influences on the complex interplay between social behaviors and drug abuse behavior. Also includes changes in social repertoire that emerge during the developmental course of addiction. Contact: Dr. Minda Lynch, 301-435-1322, mlynch1@nida.nih.gov **01-DA-103 Identifying phenotypic markers for positive behavioral change.** Identify intermediate phenotypes that predict sensitivity to interventions designed to block the development of drug abuse, block or reduce compulsive drug- taking, or promote abstinence. Phenotypes can be identified using physiological, behavioral, cognitive or neurobiological assessments in animal models or human studies. Research with animal models should manipulate environmental, behavioral or neurobiological variables that alter the sensitivity to these interventions. Contact: Dr. Minda Lynch, 301-435-1322, mlynch1@nida.nih.gov

Broad Challenge Area	Specific Challenge Topic
	01-DA-104 Functional Roles of Glia-Derived Factors in Mediating Drug Abuse Behavior. Emerging data suggest that the physiological functions of neuroimmune factors such as cytokines and chemokines, and of other factors derived from glia residing within the nervous system actively participate in modulating neuronal function and processes that contribute to and underlie behavioral change. This offers a new framework towards understanding the roles of glia-derived factors in the development and progression of drug abuse and addiction. Contact: Dr. Roger G Sorensen, 301-443-3205, rsorense@mail.nih.gov **01-DA-105 Capturing social network information for groups at high risk for negative health behaviors.** Research in this area is needed to enhance existing methodologies and/or devise novel methods that will capture social network information among groups at heightened risk for particular negative health behaviors such as smoking, and use or abuse of illicit drugs and prescription medications. Furthermore, research on characterizing social networks (e.g., sexual networks, drug use networks) to identify protective and risk factors that affect HIV transmission among drug using populations is needed. Novel methods and strategies for doing so are encouraged. Contacts: Dr. Harold Perl, 301-443-9982, hperl@nida.nih.gov; Dr. Jacques Normand, 301-443-1470, jnormand@nida.nih.gov; and Dr**.** Jessica Chambers, 301-443-2237, jcampbel@mail.nih.gov **01-DA-106 Development of behavioral and social interventions that reduce stigma and improve quality and accessibility of health care services in low resource settings.** Residents of economically deprived neighborhoods in this country have limited access to health care. Accessing HIV/AIDS health care services, including HIV testing is further exacerbated by the stigma associated with drug abuse and HIV infection in those settings. This initiative is soliciting applications that would translate existing knowledge related to the causes and consequences of stigma into pilot interventions that can prevent or mitigate stigma and its associated negative effects on HIV/AIDS health care services among drug users. Contact: Dr. Jacques Normand, 301-443-1470, jnormand@nida.nih.gov **01-DA-107 Identifying phenotypic markers for positive behavior change.** Identify reliable, robust intermediate phenotypic markers (using cognitive neuroscience and behavioral economics) that can be used to personalize approaches to support positive health behavior change related to substance abuse and HIV risky decision making behavior. Examples include behavioral disinhibition, delay discounting and other measures of impulsivity, risk perception, sensitivity to reward and punishment, and implicit cognition. Contact: Dr. Lynda Erinoff, 301-443-1470, lerinoff@nida.nih.gov **01-DA-108 Test default options to promote healthier behaviors.** Exploration by behavioral economists and clinicians to develop and test default options (e.g., placement of fresh fruit displays in stores, the location of parking spaces at the workplace) to promote healthier behaviors. Studies may include incentives and policies for healthier behavior by program staff and providers (e.g. stop smoking programs for drug abuse treatment staff). Contact: Ms. Debbie Grossman, 301-443-2249, Dg9a@nih.gov **01-DA-109 Behavioral and/or pharmacotherapeutic intervention research in the area of neonatal exposure to substances of abuse.** Develop and test behavioral and or pharmacotherapeutic interventions for the neonate to regulate behavior in problem areas, such as feeding problems, irritability, and vomiting problems that ensue due to substance exposure *in utero.* The behaviors of the neonate exposed to substances are going to

Broad Challenge Area	Specific Challenge Topic
	constantly change with a developing nervous system and in a milieu in which the mother may have non-appropriate caregiver response**.** Contact: Dr. Steve Oversby, 301-435-0762, soversby@mail.nih.gov **01-DA-110 Identify and/or evaluate dietary supplements that could be used in treating substance abuse disorders.** There is abundant preclinical and clinical evidence that suggest dietary therapies and behavioral interventions can promote neurogenesis, diminish susceptibility to metabolic and excitotoxic injury (e.g., diets rich in antioxidants), and/or counteract stress responses within the brain. Dietary regimens or supplements can be evaluated as individual treatments or as adjuncts to FDA-approved medications. Contact: Dr. Kris Bough, 301-443-9800, boughk@mail.nih.gov **01-DA-111 Approaches to study the interactions among individual behaviors, social and physical environments, and genetic/epigenetic processes during critical developmental periods.** NIDA is soliciting research that integrates environmental and developmental variables with genotypic information in order to permit comprehensive model-building and hypothesis testing for determining genetic, environmental, and developmental contributions to substance abuse and related phenotypes. Contact: Dr. Karen Y. Sirocco, 301-451-8661, Sirocco@nida.nih.gov **01-DE-101 Mechanisms of Behavior Change Research.** Understanding how behavior change happens, and how and for whom behavioral interventions work, are key components of a strong science of oral health behavior. Goal: Research is encouraged that identifies and tests the mechanisms of behavior change related to oral health. Basic science studies are encouraged that identify the mechanisms underlying the initiation and maintenance of oral health behaviors, and the mechanisms of action of behavioral interventions targeting oral health, across a variety of populations. Responsive studies include, but are not limited to, laboratory-based studies testing the causal relationships between hypothesized key variables; analysis of archived or existing observational and/or self-report data testing mechanisms of action hypotheses; and enhancement of ongoing intervention studies with additional assessments or methods that allow for mechanisms of action tests. **Contact**: Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov **01-DE-102 Behavioral and Social Intervention Research.** Studies are encouraged that develop behavioral interventions for oral health. Goal: For populations for which data suggest tailored interventions are needed, adaptation and testing of tailored behavioral interventions is appropriate. For populations for which data do not identify a need for tailoring, testing of evidence-based behavioral interventions is encouraged. For populations for which inadequate data are available, collection of foundational data followed by intervention development and/or testing would be responsive. Contact: Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov **01-DK-101 Behavioral research in NIDDK diseases.** Evidenced based medical management is essential to disease prevention and treatment but optimizing health outcomes also requires attention to non-biomedical factors in the individual, healthcare setting, and community. Basic and applied research is needed to examine the behavioral, cognitive, affective, interpersonal/social, and environmental factors that influence disease onset, course and complications. Where applicable, research should also examine the interaction between these factors and the biomedical aspects of disease (e.g. genetics, medication use and effectiveness, and physiologic/neural functioning). Contact: Dr. Christine Hunter, 301-594-4728, hunterchristine@mail.nih.gov

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	01-DK-102 Discovery of behavioral mechanisms relevant to obesity. There is a gap in knowledge about basic behavioral aspects of obesity which limits the development of novel clinical approaches to obesity prevention and treatment. Basic behavioral research is needed to uncover the mechanisms and pathways of eating and activity related decision making, preferences, and behavioral response in humans. Where relevant, targets of research should include study of the interaction between biological factors (e.g. genetics, sensory or neural processing, and sleep) and behavioral, psychological, cognitive, economic, and social factors relevant to obesity. Research is sought that targets critical periods of obesity risk across the lifespan. Contact: Dr. Christine Hunter, 301-594-4728, hunterchristine@mail.nih.gov **01-DK-103 Improved understanding of behavioral and social factors related to non-Adherence in people with diabetes.** Optimal management of diabetes requires adherence to a complex and ongoing regimen that often includes attention to medication, blood glucose monitoring, diet, physical activity, other self-management behaviors, and medical monitoring. However, adherence to one or many of the recommendations for optimal care is also a complex process and requires attention to factors such as the interaction between patient and provider, patient preferences and cultural values, health literacy, economic factors and competing life demands. Basic behavioral and social science research is needed to better understand the factors that influence adherence and identify potential targets for intervention to improve diabetes relevant adherence. Contact: Dr. Christine Hunter, 301-594-4728, hunterchristine@mail.nih.gov **01-EB-101 Technologies to Enhance Patient Safety and Avoid Errors in the Clinical Setting.** Many people die each year from accidental medical errors in the hospital. The behavior and actions of medical personnel need to be changed through the incorporation of intelligent communication reminders, safety checks, and skill retraining. Proposals for the development of intelligent medical devices and tools, training simulators, work flow systems, standards, and a plan for rigorous testing, validation and evaluation to prove a reduction or elimination of medical errors are encouraged. Contact: Dr. Grace Peng, 301-451-4778, pengg@mail.nih.gov **01-ES-101 The role of environmental exposure on genotype-phenotype interaction in behavioral toxicology.** Support research to elucidate the role of gene-environment interactions by incorporating behavior as a parameter in toxicology study in model systems such as c. elegans, drosophila, zebrafish, and rodents. These more clearly defined genetic models have considerable advantages for understanding the relationship between toxicant actions and genetics on neurobehavioral function. Contact: Dr. Annette Kirshner, 919-541-0488, Kirshner@niehs.nih.gov **01-GM-101* Individual-based model of social behavior.** Development of a robust and well-characterized individual-based model of social behavior that includes the dynamics of social interactions and that matches observed patterns of behavior. Contact: Dr. Irene Eckstrand, 301-594-0943, eckstrai@nigms.nih.gov **01-GM-102 Model organisms for social behavior studies.** Identification and development of model organisms that allow for integrative analyses of the genetic, biochemical, physiological, and environmental components of social behavior. Contact: Dr. Irene Eckstrand, 301-594-0943, eckstrai@nigms.nih.gov **01-GM-103 Formation and evolution of social organization.** Development of pilot projects to demonstrate how virtual or e-communities may provide information and insights

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	into the formation and evolution of social organization. Contact: Dr. Irene Eckstrand, 301-594-0943, eckstrai@nigms.nih.gov **01-HD-101 Behavioral Interventions.** Behavioral interventions are especially needed: to increase women's and couples' correct and consistent use of family planning methods; and to improve parental adherence with medical and health recommendations, such as well-baby/well- child visits and vaccination schedules. New technology has created opportunities for the development and/or testing of interventions such as automated reminders, electronic records checks, and other innovative methods to improve adherence. Development and/or testing of interventions that work on multiple scales (e.g., the individual, family, community, school, religious congregation, organized social group, etc.), or examine the roles of social networks are particularly encouraged. Contact: Dr. Rebecca L. Clark, 301-296-1175, rclark@mail.nih.gov **01-HL-101 Develop innovative technologies and measurements to assess and provide real-time feedback on behavioral and environmental exposures for disease onset and progression for heart, lung, and blood diseases.** In the area of risk factors, tools and measures are needed to assess dietary habits, physical activity, and psychological stress. Current approaches mostly rely on self-report and are, therefore, of limited reliability and validity while also being costly and imposing a high respondent burden. In the area of clinical outcomes, tools and measures are needed to assess early contributions to health care disparities and patient and provider adherence to medical regimens. Contact: Dr. Lawrence Fine, 301-435-0305, lf128x@nih.gov **01-MH-101 Social networks and negative health behaviors related to HIV/AIDS.** Enhance the methodology and/or devise novel methods to capture social network information for groups at high risk for negative health behaviors related to HIV/AIDS. Contact: Dr. Emile Brouwers, 301-443-4526, ebrouwer@mail.nih.gov **01-NS-101 Limiting neurological disability through behavior change.** Research on behavior change could advance the neurological health of patients at risk for, or affected by, a wide range of neurological disorders. The challenge is to test behavioral models that improve compliance with treatment regimens, stress reduction to attenuate neurologic symptoms, exercise regimens, accessing emergency care, or management of pseudo-seizures. Contact: Dr. Emmeline Edwards, 301-496-9248, ee48r@nih.gov **01-OD(OBSSR)-101* Tools for studying cultural phenomena.** Development of new tools for: the measurement of culturally-shared mental phenomena (e.g., representations, scripts, prejudices); studying mechanisms by which these phenomena are transferred and adapted across individuals; and advancing research on the distribution and transmission of cultural phenomena within populations. Contact: Dr. Christine Bachrach, 301-496-9485, cbachrach@nih.gov; NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; FIC Contact: Dr. Aron Primack, 301-496-1653, aron_primack@nih.gov **01-OD(OBSSR)-102* Methods for studying the interactions among behaviors, environments, and genetic/epigenetic processes.** Research is needed to develop analytic methods, systems science approaches, or computational models designed to address the interactions among individual behaviors, social and physical environments and genetic/epigenetic processes during critical developmental periods and over time. This research is essential to incorporating the dynamic complexity of behavior and

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	environments in the study of gene-environment interactions in health. Contact: Dr. Kay Wanke, 301-435-3718, wankek@od.nih.gov; NHLBI Contact: Dr. Peter Kaufmann, 301-435-2467, kaufmannp@nhlbi.nih.gov **01-OD-101*** **Test default options to promote healthier behaviors.** Exploration by behavioral economists and clinicians to develop and test default options (e.g., placement of fresh fruit displays in stores, the location of parking spaces at the workplace) to promote healthier behaviors. Contact: Dr. Jonathan King (NIA), 301-402-4156, kingjo@mail.nih.gov **01-OD-102** **Innovative Approaches to Improve Patient and Provider Adherence.** Both poor patient adherence to prescribed medical regimens and poor utilization of adherence-enhancing strategies in clinical practice severely limit the public health impact of efficacious treatments and preventive regimens. The challenge is to integrate and improve existing technologies to improve patient self-monitoring, provide automatic reminders, and link service providers, patients, and pharmacies through electronic medical records. These technologies will allow the rapid identification of probable patient non-adherence and will help clinicians generate individualized treatment plans that could enhance patient outcomes. OD Contact: Dr. Lynn Bosco, (OBSSR) 301-451-4286, boscol@od.nih.gov. **01-OD-103** **Methodologies or technologies that facilitate understanding of the biological effects of behavioral interventions.** The ability to modify behavior is critical for preventing, managing and treating many important health conditions. Approaches are needed that will identify, quantify, and document biological changes associated with initiation and maintenance of human behavior change. Contact: Dr. Lisa Onken (NIDA), 301-443-2235, lonken@mail.nih.gov. **01-OD-104** **Mechanisms of Behavior Change.** The challenge is to identify mechanisms and controllable variables that underlie positive change in health behaviors. This will require use of models that incorporate and relate findings at different levels of analysis from the genomic through the physiologic to the psychological and social. Contact: Dr. Mark Willenbring (NIAAA), 301-443-1208, mlw@niaaa.nih.gov **01-TW-101*** **Novel strategies to improve health care access for stigma-related conditions**. Design and evaluate pilot interventions to improve access to health care for stigma-related health conditions, identify the qualitative characteristics of successful interventions, and demonstrate successful interventions that can be scaled up or generalized to other stigmatized public health problems and/or to other populations and cultures. Develop valid and reliable methods and measures for assessing stigma as an impediment to access to health care services that allow for comparisons over time and locations. Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov **01-TW-102*** **Improving health through ICT/mobile technologies: enhancing patient compliance**. Develop theory-based social and behavioral principles that influence the utility of evidence-based interventions using Information and Communication Technology (ICT) to effect patient compliance and adherence. Test effectiveness, feasibility and scalability of an ICT approach in real-world settings, including development and use of intermediate and end-point health outcomes measures. Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov

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(02) Bioethics	**02-CA-101 Examining the Use and Impact of New Genomic Technologies in Clinical Practice.** Studies that examine the physician utilization and/or patient acceptability of new cellular, molecular and genomics technologies in clinical and public health settings and the potential impact of these technologies on cancer outcomes such as incidence, progression, mortality, survival, and quality of life. Contact: Dr. Andrew Freedman, 301-435-6819, Andrew_Freedman@nih.gov **02-CA-102 Unified informed consent document for biobanking and subsequent analysis of human biospecimens.** Obtaining adequate informed consent from research participants for broad future research use of biospecimens remains a challenge that impedes efforts related to biobanking as well as downstream research that uses biospecimens. Development of a unified informed consent document that describes the risks and benefits of both biobanking and potential downstream analyses such as genomics or proteomics would be of broad use to the research community. Development of such an informed consent document would include synthesis of existing empirical data on informed consent for biobanking with current recommendations in the ethics literature. In addition, all documents related to informed consent would be evaluated using focus groups and other techniques in order to ensure patient understanding. Contact: Dr. Nicole Lockhart, 301-496-0556, lockhani@mail.nih.gov **02-CA-103 Optimizing the Timing of Consent for Biobanking to Achieve Ethical and Research Objectives.** In order to promote both ethical and research objectives the informed consent process must provide opportunities for biospecimen contribution to all appropriate patients while at the same time ensuring a robust consent process that allows research participants to carefully consider risks and benefits. In response to this challenge, two alternative models have been proposed: a “front-door” consent model in which an institution actively invites all patients to contribute to a biospecimen resource and a post-operative consent model which seeks consent from patients who have appropriate biospecimens for banking after surgery has occurred. In order to determine which approach would best meet ethical and research objectives, empirical research must be performed to assess how the timing of informed consent affects: patient understanding of the proposed research, the psychological state of the patient; and accrual rates of biospecimens. Ideally, both approaches would be piloted and compared for these and other key parameters. Contact: Dr. Nicole Lockhart, 301-496-0556, lockhani@mail.nih.gov **02-DA-101 Research on Obtaining Consent for Illicit Drug Users.** NIDA is soliciting research to evaluate the consent form and the procedure to obtain consent from individuals seeking to participate in drug abuse clinical trials. Research to determine their impact on the ability to recruit potential study subjects into drug abuse trials would be needed to determine what measures may be necessary to ensure research subjects are protected. Contact: Bob Walsh, (301) 443-9825, rwalsh@nih.gov **02-DA-102 Confidentiality in Electronically Shared Information of Illicit Drug Use Behaviors.** NIDA is soliciting research assessing current areas of risk with web-based electronic capture of research data in drug abuse treatment clinical trials as well as suggestions for improvements to existing paradigms to ensure secure transmission of data. Identification of potential future areas of risk regarding the use of data standards and changing regulatory requirements should also be explored. Contact: Bob Walsh, (301) 443-9825, rwalsh@nih.gov **02-DA-103 Translation of genetic knowledge to clinical practice**. Address ethical issues related to access to broad sharing and use of new genetic information and

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	technologies for addiction research to improve treatment and prevention options for addicts. Important issues include the identifiability of genetic/genomic information, return of research results and incidental findings to high risk subjects, and alternative models of informed consent for broad data sharing for research. Contact: Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **02-DK-101 Ethical issues related to genetic and epigenetic information.** Genotype and genome-wide association studies, as well as the large databases containing this information for many individuals create a series of challenging ethical issues. In genome wide epigenetic studies have the potential to identify specific environmental exposures linked to genotyped individuals. Relevant studies will address issues such as recontact, return of research results and incidental findings, informed consent in the context of possible identifiability, and implications for related individuals for diseases that fall within the scope of the NIDDK mission. Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@mail.nih.gov **02-DK-102 Informed consent.** Evolving research paradigms using large databases of genomic and health information and the growth of personalized medicine challenge long-held assumptions about informed consent. New paradigms of informed consent should be developed for individuals with diseases within the scope of the NIDDK mission. Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@mail.nih.gov **02-DK-103 Unique issues posed by emerging technologies.** Identify how emerging technologies, in areas such as biotechnology, tissue engineering, nanomedicine, and synthetic biology, raise unique ethical concerns related to dual use research, privacy, safety, intellectual property, commercialization and conflict of interest, among others. Assess how these novel issues are adequately addressed under current oversight and regulatory structures, and identify where there may be gaps and/or need for revised or new oversight approaches focusing specifically on studies of diseases within the scope of the NIDDK mission. Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@mail.nih.gov **02-DK-104 Enhancing privacy and confidentiality in electronically shared information.** Identify novel approaches for enhancing the privacy, confidentiality and data security of health information that is shared electronically on diseases that fall within the scope of the NIDDK mission, especially within minority populations. Examination could include analysis of current oversight paradigms and suggestions for enhancements, as well as assessment of current and future privacy risks. The challenges of sharing health information in U.S. projects involving international collaborations should also be explored. Contact: Dr. Paul Eggers, 301 594-8305, eggersp@extra.niddk.nih.gov **02-DK-105 Allocation of scarce transplanted organs.** Identify causal factors that contribute to decisions of patients and families to contribute to kidney, liver, and pancreatic organ transplantation programs, particularly in minority communities. Develop novel strategies to enhance the availability of organs for transplant. Contact: Dr. Catherine Meyers, 301-451-4901, meyersc@mail.nih.gov **02-ES-101 Responsible dissemination of research results.** The health effects of environmental exposures are of great interest to public health officials, affected communities and to the general public, yet the quality of reporting and interpretation of research results is uneven and leads to much confusion and uncertainty. There is an urgent need to develop and evaluate methods and strategies to promote more responsible dissemination and improved understanding of scientific research results emerging from

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	studies in environmental health sciences. Partnerships with community are essential to tackle community concerns regarding reporting results to individuals who participate in studies of exposures in their home, school and community and who provide biospecimens for studies of exposure and disease relationships. Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov **02-HG-101*** **Informed consent and data access policies.** The creation of large databases that include genomic information on individual participants, coupled with the move to universal electronic medical records, makes it increasingly possible to identify individual research participants in databases, despite efforts to "de-identify" their data, and potentially to unearth an individual's private medical information. Research is urgently needed to address the implications of this for recruitment, informed consent, and data access policies in biomedical research. Contact: Dr. Jean McEwen, 301 402-7997, jm552n@mail.gov.nih; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIDA Contact: Dr. Marsha Lopez, 301-402-1846, lopezmar@nida.nih.gov **02-HG-102** **Direct to Consumer (DTC) Personal Genomics--Ethical, Legal and Social Implications Research.** Direct-to-consumer marketing of targeted genetic scans for particular disease mutations and for ancestry-informative markers has been available for several years, and a growing number of companies now offer direct-to-consumer (DTC) personalized genomic services based on more comprehensive genomic analyses. The emergence of these DTC genetic testing services raises many issues: Are such services a generally positive advance that empowers the public, or are they premature? What is the potential for consumers to be educated, helped, confused, or even misled by these services? How do those who use these services react to the information they receive? How do health care providers deal with this information? Research is needed to address these and other issues related to DTC marketing of genetic tests. HHGRI Contact: Dr. Jean McEwen, 301-402-7997, jm552n@mail.gov.nih **02-HG-103** **Natural selection in the human genome--Ethical, Legal and Social Implications Research.** The characterization of signatures of recent positive selection in genes that are of adaptive significance in humans can have great medical relevance, by helping to identify functionally significant variants that play a role in health and disease. However, research on recent positive selection in the human genome has methodological challenges and can have significant ethical and social implications. The results of studies that attribute differences in allele frequencies between populations to recent positive natural selection may challenge past understandings about human history and the way that we think about differences. Where the frequencies differ substantially between populations (as defined by ancestral geography), these findings may affect the way we think about differences (both real and perceived) between people from various ancestral backgrounds. Research is needed on the ethical, legal and social issues associated with the way that natural selection research is designed, conducted, and the results communicated to the public. NHGRI Contact: Dr. Jean McEwen, 301-402-7997, jm552n@mail.gov.nih **02-HG-104** **Uncovering Genomic Contributions to Human Traits and Behaviors: Ethical, Legal and Social Implications Research.** Many studies are underway that explore the genetic contribution to non-disease attributes (e.g., the aging process, diurnal rhythms) and to behavioral traits (e.g., cognition, personality traits). These types of studies raise ethical issues similar to other types of genetic studies, but can raise heightened or in some cases unique concerns, relating especially to such issues as: definitions of "normalcy"; the potential for genetic determinism (and its societal implications); and the potential for stigmatization of individuals or groups. Research is needed that addresses

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	these and other implications of research in this area. Contact: Dr. Jean McEwen, 301 402-7997, jm552n@mail.gov.nih **02-HG-105 Genotype-Tissue Expression (GTEx): Ethical, Legal and Social Implications Research.** The GTEx project is an NIH Roadmap Initiative (http://nihroadmap.nih.gov/GTEx/) to create a public resource that will help reveal the role of genetic variation in human gene expression and regulation. This project is designed to collect and analyze multiple human tissues from diverse populations in a variety of settings, including organ transplant settings, medical examiner offices, low-post mortem interval autopsy programs and surgical settings. The phenotypic and genomic information derived from these samples will be placed in a database and made widely available for research use. Research is needed that addresses the ethical, legal and social issues related to the collection and use of this information. Contact: Dr. Joy Boyer, 301-402-7997, jb40m@nih.gov **02-HL-101 Informing the ethical and practical guidelines for providing genetic research results to study participants**. Following completion of the Human Genome Project, genome-wide association studies, candidate gene studies, and sequencing studies have proliferated and are now providing significant, clinically-relevant, and sometimes actionable, findings for study participants. However, investigators are at a loss with respect to ethical and practical issues to consider in providing results to study participants. Research is needed to inform the development of guidelines that could be followed by investigators who confront the issues of who, what, when and how genetic research results should be provided to study participants. Contact: Dr. Paul Sorlie, 301-435-0456, sorliep@nhlbi.nih.gov **02-MH-101 Evidence–based practice guidelines for HIV prevention strategies.** Develop evidence-based practice guidelines for informed consent, standards of care, and comprehension of partial efficacy for new HIV prevention strategies (e.g., microbicides, vaccines, circumcision, PrEP). Contact: Dr. Andrew D. Forsyth, 301-443-8403, aforsyth@mail.nih.gov **02-OD(OSP)-101* Unique Ethical Issues Posed by Emerging Technologies.** Advances in biotechnology and biomedical science raise novel ethical, legal, and social issues. Research in this area is needed to understand the unique ethical concerns related to emerging technologies (e.g. biotechnology, tissue engineering, nanomedicine, and synthetic biology). These include issues such as dual use research, privacy, safety, intellectual property, commercialization and conflict of interest, among others. Research is also needed to assess how these novel issues are addressed under current oversight and regulatory structures and identify where there may be gaps and/or need for revised or new oversight approaches. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103, killenj@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NCI Contact: Dr. Jerry Lee, 301-594-0255, leejerry@mail.nih.gov; NIDA Contact: Dr. Kathy Etz, 301-402-1749, ketz@nida.nih.gov; NIDCR Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov; NIDDK Contact: Dr. Olivier Blondel, 301-451-7334, blondelol@niddk.nih.gov; NIBIB Contact: Dr. Belinda Seto, 301-451-6768, setob@mail.nih.gov; NIEHS Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov; NIGMS Contact: Dr. Richard Anderson, 301-594-0943, andersor@nigms.nih.gov; NICHD Contact: Dr. James Hanson, 301-496-8535, hansonj@mail.nih.gov; NHGRI Contact: Dr. Joy Boyer, 301-402-7997, jb40m@nih.gov; NHLBI Contact: Dr. Gail Weinmann, 301-435-0233, weinmanng@nhlbi.nih.gov NIMH

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	Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Joe Pancrazio, 301-496-1447, jp439m@nih.gov **02-OD(OSP)-102* Ethical Issues in Health Disparities and Access to Participation in Research.** Research is needed to assess the under-representation in biomedical and clinical research of U.S. minority populations, underserved populations, and populations who may be vulnerable to coercion or undue influence, to identify barriers to participation in research and to develop approaches for overcoming them. Additionally, studies are needed to assess the impact and ethical considerations of conducting biomedical and clinical research internationally in resource-limited countries. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov NCI Contacts: Dr. Alexis Bakos, 301-443-0542, bakosa@mail.nih.gov; Dr. Martha Hare, 301-594-1908, harem@mail.nih.gov; Dr. Shobha Srinivasan, 301-435-6614, Sriniva2@mail.nih.gov; NIDCR Contacts: Dr. Ruth Nowjack-Raymer, 301-594-5394, nowjackr@nidcr.nih.gov and Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov; NICHD Contact: Dr. Regina James, 301-435-2692, rjames@mail.nih.gov; NHGRI Contact: Dr. Jean McEwen, 301-402-4997, mcewenj@mail.nih.gov; NHLBI Contact: Dr. Patrice Desvigne-Nickens, 301-435-0515, desvignp@nhlbi.nih.gov; NCMHD Contact: Dr. Nathaniel Stinson, 301-402-1366, stinsonn@mail.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Salina Waddy, 301-496-3102, Salina.Waddy@nih.gov**;** FIC Contact: Dr. Barbara Sina, 301-402-9467, sinab@mail.nih.gov **02-OD(OSP)-103* Ethical Issues Associated with Electronic Sharing of Health Information.** The development of an electronic health information infrastructure and the sharing of health information for patient care and research offer enormous promise to improve health care and promote scientific advances. However, the broad sharing of such data raises numerous ethical issues that may benefit from additional studies (e.g. those related to privacy and confidentiality). Examples include studies to assess risks associated with health information technology and the broad sharing of health information for research, and novel approaches for mitigating them. Examination could also include analysis of current oversight paradigms and suggestions for enhancements, as well as assessments of how privacy risks may change in the future. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIAAA Contact: Dr. Patricia Powell, 301-443-5106, ppowell@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103,killenj@mail.nih.gov; NCI Contacts: Dr. Chris Kinsinger, 301-436-1550, kinsingc@mail.nih.gov; Dr. Marsha Reichman, 301-534-7032, reichmam@mail.nih.gov; NIDCD Contact: Dr. Gordon Hughes, 301-435-4085, hughesg@nidcd.nih.gov; NIDCR Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov; NIDDK Contact: Dr. Christine Hunter, 301-594-4728, hunterchristine@mail.nih.gov; NIBIB Contact: Dr. Belinda Seto, 301-451-6768, setob@mail.nih.gov; NHLBI Contact: Dr. Dina Paltoo, 301-435-0513, paltood@nhlbi.nih.gov; NLM Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NCRR Contact: Dr. Elaine Collier, 301-435-0794,

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	colliere@mail.nih.gov **02-OD(OSP)-104* Ethical Issues in the Translation of Genetic Knowledge to Clinical Practice.** Genetics and genomics have great promise for the development of personalized medicine, yet the ethical, legal and social implications of both the research and application of genetic and genomic knowledge and technology are far reaching. Studies are needed to better understand the factors that influence the translation of genetic information to improved human health and the associated ethical issues. Examples of studies include those to address ethical issues related to broad sharing and use of new genetic information and technologies for research to improve human health, human subjects protection in genetic and genomic research, the identifiability of genetic/genomic information and how our understanding of identifiability is evolving, return of research results and incidental findings to subjects, alternative models of informed consent for broad data sharing for research, and the impact of intellectual property (IP) issues on development of new technologies. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NIAAA Contact: Dr. Patricia Powell, 301-443-5106, ppowell@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; NCI Contacts: Dr. Mehdi Mesri, 301-496-1550, mesrim@mail.nih.gov; Dr. Leah Sansbury, 301-435-4910, sansburl@mail.nih.gov; NIDCD Contact: Dr. Bracie Watson, Jr., 301-402-3458, watsonb@nidcd.nih.gov; NIDCR Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov;NEI Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov; NICHD Contact: Dr. James Hanson, 301-496-8535, hansonj@mail.nih.gov; NHGRI Contact: Dr. Elizabeth Thomson, 301-402-4997, et22s@nih.gov NHLBI Contact: Dr. Dina Paltoo, 301-435-0513, paltood@nhlbi.nih.gov; NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Danilo Tagle, 301-446-5748, dt39y@nih.gov **02-OD(OSP)-105* Ethical Issues Raised by the Blurring between Treatment and Research.** The distinction between clinical practice and research is growing less clear, a trend that may be more pronounced with respect to genetic information and medical records research. Studies are needed to better understand the ethical issues associated with this trend. Examples of studies include those to identify how this blurring in roles affects traditional human subjects protections, including, for example, essential practices such as informed consent, conceptions of the doctor/patient and investigator/subject relationship, and privacy protections. Contact: Abigail Rives, 301-594-1976, rivesa@od.nih.gov; NCCAM Contact: Dr. Jack Killen, 301-594-7103, killenj@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIAID Contact: Dr. Liza Dawson, 301-496-6179, dawsonl@niaid.nih.gov; NCI Contact: Dr. Paul Han, 301-594-6642, hanp@mail.nih.gov; NIDCD Contact: Dr. Gordon Hughes, 301-435-4085, hughesg@nidcd.nih.gov; NIDCR Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov; NIDDK Contact: Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@EXTRA.NIDDK.NIH.GOV; NIEHS Contact: Dr. Kim Gray, 919-541-0293, Gray6@niehs.nih.gov; NHGRI Contact: Dr. Elizabeth Thomson, 301-402-4997, et22s@nih.gov; NHLBI Contact: Dr. Carol Blaisdell, 301-435-0219, blaisdellcj@nhlbi.nih.gov NIMH Contact: Dr. Jean Noronha, 301-443-3367, jnoronha@mail.nih.gov; NINDS Contact: Dr. Brandy Fureman, 301-496-9135, bf103s@nih.gov**;** FIC Contact: Dr. Barbara Sina, 301-402-9467, sinab@mail.nih.gov.

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	02-OD-101 Bioethical concerns unique to epigenomic research. Emerging evidence suggests that epigenetic changes may have an important role in a variety of diseases. Although our understanding of the bioethics of genomic studies is mature, our understanding of the bioethics of epigenomic studies is very much in its infancy. Specific environmental exposures (use of illicit drugs or alcohol, HIV infection, psychosocial stress, etc) or disease states (depression, HIV infection status, etc) may be correlated with specific epigenomic changes. Thus epigenomic research may lead to unique and unanticipated bioethical challenges that must be overcome. Studies exploring bioethical concerns unique to epigenomic research would identify unanticipated ethical problems and help identify appropriate solutions to be sure human subjects involved in epigenomic research are properly protected. Contact: Dr. Joni Rutter (NIDA), 301-435-0298, jrutter@mail.nih.gov. **02-RR-101* Recontact Issues in Genotype and Genome-Wide Association Studies.** Genotype and genome-wide association studies create challenging re-contact issues if subjects are later to be asked to return for clinical research including phenotyping. Applicants would propose 2-year awards for pilot programs that would be implemented at 3 or more affiliated sites to develop and apply IRB guidelines that addressed ethical barriers (e.g., re-contacting) in genotype – phenotype studies. This idea is submitted through NCRR on account of the ethics work underway at the Clinical and Translational Science Awards (CTSAs) and, if accepted, would be developed with NHGRI's ELSI Division. NCRR Contact: Dr. Andrea Sawczuk, 301-435-0792, sawczuka@mail.nih.gov; NIA Contact: Dr. Robin Barr, 301-402-7715, BarrR@mail.nih.gov; NIDA Contact: Dr. Louise Wideroff, 301-443-8663, wideroffl@nida.nih.gov; NHGRI Contact: Dr. Jean McEwen, 301-402-4997, mcewenj@mail.nih.gov

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(03) Biomarker Discovery and Validation	**03-AA-101 Identification of Intermediate Phenotypic Markers of Alcohol Use Disorders.** Alcohol use disorder is a heterogeneous disease resulting from complex interactions of genes and environment to yield a range of phenotypes. Because of this heterogeneity, available treatments work for some, but not, all individuals. Being able to distinguish subtypes will advance personalized medicine by identifying those who respond favorably to specific treatments. One approach to identify subgroups is to measure intermediate phenotypic markers. These markers are found in groups that share a common neurobiology, usually controlled by only a few genes. Alcohol researchers have begun to investigate a variety of intermediate phenotypes using basic behavioral, clinical, and neuroscience approaches. Examples include P300 event-related potential, facial flushing syndrome, pathologic anxiety as measured by low-voltage alpha electroencephalogram, and aspects of disinhibition as determined by impaired prefrontal cognitive function. However, the discovery of more sensitive, specific markers is needed to more clearly delineate complex alcoholic phenotypes. Research is encouraged in promising areas such as electrophysiology, social and cognitive neuroscience, behavioral economics, neuroimaging, and subjective and physiological responses to alcohol. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **03-AA-102 Validating Human Laboratory Models as Predictors of Clinical Efficacy.** Developing medications is a long, costly process with a low probability of success for any single agent. In particular, human clinical trials are particularly time consuming. Therefore, development and validation of screening procedures that are predictive of performance in clinical trials are needed. Currently, there are numerous promising compounds in the developmental pipeline, but there are no proven ways to select which of them should be tested clinically. Development and validation of screening paradigms using human laboratory procedures offers one potential avenue for screening novel compounds. To be a successful screening model, clinical indicators from the human lab models should be predictive of treatment outcome. Several human lab paradigms currently exist, including cue reactivity, alcohol self-administration and alcohol administration models. Examples of clinical indicators used in these models are craving, physiological measures (heart rate, blood pressure, skin conductance), self-administration measures, motivation to drink, alcohol reinforcing behavior, and impulsive behavior. Currently, none of these indicators have been shown to reliably predict clinical performance. Research is encouraged to discover new indicators that are predictive of clinical performance. Validation of these indicators will require both “upstream” validation by examining their predictive power in human clinical trials, as well as “downstream” validation by examining the relationship between performance testing various animal models with human laboratory indicators. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **03-AA-103 Molecular Markers of Alcohol-induced Tissue Injury.** High-throughput bioinformatic investigations of alcohol's impact on, for example, the epigenome, transcriptome, proteome, metabolome, etc. are needed to inform our understanding of the mechanisms involved in alcohol-induced injury to adult and fetal tissues. Additionally, these approaches have the potential to reveal candidate biomarkers of alcohol-induced pathology and alcohol exposure. Research is sought to develop diagnostic biomarker signatures of alcohol consumption and alcohol-induced organ damage. Contact: Dr. Dale Hereld, 301-443-0912, hereldd@mail.nih.gov or Dr. Kathy Jung, 301-443-8744, jungma@mail.nih.gov **03-AG-101 Novel assays for dried blood spots.** Population surveys including biomarkers have invigorated the social sciences, but requirements for very large sample

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	sizes frequently make the collection of blood unfeasibly expensive, while storage costs and conditions are quite high. Recent advances in biochemistry, however, have made it possible in principle to derive rich profiles of important lipids, proteins, metabolites, and genetic information from dried blood spots that could be more systematically exploited through the development and perfection of new assays and their eventual implementation in larger biobanking facilities. Contact: Dr. John Haaga, 301-496-3131, haagaj@mail.nih.gov **03-AG-102 Novel biomarkers for Alzheimer's Disease.** Development and testing of novel tissue or fluid (e. g. blood, cerebrospinal fluid) biomarkers of Alzheimer's disease for mechanism based therapeutic target validation, early disease diagnosis, disease progression, or response to therapeutic interventions. Contact: Dr. Neil Buckholtz, 301-496-9350, BuckholN@mail.nih.gov **03-AG-103 Biomarkers for neurodegenerative diseases.** Identification of sensory and/or motor biomarkers for age-related neurodegenerative diseases in relevant animal models or human subjects. Contact: Dr. Neil Buckholtz, 301-496-9350, BuckholN@mail.nih.gov **03-AG-104 Biomarkers, stress, and immune function.** Identification of biomarkers to assess the impact of stress, both social and biological, on immune function. Contact: Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **03-AG-105 Biomarkers, oxidative stress, and dietary supplements.** Development and validation of biomarkers of oxidative stress that could be used to assess the antioxidant effects of dietary supplements *in vivo* and to examine their mechanisms of action, efficacy, and effectiveness with respect to human health. Contact: Dr. David Finkelstein, 301-496-7847, FinkelsD@mail.nih.gov **03-AG-106 Biomarkers for pain.** Pain research has been greatly hampered by the unreliable nature of self-report based instruments. The establishment of objective, affordable, and reliable pain biomarkers would advance our understanding of pain mechanisms, provide a basis for improved clinical management of pain, help assess an individual's risk for becoming addicted to opiate analgesics, and establish much needed objective measures of treatment success or failure. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **03-AG-107 Role of immunity in neurodegenerative diseases of the eye.** Oxidative stress/injury and host immune response are postulated to be involved in many degenerative eye diseases such as age-related macular degeneration, diabetic retinopathy, uveitis, glaucoma, and keratoconus. Characterizing the molecular events and how the host responds to these insults will allow us to identify biomarkers for the diagnosis and treatment of these blinding diseases. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **03-AG-108 Developing high-throughput biomarker assays from finger-stick dried blood spots.** Develop, using finger-stick dried blood spots, novel high-throughput biomarker assays, to identify lipids, proteins, metabolites, and genetic information to expand the array of available biomarkers for use in large community-based biosocial surveys. Contact: Dr. John Haaga, 301-496-3131, haagaj@mail.nih.gov

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	03-AG-109 Biomarkers of persistent damage after acute joint injury. Define early biochemical and structural changes that arise after joint injury, such as trauma or anterior cruciate ligament (ACL) tears, which would serve as indicators that could be analyzed in subsequent longitudinal studies to seek biomarkers for progression to early osteoarthritis (OA). These could be used for both preventive intervention, and as preliminary indications for pathways of disease pathogenesis to guide therapeutic development. Contact: Dr. Chhanda Dutta, 301-435-3048, DuttaC@mail.nih.gov **03-AG-110 Develop novel imaging, proteomic, or genomic approaches to identify risk for fragility fractures.** Projects may use existing data sets to define and validate measures of bone quality that are more predictive than bone mineral density measurements. Contact: Dr. Sherry Sherman, 301-435-3048, ShermanS@mail.nih.gov **03-AG-111 Validation of biomarkers that bridge animal models with proof of concept (Early Phase IIa) studies for mental/nervous system disorders.** Identify and validate useful biomarkers that associate with a beneficial response to treatment in animal models and can be measured in patients. These can then be utilized as targets in early Phase IIa Proof of Concept studies to determine whether a therapeutic intervention has engaged the intended biologic target. Contact: Dr. Neil Buckholtz, 301-496-9350, BuckholN@mail.nih.gov **03-AG-112 Identify and validate clinically relevant, quantifiable biomarkers of diagnostic and therapeutic responses for blood, vascular, cardiac, and respiratory tract dysfunction.** Patients who appear to be similar because of their clinical characteristics often demonstrate substantially different morbidity, mortality, and responses to drugs. Identification and validation of biomarkers from cell culture to animal models and human studies could be used to determine the most effective care for individual patients and more precisely identify those who are most likely to benefit from specific interventions for prevention or treatment. Contact: Ms. Winifred Rossi, 301-496-3836, rossiw@mail.nih.gov **03-AI-101 Identification, characterization and evaluation of novel pathogen or host targets that may lead to the development of antimicrobials with broad spectrum activity.** Contact: Dr. Kent Peters, 301-402-8643, petersn@mail.nih.gov **03-AR-101* Biomarkers Of Persistent Damage After Acute Joint Injury.** Define early biochemical and structural changes that arise after joint injury, such as trauma or anterior cruciate ligament (ACL) tears, which would serve as indicators that could be analyzed in subsequent longitudinal studies to seek biomarkers for progression to early osteoarthritis (OA). These could be used for both preventive intervention, and as preliminary indications for pathways of disease pathogenesis to guide therapeutic development. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; OD(ORWH) Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **03-AR-102* Develop Novel Imaging, Proteomic, Or Genomic Approaches To Identify Risk For Fragility Fractures.** Projects may use existing data sets to define and validate measures of bone quality that are more predictive than bone mineral density measurements. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; OD(ORWH) Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov

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	03-AR-103 Biomarkers: Bench to Bedside for Autoimmune and Inflammatory Skin and Rheumatic Diseases. Define biomarkers in autoimmune disease for early diagnosis, use as predictors of clinical outcome, and as surrogates of clinical response. Create the resources required to move promising biomarkers from the bench to the clinic using state of the art statistical, analytical, and computational methods. These include development of new technologies to identify markers of disease onset and clinical response measured by changes in blood or bodily fluids, genetic biomarkers, or by in vivo imaging of cells and tissues. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **03-AR-104 Imaging Biomarkers**. Apply existing and newly developed imaging technologies to improve understanding of musculoskeletal or skin disease, and to enable identification of possible imaging biomarkers associated with disease onset and progression. Broad, innovative use of imaging techniques could enable early identification of disease onset, predict disease progression, and make possible direct monitoring of responses to therapeutic interventions. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **03-AT-101* Psychoneuroimmunology biomarkers of stress.** Identification of biomarkers to assess the impact of stress, both social and biological, on immune function. Contact: Dr. John Glowa, 301-496-0527, glowaj@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **03-AT-102* Antioxidant biomarkers.** Development and validation of biomarkers of oxidative stress that could be used to assess the antioxidant effects of dietary supplements *in vivo* and to examine their mechanisms of action, efficacy, and effectiveness with respect to human health. Contact: Dr. Laura Moen, 301-402-5867, moenl@mail.nih.gov **03-AT-103 Omega-3 fatty acid biomarkers.** Development of strategies to test the impact of fatty acids/omega-3 fatty acids on lipid composition and membrane function. Contact: Dr. Laura Moen, 301-402-5867, moenl@mail.nih.gov **03-CA-101 Fingerprints for the Early Detection and Treatment of Cancer.** Early detection is a proven approach to successfully preventing and treating cancer. Because cancer arises through a complex interaction of multiple molecular signals and pathways often confounding the eventual effect, we need to identify key pathways or profiles that better reflect the underlying transforming processes. These “fingerprints”, which could include a myriad of indicators including mutations, proteins and metabolites, would have biological relevance and be appreciate in the detection and management of the disease. Contact: Dr. Dan Gallahan, 301-496-8636, gallahad@mail.nih.gov **03-CA-102 Biological Predictors of Progression in Barrett’s Esophagus.** The incidence of adenocarcinoma of the lower esophagus and esophagogastric junction has increased at an alarming rate in the last few decades. Risk factors including obesity, alcohol consumption, smoking, and gastroesophageal reflux disease (GERD) have contributed to the increase in this cancer. Research is needed on Barrett’s transformation to cancer to identify unique biological pathways that predict the progression of Barrett’s epithelium to adenocarcinoma and lead to an understanding of their relation to lifestyle risks such as obesity and GERD. The goal is to increase our understanding of Barrett’s associated cancer, facilitate the development of more translational strategies for early detection, and benefit the clinical management of Barrett’s patients at increased risk for esophageal cancer perhaps through lifestyle changes. Contact: Dr. Rihab Yassin, 301-

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	496-7028, yassinr@mail.nih.gov **03-CA-103 Reagents for rapid screening of human tumor cells for defects in DNA repair and/or replication**. A surprisingly high percentage of human tumors are showing mutations in DNA repair that make them overly dependent on alternative backup DNA repair pathways for survival. As a consequence, cancer cells from such tumors tend to be highly vulnerable to the inhibition of the backup pathway(s). Such effects have been observed for Fanconi anemia mutation in breast and ovarian cancer but similar mutations in other pathways are likely to exist also but are difficult to predict a priori. What is needed is a systematic screening of large numbers of patient samples from a variety to human tumors to identify such patterns of DNA repair mutations and consequent vulnerabilities from the over-dependence on compensatory pathways. This would be followed by confirmatory validation of putative targets in cultured human cancer cells and animal models. Contact: Dr. Dick Pelroy, 301-496-9326, pelroyd@mail.nih.gov **03-CA-104 Enhancing Biomarker Discovery Through Mass Spec Spectral Libraries.** The rapidly emerging field of proteomics has reached a development point where it now needs a catalog or map of all detectable peptides. Such a map would unite researchers across the field to common metrics for detection, identification, and quantitation of proteins. Ultimately, this national resource would enable discovery of biomarkers as well as their translation to clinical validation. Contact: Dr. Christopher Kinsinger, 301-496-1550, kinsingc@mail.nih.gov **03-CA-105 Enhancing Biomarker Discovery Through Targeted Antibody Production.** Development of affinity capture reagents against the National Institute of General Medical Sciences' Protein Structure Initiative project. This program will explore the mapping of affinity reagents to a subset of proteins in the PSI. This global resource will empower the biomarker discovery field with critical resources (reagents and data) on translating basic science to clinical utility. Contact: Dr. Henry Rodriguez, 301-496-1550, rodriguezh@mail.nih.gov **03-CA-106 Utilizing data from the TCGA and TARGET projects to support a large scale bioinformatics effort to identify biomarkers that lie within a pathway or are epi-pathway indicators of tumor formation or progression.** Epi-pathway markers lie outside of typical pathways but can be identified as indicators when statistically significant numbers of tumors are characterized as is being done in these projects. Potential markers would be validated under other funding mechanisms. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **03-CA-107 Biospecimen Research to Improve Biomarker Identification and Validation**. The human biospecimens that form the basis of medical research are collected, processed and stored under very different, non-standardized methods in multiple institutional settings. The molecular changes induced by these pre-analytical biospecimen variables can significantly confound research studies, particularly in the study of disease biomarkers. New biospecimen research is needed to better understand the contribution of biospecimen pre-analytical variables to molecular profiles. Potential topics under this research area are: 1) How do differences in how blood biospecimens are collected, processed and stored affect molecular profiles?; 2) How can the relative molecular integrity of banked biospecimens be assessed?; and 3) Normal human tissues are needed for studies that seek to understand early development of disease. How do differences in methods for obtaining normal human tissues affect resulting molecular profiles? How does post-mortem interval affect the molecular integrity of different tissues? Contact: Dr. Helen

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	M. Moore, 301-496-0206, moorehe@mail.nih.gov **03-CA-108 Biomarker Discovery and Validation among racial and ethnic minority Populations**. Support community-targeted prevalence studies in co-morbidities (co-occurring conditions) and design research pilots to educate and engage these communities in participating in studies to identify and validate biomarkers of stress-related changes in immune function. Link the value of this research to the health of the community. Contact: Dr. Ken Chu, 301-435-9213, chuk@dcpcepn.nci.nih.gov **03-CA-109 Enhancing biomarker discovery and validation using high quality, unbiased PLCO specimens.** The current process for cancer biomarker development is hindered by unsuitable specimens. The problem is two-fold: the lack of specimens specifically collected for biomarker development; and the lack of attention to potential sources of biases in the samples. These biases have resulted in numerous false positive results, leading to wasted efforts and funds invested in those early phase discovery research efforts. The PLCO biospecimens resource is designed for prospective studies of early detection biomarkers and cancer etiology. It is ideal for nested case control design for biomarker discovery and validation. We propose that this resource should be used for coordination of projects of discovery and validation of early detection biomarkers. Specifically, samples will be divided into two identical aliquots. One will be used for laboratory discovery, and one will be used for validation of the biomarkers. This design will eliminate many confounding factors that may lead to false discovery. Contact: Dr. Christine Berg, 301-496-8544, bergc@mail.nih.gov **03-CA-110 Validation of Known Biomarkers.** Biomarkers in cancer prevention, detection and treatment continue to challenge the scientific community from realizing its potentials and translating them into clinical use. The pathway to clinical application remains elusive. The challenge grants will ask researchers to take up validation studies of known biomarkers with clearly defined milestones with measurable outcomes in a two-year period. The outcomes may include proof-of-principle studies for select risk groups, cohorts, and populations that may benefits from risk assessment, and early detection and diagnosis. Contact: Dr. Sudhir Srivastava, 301-435-1594, srivasts@mail.nih.gov **03-DA-101* Biomarkers for Pain.** Pain research has been greatly hampered by the unreliable nature of self-report based instruments. The establishment of objective, affordable and reliable pain biomarkers and measurements would advance our understanding of pain mechanisms, provide a basis for improved clinical management of pain, help assess an individual's risk for becoming addicted to opiate analgesics, and establish much needed objective measures of treatment success or failure. Contact: Dr. Yu Lin, 301-435-1318, ylin1@nida.nih.gov; OD(ORWH) Contact: Dr. Janine A. Clayton, 301-402-1770, Smithja2@od.nih.gov **03-DA-102* Novel Molecular Targets From Unexpected Sources.** The quiescent databases left behind by unsuccessful medication trials represent an incredibly rich resource with the potential to turn failure into success. Through the use of strategic alliances (e.g., with FDA Critical Path Initiative) and novel approaches, such as target deconvolution and network pharmacology, these databases, can be transformed into engines of discovery to dramatically increase our ability to recognize novel molecular targets that underlie robust biological responses such as liability to drug abuse. Contact: Dr. Elena Koustova, 301-496-8768, koustovae@mail.nih.gov

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	03-DA-103* **Comprehensive biomolecular mass spectrometry.** Current detection methodologies provide a narrow window into just 1% of the molecular universe. As a consequence, there is a strong need to develop new mass spectrometric technologies for the faster, more sensitive, more specific, and more comprehensive identification of biomolecules (both charged and neutral proteins and lipids) in tissue samples and single cells. This initiative seeks to leverage the potential of cutting edge technologies in the areas of ion mobility and vacuum ultraviolet photofragmentation for developing molecular identification and quantitation instruments that could be deployed in the clinical as well as research environments. Contact: Dr. Christine Colvis, 301-443-6480, ccolvis@nida.nih.gov **03-DA-104*** **Biosignatures of Drug Exposure.** Chronic exposure to a pathogenic agent is one of the defining features of conditions such as infectious diseases and substance use disorders. This characteristic presents a unique opportunity to develop and harness the power of biosignatures that could reliably predict disease vulnerability, trajectory, and treatment outcome. This initiative is specifically designed to uncover and validate peripheral endogenous biomarkers in animal models exposed to chronic drug exposure, withdrawal, or relapse that may serve as surrogates for CNS changes in humans. The results are also likely to spur significant advances in a host of related disorders. Contacts: Dr. Ivan D. Montoya, 301-443-8639, Imontoya@mail.nih.gov; Dr. Jeffrey Schulden, 301-402-1526, schuldenj@nida.nih.gov; Dr. Elena Koustova, 301-496-8768, koustovae@mail.nih.gov **03-DA-105** **Biomarkers, stress and immune function.** Stress is known risk factor for substance abuse and relapse, and stress, substance abuse and withdrawal are known to impact immune function. There is a need to identify biomarkers to assess the impact of stress, both social and biological (including substance abuse and withdrawal), on immune function. Studies addressing specific immune or inflammatory responses to HIV/SIV infection are of particular interest. Contact: Dr. Diane Lawrence, 301-443-1470, lawrencedi@nida.nih.gov **03-DA-106** **Biomarkers in mental disorders.** There is a need for innovative approaches to identify biomarkers that can predict illness onset, define diagnosis, identify potential individualized therapeutic targets, and/or assess treatment responses related to HIV-associated neurological and neurocognitive impairment. Studies incorporating substance abusers or model systems that include exposure to abused substances would be appropriate. Contact: Dr. Diane Lawrence, 301-443-1470, lawrencedi@nida.nih.gov **03-DA-107** **Biomarkers of substance abuse comorbidity.** This initiative will support the development of molecular/proteomic biomarkers that will help in the detection, assessment and treatment of drug abuse comorbidity consisting of infections; and provide objective testing methods, help in the understanding of molecular bases of diseases, disease processes and progression. Contact: Dr. Jag H. Khalsa, (301) 443-2159 jk98p@nih.gov **03-DE-101** **Development, Refinement, or Validation of Biomarkers Relevant to Oral or Craniofacial Disorders.** Clinical trials evaluating treatments for oral diseases such as periodontal disease or autoimmune salivary gland diseases are well suited to complementary biomarker studies. Biofluids such as parotid saliva or gingival crevicular fluid can be collected using non-invasive techniques. **Goal**: Identification of biomarkers from oral fluids, validation against other biofluids or bioassays, and development of diagnostic platforms to predict, diagnose or profile oral and systemic health, and to determine if therapeutic interventions are impacting the biological target. Other biomarker

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	studies of interest to NIDCR include those seeking to define novel pain biomarkers, biomarkers associated with stress-related responses, and objective and quantifiable measures of pain severity that are independent from self-report based instruments. Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov **03-DK-101 Discovery of biomarkers for disease risk, progression or response to therapy in diseases of interest to NIDDK.** A barrier to understanding and treating diseases of interest to NIDDK is the paucity of sensitive and validated biomarkers. Research is needed at all levels including identifying new targets, developing new imaging or non-invasive methods and validating promising biomarkers in well-characterized populations. **Contact:** Dr. Teresa Jones, 301-435-2996, jonester@mail.nih.gov **03-DK-102 Development and validation of novel, non-invasive methods to detect and monitor disorders of relevance to NIDDK at early stages of disease before major organ damage and dysfunction has occurred.** Novel diagnostic methodologies relevant to disorders that are currently difficult to detect early in the course of disease and/or that require invasive procedures (such as tissue or organ biopsies) are of highest priority. Contact: Dr. Teresa Jones, 301-435-2996, jonester@mail.nih.gov **03-DK-103 Identify the normal and diseased proteome of subcellular organelles of relevance to NIDDK diseases.** Studies are needed to identify ciliary or other organelle proteins in model organisms and human cells, using tissue from both healthy and diseased (Bardet-Biedel, PKD, nephronophthesis, etc.) sources. Contact: Dr. Teresa Jones, 301-435-2996, jonester@mail.nih.gov **03-DK-104 Development of drug toxicity biomarkers for kidney, liver, and other organs of NIDDK interest for use in assessing human drug toxicity.** Studies are needed to identify markers of organ toxicity that can be used to screen potential therapeutic agents for diseases of relevance to NIDDK. Markers are also needed to identify organ specific damage in organs and tissues of interest to NIDDK. Contact**:** Dr. Teresa Jones, 301-435-2996, jonester@mail.nih.gov **03-DK-105 Nutrient biomarkers.** Identification and validation of sensitive and predictive biomarkers are needed that evaluate status of a specific nutrient, that assesses biological effects that may be related to disease, and that may indicate individual response to nutrient-gene or nutrient-nutrient interactions. Such studies may be important for determining which diseases will respond to dietary interventions. Contact: Dr. Michael (Ken) May, 301-594-8884, maym@mail.nih.gov **03-ES-101 Validation of new exposure assessment methodologies.** NIEHS supports research in the development of biosensors, biomarkers and signatures of response to environmental exposures. An important aspect of this research is the validation of biomarkers and analytical methods in on-going cohorts, studies preferably with well-characterized exposures. Support is needed for pilot studies to test biomarkers of exposure and response in archived samples from previous or ongoing population studies. Contact: Dr. Daniel Shaughnessy, 919-541-2506, Shaughn1@niehs.nih.gov **03-EY-101* Role of immunity in identifying relevant markers in ocular diseases.** Oxidative stress/injury and host immune response are postulated to be involved in many degenerative eye diseases such as age-related macular degeneration, diabetic retinopathy, uveitis, glaucoma, and keratoconus. Other disorders such as Sjögren's syndrome remain difficult to diagnose and treat. Characterizing the molecular events and

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	the host immune response during disease progression, and the understanding of how genes and their products interplay between systemic inflammation, vascular disease and photoreceptor cell death will allow us to identify biomarkers for the diagnosis and treatment of these blinding diseases. Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov **03-HD-101 Biomarkers to Assess Maternal and Child Health.** Research is needed to accelerate the development and validation of biomarkers that can be used to assess normal and abnormal child development and human reproductive function. Biomarkers could help identify individuals at risk for serious disorders or help physicians determine the severity of conditions where symptoms develop over longer periods of time. Examples where biomarker discovery would make a significant advance include: o Gamete quality - assessment of gamete quality and ovarian and testicular reserve, and as indices of normal sexual maturation; o Reproductive diseases - use as minimally invasive or non-invasive diagnostic markers of reproductive diseases and disorders such as endometriosis and fibroids; o Pregnancy-related complications - detection of early pregnancy-related complications (i.e., during implantation, placental development) that could result in pregnancy failure; o NEC - identifying low birthweight infants that are at high risk of necrotizing enterocolitis (NEC). o TBI - identifying molecules that are sensitive indicators of severity and outcome in traumatic brain injury (TBI). Contact: Dr. Louis DePaolo, 301-435-6970, ld38p@nih.gov; Dr. Michael Spittel, 301-435-6983, spittelm@mail.nih.gov; Dr. Gilman Grave, 301-496-5593, gg37v@nih.gov; Dr. Beth Ansel, 301-496-5289, ba25e@nih.gov **03-HL-101* Identify and validate clinically relevant, quantifiable biomarkers of diagnostic and therapeutic responses for blood, vascular, cardiac, and respiratory tract dysfunction.** Treatment paradigms have evolved from studies of patients who, despite similar presentations, may have experienced disparate environmental exposures or clinical courses and may have varied underlying pathobiologies. As a result, patients who appear to be similar because of their clinical characteristics often demonstrate substantially different morbidity, mortality, and responses to drugs. Identification and validation of biomarkers from cell culture to animal models and human studies that can be efficiently and reproducibly quantified in a clinical setting could be used to determine the most effective care for individual patients and identify more precisely those who are most likely to benefit from specific interventions for prevention or treatment. Contact: Dr. James Kiley, 301-435-0233, kileyj@nhlbi.nih.gov **03-HL-102 Identify molecular addresses (zip codes) in blood vessels to enable specifically targeted therapy.** Every organ appears to display a unique signature or molecular address (“zip code”) on the luminal surface of its blood vessels that can serve as a target for agents such as peptides, small molecules, or nanoparticles. Such agents could be used as carriers to transport drugs, genes, or imaging markers to diseased tissues/organs while sparing normal tissues. Contact: Dr. Stephen Goldman, 301-435-0560, goldmans@nhlbi.nih.gov **03-MH-101* Biomarkers in mental disorders.** Search for innovative approaches to identify candidate biomarkers for mental disorders that are suitable for subsequent validation efforts. Potential biomarkers would predict disease risk and course, prognosis, and/or treatment response. Techniques could include behavioral assessments, electrophysiology, neuroimaging, genomics, proteomics, metabolomics, or any

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	combination thereof. Contact: Dr. Steven J. Zalcman, 301-443-1692, szalcman@mail.nih.gov **03-NS-101* Identification and validation of biomarkers for Proof of Concept (early Phase IIa) studies for Nervous System Disorders.** For many neurological disorders, moving potential therapies from promising studies in animal models to clinical trials that demonstrate effectiveness in patients remains a major hurdle. Identifying and validating biomarkers that associate with a beneficial response to treatment in the human (or in the animal model) which can also be measured in patients would help overcome this hurdle. These biomarkers could be used in Phase IIa Proof of Concept studies to determine whether a therapeutic intervention has engaged the intended biologic target. Contact: Dr. Ursula Utz, 301-496-1431, utzu@ninds.nih.gov **03-NS-102 Standardization and validation of neurological biomarkers.** There are many promising biomarkers for neurological disorders whose usefulness for research or health care is limited due to lack of standardization and/or multi-center validation of sensitivity and specificity. These include, for example, tests of mitochondrial dysfunction, identification of specific cell types in brain (stem cells, malignant cells, inflammatory cells, etc.), perfusion imaging in acute stroke, diffusion –based imaging in traumatic brain injury, and objective measures linked to the progressively disabling pathology in Parkinson's disease, multiple sclerosis, spinal muscular atrophy, and other neurological disorders. Contact: Dr. Ursula Utz, 301-496-1431, utzu@ninds.nih.gov **03-OD(OBSSR)-101* Developing high-throughput biomarker assays from finger-stick dried blood spots.** Develop, using finger-stick dried blood spots, novel high-throughput biomarker assays, to identify lipids, proteins, metabolites, and genetic information to expand the array of available biomarkers for use in large community-based biosocial surveys. OD(OBSSR)Contact: Dr. Kay Wanke, 301-435-3718, wankek@od.nih.gov NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NIEHS Contact: Dr. Daniel Shaughnessy 919-541-2506, Shaughn1@niehs.nih.gov; NHLBI Contact: Dr. Catherine Stoney, 301-435-6670, stoneyc@nhlbi.nih.gov **03-OD(ORDR)-101* Validating biomarkers for functional outcomes in rare diseases.** This initiative will provide a program of an expert consultative group to work with research investigators in the design to validate biomarkers and collect the data necessary to relate the biomarker with functional outcome in rare diseases. This program will be designed to stimulate development of new treatment trials. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **03-OD-101 Use of epigenetic signatures in blood cells to predict disease.** Although epigenomic changes appear to be important in many diseases, disease diagnosis may be quite challenging if epigenomic analysis of tissues that are not readily accessible (brain, heart, etc) is required. Blood cells are readily accessible and could serve as powerful "sentinels" or biomarkers for a variety of complex diseases. Characterization of epigenomic signatures in blood cells in a variety of disease situations could lead to the development of entirely new non-invasive diagnostic strategies. Contact: Dr. Phil Smith (NIDDK), 301-594-8816, smithp@mail.nih.gov

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(04) Clinical Research	**04-AA-101*** **Medication Development for Hepatic Fibrosis.** Alcohol and infectious disease induced hepatic fibrosis affects millions of patients worldwide and remains an unresolved challenge for clinicians. Given the morbidity/mortality associated with this disease, there is an urgent need for translation of emerging antifibrotic molecules into effective therapies. Expediting clinical trials for compounds that have successfully undergone preclinical studies has the potential to make much needed medications available and reduce the need for liver transplantation. Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AA-102** **Use of *in silico* techniques to develop compounds to treat alcohol dependence.** Recent advances in computational software and hardware have revolutionized the process of drug discovery. This initiative will support the use of *in silico* computational methods to facilitate the development of new compounds for the treatment of alcohol dependence. *In silico* modeling may be used for all aspects of the drug discovery and drug design process including identifying and characterizing brain targets of alcohol effects for possible binding sites; designing and generating candidate molecules; virtual screening of compound libraries to identify lead structures; optimizing lead compounds; as well as use of *in silico* models to predict absorption, distribution, metabolism and excretion properties of molecules to address early toxicity issues. The goal is to streamline and expedite the traditional process of drug development and produce novel compounds for the treatment of alcohol dependence. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **04-AA-103** **Novel Models of Service Delivery.** Fewer than 10% of people with alcohol use disorders ever receive professional treatment. Furthermore, most specialty treatment programs have not implemented NIAAA-funded research findings on behavioral or pharmacologic treatment. Thus, the public has no effective access to research-based treatment. Obviously, research on implementation will be important for increasing adoption of such findings in specialty treatment programs, but it is not sufficient. Two year studies are encouraged to develop and test additional models of care. Key to the impact of this research is that these models will need to be accessible, affordable, culturally sensitive, and acceptable to the patients. Research should also examine strategies for integrating prevention and treatment services into other service components to enhance access including medical, mental health care, employment and social services, and criminal justice. Enhanced collaboration among the various treatment providers and treatment sectors should also be emphasized. Given the small percentage of individuals with alcohol use disorders who receive treatment, it is important that future research focus on personal barriers (i.e. stigma, denial, etc.) as well as on organizational barriers (availability, costs, etc.) that affect treatment access. It is important that this research examine the unique barriers faced by at-risk populations. Also key to addressing the chronic nature of this illness will be studies that examine models that support long term access for individuals who may need additional help, such as booster sessions or rapid re-entry into care rather than waiting until a relapse has become serious enough to warrant re-treatment. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **04-AA-104** **Disease Management of Chronic or Relapsing Illness.** About 30% of people with a lifetime diagnosis of alcohol dependence have a chronic form of the illness; those with more than one episode have an average of five episodes. Yet our models are almost all time-limited, and focus exclusively on relapse prevention among people who have already stopped drinking. Two year research studies are sought to determine how services should most effectively be structured and financed in order to provide effective

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	care. Since many of these individuals have serious co-morbidities, research care models should integrate care for different disorders, co-locate them, or coordinate them. In addition, many chronically ill people are unable to make use of current treatments because they have sensory or cognitive deficits and research should also address how to provide care in these situations. Research is also sought to develop and test alternative modes of care delivery, especially tele-medicine, telephone care, internet, and toll-free telephone numbers. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **04-AA-105 Adaptive Screening and Intervention Technology.** Decisional models are being developed to characterize the interaction of prevention and treatment modalities for at-risk and HIV infected individuals in order to prevent acquisition, transmission, and progression of infections resulting in death. Research is encouraged to explore these models more systematically and identify choice points in interventions where optimal prevention and treatment strategies can be put into place. The goal is to develop and test models tied to specific end points (antiretroviral treatment failure, mortality, cost, etc) using appropriate Operations Research methodologies to prioritize among multiple alcohol interventions, construct portfolios of alcohol interventions that deliver the maximum value, and consider capacity constraints in the infrastructure, and consider investments to reduce those capacity constraints within the portfolio of possible interventions. This approach calls for development of a broader systems science that focuses on optimization and is a natural extension of operations research. Contact: Dr. Kendall Bryant, 301-402-9389, kbryant@mail.nih.gov **04-AG-101* Therapeutic algorithms for older patients with multiple conditions: data analyses and pilot testing.** Analysis of existing medical record data sets (e.g., from the VA or HMOs) to identify problems associated with the combination of therapies for two or more specific conditions in older patients with multiple conditions. This information could be used to develop new therapeutic algorithms or refine existing algorithms to address problems related to the use of multiple algorithms in older clinically complex patients and to inform short-term intervention studies to assess their efficacy and practicality. Contact: Dr. Susan Nayfield, 301-496-6949, nayfiels@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AG-102 Pain and Neurodegenerative Diseases.** Research to understand the impact of aging or age-related neurodegenerative diseases on the neural pathways underlying pain experience as well as the underlying mechanisms and the influence of aging or age-related neurodegenerative diseases on the assessment and treatment of pain in the elderly. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **04-AG-103 Development of treatments for the metabolic syndrome.** The metabolic syndrome, which is a combination of medical disorders manifested as central obesity, dyslipidemias, fatty liver disease, hyperinsulinemia and insulin resistance, affects at least one in five (maybe even one in four) people in the USA and prevalence increases with age. It leads to shortening of life and increasing morbidity because of diabetes and cardiovascular disease. Rather than treating each component of the metabolic syndrome separately, it would be beneficial and less expensive in the long run, if a unifying pathophysiology for metabolic syndrome were uncovered. This could then potentially lead to developing of treatments for its prevent and treatment. Contact: Dr. Susan Nayfield, 301-496-6949, nayfiels@mail.nih.gov

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	04-AG-104 Development of Less Expensive and More Effective Treatments for Medical Conditions, e.g., Restless Legs Syndrome. It is estimated that approximately 16 million Americans have symptoms of Restless Legs Syndrome with 1/3 reporting significantly diminished quality of life because of those symptoms. Current FDA-approved treatments are limited, costly, do not have sustained, long-term benfits, and in fact may lead to worsening of the condition with very long-term treatment. Alterantive and less costly treatments are now ready and waiting to be developed that would both save money for the health care system and potentially improve treatment of the RLS patient, possibly even correcting an underlying pathology of the diseease, but as these offer no potential commercial gain they require federal support for development and clinical evaluation. Contact: Dr. Brad Wise, 301-496-9350, WiseB@mail.nih.gov **04-AG-105 Development of experience-based measures of well-being.** Almost all measures of the quality of life and life satisfaction are based on self-evaluations and judgments rather than on cumulating actual experience over the course of a day, week, etc. Studies of how people remember and report these experiences show that systematic distortions can prevent reporting of accurate experiences after the fact. Brief, standardized measures of experienced, subjective well-being, based on experience sampling approaches, would offer a unique tool for clinical and epidemiological research, augmenting and complementing current indicators of population wellbeing and quality of life. Such measures are not included in PROMIS or the NIH Toolbox. Measuring both the evaluative and experiences facets of well-being is likely important for understanding health, which is not just the absence of illness, but the presence of wellness. Contact: Dr. Lis Nielsen, 301-402-4156, NielsenLi@mail.nih.gov **04-AG-106 Development of better methods to measure "real world" caloric intake and physical activity in people.** Precise quantitative knowledge of individuals' caloric intake and level of physical activity in their daily lives is crucial to assessing the success of interventions designed to modify them, as well to assess their health effects. To date, both objective and self-reported measures of these variables have remained very imperfect. Research to improve reliability and practicality of stable-isotope metabolic methods and body composition measures used in objective estimation of caloric intake, and of accelerometers or other objective measures of physical activity, as well as improved self-report instruments, could play an important role in developing better interventions to control weight and assess their effects. Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **04-AG-107 Mechanisms of specific benefits of different types of physical activity.** Different types of physical activity (e.g., resistance exercise, endurance exercise, walking) have different physiologic effects and differing effects on specific health outcomes and risk factors. Greater knowledge of the physiologic and cellular effects (e.g., on muscle, body composition, blood vessels, metabolism, and bone) of specific types of physical activity could lead to better physical activity interventions targeted for specific conditions, risk factors, or disabilities. This information could be obtained through short-term physical activity or exercise intervention studies that combine measures of clinical or functional outcomes with physiological or cellular information from biospecimens. Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **04-AG-108 Drug response and toxicity.** Application of pharmacogenetics and pharmacogenomics, quantitative and systems pharmacology (this could be part of a larger grouping to include systems biology and systems genetics), ADMET pharmacology, pre-clinical models, new technologies and approaches to complement pharmacogenomic

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	studies to enhance signal to noise ratios and aid mechanistic studies, and consensus standards for normal and altered phenotypes in drug response and toxicity. Contact: Ms. Winifred Rossi, 301-496-3836, rossiw@mail.nih.gov **04-AG-109 Develop and validate behavioral metrics to measure the impact of chronic pain.** It will also be important to identify and measure the factors influencing human pain perception and transitions to chronic pain after an acute insult. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **04-AG-110 Methods to enhance palliative care and end-of-life research.** Develop and test interventions to enhance the quality of care for persons with a life-threatening illness. This research will provide the foundation for the development of evidenced-based guidelines to standardize palliative and end-of-life care. Contact: Dr. Lis Nielsen, 301-402-4156, NielsenLi@mail.nih.gov **04-AG-111 Development of effective approaches to increase minority recruitment and retention into clinical trials.** Focus on research activities that reduce barriers to diversity and participation in clinical trials and on initiatives that build partnerships and utilize new and non-traditional recruitment approaches. Specific health disparity diseases/conditions of concern include but are not limited to diabetes, obesity, cardiovascular disease, infant mortality, cancer, substance abuse, mental health, and HIV/AIDS. Contact: Dr. Taylor Harden, 301-496-9265, hardent@mail.nih.gov **04-AI-101* Develop novel methods and address key questions in mucosal immunology:** Human mucosal immunology has been an extremely difficult area of study, despite its importance for developing interventions for immunologic and infectious diseases of the airway, GI, and vaginal tract, and for improving human vaccine responses. Greater understanding of the immunology of the mucosa will also be important in the design and development of topical microbicides and a variety of immune-based therapies. Furthermore, immunizations of the mucosa are likely to be more relevant, simpler, and less expensive than systemic immunizations. Contact: Dr. Annette Rothermel, 301-496-5429, arothermel@mail.nih.gov **04-AI-102* The human immune response to infection and immunization – Profiling via modern immunological methods and systems biology.** Challenge grants in this area will capitalize on recent advances in immune profiling and systems biology to understand the diversity of human immune responses to vaccination and generate profiles of protective as well as ineffective immune responses. This effort will rely on existing, phenotypically well-characterized cohorts (e.g., human microbiome project, various longitudinal birth cohorts, etc.) and apply a variety of modern analytic tools, including transcriptional, cytokine, and proteomic profiling, and analysis of leukocyte subsets and functional status. Parallel efforts will focus on development of a wide range of human sample-sparing assays. The resulting challenge grants will expand ongoing NIAID-sponsored efforts in immune profiling and accelerate a planned expansion of these activities. The results of these studies will have immediate implications for rational design and development of safe and effective vaccines and improved immunization schedules. Contact: Dr. Dan Rotrosen, 301-496-1886, drotrosen@mail.nih.gov **04-AR-101* Autoimmunity For Diseases Of The Skin, Joints, Muscle And Other Tissues.** Develop reagents and analytic methods to identify, characterize, track, and inhibit human B and T cells specific for defined self-antigens, and antigen-presenting cells in diseases of the skin, joints, and other tissues. Define mechanisms by which autoreactive

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	lymphocytes contribute to tissue damage. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Janine A. Clayton, 301-402-1770, Smithja2@od.nih.gov **04-AR-102 Clinical Research in Rheumatic, Muscle and Skin Diseases of Childhood**. Studies suggest that children with chronic life-threatening diseases who are treated under a clinical protocol have significantly reduced mortality and morbidity. This also enhances and accelerates understanding of disease and testing of new therapies. The goal is to establish a coordinating mechanism and database software for a pediatric rheumatology consortium, with the goal of having every child with a rheumatic disease entered into a clinical study. Development of consortia for studying children with muscular dystrophies and for rare skin or bone diseases may also facilitate and accelerate research in patients with these diseases. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AR-103 Targets for Intervention in Chronic Pain in Musculoskeletal, Skin and Rheumatic Diseases.** There is significant variability in the amount of pain individuals experience in spite of having the same degree of the tissue injury and destruction due to chronic disease. Complete pain relief is not always achieved even after the replacement of the injured organ, such as in joint replacement. This indicates that many mechanisms in addition to organ damage affect the duration, intensity, and emotional response to pain. The goal is to establish collaborative approaches and private-public partnerships to discover key genetic, biochemical and cellular pathways and processes that can be targeted for intervention to provide long-term pain relief in patients with chronic rheumatic and musculoskeletal diseases. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AR-104 Standardized Use of Patient Reported Outcomes (PRO) for Pain Assessment in Arthritis and Musculoskeletal Diseases Outcomes Studies.** Disease and treatment impact on patients are best evaluated by PROs, which are better overall predictors of long-term morbidity and mortality than many clinical and laboratory tests. The objective is to systematically validate pain PROs developed through the NIH Roadmap PROMIS initiative (http://nihroadmap.nih.gov) in clinical trials and observational studies of chronic diseases of interest to the NIAMS. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AR-105 Critical, Ready To Be Deployed Clinical Research Infrastructure**. Investigators are encouraged to propose, implement and utilize research infrastructure that will accelerate progress and make efficient use of current investments in research. The objectives are to develop shared core resources including state-of-the-art new technologies and instrumentation and to expand and intensify research collaborations and communication between disease-focused research centers, medical research centers and patient care communities. Existing registries and repositories of autoimmune and rare genetic diseases of bone, muscle, skin and connective tissue require new networking systems for linking them to laboratories, research clinics and other national datasets to accelerate genetic research and early validation of biomarkers. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-AR-106 Cellular, Molecular and Genetic Therapies for Rare Inherited Diseases of Muscle, Skin and Connective Tissue and Bone.** These novel therapeutic approaches offer the possibility of restoring function to a defective gene or compensating for the loss of gene function. These approaches are potentially quite powerful and could

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	lead to significant advances in the treatment of diseases of muscle and other tissues. The goal of the projects will be to find creative approaches to overcome some of the current technical obstacles and resolve remaining ethical issues. Areas of interest include promising vectors, therapeutic genes, local and systemic delivery methods for viral gene therapy; study the immune reaction to gene therapy approaches, methods to improve long-term expression, methods for editing gene products in vivo, such as exon-skipping antisense oligonucleotides and small RNAs. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-CA-101 Enhanced infrastructure for Brain Cancer Research.** Progress in the treatment of brain metastases has been hampered by a lack of focus on the clinical problem over many years. The most critical need is for coordinated efforts toward creating infrastructure for biospecimen collection, banking, and distribution of clinically annotated tissue available for research focused on all aspects of the process by which a tumor cell metastasizes to the brain are needed. Multidisciplinary approaches should be encouraged to explore: the molecular signature of tumors that metastasize to the brain, homing of tumor cells to the brain microenvironment, the blood brain barrier, the role of brain microenvironment in successful growth of brain metastases and the use of novel imaging and other technologies to target and validate novel therapeutics. Contact: Dr. Judy Mietz, 301-496-9326, mietzj@mail.nih.gov **04-CA-102 Understanding the Impact of Cultural Beliefs on Biospecimen Collection and Use.** Research is needed to understand the impact of cultural beliefs on biospecimen collection and use, and begin to build the interdisciplinary scientific teams and community partnerships that will be required to stimulate an effective, high quality biospecimen collection, processing and banking and analysis system within diverse communities. Building on current research (in CNP and PNRP), focused studies in this area will not only contribute to jobs within multi-ethnic communities, but also help ensure that advances in personalized cancer care among racially and ethnically diverse communities keep pace with broader national biospecimen collection and research efforts. Contact: Dr. Mary Ann S. Van Duyn, 301-451-4284, vanduynm@mail.nih.gov **04-CA-103 Augment Clinical Trial Recruitment/Retention of Multi-Ethnic Patients through Patient Navigators.** Support research to increase representation of multi-ethnic patients in clinical trials through the development and testing of innovative, multi-pronged, multi-cultural, and incentivized approaches to enhancing multi-ethnic accrual to and retention within clinical trials. Promising approaches, based on current research, include employing navigators to help patients through the system and engaging the community. Further studies are needed to define the role of navigators and the community, as part of broader multi-ethnic outreach approaches, to improving access to clinical trials among underserved populations with unusually high cancer rates. Contact: Dr. Martha L. Hare, 301-594-1908, Martha.hare@nih.gov **04-CA-104 Policy for Challenge Grants: Incorporation of Analysis of Race/Ethnicity Differences into Challenge Grants.** Applicants for Clinical Research Challenge Grants must set forth race/ethnicity-based hypotheses based on a consideration of the relevant literature if the proposed study has the potential for such consideration. The purpose of this requirement is three-fold: to ensure compliance with NIH strategic focus on eliminating health disparities; to capitalize on the growing body of research demonstrating race/ethnicity differences in all areas of NIH research; and to ensure that any race/ethnicity-specific solutions/answers to the stubborn questions are not overlooked, thus resulting in incorrect conclusions. If these requirements are not relevant to the

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	proposed research, applicants would be required to provide scientific justification for why racial/ethnic analysis would not be relevant. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **04-CA-105 Oversampling Minority populations in Clinical Research.** Provide financial incentives/supplements to NCI-supported clinical trials where oversampling for minority populations would be feasible. Efforts to reach minority populations and barriers to access trials should be documented for further study, e.g., non-participation by choice, ineligible based on study design and/or health condition. Contact: Dr. Martha L. Hare, 301-594-1908, Martha.hare@nih.gov **04-CA-106 Designing Clinical Research Studies based on unique health characteristics of a Minority Community Cohort with regard to Co-morbidities (domestic and international).** Support the development of treatment protocols for co-morbid conditions including the development of clinical guidelines, development of effective low cost diagnostic and treatment techniques, upgrading surveillance and tracking systems in these communities that are effective in capturing critical information in disease tracking and surveillance, designing patient navigation networks to support the needs of patients and families, etc. Particular attention should be paid to projects that include HIV/AIDS, mental health, tropical diseases, tuberculosis, and cancer. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **04-CA-107 Developing innovative comprehensive trans-NIH approaches to address global health disparities**. Provide support to stimulate the creation of innovative comprehensive trans-NIH approaches to address global health disparities through the development of scientific teams to strengthen the current international research agenda to include initiatives that provide the region/country with benefits and improve the impact of the NIH research investment in low to middle income countries, e.g., improve research capacity and research translation to contribute to the improvement of health outcomes, expansion of in-country research training efforts, the introduction of community-based participatory research, and health services research to address cancer and other co-morbidities. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **04-CA-108 Policy for Conducting Clinical Research in low- and middle income countries.** Require all NIH grants proposing to conduct research in low-middle-income countries to demonstrate/articulate what the benefit is to the country being studied, and to what extent the researcher intends to engage in capacity-building during, and/or at completion of the research project, e.g., what would be provided to the country to address disparities, including capacity-building, research training, financial or in-kind support targeted to improve community health, etc. Encourage partnering/collaborating with existing NCI/NIH health disparities programs (CNP, PNRP) to introduce community-based approaches to addressing disparities. US Jobs: Hire pre-and post-docs to develop and manage foreign relations and community networks and develop linkages with other US programs to address critical health gaps found in the targeted country. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **04-CA-109 Biospecimen standardization for Clinical Assays**. Emerging clinical markers for cancer diagnosis, prognosis, and treatment efficacy need standardized biospecimen collection, processing and storage protocols to reduce assay variability and improve patient care. Systematic studies are needed to determine the most important standardization steps for biospecimen preparation for markers that have shown particular utility, and to determine the specific biospecimen preparation needs of different marker

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	assays. Contact: Dr. Helen M. Moore, 301-496-0206, moorehe@mail.nih.gov **04-CA-110 Treatment of Prostate Cancer.** Currently there is evidence that Androgen Deprivation Therapy (ADT) may be effective in the palliative management of advanced prostate cancer and may be effective for high-risk patients treated with radiation therapy for localized disease. In other clinical settings the balance of the clinical costs and benefits of ADT, including adverse effects on quality of life, are not well characterized. This project would use the data resources of the HMO Cancer Research Network (CRN) to identify a large, multi-center historical cohort of men with prostate cancer who received some form of treatment for their cancer. Using a broad array of clinical and pathological data, the analysis would compare clinical outcomes among men with similar prognostic characteristics and primary therapy (surgery, radiation, etc.) who received and didn't receive ADT. The cohort will have to be very large involving several sites the budget is likely to $2-3 million over 4-5 years. NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **04-CA-111 Quality of Cancer Surgery and Outcomes.** This collaborative project would use electronic data resources in the CRN and the University of Vermont to identify a large cohort of patients operated on to remove breast and colorectal cancers. From national cancer quality measurement initiatives and the literature, a set of quality indicators (e.g., number of lymph nodes removed, necessity for reoperation, etc.) will be determined for each cancer. Using existing databases and electronic medical records, investigators will assess the quality of each patient's surgery on each indicator. The analysis will examine the ability of the quality indicators singly and in combination to predict outcomes such as survival. Because this study plows new ground, we would propose a large pilot involving the University of Vermont's existing breast cancer surgery database and two CRN sites, Marshfield and GHC. NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **04-CA-112 Appropriate Use of Colony Stimulating Factors.** Studies suggest that colony stimulating factors (CSF) are not used as approved by FDA label and clinical indication; namely, patients are often given these agents as treatment rather than prophylaxis for chemotherapy-induced neutropenia. Furthermore, in the correct setting, using these agents as prophylaxis could improve outcomes and at the same time be cost-neutral or perhaps minimally cost increasing. These issues represent testable hypotheses, and are of great interest to health plans facing rising costs for cancer-related care. Therefore, the purpose of this Phase IV study is to determine if an intervention designed to improve use of Neulasta as primary prophylaxis improves health outcomes (episodes of grade 4 neutropenia and febrile neutropenia, quality of life) and is cost-neutral compared to standard care for newly diagnosed breast cancer patients undergoing moderately suppressive chemotherapy. NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **04-CA-113 The Use of Health Informatics to Increase the Effectiveness of Cancer Prevention.** Using the electronic medical records systems of integrated health care systems to provide feedback to primary care physicians to increase their effectiveness in providing cancer prevention services, such as tobacco cessation. A proof of principle trial in the Cancer Research Network has shown that this approach is potentially effective for tobacco cessation. But a larger dissemination/implementation study is needed to generalize these results. NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov

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	04-CA-114 Chemoprevention of Breast Cancer. In adult women without pre-existing breast cancer, what is the comparative effectiveness of selective estrogen receptor modulators (SERMs), tamoxifen citrate (Tamoxifen) and raloxifene (Evista), used for the primary prevention of breast cancer on improving short-term and long-term outcomes including: invasive breast cancer; ductal carcinoma in situ (DCIS); breast cancer mortality; osteoporotic fractures ; and all cause mortality. In adult women without pre-existing breast cancer, what is the evidence for harms of tamoxifen citrate and raloxifene? Harms may include but are not limited to: thromboembolism (i.e. deep vein thrombosis, pulmonary embolism); cardiovascular disease (i.e. stroke, myocardial infarction); metabolic disorders (i.e. hypertriglyceridemia); musculoskeletal symptoms (i.e. arthralgia syndrome); mental health (i.e. mood changes); gynecological outcomes (i.e. vaginal dryness, dyspareunia, sexual dysfunction, endometrial hyperplasia/dysfunctional uterine bleeding, and endometrial cancer; ophthalmologic disorders; other adverse events that would impact quality of life such as vasomotor symptoms; and cross-reactively with other medications or therapies. This could include an examination of whether outcomes vary by subgroups such as age, menopausal status, breast cancer risk, race and ethnicity and metabolism status (i.e., CYP2D6 mutation). NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **04-CA-115 Comparative Effectiveness of Computer Assisted Diagnostic Devices.** For over a decade, Computer Assisted Diagnostic devices have been developed to aid clinicians in a variety of ways. Many, but by no means all, of these devices have been developed for use with imaging technologies. This supplement proposes studies regarding comparisons between CAD devices and alternative diagnostic approaches. Some of these CAD devices are intended to remove large numbers of likely negative cases to make the radiologists' time more efficient. Others are used to point to regions of an image for special attention. These Computer Assisted Diagnostic devices have been approved by the US FDA with varying degrees of evidence depending on the particular clinical application. There are opportunities to do short term trials (which can be simulated with outcomes and do not need to wait for clinical course to occur) that compare various CAD algorithms to standard of care, to double reading, and to expert panel approaches. Each project would have three phases: Review the clinical and statistical evidence used to place the product on the market and any evidence accrued since marketing application. Develop a standard protocol and data system (unless data already exist) that can be used for future studies of other algorithms or other was of using imaging data to optimize diagnosis. Perform a head-to-head comparison of CAD with standard of care, with double reading, and with an expert panel approach. NCI Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **04-CA-116 Comparative Effectiveness of Different Modalities for Breast Cancer Screening.** Film screen mammography was initially established, through randomized clinical trials to be an effectiveness screening modality for breast cancer. Over time other innovative technologies, such as digital mammography and MRI, have become disseminated into the practice of breast cancer screening. The existing NCI sponsored Breast Cancer Surveillance Consortium, which currently contains information on over 7.5 million mammographic examinations, over 2 million women and over 87,000 cases of breast cancer, can be used as a platform to evaluation the comparative effectiveness of these newer modalities. NCI Contact: Dr. Stephen Taplin, 301-402-1483, taplins@mail.nih.gov **04-DA-101 Evaluation of novel, rationalized poly-pharmacotherapeutic treatment strategies for substance abuse.** Phenotypic robustness is underpinned by redundant

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	and compensatory functional signaling routes. Network biological analysis predicts that modification of a single target by a drug is not nearly as likely to affect disease outcome as would rational combinations of drugs that target multiple, complementary mechanisms. Applications will focus on combination of medication strategies for the treatment of substance use disorders. Contact: Dr. Kris Bough, 301-443-9800, boughk@mail.nih.gov **04-DA-102 A New Look at Longitudinal Data.** NIH has funded numerous prospective longitudinal epidemiologic, developmental, prevention, and treatment studies that have resulted in extensive data sets. A real need exists for additional funding to analyze these rich data resources; much of these data remain unmined due to budget and time constraints. The Challenge Grants could provide support for new research questions from already collected data. The grants could also support research to add outcome measures that were not originally included in the longitudinal project, for example, adding substance use and other behavioral outcomes to a study of smoking and asthma. Contact: Dr. Nicolette Borek, 301-402-0866, nborek@nida.nih.gov **04-DA-103 Extending the Reach of Web-Based Drug Abuse Prevention and Treatment to Rural and Other Remote Locations.** Many persons living in remote or rural locations have limited opportunities to obtain drug abuse treatment services, due to a lack of available service settings, the barrier of traveling long distances, and/or the perceived lack of private and confidential treatment options. This program seeks to develop web-based drug abuse treatment interventions that do not necessitate frequent in-person visits to a central facility. The interventions could take various forms, including: accessing interactive web-sites, video linkages with an individual counselor, video linkages with counselor-led group sessions, and asynchronous linkages with moderated chat rooms. Contacts: Dr. Harold Perl, 301-443-9982, hperl@nida.nih.gov and Dr. Jacqueline Lloyd, 301-443-8892, Lloydj2@nida.nih.gov and Dr. Cecelia Spitznas, 301-402-1488, spitznasc@mail.nih.gov **04-DA-104 Primary Screening for Psychiatric Problems.** A standardized screening assessment for behavioral and psychiatric problems would greatly increase the identification of patients' problems in medical settings and would also promote adoption of a standardized core research assessment, facilitating substance abuse, comorbidity and other psychiatric disorder identification across multiple clinical and research settings and maximize data utilization and cross situational analyses. It would also facilitate research use of diagnostic and treatment data from the intervention field and the translation of empirical data into applied contexts. The goal is to develop a relatively brief, easily administered and scored assessment with strong abuse and addiction validity. Contact: Dr. Jeffrey Schulden, 301-402-1526, schuldenj@nida.nih.gov **04-DA-105 HIV - Viral Hepatitis Co-Morbidity.** The aims of this research topic area are to investigate the feasibility, acceptability, efficacy, and effectiveness of combined screening for HIV, Hepatitis-B and Hepatitis-C at general and specialty medical clinics, emergency departments, trauma centers, intensive care units, community treatment centers for alcohol and substance abuse, sexual transmitted disorders clinics, detention centers, educational centers, etc. Furthermore, research is needed to examine the effectiveness of linking screening for HIV and viral hepatitis to appropriate medical care for those infected. Contact: Dr. Raul N. Mandler, 301-435-0645, mandlerr@nida.nih.gov **04-DA-106 Integrating cost-effectiveness analysis into clinical research.** This initiative calls for cost-effectiveness analysis of new and innovative HIV/AIDS interventions (i.e., prevention and treatment) as well as of existing interventions with demonstrated

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	effectiveness. Such cost-effectiveness research should provide information that can inform and guide future policies that support the allocation of health resources for the prevention and/or treatment of HIV/AIDS. Contact: Dr. Jacques Normand, 301-443-1470, jnormand@nida.nih.gov **04-DA-107 Improving quality of life of patients and family following a war-related traumatic injury.** Develop and test personalized behavioral or pharmacological interventions to prevent development of or treat psychiatric disorders, addictions, or other complications in persons with war-related traumatic injuries both in theatre and during the post hospitalization transition period, with the ultimate goal of improving the health and quality of life of affected individuals and families. Preventive and treatment interventions for families would be applicable during pre-deployment, deployment, and post-deployment stages. Contact: Dr. Steve Sparenborg, 301-496-4844, Sparenborgs@nida.nih.gov ; Dr. Eve Reider, 301-402-1720, ereider@nida.nih.gov; and Dr. Cecelia Spitznas, 301-402-1488 spitznasc@mail.nih.gov **04-DA-108 Development of effective approaches to increase minority recruitment and retention into clinical trials.** Minority participation in substance abuse and HIV/AIDS clinical trials has been very low and new tools are needed to improve this in order to advance knowledge in treatments that are most effective in helping minority groups. This initiative encourages researchers to develop and evaluate innovative approaches to promote subject retention and initiatives that build partnerships and utilize new and non-traditional approaches to recruitment and retention. Contacts: Dr. Lynda Erinoff, 301-443-1470, lerinoff@nida.nih.gov and Carmen L. Rosa, M.S., 301-443-9830, crosa@nida.nih.gov **04-DA-109 Medication development for hepatic fibrosis.** HIV/HCV co-infection among drug abusers is a major cause of hepatic fibrosis, and HCV-related liver disease is the leading cause of death among those on HAART therapy. Given the morbidity/mortality associated with this disease, there is an urgent need for translation of emerging antifibrotic molecules into effective therapies. Expediting clinical trials for compounds that have successfully undergone preclinical studies has the potential to make much needed medications available and reduce the need for liver transplantation. Contact: Dr. Lynda Erinoff, 301-443-1470, lerinoff@nida.nih.gov **04-DA-110 Screening, Brief Intervention, and Referral to Treatment (SBIRT)**. Excessive use, abuse, and/or dependence on drugs and alcohol have a tremendous impact on individual health status, contributing to a variety of medical conditions having high levels of associated mortality and morbidity. The attention required to attend to these conditions also places increased burden on the medical system, including considerable costs that are often not recovered. Under the NIH Challenge Initiative, the aim of this research topic area is to investigate the feasibility, efficacy, effectiveness, sustainability and cost benefits of using screening, brief intervention and referral to treatment (SBIRT) strategies to decrease the medical and social burden of alcohol and/or drug abuse in the US. Contact: Dr. Raul N. Mandler, 301-435-0645, mandlerr@nida.nih.gov and Dr. Cecelia Spitznas, 301-402-1488, spitznasc@mail.nih.gov **04-DA-111 Clinical Neurobiology of Chronic Opioid Use and Misuse.** There is an urgent need for research that will more thoroughly delineate the neurobiological implications of long-term opioid use. This knowledge gap is of particular concern when it comes to the developing brain - and the urgency is underscored by the fact that increasing numbers of adolescents and young adults are using opioid medications, prescribed and

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	otherwise. Research funded in this area could be instrumental in the development of evidence-based clinical guidelines for prescribing and managing long-term opioid pharmacotherapy for chronic pain and opioid dependence, and in furthering our understanding of the treatment needs of opioid dependent patients. Contact: Dr. David Liu, 301-443-9802, dliu@nida.nih.gov **04-DA-112 Enhancing the Impact of Behavioral Interventions using New and Innovative Technology.** The ultimate goal of the NIH is to improve public health as measured in terms of biological well-being, which is multidimensional and is strongly shaped by behavioral variables. Neuroscience research on brain plasticity has demonstrated, unequivocally, that the brain changes as a result of behavior changes. Technological advancements have made it possible to better measure the impact of behavioral interventions on specific biological targets and processes. Innovative 2-year projects that will utilize technology to enhance efficacious behavioral interventions by targeting specific neurobehavioral and/or biological processes (e.g., risk taking, impulsivity, decision making) involved in drug abuse/addiction. Contact: Dr. Lisa Onken, 301-443-2235, Lisa_Onken@nih.gov **04-DA-113 Development of behavioral and social interventions that reduce stigma and improve quality and accessibility of health care services in low resource settings.** In the same manner that the effects of stigma magnify the personal and societal problems related to substance use disorders and HIV infection, addressing, preventing, or mitigating stigma of these disorders and their effects on recovery can profoundly improve the lives of individuals with these disorders, their families, and the larger society. The engagement of key stakeholders (such as professional treatment programs, healthcare-delivery disciplines, and informal care-giving networks) in offering viable treatments that reduce the stigma of substance use disorders and HIV infection may be critical to implementation of treatments that enhance and sustain positive health. Thus, there is a critical need in substance abuse and HIV treatment to translate existing knowledge related to the causes and consequences of stigma into scalable pilot interventions that can measure stigma and prevent or mitigate its negative effects on recovery from these disorders. Contact: Dr. Udi E. Ghitza, 301-443-9983, ghitzau@nida.nih.gov **04-DA-114 New and innovative technologies to monitor patient behaviors and clinical status in clinical trials.** Develop and test new affordable, technologies to enable remote, centralized monitoring of physiologic, behavioral and neurologic indices across various health and mental disorders as well as study medication compliance and overall treatment compliance, and adverse effects in clinical trials. These technologies should provide opportunities to enhance efficiency in clinical trials, as well as to collect more “real life” data. Identity verification and time stamp information will be needed in some cases. Contacts : Dr. Cecelia Spitznas, 301-402-1488, spitznasc@mail.nih.gov **04-DA-115 The effect of drug addiction treatment immunotherapies (monoclonal antibodies or vaccines) on the fetus**. Preclinical assessment of changes in maternal and fetal (organ) drug distribution following maternal administration of an immunotherapy. Preclinical studies to assess teratology and pharmacokinetics of immunotherapies, alone and in combination with drugs of abuse or nicotine. Contact: Dr. Jamie Biswas, 301-443-8096, jb168r@nih.gov **04-DA-116 Research to develop novel pharmacotherapy strategies for the treatment of pregnant/postpartum women with substance related disorders.** Substance abuse during pregnancy often occurs in the context of complex environmental

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	factors and poly-drug exposure, as well as medical conditions which are associated with adverse neonatal consequences. Much is known in regard to the negative effects of substances of abuse on the pregnant/post partum women and their substance exposed neonates but relatively little is known in regard to medication treatment strategies and research methodology. Contact: Dr. Steve Oversby, 301-435-0762, soversby@mail.nih.gov **04-DA-117 Drug response and toxicity.** Application of pharmacogenetics and pharmacogenomics to addiction research by the development or use of pre-clinical models, new technologies and approaches to complement pharmacogenomic studies to enhance signal to noise ratios and aid mechanistic studies, and consensus standards for normal and altered phenotypes in response to drugs of abuse, or treatments for drug addiction. Contact: Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **04-DA-118 Role of the human gut microbiome in chronic diseases.** Applications will be invited to understand the interactive effects of drugs of abuse and gut microbiome on the pathogenesis of chronic diseases such as HIV and HCV. Contact: Dr. Vishnu Purohit, 301-594-5754, vpurohit@nida.nih.gov **04-DA-119 Novel methods in mucosal immunology.** Gut-associated lymphoid tissue (GALT) is the largest mucosal lymphoid organ and the major site of HIV replication which is associated with severe CD4+ T cell depletion. Various drugs of abuse have also been shown to compromise immune system as well as disrupt intestinal integrity. Understanding the interactive effects of drugs of abuse and HIV infection on GALT may help prevent progression of HIV-associated pathological conditions. Contact: Dr. Vishnu Purohit, 301-594-5754, vpurohit@nida.nih.gov **04-DA-120 Medication development for hepatic fibrosis**. Liver fibrosis is a common feature of chronic liver diseases such as Hepatitis C, alcoholic liver diseases and nonalcoholic steatohepatitis, and it can progress to cirrhosis without intervention. There is an urgent need for translation of potential antifibrotic molecules into effective therapies. Activation of cannabinoid 2 (CB2) receptors and inactivation of cannabinoid 1 (CB1) receptors have been shown to attenuate liver fibrosis in animal model of fibrosis. Preclinical studies are required to test the efficacy of various CB1 antagonists and CB2 agonists in the treatment of liver fibrosis. Contact: Dr. Vishnu Purohit, 301-594-5754, vpurohit@nida.nih.gov **04-DC-101* Prevention of Otitis Media.** Otitis media, or middle ear infection, is a major public health problem in young children. Resistance of bacterial pathogens to traditional antibiotic therapy is making this approach to treating this disorder increasingly problematic. The Challenge is to develop and utilize knowledge of the basic biology underlying bacterial colonization and infection of the middle ear to create new approaches to preventing infection. Contact: Dr. Bracie Watson 301-402-3458, watsonb@nidcd.nih.gov **04-DE-101 Clinical Outcomes of Dental Procedures:** Many approaches are used to treat oral diseases and conditions. The long term successes of different treatment and restorative approaches have not been assessed completely, particularly in patients with complex medical problems or rare dental diseases. Goal: Assessment of the comparative effectiveness of diagnostic technologies with differing costs, or cost-effectiveness of new and innovative interventions; cost-effectiveness or comparative effectiveness of existing interventions with demonstrated effectiveness, including in patients with compromised oral

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	health such as those having undergone head and neck radiation, Sjögren's syndrome or rare syndromes such as the Ectodermal Dysplasias. Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov **04-DE-102 Classification Criteria for Craniofacial Diseases.** New classification criteria have been proposed for genetic diseases that significantly impact the oral structures, but validation studies are needed to establish their utility. Goal: Refinement or validation of current classification criteria for rare genetic diseases with significant oral and craniofacial manifestations. Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov **04-DE-103 Feasibility of Evaluating Effectiveness Using Current Infrastructure.** There is a limited evidence base to support common interventions in dental care and management options in craniofacial disorders. It is not certain to what degree the current infrastructure can support evaluation of effectiveness in oral health or craniofacial conditions. Goal: Assessment of, or demonstration of the usefulness of current infrastructure for evaluating the effectiveness of prevention or treatment approaches in oral health or craniofacial conditions. Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov **04-DE-104 Survival of Resin Dental Composites.** Resin dental composites are one of the most frequently used materials for restoration of teeth. Multiple formulations are available commercially. The long-term outcomes of different composite materials have not been compared extensively. For example, resin dental composite shrinkage is implicated as the main cause of failure of dental restorations. However, this hypothesis has not been clinically evaluated by comparing outcomes of low shrinkage and high shrinkage resin composite restorations. Studies allowing survival comparisons of different resin dental composites are encouraged. This could be accomplished by examining patients treated previously, or through analyses of records that indicate the type of resin material used for restoration. NIDCR Contact: Dr. James Drummond, 301-402-4243, drummondj@nidcr.nih.gov **04-DK-101* Role of the human gut microbiome in NIDDK diseases.** This effort would support metagenomic studies aimed at understanding the role of the human microbiome in contributing to NIDDK diseases and conditions. Studies are needed that would evaluate appropriate sampling techniques, high throughput platforms, and analytic techniques that would provide sufficient data to serve as the foundation for further hypothesis driven studies in the disease or condition of interest. Contact: Dr. Robert Karp, 301-451-8875, karpr@mail.nih.gov **04-DK-102 Develop improved techniques for clinical diagnosis, detailed clinical phenotyping, and clinical disease staging and activity for conditions of interest to NIDDK, including endocrine and metabolic diseases, digestive and liver diseases, renal and benign urologic and hematological diseases.** Examples include developing a comprehensive disease profile, defining informative immunophenotypic profiles, and developing new technologies for anatomic and functional diagnosis. Contact: Dr. Myrlene Staten, 301-402-7886, statenm@mail.nih.gov **04-DK-103 Develop novel approaches to understand and treat functional disorders**. Examples include characterizing the factors in diabetes that lead to the development of functional GI and motility diseases; Determine how genotype contributes to or predisposes patients to the development of functional GI and motility disorders;

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	Determine the role of diet in the development of functional GI and motility disorders**;** Develop new technologies and therapeutic approaches to effectively treat patients with functional GI and motility disorders; Evaluate therapeutic outcomes and the impact of doctor/patient interactions to determine effective treatments for functional GI and motility disorders. Contact: Dr. Frank Hamilton, 301-594-8877, hamiltonf@mail.nih.gov **04-DK-104 Improve the diagnosis, staging and treatment of diseases of the liver**. Examples include: viral hepatitis, non-alcoholic steatohepatitis, genetic diseases such as hemachromatosis and Wilson's disease, inborn errors of metabolism, liver disease associated with cystic fibrosis, and biliary atresia, autoimmune liver diseases, and drug induced hepatotoxicity. Examples include devise novel diagnostic tests, biomarkers, imaging and other modalities to non invasively assess fibrosis and inflammation. Contact: Dr. Edward Doo, 301-451-4524, dooe@mail.nih.gov **04-0DK-105 Develop resources needed to support clinical research**. Examples include assembling sample collections for uncommon conditions, developing centralized core reagents and assays for clinical research, and assembling clinical data for cross sectional epidemiological studies. Contact: Dr. Beena Akolkar, 301-594-8812, AKOLKARB@mail.nih.gov **04-DK-106 Preservation/Recovery of endogenous insulin secretion.** Insulin response to hyperglycemia in humans with type 2 diabetes diminishes with duration and severity of the disease but the mechanisms underlying this loss are only partly understood. Causes may include progressive loss of beta cell function due to the underlying disease or be a consequence of hyperglycemia and other metabolic derangements of diabetes. Failure of insulin response is at least partially reversible. New human pilot studies or ancillary studies within ongoing investigations are requested to explore the mechanisms of failure/recovery of insulin secretion. These could include strategies to reduce stress on endogenous insulin secretion to "rest" the beta cells or to reduce insulin resistance. New drugs, devices and therapeutic strategies provide opportunities for investigations that can pioneer new approaches to delaying onset or progression of type 2 diabetes. Contact: Dr. Peter Savage, 301-594-8858, savagep@mail.nih.gov **04-DK-107 Understanding the mechanism by which bariatric surgery improves diabetes and cardiovascular risk factors.** Resolution or amelioration of Type 2 diabetes after bariatric surgery has been observed both before and after substantial weight loss. Understanding the underlying mechanisms for this saluatory effect will help define optimal surgical approaches and identify new targets for therapy and prevention of diabetes and other obesity-associated co-morbidities. Contact: Dr. Myrlene Staten, 301-402-7886, statenm@mail.nih.gov **04-DK-108 Nutritional status of bariatric surgery patients.** Studies to evaluate the nutritional status of bariatric surgery patients, including changes in blood/tissue levels of micronutrients or body stores of these nutrients before and after surgery. Also includes studies to determine the optimal nutrient supplementation needed in patients after different bariatric surgery procedures. Contact**:** Dr. Carolyn Miles, 301-451-3759, milesc@mail.nih.gov **04-DK-109 Optimal nutritional support in acute and chronic diseases/conditions.** Includes studies to determine optimal macronutrient/energy composition, micronutrient supplementation, and delivery mode/timing of nutrition support formulas in patients with both acute and chronic nutrition support needs. Contact: Dr. Carolyn Miles, 301-451-3759,

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	milesc@mail.nih.gov **04-DK-110 Phenotyping eating and activity behaviors**. Studies assessing methods for phenotyping eating or activity behaviors that can be used to inform behavioral genetic studies, including but not limited to methodologies to capture propensity for sedentary behaviors vs. vigorous activity, differing hedonic responses to high fat or high sugar foods, or differences in hunger and satiety. Contact: Dr. Susan Yanovski, 301-594-8882, yanovskis@mail.nih.gov **04-DK-111 Pilot and feasibility clinical research studies in diabetes, obesity, and metabolic, endocrine, digestive, liver, renal and urological diseases.** Translation of new research discoveries from preclinical phase to phase 3 randomized trials requires preliminary data on the safety, efficacy and feasibility of new interventions. Mechanistic studies may help explain response to therapy. In addition, new epidemiological research is required to estimate disease incidence, prevalence, and potential risk modifiers in the United States. These areas of investigation are required for the design of larger, long-term clinical trials and observational studies. Contact: Dr. Barbara Linder, 301-594-0021, linderb@mail.nih.gov **04-DK-112 Comparative effectiveness research (CER) in diabetes, obesity, and metabolic, endocrine, digestive, liver, renal and urological diseases.** Pilot feasibility studies and planning grants for CER that can be accomplished within two years are needed to plan long term multi center randomized controlled trials in diseases within the mission of NIDDK. Proposals must address a rigorous evaluation of the impact of different options that are available for treating a given medical condition for a particular set of patients. Studies may compare similar treatments, such as competing drugs, or it may analyze very different approaches, such as surgery and drug therapy. The analysis may focus only on the relative medical benefits and risks of each option, or it may also weigh both the costs and the benefits of those options. Examples include comparisons of multiple currently approved medical treatments and comparison of medical and surgical treatments for diabetes. Contact: Dr. Peter Savage, 301 594-8858, savagep@niddk.nih.gov. **04-ES-101 Intervention strategies for environmentally-induced diseases.** Capitalizing on the knowledge that has been gained to understand the relationship between environmental exposures and disease, studies are being sought to initiate the development of prevention/intervention strategies that can reduce the body burden of chemicals and/or reduce its adverse effects on biological systems through dietary, nutritional or other treatments. Studies that use animal models and/or build on current human studies will be considered appropriate. Prevention/intervention strategies that focus on modulating absorption, disposition, metabolism and excretion of chemicals or modify signaling and other stress induced pathways that lead to disease are examples of approaches that could be considered. Contact: Dr. Claudia Thompson, 919-541-4638, Thomps14@niehs.nih.gov **04-ES-102 Investigating gene x environment interaction using controlled human exposures.** Carefully controlled exposures of human subjects to low levels of environmental toxicants, such as ambient particulate matter, ozone, or diesel exhaust, provide an opportunity to help augment animal studies and population-based studies to better understand the interaction of genetics and exposure (GxE). Valuable GxE data could be generated in two-year projects by 1) exposing previously genotyped individuals to environmental agents and measuring appropriate endpoints or 2) genotyping individuals

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	who have been exposed to environmental agents and subsequently evaluated. Contact: Dr. Sri Nadadur, 919-541-532, Nadadurs@niehs.nih.gov **04-GM-101*** **Personalized drug response and toxicity.** Application of pharmacogenetics and pharmacogenomics, quantitative and systems pharmacology (this could be part of a larger grouping to include systems biology and systems genetics), ADMET pharmacology, preclinical models, and new technologies and approaches to complement pharmacogenomic studies to enhance signal-to-noise ratios and aid mechanistic studies, and consensus standards for normal and altered phenotypes in drug response and toxicity. Contact: Dr. Rochelle Long, 301-594-3827, longr@nigms.nih.gov; Dr. Richard Okita, 301-594-3827, okitar@nigms.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **04-GM-102** **Integrative bioinformatics systems for critical care**. Development of highly flexible and viable integrative bioinformatics systems for the unique, data-rich and time-sensitive environments found during the care of injured or critically ill patients in the emergency department or intensive care unit. Contact: Dr. Scott Somers, 301-594-3827, somerss@nigms.nih.gov **04-GM-103** **Perioperative pain.** Studies to inform, develop, and validate new animal models of perioperative pain conditions; develop new measures of perioperative pain in animals that are noninvasive and objective, and that permit a behavioral or functional assessment of pain and pain treatment outcomes; and identify gene polymorphisms and gene-environment interactions that predict the development of perioperative pain and response to drug therapy. Contact: Dr. Alison Cole, 301-594-3827, colea@nigms.nih.gov **04-HD-101*** **Identify the Factors that Place Women at Risk for Preterm Birth.** Over 12 percent of births happen prematurely, and the rate is rising--increasing the risk of adverse outcomes for babies and mothers. However, most of these births occur in women who do not have any of the few known risk factors for preterm birth. New approaches and technologies (such as fetal imaging, fetal EKG, blood or urine tests, or response to maternal position or exercise) are urgently needed to improve physicians' ability to identify women at increased risk for preterm birth, so that preventive interventions can be developed. Contact: Dr. Catherine Spong, 301-435-6894, spongc@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, MD, 301-402-1770, jevajiip@od.nih.gov **04-HD-102*** **Development of Pediatric Medical Devices**. Currently, many cardiovascular, surgical, prosthetic, and diagnostic devices originally designed for adults are also being adapted for use in young children, without having demonstrated that they are safe, effective, and appropriately sized. Pediatric medical devices need to be developed that are properly designed for children, with safety and effectiveness demonstrated rather than presumed, and with accurate risk assessments. Contact: Dr. Steven Hirschfeld, 301-496-0044, hirschfs@mail.nih.gov. **04-HD-103** **Vaginal Microbicides.** Vaginal microbicides are currently under study as female-controlled interventions to prevent heterosexual HIV transmission, but the effect of the microbicides on normal vaginal physiology, including during pregnancy, has not been evaluated. Studies are needed to assess vaginal physiology and milieu (including cytokines), and the effect of candidate microbicide formulations, in normal women; in women with various co-infections; and in pregnant women. Contact: Dr. Lynne Mofenson, 301-435-6870, mofensol@mail.nih.gov

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	04-HD-104 Glucose Levels and Brain Development. Young children with type 1 diabetes experience large daily fluctuations in levels of plasma glucose ranging from brain-threatening levels of hypoglycemia to organ- damaging levels of hyperglycemia. Studies are needed on 4-8-year-old diabetic children using the new technology of minimally invasive continuously monitored glucose sensing in conjunction with periodic MRI studies of brain anatomy and function to ascertain how conditions of hyper- and hypoglycemia affect brain development prospectively. These studies should determine the neurodevelopmental changes that occur over the course of two years in diabetic children in comparison with (1) control children without diabetes, and (2) publicly available normative data in the NIH Pediatric MRI Study of Normal Brain Development. Contact: Dr. Karen Winer, 301-435-6877, winerk@mail.nih.gov **04-HD-105 Advanced Imaging to Assess Impact of HIV on Child Development.** In the United States, perinatally infected children are surviving into young adulthood; however, complications of multiple organ systems are in need of study. For example, a critical need is to assess the cardiovascular impact of HIV and its treatment in perinatally infected adolescents using newer cardiac and vascular imaging techniques. Moreover, new neuroimaging technologies offer opportunities to assess the effect of HIV on the brain in children and to assess the effect of in utero exposure to antiretroviral drugs in uninfected children. Contact: Dr. Lynne Mofenson, 301-435-6870, mofensol@mail.nih.gov **04-HL-101 Identify Mechanisms Linking Cardiopulmonary Disease Risk and Sleep Disordered Breathing**. Sleep Disordered Breathing (SDB) is pervasive among the overweight and elderly; it more than doubles their risk of cardiovascular disease, stroke, respiratory problems, diabetes, and all-cause mortality. However, gaps in translational research defining how SDB treatment reduces cardiopulmonary morbidity have led to inconsistencies in whether SDB is treated in the course of usual cardiopulmonary care. Clinical approaches need to be applied to elucidate biomarkers, mechanisms, and clinically relevant pathways from animal models, clinical studies, and/or existing cohorts. Advances are urgently needed to move recent discoveries into practical application and improve cardiopulmonary disease outcomes. Contact: Dr. Michael Twery, 301-435-0199, twerym@nhlbi.nih.gov **04-HL-102 Develop Integrative Strategies to Elucidate the Mechanisms of Lung Diseases**. Integrative approaches are needed to move beyond the limitations of traditional disease models based on single pathway/gene analyses. Studies are needed to elucidate biologically relevant patterns of cellular pathophysiology as a dynamic process and identify gene regulatory networks that control such processes as normal lung alveolization and development or that contribute to dysregulated vascular cell proliferation in pulmonary hypertension. Data developed through such studies are expected to support the development of molecular models for the study of lung cell interactions, the lung tissue injury cascade, immunophenotypes of lung disease, identification of regulatory and shared “control points” in the systems biology of lung disease, and molecular elements that predict disease susceptibility and therapeutic response. Contact: Dr. Dorothy Gail, 301-435-0222, gaild@nhlbi.nih.gov **04-HL-103 Assess the role of leukocyte interaction with platelets, erythrocytes, and endothelium in the pathogenesis of heart, lung, and blood diseases.** The intercellular interface that emerges among leukocytes, platelets, and endothelial cells as a result of inflammation enables transfer of both beneficial and potentially injurious locally generated bioactive molecules. The mechanisms for recruitment, activation and retention of platelets and leukocytes and the associated sequelae on the behavior of endothelium

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	and underlying tissue cells require more in-depth analysis. The identification of the key points controlling such communication may lead to new pharmaceutical interventions for both thrombosis and inflammation. Contact: Dr. Andrei Kindzelski, 301-402-0658, kindzelskial@mail.nih.gov **04-HL-104 Perform secondary analyses of existing data to answer important clinical and preventive medicine research questions**. Numerous data sets have been created from completed and ongoing population-based longitudinal observational studies and clinical trials that include rich data on phenotypes, behaviors, genetic markers, environmental factors, physiological risk factors, subclinical cardiovascular disease, clinical care, and clinical outcomes. Those data sets may be not only be mined further to explore new hypotheses but also combined to increase statistical power and representativeness of the study populations. Selective addition of new data, such as data extracted from medical records of participants or data on costs, has the potential to provide valuable new information to the existing data. Efforts are needed to obtain additional data, combine data sets where appropriate, conduct additional analyses, and disseminate findings of clinical importance. Examples of areas of interest include: ▪ Analysis of data from completed randomized clinical trials that may have ascertained atrial fibrillation to identify potential prevention approaches ▪ Determination of cost-effectiveness of preventive interventions ▪ Identification of prevention approaches or analyses of important demographic subgroups ▪ Analysis of risk factors for heart failure ▪ Identification of biomarkers for clinical outcomes, such as heart failure and atrial fibrillation ▪ Evaluation of predictors of recurrent clinical cardiovascular disease ▪ Exploration of associations of treatment and control of risk factors with severity of incident clinical events, recurrent clinical events, and prognosis ▪ Analysis of genetic markers related to risk factors and disease in relation to their genetic and environmental context and how these may be used to inform preventive medicine and clinical care. Contact: Dr. Diane Bild, 301-435-0547, bildd@nhlbi.nih.gov **04-HL-105 Treatment of heart failure with preserved systolic function.** Nearly half of all patients with heart failure have preserved left ventricular systolic function, yet still have a poor prognosis. Commonly used strategies for treating such patients include treatment with diuretics, nitrates, angiotensin converting enzyme inhibitors, and/or beta-blockers, but it is not clear how the agents, or combinations of them, compare with one another with respect to their effect on quality and length of life and health care costs. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Lauer, 301-435-0422, lauerm@nhlbi.nih.gov **04-HL-106 Implantable cardioverter defibrillators and cardiac resynchronization therapy in heart failure.** Implantable cardioverter defibrillators and cardiac resynchronization therapy have been shown to improve clinical outcome in chronic heart failure, but they are expensive technologies and have been studied primarily in the context of carefully managed randomized controlled trials. It is not clear how they compare with standard medical therapy in routine clinical practice and among certain patient subsets, such as women, the elderly, and minorities. Projects that address this challenge could

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	include analyses of existing data registries. Contact: Dr. Michael Lauer, 301-435-0422, lauerm@nhlbi.nih.gov **04-HL-107 Treatment of insomnia.** Insomnia is common and is associated with poor quality of life at increased risk for clinical events. Available treatment strategies include sedatives, melatonin, and behavioral interventions. However, it is not clear how they compare with one another with respect to their effect on quality and length of life and health care costs. Projects that answer this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Twery, 301-435-0199, twerym@nhlbi.nih.gov **04-HL-108 Improving clinical outcomes in critically ill patients with respiratory failure.** Treatment of critically ill patients involves multiple diverse interventions that affect all organ systems. While many have been viewed as merely supportive and comforting, they may in fact have important effects on outcomes. For example, studies of glucose management and sedation practices have shown reductions in hospital time and even mortality. The evidence base for intensive care medicine is improving in recent years, but many aspects of care are not systematically applied and should be compared and studied. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries Contact: Dr. Andrea Harabin, 301-435-0222, harabina@nhlbi.nih.gov **04-HL-109 Management of sarcoidosis.** Sarcoidosis is a systemic granulomatous disease of unknown origin that affects the lungs in about 90 percent of patients. Management is primarily based on the use of corticosteroids, anti-inflammatory agents, and cytotoxic drugs, such as methotrexate. Depending on the organs involved and the severity of disease regimens vary, although sometimes treatment is maintained for prolonged periods, often for many years. It is not clear which regimens and drug combinations and duration of therapy are most effective in controlling the disease, especially lung disease. Regimens for improving or maintaining lung function, other organ function, quality and length of life, and for reducing costs of health care would be of particular interest. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries Contact: Dr. Hannah Peavy, 301-435-0222, peavyh@nhlbi.nih.gov **04-HL-110 Treatment of pulmonary hypertension and right heart failure.** Pulmonary hypertension is a devastating, rapidly progressive disease characterized by progressive elevation of pulmonary arterial pressure and pulmonary vascular resistance that leads to right ventricular failure. Current therapies include prostacyclins, phosphodiesterase inhibitors, and endothelin receptor antagonists. The availability of these agents has improved hemodynamic measures and quality of life, but patient response varies significantly, and deterioration in outcomes is not uncommon. Morbidity and mortality remain high, and it is not known how the agents or, particularly, their combinations compare with each other affect outcome and quality of life. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Dorothy Gail, 301-435-0222, gaild@nhlbi.nih.gov **04-HL-111 Personalized algorithms for treatment of COPD.** Although many different treatments are efficacious for treating COPD, individuals vary widely in their responsiveness to therapies and few data are available to guide the choice of drug combinations for particular patients. Comparative effectiveness studies are needed to

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	assess both the benefits of combination therapies and to identify individual characteristics that are predictive of treatment responsiveness. Studies that address this challenge area will design and demonstrate feasibility for later studies that will directly test effectiveness of alternative treatment strategies which incorporate substantial stratification of subjects by baseline characteristics, such as biomarkers, genotype, and gene expression profiles. Contact: Dr. Antonello Punturieri, 301-435-0230, punturieria@nhlbi.nih.gov **04-HL-112 Screening for cardiovascular risk factors in children.** Cardiovascular risk factors – such as hypertension, elevated cholesterol, and obesity – often begin in childhood. There is substantial evidence that these risk factors in childhood will translate to increased risk of disease later in life. However, there are inconsistent recommendations about the clinical utility of screening children for these risk factors or how broad such screening should be. It is unknown, for example, whether universal screening for high blood cholesterol would be beneficial and cost-effective in youth, or whether it would be harmful and wasteful of clinical resources. Nor is it known whether only some children, and not all, should be screened. Projects that answer this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Denise Simons-Morton, 301-435-0384, simonsd@nhlbi.nih.gov **04-HL-113 Cost-effective trials of CVD prevention in persons with low short-term risk.** Traditional clinical trials have provided a powerful evidence base for preventing cardiovascular (CV) events in patients at known high short-term CV risk, but are less suited to addressing the larger problem of preventing or slowing the chronic disease process that creates that risk. Late-stage interventions tend to be resource-intensive, and they come too late for the many persons whose first clinical manifestation of CV disease is a fatal heart attack or stroke. Unfortunately, the duration and sample sizes required for clinical trials employing less intensive interventions in patients whose CV risk lies many years down the road are often prohibitive. The use of modern information technology may provide the means to facilitate more economical large early prevention trials, while preserving patient safety. Projects that answer this challenge could include planning grants for specific large-scale trials comparing strategies of early prevention. Contact: Dr. David Gordon, 301-435-0466, gordond@nhlbi.nih.gov **04-HL-114 Using existing datasets to plan effectiveness trials in pediatric cardiology.** Promoting guideline development or comparative effectiveness research in pediatrics is limited by the rarity of diseases, small patient populations, and difficulty (logistical, cost, ethical) in performing randomized, controlled trials. These constraints necessitate creative and novel approaches, such as developing new analytic, statistical, or theoretical strategies for evaluating comparative treatment effects of pediatric medications or interventions. Examples include innovative approaches to evaluating extant data (e.g., making use of administrative databases, or, increasingly, electronic health records to assess, for example, the comparative effectiveness of different medications administered in the cardiac intensive care unit) or development of novel, computational theoretical models or adaptation of existing procedures (e.g., decision analysis to assess, as an example, the comparative effectiveness of incorporating ECG screening into risk assessment of children receiving stimulant medications). These and similar approaches could be developed and tested using existing data sets in a two-year time frame, and could benefit not only pediatrics, but all research into rare diseases. Contact: Dr. Gail Pearson, 301-435-0510, pearsong@nhlbi.nih.gov

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	04-HL-115 Treatment of stenosed coronary arteries with hybrid coronary revascularization versus multi-vessel percutaneous intervention with drug eluting stents (DES). The prevalence of coronary artery disease (CAD) is increasing and as a result advances have been made in surgical and percutaneous techniques for revascularization as well as concomitant medical therapy for CAD. The American College of Cardiology Foundation, among other collaborating groups, conducted an appropriateness review of common clinical scenarios in which coronary revascularization is frequently considered. The findings indicate that clinical evidence is insufficient for new interventions for three vessel CAD including disease of the Left Anterior Descending Coronary Artery. It is unknown whether hybrid coronary revascularization using a minimally invasive surgical approach with PCI (hybrid procedure) is associated with improved patient outcomes as compared to PCI with DES alone. A randomized, controlled clinical trial targeting a large segment of the CAD population is needed to answer this important public health question. Without scientific evidence, this question will be answered through clinical practice patterns that may not optimize patient outcomes or be cost effective. Projects that answer this challenge could include planning projects for large-scale definitive clinical trials or development of data registries to collect prospective outcomes information on CAD patients receiving different treatments. Contact: Dr. Marissa Miller, 301-594-1542, millerma2@nhlbi.nih.gov **04-HL-116 Cost-effective strategies to achieve smoking cessation in hospitalized patients with cardiovascular cisease and COPD.** In 2007, 20% of adult Americans were current cigarette smokers, but significant disparities exist by age, race/ethnicity, level of education and socioeconomic status. Smoking is particularly problematic among hospitalized patients; those who continue to smoke after an MI have a 50% higher risk of recurrent coronary events compared to nonsmokers, but the risk for those who quit equals that of nonsmokers after 3 years. Providers are faced with uncertainty regarding optimal and cost-effective strategies to initiate smoking cessation for their hospitalized patients. Options include simple counseling, intensive behavioral interventions, financial incentives, and pharmacotherapy (nicotine replacement, buproprion, and veraclinine). Projects that answer this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Endpoints for comparisons could include safety and effectiveness, quality of life, and cost-effectiveness. Contact: Dr. Jared Jobe, 301-435-0407, jobej@nhlbi.nih.gov **04-MD-101* Development of effective approaches to increase minority recruitment and retention into clinical trials.** NCMHD will focus on research activities that reduce barriers to diversity and participation in clinical trials and on initiatives that build partnerships and utilize new and non-traditional recruitment approaches. Specific health disparity diseases/conditions of concern include but are not limited to diabetes, obesity, cardiovascular disease, infant mortality, cancer, substance abuse, mental health, and HIV/AIDS. Contact: Dr. Derrick Tabor, 301-402-1366, tabord@mail.nih.gov **04-MH-101* Autism: Addressing the challenge.** Target research gap areas identified by the Inter-Agency Autism Coordinating Committee (IACC) Strategic Plan for Autism Spectrum Disorder Research, including biomarkers, novel interventions, and new tools for screening, among other topics. Contact: Dr. Ann E. Wagner, 301-443-5944, awagner@mail.nih.gov **04-MH-102 Refining categories of clinical phenotypes for mental health research purposes.** Support research to refine and validate categories of clinical phenotypes to be used in mental health research. NIMH is in the process of developing these categories,

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	defined as dimensions of cognition or behavior that map on to brain circuits, genetic architecture, or conserved behaviors. Contact: Dr. Jane Steinberg, 301-443-3658, jsteinbe@mail.nih.gov **04-MH-103 Interventions that target symptom dimensions of childhood-onset mental disorders.** Conduct studies to develop novel interventions that target symptom dimensions of childhood-onset mental disorders, as well as related syndromes. Two-year awards will support initial technical development and proof-of-principle, pre-clinical studies, pilot studies of novel interventions, and novel strategies for matching individuals to available treatments. Contact: Dr. Lisa Gilotty, 301-443-3825, gilottyl@mail.nih.gov **04-MH-104 Access to services by individuals with autism and their families.** Engage well-characterized subjects and families in existing autism research activities in preliminary studies exploring variations in access to and use of services, identification of targets for services interventions, and exploration of how variations in service use affect family functioning in diverse populations. Contact: Dr. Denise M. Juliano-Bult, 301-443-3364, djuliano@mail.nih.gov **04-MH-105 Conduct pilot studies to develop and test developmentally appropriate, evidence-based prevention interventions and service delivery models for youth with who are at high risk for, or experiencing severe mental illnesses who are transitioning to adulthood.** Studies would propose strategies to address discontinuities in service systems and health care financing. Contact: Dr. Joel Sherrill, 301-443-2477, jsherril@mail.nih.gov **04-NR-101* Integrating Cost-Effectiveness Analysis into Clinical Research.** This initiative calls for the inclusion of rigorous cost-effectiveness analysis in the design and testing of new and innovative interventions as well as existing interventions with demonstrated effectiveness. Cost-effectiveness research will provide accurate and objective information to guide future policies that support the allocation of health resources for the treatment of acute and chronic diseases across the lifespan. Contact: Dr. Linda Weglicki, 301-594-6908, weglickils@mail.nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **04-NR-102* Methods to Enhance Palliative Care and End-of-Life Research.** This initiative will develop and test interventions to enhance the quality of care for persons with a life-threatening illness. This research will provide the foundation for the development of evidenced-based guidelines to standardize palliative and end-of-life care. Contact: Dr. Josephine Boyington, 919-316-4560, boyingtonje@mail.nih.gov **04-NR-103* Improving Quality of Life of Patients and Family Following a War-Related Traumatic Injury.** This initiative will develop and test personalized interventions to prevent complications in persons with war-related traumatic injuries during the post hospitalization transition period, with the ultimate goal of improving the health and quality of life of individuals and families following a war-related traumatic injury. Contact: Dr. Karen Huss, 301-496-9558, hussk@mail.nih.gov **04-NS-101 Constructing a relational database for neurological diseases.** A dynamic, biologically clustered, publicly accessible, relational database of neurological diseases that reflects current scientific understanding would be highly valuable to the NINDS and the scientific and lay community. It could also serve to illustrate the "knowledge landscape" of specific neurological disorders and their interrelationships and

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	help in analyzing scientific opportunities with respect to the current state of relevant research supported by NINDS as well as other Institutes, foundations, industry, and disease-related organizations. Contact: Dr. Yuan Liu; 301-496-0012, liuyuan@ninds.nih.gov **04-NS-102 Developing web-based entry and data-management tools for clinical research.** The construction of open source, user-friendly, web-based data entry and data management tools that could be customized by investigators would serve as a core resource for the community. In addition, the inclusion of common data elements in such databases in collaboration with NINDS would greatly facilitate the ability to combine datasets, facilitate data sharing, and perform data mining among clinical research datasets and report trial results to clinicaltrials.gov. Contact: Ms. Joanne Odenkirchen; 301-496-3104, odenkirj@ninds.nih.gov **04-NS-103 Developing consortia for clinical research.** Research progress in rare as well as common neurological disorders is often limited by the lack of a sizeable consortium with shared goals and ability to coalesce around a specific clinical research project. Applicants would have to demonstrate need and immediate impact by providing details on what research would be performed in the near future. Clinical protocols should be generated at the time of submission, but probably not yet IRB-reviewed/approved. Contact: Dr. Scott Janis, 301-496-9135, janiss@ninds.nih.gov **04-OD-101* Develop and validate behavioral metrics to measure the impact of chronic pain.** Standardized and validated measures of behaviors commonly associated with spontaneous pain in human chronic pain conditions are needed. These metrics can provide a basis for understanding the role and potential therapeutic impact of behavior in initiating and modulating chronic pain. Contact: Dr. Linda Porter (NINDS), 301-496-9964, porterl@mail.nih.gov **04-OD-102 Identify and measure the factors influencing human pain perception and transitions to chronic pain after an acute insult.** Quantitative and qualitative assays are needed that will reveal and measure the biological and behavioral mechanisms underlying pain perception and chronicity. Contact: Dr. Linda Porter (NINDS), 301-496-9964, porterl@mail.nih.gov **04-TW-101* Examining the clinical and mechanistic link between diabetes mellitus and cardiovascular disease in low- and middle-income countries.** The rising epidemic of obesity, insulin resistance, and type 2 diabetes has placed societies at dramatically elevated risks for atherosclerotic disease. Epidemiologic studies involving global populations exposed to different environmental and genetic risk will improve understanding of the complex clinical and mechanistic links between diabetes and heart disease, and help create the next generation of control measures. Contact: Dr. Aron Primack, 301-496-1653, aron_primack@nih.gov; NHLBI Contact: Dr. Cristina Rabadan-Diehl, 301-435-0550, rabadanc@nhlbi.nih.gov

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(05) Comparative Effectiveness Research	**05-AA-101* Innovative Analyses of Existing Clinical Datasets.** Typically secondary analyses of administrative and clinical data have been utilized for multiple objectives that include estimating incidence and prevalence of alcohol use and alcohol disorders, estimating treatment needs, developing health policy, testing clinical hypotheses, and performing meta-analyses that may contribute insights on the comparative effectiveness of behavioral and pharmacological therapies. Under this Challenge Grant initiative, researchers are encouraged to use secondary data analyses in methodologically innovative ways. An example is the use of cross-design synthesis to standardize and compare clinical data collected by different methods, thereby expanding the scope of knowledge on comparative treatment effectiveness. Another example is evaluation of the impact of new statistical models and methods on treatment effectiveness outcomes, for instance, comparing the relative impact of linear models and dynamic models on clinical trial outcomes. Both clinical and health services research proposals based on secondary analyses are invited under this initiative. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AA-102* Adaptive Designs and Person-Centered Data Analysis for Alcohol Treatment Research.** Simple trials comparing two treatments, or a treatment and a control condition, are essential in determining the efficacy of various treatments. However, such studies often do not answer questions of particular import to clinicians, who have to make a series of decisions in the same patient based upon response to initial and subsequent treatment. Adaptive designs offer a potential solution, but they are methodologically complex, are difficult to implement and require large numbers of subjects. Similarly, statistical analyses using variable-centered approaches (e.g., comparison of means) may miss important variability in outcomes, especially since statistical assumptions (e.g. normality) are routinely violated. Person-centered approaches such as trajectory analysis may offer an alternative that better captures differences in outcomes and also is more clinically intuitive. Research and development are needed to further develop such approaches and especially to make them easier to use. Also, additional new approaches are needed in order to speed the process of comparing effectiveness of different treatments. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AA-103* Use of Innovative Technologies in Alcohol Treatment Research**. Although progress has been made to standardize methods for measuring alcohol consumption in research on treatment of heavy drinkers, the best methods currently available still rely on retrospective accounts. Recent research comparing these interview methods with interactive voice response (IVR) has demonstrated that the interviews have reasonable validity for overall consumption, but day-to-day variability does not adequately characterize true consumption. More research is needed on the best type of technologies to use (IVR, pagers, etc.) and how best to integrate it into clinical trials. A related challenge has been standardizing behavioral interventions through the use of extensive training, monitoring and supervision. However, substantial variability exists with regard to the outcome of individual therapists. In addition, these therapies are not feasible to implement in community settings. Research is needed to develop and validate computerized behavioral interventions that can be used in clinical trials, especially for pharmacotherapy trials, and that offer easy adoption in the community. NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mwillenb@mail.nih.gov **05-AG-101* Data Infrastructure for Post-Marketing Comparative Effectiveness Studies.** The challenge is to create the data infrastructure that will enable comparisons of particular therapies, prescribing patterns, and benefit designs on health outcomes. Problems with currently available studies include omission of key patient groups (such as

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	the elderly in nursing homes), lack of information on adherence and outcomes in polypharmacy, lack of information on outcomes across different insurance benefit designs, and lack of information on actual prescribing patterns and outcomes across regions and over time. Responsive projects could include: (1) Data linkages to allow studies of diffusion of therapies and comparisons of their effects on outcomes, health care utilization and expenditures across hospital referral regions, hospitals, and physician practices; (2) Linkage of Medicaid administrative data and Medicare Part D claims data for comparative research on prescribing patterns and patient outcomes in the nursing-home population; (3) Linkage of prescription drug data to data banks such as those maintained by the Alzheimer's Disease Neuroimaging Initiative to allow comparative research on outcomes in defined patient populations; (4) Supplements to longitudinal data sets and ongoing clinical trials to allow comparisons of the effects of alternative benefit designs on adherence, patient outcomes and health care expenditures; (5) Analyses of how context (geographic region, hospitals, insurance) affects comparative effectiveness studies of two or more interventions; (6) Data linking features of health and prescription drug insurance (public or private) to utilization of health services and health outcomes; and (7) Planning grants for comparative effectiveness research using and building the data infrastructure on these topics. NIA Contacts: Dr. John Haaga, 301-496-3131, haagaj@nia.nih.gov; and Dr. John Phillips, 301-496-3138, PhillipJ@nia.nih.gov **05-AG-102* Prevention and Risk Factor Reduction Strategies for Disabilities.** A variety of risk factors contribute to disabilities in activities of daily living and instrumental activities of daily living in older persons. Reduction in the number of individuals' risk factors has been shown to reduce risks of certain causes of disabilities, such as falls. However, effective risk-factor reduction strategies require a high degree of coordination of care across diverse health services and settings. Alternative strategies to achieve this coordination in risk-reduction interventions could be tested in two-year studies. In addition, planning grants could develop protocols for clinical trials to compare the effectiveness of different pharmacologic (e.g. analgesic) and lifestyle (e.g. physical activity) interventions to prevent a variety of disability outcomes, such as loss of walking ability and cognitive disability, for which current data do not provide a clear basis for comparison. Secondary analyses of existing clinical trial data and expanded data collection on ongoing trials could also address these issues. NIA Contacts: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov and Ms. Georgeanne Patmios, 301-496-3138, patmiosg@nia.nih.gov **05-AG-103* Imaging and Fluid Biomarkers for Early Diagnosis and Progression of Aging-related Diseases and Conditions including Neurodegenerative Diseases.** Diseases and conditions of aging have a huge public health burden, and the ability to diagnose these early and follow their course would greatly help in treating and managing them. Various imaging modalities and fluid biomarkers have been proposed as being useful for early diagnosis and following the course of diseases and conditions of aging including neurodegenerative diseases such as Alzheimer's disease. However, most studies have not compared multiple imaging and/or fluid biomarkers in the same study with the same study participants to evaluate their comparative effectiveness at being able to provide for the early diagnosis or for following the progression of disease. Two-year grants could be used to analyze data from available studies which include multiple imaging and fluid biomarker measures (e.g. MRI and PET imaging; blood, urine, or cerebrospinal measures of disease-associated molecules) or to plan or implement new studies which would incorporate multiple imaging and/or fluid biomarker modalities for early diagnosis and/or progression of conditions and diseases of aging including neurodegenerative

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	diseases. NIA Contact: Dr. Neil Buckholtz, 301-496-9350, buckholn@gw.nih.gov **05-AG-104* Planning Grants and Pilot Studies for Comparisons of Management Strategies for Older Patients with Multiple Coexisting Conditions.** The majority older individuals suffer from multiple coexisting conditions. This poses challenges for medical management in regard to factors such as adverse interactions of drugs used for different conditions, and conflicting recommendations from treatment guidelines for different individual conditions. Different treatment strategies to optimize health and quality-of-life outcomes need to be compared to identify strategies that provide the best risk-benefit ratios for such older patients. Two-year planning grants, and pilot feasibility testing for different management strategies could contribute to this goal. Although many clinical trials testing pharmacological, behavioral, or community-level interventions to remediate or prevent aging-related disorders or declines in function have established the efficacy of specific interventions, we know much less, however, about the comparative effectiveness of these approaches. Two-year planning grants to develop protocols for clinical trials directly testing the comparative effectiveness of these different intervention types would be appropriate, as would comparative effectiveness analyses of data from existing clinical trials data. Specific examples of target domains that could benefit from either further analysis or planning activities include the following: (1) The comparison of different types of interventions (e.g., different anti-inflammatories and behavioral interventions) for the prevention of Alzheimer's disease; (2) The comparison of efficacious treatments (e.g., physical exercise vs. cognitive training) for the remediation of age-related cognitive decline exclusive of dementia. NIA Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **05-AG-105* Comparative Intervention Trials for Diseases and Syndromes of Aging Including Neurodegenerative Diseases.** Although many clinical trials testing pharmacological, behavioral, or community-level interventions to remediate or prevent aging-related disorders or declines in function have established the efficacy of specific interventions, we know much less, however, about the comparative effectiveness of these approaches. Two-year planning grants to develop protocols for clinical trials directly testing the comparative effectiveness of these different intervention types would be appropriate, as would comparative effectiveness analyses of data from existing clinical trials data. Specific examples of target domains that could benefit from either further analysis or planning activities include the following: (1) The comparison of different types of interventions (e.g., different anti-inflammatories and behavioral interventions) for the prevention of Alzheimer's disease; (2) The comparison of efficacious treatments (e.g., physical exercise vs. cognitive training) for the remediation of age-related cognitive decline exclusive of dementia; and (3) Comparisons of interventions for "geriatric syndromes", such as urinary incontinence and involuntary weight loss. NIA Contacts: Dr. Laurie Ryan, 301-496-9350, ryanl@nia.nih.gov; Dr. Jon King, 301-402-4156, kingjo@nia.nih.gov; Dr. Molly Wagster, 301-496-9350, wagsterm@gw.nia.nih.gov; and Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **05-AI-101* Accelerated Aging in Treated vs. Untreated HIV/AIDS.** There is increasing evidence that suggests that HIV-1 infected individuals experience similar immunologic changes as the uninfected elderly. This may be due to the continuous highly productive viral replication which persistently stimulates immune cells. It is not clear whether antiretroviral therapy can reverse this process. This program will aim to compare the effectiveness of different treatment regimens in reversing or preventing accelerated aging as manifested in the immune and other body systems. Contact: Dr. Robin Huebner,

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	301-402-4239, rhuebner@mail.nih.gov **05-AI-102* Comparative-effectiveness of Anti Retroviral Therapy (ART).** Challenge grants in this area would focus on collection of additional HIV/AIDS epidemiologic data and subsequent analysis of comparative-effectiveness of different regimens of anti retroviral therapy (ART) in highly representative populations in the US. Contact: Dr. Carolyn Williams, 301-402-2305, cwilliams@niaid.nih.gov **05-AI-103* Clinical Research to Reduce the Risk of Antimicrobial Resistance.** Support research to preserve antimicrobial effectiveness by targeting infectious disease areas experiencing the greatest antimicrobial selective pressure, and within these areas, develop strategies that test the safety and effectiveness of different therapeutic approaches/regimens that reduce the probability of the emergence of drug resistance by minimizing unnecessary drug exposure. Contact: Dr. Dennis Dixon, 301-435-2858, dmdixon@niaid.nih.gov **05-AR-101* Comparative Effectiveness (CE) of Biologics in Autoimmune Rheumatic and Skin Diseases.** Create a research structure to study clinical and cost-effectiveness of biologics to determine the best therapy for individual patients. Disease- and treatment-specific methodologies could include: systematic review of existing research; analysis of effectiveness from large dateset, construction of medical registries for clinical and laboratory data related to efficacy, safety, and health care utilization rates data to evaluate cost-effectiveness; and computer-based modeling of clinical trials to predict the efficacy, safety and cost effectiveness. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **05-AR-102* Comparative Effectiveness (CE) of Treatments for Chronic Childhood Arthritis and Musculoskeletal (MSK) and Skin Disease.** Create a research structure to study clinical and cost-effectiveness of pediatric rheumatic and MSK disease treatments. A number of resources exist to support the rapid implementation of this project, including networks of physicians and researchers (The Childhood Arthritis and Rheumatology Research Alliance; Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Centers) that have already developed preliminary protocols to evaluate efficacy, effectiveness, and safety of pediatric therapies for specific disease. Examples of CE studies utilizing these approaches could include a registry of all children receiving biologic therapy for JIA, to evaluate comparative clinical and cost-effectiveness, and long-term safety; A randomized, controlled trial to evaluate the efficacy and cost effectiveness of laser surgery and other non surgical approaches in the treatment of infantile hemangiomas;.CE of agents that target interleukin 1 pathways in NOMID; CE of steroid therapies and steroid administration regimens in children with DMD. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **05-AR-103* Comparative Effectiveness of Therapies to Treat Fibromyalgia.** Several drugs have been approved to treat fibromyalgia, a chronic musculoskeletal pain condition. Chronic pain, and its adverse impact on patient functioning and quality of life, will become even more of an economic and societal burden in the United States as the population ages. The purpose of this proposal is to compare recently approved drugs with differing mechanisms of action, i.e., serotonin and norepinephrine reuptake inhibitors, with tricyclic antidepressants1, and biopsychosocial approaches, such as cognitive behavioral therapy. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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	05-AT-101* Comparative Effectiveness Studies of Non-Pharmacological Treatments for Chronic Low Back Pain. Observational studies or secondary data analyses to compare the effectiveness of: non-pharmacological treatments or integrative health care approaches for chronic low back pain when used in addition to and/or as an alternative to standard conventional care. Contact: Dr. Partap Khalsa, 301-594-3462, khalsap@mail.nih.gov **05-AT-102* Comparative Effectiveness Studies of Complementary and Alternative Medicine.** Observational studies or secondary data analyses to compare the effectiveness or cost-effectiveness of: 1) CAM used in addition to standard conventional care; 2) CAM or integrative health care versus standard conventional care; OR 3) one CAM therapy to another. Contact: Dr. Richard Nahin, 301-496-7801, nahinr@mail.nih.gov **05-CA-101* Comparative Effectiveness Research in Cancer Primary Prevention.** A number of chemoprevention agents have been shown to be potentially effectiveness for the prevention of common cancers. But dissemination of chemoprevention remains low and controversy remains about the side effects associated with these agents. Comparative effectiveness research in this area would have the following aims: to document the level of dissemination of chemoprevention agents and the examine the physician, patient and health system factors that either facilitate or retard this dissemination; to conduct head to head studies of alternative chemoprevention agents and or approaches (e.g. risk stratification) to determine the relative clinical risk and benefits and economic cost of these alternatives. These studies could be conducted as adjuncts to existing controlled trials, as retrospective analysis of health system data or as prospective studies of cohorts of patients and physicians within the context of various healthcare delivery systems. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-102* Comparative Effectiveness Research on Cancer Screening.** The effectiveness of cancer screening has been established through randomized trials and other evidence for breast, colorectal and cervical cancer. However since screening for these cancers were initially introduced, there has been rapid and substantial innovation in new early detection technologies. Many of these technologies have disseminated into the practice of screening but without sufficient evidence as to their comparative effectiveness relative to earlier established technologies. In addition newer technologies may influence how the earlier technologies are most effectively used. Comparative effectiveness research in this area would augment evidence from controlled screening trials with: data from observational studies in defined populations of screening, intermediate and final outcomes; head-to-head studies of the technical performance characteristics, physician and patient acceptability and cost of alternative screening technologies, and decision models designed to project the costs and benefits of different screening technologies and strategies over the long-term at the individual, program and policy level. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-103* Cost-Effectiveness of Patient Navigation.** Patient navigation is currently being tested to determine if this approach has an impact on the timeliness of diagnostic testing and treatment. While the cost-effectiveness of patient navigation is being modeled by investigators in NCI's Patient Navigation Research Program (PNRP), studies comparing the costs associated with navigation as compared to usual care are still needed. The purpose of this pilot project would be to *implement* a cost effectiveness model

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	that has been developed within PNRP to understand and quantify the costs associated with implementing and maintaining a patient navigation program, and to determine if this model can be applied to varied patient navigation projects (i.e., screening, diagnosis, treatment). Results would help to determine whether patient navigation is providing both clinically sound and cost-effective service. This initiative would involve supplements to current Patient Navigation Research Programs (PNRP). Using data from the nine funded PNRPs, successful applicants will work collaboratively with the other PNRP PIs, CRCHD Project Scientists, and the PNRP evaluator to test the cost-effectiveness model. The results will form a basis for cost-effectiveness studies in future patient navigation research. Contacts: Dr. Martha L Hare, 301-594-1908, Martha.hare@nih.gov and Dr. Mary Ann Van Duyn, 301-451-4284, vanduynm@mail.nih.gov **05-CA-104*** **Comparative Effectiveness Research on Cancer Treatment.** The results of controlled clinical trials guide recommendations for many initial cancer treatments. But cancer treatments are also prevalent for cancers for which the evidence base in-complete, not applicable to the patient population (e.g. older patients) or non-existent. Prostate cancer is a prime, but not the only example, of this situation. Comparative effectiveness research in this area would use retrospective data and/or prospective interviews with patients, physicians and policy makers to assess the clinical benefits, risks and economic costs of commonly used treatment approaches and assess patient, physician and health system factors that effect dissemination of these treatment approaches. Contact: Dr. Martin Brown, 301-496-5716, brownm@dcpcepn.nci.nih.gov **05-CA-105*** **CISNET.** The Cancer Intervention and Surveillance Modeling Network (CISNET http://cisnet.cancer.gov/) is a consortium of NCI-sponsored investigators whose focus is to use modeling to extrapolate evidence from RCT's, epidemiologic, and observational studies to help determine the best strategies for implementing prevention, screening, and treatment strategies in the population and clinical practice. CISNET models could be applied to three areas: evaluation of competing early detection technologies, such as MRI vs digital mammography for breast cancer ; evaluation of competing diagnostic technologies, such as PET scans; evaluation of competing treatments, such as aggressive vs. conservative treatment for early stage prostate cancer. NCI Contact: Dr. Eric Feuer, 301-496-5029, feuerr@dcpcepn.nci.nih.gov **05-DA-101*** **Behavioral and Medication Interventions To Treat Drug Abuse Disorders in Non-Specialty Care Settings.** Treatment for substance use disorders has most commonly been provided in specialty care settings such as residential therapeutic communities, methadone maintenance treatment clinics, and dedicated inpatient or outpatient substance abuse treatment programs. One way to broaden access to substance abuse treatment would be to expand care in non-specialty care settings (i.e., primary care settings such as emergency departments, general medicine and public health clinics), and the criminal justice system. Research is needed on the comparative effectiveness of treatment interventions delivered in non-specialty care settings compared to those in traditional settings. Contact: Dr. Redonna Chandler, 301-443-8768, rc274k@nih.gov and Dr. Will Aklin, 301-443-3207, aklinwm@nida.nih.gov **05-DA-102*** **Treatment of Substance Abuse and Related Health Consequences Using Web-Based Technologies.** Evidence-based behavioral therapies are not routinely integrated in substance abuse treatment programs because of financial constraints or inadequate provider training. Technology is increasingly being harnessed as a low-cost option for teaching behavioral skills to substance users, thereby broadening their availability. Research is needed to compare the effectiveness of already developed web-

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	based technologies (e.g., cognitive behavioral therapy; community reinforcement; HIV risk reduction) with traditional modes of treatment delivery (e.g., counselors, physicians, etc.) in order to optimize use of the web for expanding delivery of science-based behavioral treatment, with fidelity, and in a manner that reduces cost and staff burden. Contact: Dr. Cecilia Spitznas, 301-402-1488, spitznasc@mail.nih.gov **05-DA-103* Integrated vs. Separate Treatment of Substance Abuse and Comorbid Conditions.** Comorbid psychiatric disorders as well as other serious medical conditions such as infectious diseases (e.g., HIV/AIDS) and chronic pain commonly co-occur with substance use disorders. Additionally, people addicted to one substance are frequently addicted to others. Comparative effectiveness research could fill a knowledge gap regarding the benefits of treating conditions in an integrated manner versus separately, pointing treatment providers and physicians toward the most effective intervention strategies for multiple disorders, identifying optimal methods of coordinating and delivering treatment while ensuring its quality and access, reducing costs, preventing further illness and disability, and improving community functioning and integration. Contact: Dr. Shoshana Kohana, 301-443-2261, kahanas@mail.nih.gov **05-DA-104* Comparing Drug Treatment Effectiveness in Ethnic Minority Populations.** Research suggests that treatment response can vary among different minority populations due to genetic, environmental and cultural factors. Still, it is unknown which treatments work best for which ethnicities. Comparative effectiveness studies in ethnic minorities would test pharmacotherapies and behavioral treatments for substance abuse that have already shown efficacy in some populations. Results could reveal optimal treatment types for various populations, many of which are currently under-studied or under-served in terms of treatment need, including African Americans, Native Americans, and Hispanics. Contacts: Dr. Mary Ellen Michel, 301-443-6697, michelm1@nida.nih.gov and Dr. Lula Beatty, 301-443-0441, Lb75x@nih.gov **05-DA-105* Comparing Episodic and Continuous Care for Drug Abuse Treatment**. Concerns have been raised over the mismatch between usual drug abuse treatment, which follows an acute care model, and emergent perspectives that addiction is a chronic illness. To treat drug abuse and addiction as a chronic illness implies that treatment providers should follow acute care with long-term monitoring and interventions to prevent a recurrence of drug use and to re-engage relapsed patients in treatment in order to minimize the consequences of the relapse. Research is needed on the comparative effectiveness of usual drug abuse treatment with drug treatment based on a model of continuing chronic illness care. Contacts: Dr. Shoshana Kohana, 301-443-2261, kahanas@mail.nih.gov and Dr. Bennett Fletcher, 301-443-2274, bf31v@nih.gov **05-DE-101* Validating dental caries risk assessment guidelines.** Traditionally, dental caries is prevented and managed with surgical restoration of damaged teeth and by recalling patients at regular six-month intervals. New strategies propose tailoring dental caries management to the individual's risk for dental disease. However, proposed caries risk assessment approaches have not been validated extensively. Projects that answer this challenge could include planning projects for large-scale definitive clinical trials or sophisticated analyses of existing datasets or records. NIDCR Contact: Dr. Ruth Nowjack-Raymer, 301-594-5394, nowjackr@nidcr.nih.gov **05-DE-102* Treatment of tobacco and drug dependence in dental settings.** Use of tobacco and other drugs is a major culprit in oral diseases. The dental office provides a potentially important entry point for supporting drug-abusing patients in cessation efforts.

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	However, busy dental practices may have difficulty finding the resources, staff, training time, and patient acceptance to incorporate comprehensive drug abuse treatment into clinical practice. Approaches that involve Screening for drug use, Brief Intervention, and Referral to Treatment (SBIRT) provide a promising, practical solution. Studies in other busy clinical settings have found that simple provider-delivered and computer-assisted SBIRT approaches increase identification of drug use, and importantly, increase cessation rates. Similar studies are needed in the dental setting comparing provider-delivered substance abuse SBIRT to computer-assisted SBIRT for tobacco use, or abuse of alcohol or other drugs. Projects that answer this challenge could include proposals to design and pilot a randomized clinical trial comparing different therapies in the dental setting. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. NIDCR Contact: Dr. Melissa Riddle, 301-451-3888, riddleme@nidcr.nih.gov **05-DE-103* Treatment and Outcomes Cleft Palate/Cleft Lip Anomalies.** Cleft lip and/or palate are among the most common of all birth defects, occurring once in every 600 to 800 births. The care of affected infants is complex and requires coordination with surgeons, orthodontists, dentists, surgical support staff, speech therapists, audiologists, and other specialists. Surveys of care centers in the United States and Europe demonstrate that there are enormous variations in timing and type of reconstruction procedures. Practices associated with best outcomes need to be identified. Projects that answer this challenge could address: (1) Presurgical appliances, whether to use and what type (NAM or Latham); (2) Surgical timing, at what age to repair unilateral and bilateral cleft lip and with what technique; (3) Use of lip adhesion and indication for its use; (4) Cleft palate repair technique and timing of repair. Investigators could compare existing approaches to repair of cleft lip and cleft palate, evaluating efficacy, cost effectiveness, speech outcomes and quality of life measures. Approaches could include: 1) establishment of observational patient registries to follow outcomes and identify best practices; or 2) planning grants for a definitive RCT or practical trial to address a significant issue. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. Contact: Dr. Holli Hamilton, 301-451-3852, hamiltonho@nidcr.nih.gov **05-DE-104* Adjunctive techniques for detection of oral premalignant and malignant lesions.** Approximately 35,000 Americans are diagnosed each year with oral cancer, and early detection, usually during a regular dental check-up, is critical to successful treatment of this disease. Adjunctive techniques have been developed to enhance visual detection of oral premalignant and malignant lesions. Overall, there is insufficient evidence to support their effectiveness. Projects that answer this challenge could include planning for randomized clinical trials that compare visual and tactile oral mucosal examination with adjunct-assisted examination in dental settings. Projects responsive to this challenge could estimate the effectiveness of existing adjunctive techniques for detection of oral premalignant and malignant lesions from available datasets or records, including cost effectiveness analyses. Applicants would need to submit a future NIDCR Clinical Trial Implementation grant for support of any proposed clinical trials, which could be considered for support through regular NIDCR appropriated funds. Contact: Dr. Jane Atkinson, 301-435-7908, jatkinso@nidcr.nih.gov **05-DE-105* Infrastructure for Comparative Effectiveness Studies in Oral Health and Craniofacial Conditions.** There is a limited evidence base to support common

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	interventions in dental care and management options in craniofacial disorders. Having adequate infrastructure for evaluating effectiveness in oral health and craniofacial conditions, as distinguished from effectiveness in medical care, is critical because much of oral health care is delivered outside of medical care (e.g., dental offices) or fragmented to address the complex needs of individuals with certain conditions affecting oral/craniofacial structures (e.g., birth defects such as cleft lip and palate, ectodermal dysplasias, or conditions resulting in hypodontia). Projects that answer this challenge could support planning grants to develop infrastructure as well as feasibility studies to assess existing infrastructure. Support for planning grants to develop infrastructure will be provided, as well as support for feasibility studies to assess existing infrastructure. Successful two-year projects may lead to applications to: implement and assess infrastructure (e.g. development of datasets or registries); enhance and re-assess existing infrastructure; or conduct comparativeness effectiveness studies. Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov. **05-DK-101* Selecting the Optimal Initial Treatment Regimen for Patients With Newly Discovered Type 2 Diabetes.** The natural history of type 2 diabetes, treated by widely used current regimens, is marked by gradual increases in glucose levels, loss of insulin secretion, progressive increases in drug therapy, and frequent development of chronic complications. Clinical trial data suggests that aggressive early therapy attempting to keep glucose levels near normal is associated with a more benign long-term course. The optimal treatment regimen (effectiveness and avoidance of hypoglycemia) is not known, but current drugs provide options for multiple treatment approaches. In view of the numerous options, pilot studies are needed to assess the short-term effectiveness of common treatment strategies. Studies of treatments comparing different drugs and levels of glucose control or studies to use insulin sparing versus Insulin-intensive regimens will help to define the most effective short-term therapy. Impact of the approaches at one and two years can be assessed. These studies can measure effects on glucose control, hormone responses, adverse events, and cost of therapies, providing crucial data for designing future clinical trials to assess the long-term clinical effectiveness and cost of the most promising therapeutic approaches. Contact: Dr. Peter Savage, 301-594-8858, savagep@niddk.nih.gov **05-DK-102* Understanding the Effects of Bariatric Surgery on Type 2 Diabetes and Cardiovascular Risk Factors.** Interest has been building in the scientific and medical communities regarding the risks and benefits of the different types of bariatric surgery in obese patients, with type 2 diabetes, particularly in those with lesser degrees of obesity. A randomized clinical trial to compare the impact of various types of bariatric surgery versus intensive medical weight loss treatment on type 2 diabetes is needed to understand the balance of risks and benefits of the different approaches. This is critically necessary given the increasing numbers of bariatric surgeries being performed and the lack of well-controlled studies to inform clinicians in selecting the best approach for a given patient and health care payors in their decision to cover specific procedures. Investigators could compare the impact of bariatric surgery compared with intensive medical weight loss treatment on insulin resistance, beta cell function, and resolution of type 2 diabetes in adults with type 2 diabetes and BMI between 30 and 40. Pilot and feasibility projects to explore different study designs and test feasibility of methods and implementation could be conducted using short term funding (~2 years). Evidence of feasibility in pilot studies would be expected to lead to a larger multi-site trial to determine long-term (3-5 year) impact of bariatric surgery on type 2 diabetes. Contact: Dr. Myrlene Staten, 301-402-78896, statenm@mail.nih.gov

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	05-DK-103* Antihypertensive Drugs and Level of Blood Pressure Control in Hemodialysis Patients. End-stage renal disease requiring dialysis is a burdensome, expensive medical and public health problem. Hypertension, present in nearly all dialysis patients, is a prime risk factor for cardiovascular disease (CVD) death and complications. Commonly used anti-hypertensive drugs including renin-angiotensin-aldosterone system (RAAS) inhibitors and non-RAAS agents (i.e., beta-blockers) improve survival in other populations, but it is not known whether a specific class of drug or level of blood pressure control can significantly reduce CVD morbidity and mortality in vulnerable hemodialysis patients. Projects that address these challenges could include planning or feasibility studies for a randomized trial of a representative subset of hemodialysis patients to better inform choices of anti-hypertensive therapy (RAAS vs. non-RAAS) and blood pressure targets. Short-term funding could be used for 1) meta-analysis of existing datasets or registries (for example, the United States Renal Data System), 2) planning grants for a randomized controlled trial, or 3) pilot studies of recruitment feasibility or implementation strategies. The NIDDK could fund a more definitive randomized clinical trial in subsequent years from its base. Contact: Dr. Catherine Meyers, 301-451-4901, meyersc@amil.nih.gov **05-DK-104* Fascial Versus Mid-Urethral Sling Surgery in Stress Urinary Incontinence Treatment Failures**. Urinary incontinence affects 17-50% of all U.S. women, is increasing as the population ages, and is associated with diminished quality of life. Approximately 30% of women with urinary incontinence treated surgically undergo repeat procedures for recurrent stress urinary incontinence (SUI). Fascial sling surgery and mid-urethral sling surgery are used commonly in women with recurrent SUI who failed initial surgical treatment; however, it is not clear which strategy is better for improving continence, quality of life, and for reducing costs of health care. Short-term funds could be used for 1) planning grants for a RCT, or 2) pilot feasibility studies of recruitment or other implementation strategies. The NIDDK could fund a full randomized clinical trial in subsequent years from its base. Contact: Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov **05-DK-105* Medical Treatment of Calcium Stones: Calcium Stone Trial.** Urolithiasis affects approximately 10 to 15 percent of the United States population, with a cost of at least $2.1 billion per year. The lifetime recurrence rate is 50 percent. After initial treatment, patients are commonly treated with potassium citrate or thiazide diuretics. However, the relative efficacy and durability of these two strategies has not been determined. Projects that address these challenges include planning or feasibility studies of a randomized trial of a representative sample of recurrent stone formers stratified by initial therapy, then randomized to receive potassium citrate or a thiazide diuretic to measure treatment durability, stone formation and passage, quality-of-life, and cost. Short-term funds could be used for 1) meta-analysis of existing datasets or registries (for example, *Urologic Diseases in America*), 2) planning grants for a randomized clinical trial, or 3) pilot studies of recruitment feasibility or implementation strategies. The NIDDK could fund a full randomized clinical trial in subsequent years from its base. Contact: Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov and Dr. Paul Kimmel, 301-594-7713, kimmelp@mail.nih.gov **05-EB-101* Comparative Effectiveness of Advanced Imaging Procedures.** Medical imaging is the fastest growing component of medical spending in the United States. This is due to increases in both the cost and utilization of advanced imaging procedures. The NIH invites applications that explore the comparative effectiveness of advanced imaging procedures in providing optimal clinical treatment. Evaluation of hybrid imaging such as combined PET-CT is particularly encouraged. Contact: Dr. Alan

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	McLaughlin, 301-496-9321, mclaugal@mail.nih.gov **05-EB-102*** **Screening Methodologies for Breast Cancer.** Phase II trials suggest that dedicated breast CT approaches can detect earlier stage cancer (i.e., smaller lesions) than mammography. Comparative effectiveness studies are invited to determine if the information obtained from earlier detection can be used to better treat breast cancer, and improve clinical outcome in terms of survival and quality of life. Contact: Dr. Alan McLaughlin, 301-496-9321, mclaugal@mail.nih.gov **05-EB-103*** **Comparative Effectiveness of Non-Invasive Ultrasound Techniques.** Non-invasive High Intensity Focused Ultrasound (HIFU) techniques have the potential to destroy tumors without the need for invasive surgery. Comparison of non-invasive HIFU approaches with invasive or minimally-invasive surgical procedures are encouraged. Comparison of technologies for assessing the level and extent of non-invasive tissue ablation are also encouraged. Contact: Dr. Victor Lopez, 301 451-4775; lopezh@mail.nih.gov. **05-EB-104*** **Comparative Effectiveness of Robotic Surgery.** Compared to standard invasive surgical procedures, minimally-invasive robotic surgical procedures have the potential to provide a safer and more precise treatment for a variety of conditions including prostate cancer. Comparison of robotic procedures with standard invasive treatments should demonstrate the comparative effectiveness and comparative cost of robotic interventions for the clinical treatment of disease**.** Contact: Dr. John Haller, 301 451-3009; hallerj@mail.nih.gov **05-EB-105*** **Comparative Effectiveness of Medical Implants.** The utilization of medical implants such as artificial hips varies significantly between different locations and between different countries. Proposals are invited that would make use of this utilization variability to assess the comparative effectiveness of medical implants. Contact: Dr. Christine Kelley, 301-451-4778, Kelleyc@mail.noh.gov **05-EY-101*** **Treatment of Age Related Macular Degeneration and Diabetic Eye Diseases and Disorders.** Age Related Macular Degeneration and Diabetic Eye Disease are leading causes of blindness among American adults. Commonly used treatment strategies include various combinations of drug and/or laser treatments but it is not clear how these agents or their combinations compare with each other for preventing visual loss, improving quality of life, and reducing health care costs. Projects that answer this challenge include studies that will compare agents to prevent the development and progression of age related macular degeneration or diabetic eye diseases and conditions. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-EY-102*** **Treatment of Pediatric Eye Diseases and Disorders.** There are a variety of eye diseases and disorders that lead to visual impairments and blindness among children. Eye Care Professionals can treat these disorders with certain medications, surgery, or optical instruments or devices. However, it is unclear how the strategies compare with each other for improving and maintaining vision, quality of life, and reducing health care costs. Projects that answer this challenge could include the planning and conducting of trials or analyses of existing data. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-EY-103*** **Eye and Vision Systematic Reviews**. There are a variety of eye diseases and disorders that lead to visual impairments and blindness. Eye Care

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	Professionals are treating these disorders with certain medications, surgery, or optical instruments or devices. However, in many instances it is unclear how the strategies compare with each other for improving and maintaining vision, quality of life, and reducing health care costs. Projects that answer this challenge would help health care providers and patients make well-informed decisions about healthcare. Contact: Dr. Don Everett, 301-451-2020, deverett@nei.nih.gov **05-GM-101* Anesthesiology Clinical Pharmacology Sepsis Trauma, Burn, and Peri-operative Injury Wound Healing.** NIGMS supports clinical research in the areas of anesthesiology, clinical pharmacology, sepsis, injury (trauma, burn and peri-operative) and wound healing. Within these general clinical areas are opportunities for rigorous comparative evaluation of the impact of different treatment options or standards of care in a variety of clinical conditions, settings and/or situations. Possible opportunities include but are not limited to comparisons of drugs, devices, and/or protocols Sophisticated analyses of existing data sets/registries, planning projects for subsequent larger scale clinical studies, or other activities that would provide comparative evaluations in these areas are appropriate. Applications that address the following topics are encouraged: o genetic basis of variable drug responses, both therapeutic and adverse o resuscitation strategies o therapies that influence stabilization and recovery following trauma and burn injury o post-injury nutrition management o studies of the methods, roles and predictive value of monitoring in critically ill patients o effective drug treatments for multi-organ failure o use of sedatives, analgesics and anesthetics in critically ill patients o responses related to gender or population-based differences o therapies that accelerate wound healing, that induce healing in a nonhealing wound or that reduce/eliminate scarring NIGMS Contact: Dr. Michael Rogers, 301-594-3827, rogersm@nigms.nih.gov **05-HL-101* Treatment of atrial fibrillation.** Atrial fibrillation, the most common acquired arrhythmia in adults, substantially increases risk for stroke and premature death. Percutaneous pulmonary vein ablation and the surgical Cox Maze procedure have been shown to be effective in eliminating arrhythmias, but it is not clear how they compare to standard therapies, such as anticoagulation combined with rate control drugs, with respect to their effect on quality and length of life and health care costs. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Lauer, 301-435-0422, lauerm@nhlbi.nih.gov **05-HL-102* Treatment of obstructive sleep apnea.** Obstructive sleep apnea is becoming increasingly common as the nation experiences an obesity epidemic. Patients with obstructive sleep apnea are at increased risk for poor quality of life, myocardial infarction, and stroke. Physicians can treat obstructive sleep apnea with certain medications, surgery, or mechanical devices (continuous positive airway pressure), but it is not clear how the strategies compare with one another with respect to their effect on quality and length of life and health care costs. Projects that answer this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries. Contact: Dr. Michael Twery, 301-435-0199, twerym@nhlbi.nih.gov **05-HL-103* Treatment of mild persistent asthma in children**. Physicians currently

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	choose among three alternative approaches to initiate daily, long term therapy for children with asthma that is not well controlled by intermittent therapy alone; namely, low dose inhaled corticosteroids, combination therapy of inhaled corticosteroids and long acting beta-agonists, and leukotriene receptor antagonist. Yet little data are available to inform the physician's decisions: randomized controlled efficacy trials in children have focused on comparing each drug to placebo rather than directly comparing the three options in children, especially children less than 12 years of age. Large scale, efficient studies are urgently needed to assist physicians in understanding the comparative advantages of the treatments with respect to benefits, risks, and costs. Projects that address this challenge would use existing data bases, e.g., administrative and electronic health records, and distributive data networks to conduct direct comparisons of the three treatments. Contact: Dr. Virginia Taggart, 301-435-0202, taggartv@nhlbi.nih.gov **05-HL-104* Reducing cardiovascular risk in moderate-risk and asymptomatic patients.** Evidence-based treatment guidelines exist for patients at high risk for a cardiovascular event due to existing clinical disease or risk factors including hypertension, dyslipidemia, obesity, and smoking. Nearly half of all life-threatening cardiovascular disease events occur in previously asymptomatic people, who may have undetected subclinical disease. In addition, many people are at elevated risk for whom evidence-based treatments are not clear; these include people with moderate elevations of multiple risk conditions as in the Metabolic Syndrome. Various technologies exist to detect asymptomatic subclinical disease and predict risk, including global risk scores, inflammatory biomarkers, specific genotypes, and imaging tests. Many intervention strategies to reduce risk also exist, including lifestyle interventions, various medications, combinations of medications, and combinations of lifestyle and medication. However, it is not clear how the existing technologies compare with each other or could be combined or sequenced, or what intensity of intervention is needed, to reduce disease risk. Projects are needed to address this challenge by comparing effectiveness, risks, and cost-effectiveness of various strategies for screening and treatment of moderate-risk and asymptomatic patients. Projects that address this challenge could include planning projects for large-scale definitive practical trials or sophisticated analyses of existing data registries Contact: Dr. Simons-Morton, 301-435-0384, simonsd@nhlbi.nih.gov **05-HL-105* Optimizing of anti-platelet treatment after revascularization procedures.** The long-term effectiveness of revascularization procedures to treat ischemic cardiovascular disease is limited by the risk for thrombotic complications, which may necessitate a second costly procedure, sometimes under emergency conditions, and may even be fatal. Anti-platelet therapy i to offer effective protection against thrombotic complications, though at the cost of increased risk for serious bleeding events, including (potentially fatal) cerebral hemorrhage. Comparative effectiveness trials are needed to determine the best regimens for achieving maximal benefit with minimal risk. Personalized approaches for tailoring the optimal regimen to the particular patient may be of value. Projects that answer this challenge could include planning grants for clinical trials comparing alternative strategies for optimizing anti-platelet therapy in this setting. Contact: Dr. David Gordon, 301-435-0466, gordond@nhlbi.nih.gov **05-LM-101* Effect of "Information Prescriptions" on Improving Care by Increasing Compliance with Medication Protocol Given to Discharged Emergency Department Patients.** A significant fraction of patients who are given a set of prescriptions, such as when they leave a physician office or the Emergency Department, are known to disregard or curtail recommended medications. Individually tailored information about risks, benefits, costs and treatment options are given by some clinicians

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	as "information prescriptions", but the effectiveness of "information prescriptions" is not known. Studies in this area should determine value of such "information prescriptions" in improving patient compliance as contrasted to current discharge advice systems or standard office practices. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **05-LM-102* Ability of Decision Tools in an Electronic Health Care System to Increase Use of Generic Drugs**. Although generic drugs are much less expensive than "brand name", clinicians commonly prescribe "brand name" drugs for a plethora of reasons often not related to belief that "brand name" drugs are more effective. Evaluation studies are needed to determine whether a Decision Support Tool that feeds information about generic options, presented to physicians prescribing "brand-name" drugs through a Computerized Physician Order Entry System (CPOE), would increase physician selection of less-expensive generic drugs. Studies should compare the use of such pre-decision feedback to situations where no feedback about generic options is provided. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **05-LM-103* Improving Compliance of School Children with Immunization Schedules**. An increasing problem in inner city and some rural school systems is failure of pre-school children to complete immunization schedules for common illnesses as required by the school system. Some of the problem is caused by the discontinuity of record-keeping systems, and the absence of reminder systems in physician offices and clinics where students receive immunizations. Evaluation studies should compare completion of immunization schedules where clinics and physicians use tools specifically designed to record, share and manage progress of immunization for each child with completion rates of children where such tools are not used. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **05-LM-104* Value of "Virtual Reality" Interaction in Improving Compliance with Diabetic Regimen.** Despite often intensive educational efforts, patients with diabetes commonly mismanage or undermanage their illness despite the known ability of optimal management to reduce complications and morbidity. Interactions between avatars in virtual reality environments such as Second Life are known to influence behavior. Studies should explore the effectiveness of periodic physician/nurse interaction with diabetic patients via a virtual reality environment in improving diabetic control, as compared to standard practice. Contact: Dr. Milton Corn, 301-496-4621, cornm@mail.nih.gov **05-MD-101* Social Determinants of Health**. There is a growing research that reveals the important role of social determinants of health in addressing and understanding health disparities. Social determinants of health are the economic and social conditions under which people live which determine their health. We propose research that investigates interventions that address these social determinants (e.g., employment training, school readiness programs, food stamp programs, and adequate and affordable housing programs) their relationship to health outcomes for health disparity populations. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov **05-MD-102* Prevention of Chronic Diseases in Disparity Populations.** Approximately 70-80% of all current health care costs are connected with the treatment of chronic diseases. Chronic diseases compose a large majority of health disparity conditions, such as asthma, obesity, oral health, diabetes, HIV/AIDS, heart disease, mental health, chronic pain, and substance abuse. We propose research to examine and inform the clinical and cost effectiveness of prevention efforts, including medical devices,

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	behavioral interventions, care management approaches (e.g., incorporation of nontraditional members of the healthcare team such as community health workers, pharmacists), pharmaceuticals, surgery, and other interventions for the prevention of chronic disease. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov **05-MD-103*** **Limited English Proficiency (LEP)**. Limited English Proficiency populations continue to grow and are a significant health disparity population. We propose conducting comparative effectiveness research studies on current health services delivery for LEP populations (medical interpreter, telephone language line, bilingual professional, translated educational aides) and the cost impacts of effective, cultural competent healthcare interventions for LEP populations (e.g. reductions in ER visits, diagnostic tests, hospital stay, disability and improved functional health status). Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MD-104*** **Screening of Health Disparity Conditions.** Comparing different screening approaches for diseases with increased prevalence in disparity groups with the goal to inform and determine the most effective modality that will result in reduced morbidity and mortality and improved survival rates in different disparity groups. Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MD-105*** **Health Literacy.** Research has shown that over 90 million individuals in the United States are unable to read a prescription bottle. Health literacy is the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. We propose research that investigates interventions that address health literacy issues (e.g., technology tools, literacy aides or other community health workers, language-appropriate labels for prescription and over-the-counter medications) and their relationship to health outcomes for health disparity populations. Contact: Dr. Irene Dankwa-Mullan, 301-402-1366, dankwamullani@mail.nih.gov **05-MH-101*** **Leveraging Existing Healthcare Networks for Comparative Effectiveness Research on Mental Disorders and Autism.** Existing large integrated healthcare networks are needed to more efficiently conduct large-scale effectiveness trials in “real-world” patient settings. The NIMH solicits individual or collaborative, linked grant applications from researchers with experience conducting studies within large integrated healthcare delivery systems to develop and test infrastructure to efficiently conduct trials on the effectiveness of treatment, preventive and services interventions to improve care for people with mental disorders and autism. Applicants can propose studies to 1) demonstrate the ability to identify, recruit and enroll large patient populations into clinical trials, 2) harmonize electronic medical record data across multiple integrated systems for research use, 3) pool data for common analyses, and 4) build capacity for the collection and storage of biologic material. Contact: Dr. David Chambers, 301-443-3747, dchamber@mail.nih.gov **05-MH-102*** **Cost Effectiveness of Mental Health Interventions.** Information on the cost effectiveness of promising mental health interventions is needed to ensure widespread uptake by payers and health systems. NIMH is interested in adding/extending cost-effectiveness components to randomized controlled trials of treatment, preventive and services interventions through two-year grants. Investigators should prioritize the calculation of the cost/QALY ratio by the most advanced available methodologies to ensure that findings from these projects can contribute to improving the efficiency of mental health care financing. In addition, researchers can conduct analyses of existing databases for

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	systematic cost-effectiveness, cost-benefit, benefit/harm analyses or to compare interventions on "real life outcomes" such as level of functioning or acceptability, using meta-analytic methods. Contact: Dr. Agnes Rupp, 301-443-3364, arupp@mail.nih.gov **05-MH-103* Collaboration with AHRQ Comparative Effectiveness Research Program.** In FY09 and FY10 AHRQ plans to support research grants (PA-09-070) on comparative effectiveness of clinical treatments and services as authorized in the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) Section 1013. MMA section 1013 mandates two mental health categories: Depression and other mental health disorders; and Developmental delays, attention deficit hyperactivity disorder and autism. NIMH is interested in funding ancillary studies including but not limited to: 1) studies on the comparative effectiveness of important new or existing technologies; and 2) assessment of the comparative effectiveness of treatments that are commonly administered to children but have been evaluated for safety and effectiveness in adult populations. Two year studies will contribute to successfully implement the mental disorders components of MMA Section 1013 by utilizing AHRQ networks (e.g. EPCs, DEcIDE, CERTs, PBRN, ACTION, etc) to generate information for health care decision-making. Contact: Dr. Agnes Rupp, 301-443-3364, arupp@mail.nih.gov **05-MH-104* Building ASD Registries for Use in Comparative Effectiveness Research.** Given the low base-rate and high variability of phenotypes among people with autism, comparative effectiveness trials of treatments for autism spectrum disorders (ASD) provide significant recruitment challenges to include well-phenotyped samples. Autism registries are needed to more efficiently conduct large-scale effectiveness trials in "real-world" service systems. The NIMH solicits grant applications from researchers with experience in diagnosis of ASD and database registry creation to develop and test infrastructure to efficiently identify populations to include within registries for use in future ASD comparative effectiveness trials. Grants applications to optimize current registries and leverage existing databases are encouraged. Applicants can propose studies to 1) demonstrate the ability to identify and collect relevant clinical, environmental, and genetic data from large populations with autism within multiple service settings, 2) Improve consensus on "caseness" within samples, given variability in phenotypes 3) harmonize data systems across multiple integrated systems serving populations with autism (e.g. health care, special education, Medicaid) for research use, 4) pool data for common analyses, and 5) build capacity for the collection and storage of biologic material. Contact: Dr. Lisa Gilotty, 301-443-3825, gilottyl@mail.nih.gov **05-NS-101* Consortia Building for Comparative Effectiveness Research in Clinical Neuroscience.** The development of evidence-based medicine to inform health decisions in neurology, neurosurgery and neurorehabilitation requires analysis of high quality, risk-stratified, data collection from "real world" practice. The challenge is to develop multi-center consortia that effectively utilize modern electronic data collection systems to standardize, collect and analyze high quality data in order to compare the effectiveness of alternative methods of prevention, diagnosis, or treatment in groups of patients with specific types/subtypes of neurological disorders. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov **05-NS-102* Technologies to Enable Comparative Effectiveness Research in Clinical Neuroscience.** High per patient costs limit the number of patients studied in RCTs as well as the rate at which important questions can be tested by RCTs. High per patient costs make it prohibitively expensive to study the comparative effectiveness of a treatment, prevention or diagnostic regimen as it transitions from clinical trial to the larger

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	venue of clinical practice. The challenge is to develop new technologies that can obtain clinically significant outcomes in larger numbers of patients at lower cost. The performance characteristics of such technologies in providing high quality outcome measures could be tested by comparing to standard outcome measures in the context of an ongoing RCT. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov **05-NS-103*** **Validating NIH's New Clinical Tools in Populations With Neurological Disorders.** The NIH Blueprint for neuroscience is developing a variety of standardized tests in the domains of cognition, emotion, sensation, and motor function as part of the NIH Toolbox project. The NINDS is supporting the development of quality of life outcomes in neurological disorders. The NIH Roadmap project has developed the patient reported outcomes measurement information system (PROMIS). Each of these tools utilizes computerized adaptive testing methods to obtain important clinical outcome data and will be tested in large groups of normal individuals across the lifespan. The challenge is to assess the performance and research utility of these new tools in well described patient populations for future comparative effectiveness research projects. NINDS Contact: Dr. Claudia Moy, 301-496-2789, moyc@ninds.nih.gov **05-NS-104*** **Intervention vs. Best Medical Therapy in Asymptomatic Persons With Identified Vascular Abnormalities**. A variety of vascular/cardiac abnormalities cause stroke but are treated by a surgical or endovascular intervention that itself carries risk of stroke and death, i.e. carotid stenosis, vertebral origin stenosis, berry aneurysm, arteriovenous malformation, cerebral artery dissection, patent foramen ovale, etc. In many of these conditions the risk of stroke due to the vascular abnormality is significantly lower in asymptomatic patients as compared to those who present with symptoms. Without a means to accurately stratify risk, such asymptomatic patients are faced with very difficult health decisions. The challenge to be completed over a two year period could include one or all of the following: 1) meta-analysis of existing datasets or registries (for example, Medicare, HMO, or Insurance company data to develop an evidence base for clinical-decision making. 2) pilot grants for an RCT, and 3) validation of selection criteria to stratify stroke risk in asymptomatic patients with defined anatomic abnormalities. NINDS Contact: Dr. Walter J. Koroshetz, 301-496-3167, koroshetzw@ninds.nih.gov **05-RR-101*** **Build CER Capacity Through Education**. Build capacity for subject recruitment, IRB and regulatory compliance, and data management for comparative effectiveness research conducted in community environments. Applicants could propose educational experiences and resources for study coordinators, medical auxiliaries, and data managers that would build capacity for the conduct of comparative effectiveness research in community settings. Where appropriate, these applications could develop links with existing clinical research infrastructure resources. Contact: Dr. Anthony Hayward, 301-435-0791, haywarda@mail.nih.gov **05-RR-102*** **Support Pilot CER Projects in Community Settings**. Pilot/demonstration projects using collaborations between academic health centers and community-based organizations or community-based research networks that bring CER into community settings. Contact: Dr. Anthony Hayward, 301-435-0791, haywarda@mail.nih.gov

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(06) Enabling Technologies	**06-AA-101 Analysis of Alcohol's Effects on Cell Behavior.** Projects are sought for the development of new advanced approaches such as techniques to image intact tissue slices, and three-dimensional (3D) cell culture systems that could provide the spatial and temporal dynamic pictures of the patho-physiology and dys-functioning of living cells in the presence of alcohol. Contact: Dr. Svetlana Radaeva, 301-443-1189, sradaeva@mail.nih.gov **06-AA-102 New Animal Model Systems for Alcohol Research.** Lack of good model systems has been a major obstacle in our understanding of alcohol-induced disorders, such as liver fibrosis, fetal alcohol spectrum disorders, and cardiomyopathy. The goal of this initiative is to develop new model systems, including animal models, cell culture, and in vitro biochemical or other systems, will provide critical tools and new perspective in our understanding and treatment of alcohol-induced disorders. Examples include zebrafish and planaria to study embryonic development and liver regeneration, mouse embryo and ES cells to understand FASD-related mechanisms, and canine models to study alcohol-induced cardiomyopathy. Contact: Dr. Max Guo, 301-443-0639, qmguo@mail.nih.gov **06-AA-103 Computational Models for Tissue Injury.** Recent developments in flow cytometry utilize a FACS Aria flow cytometer, which allows the simultaneous determination of as many as 18 different parameters in single cells. Using this technology, it is possible to simultaneously quantitate a large variety of cellular constituents in the same cell. For example, in a single cell one can simultaneously measure early apoptosis, late apoptosis, molecules in the caspase cascade that lead to apoptosis, key molecules of canonical signaling pathways (e.g., PI3 kinase, Akt, mTOR, BCL 2, etc.), and numerous transcription factors (e.g., Oct 3/4, Sox 2, Nanog, etc.). By using Bayesian statistics and advanced computer programs, we can establish models of various signaling pathways that are affected by alcohol. Research to develop computational models is sought as they offer a promising integrative approach to alcohol research. Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov **06-AA-104 Systems Biology Approach for the Characterization of Immune Function.** Research is encouraged that takes a systems biology approach to study the effects of alcohol on immune function, by measuring a panel of immune effectors. Such an approach includes quantitative profiling and validation of pro- and anti-inflammatory cytokines, chemokines and their receptors, (cell surface and secreted) and neuroendocrine hormones at different stages of liver disease or immune function impairment using analytical techniques with multiplex capability. The goal is to provide bases for diagnostic biomarkers and for designing intervention strategies. This approach also pertains to the combination of alcohol and infection with HCV or HIV/HCV. Contact: Dr. Kathy Jung, 301-443-8744, jungma@mail.nih.gov or Dr. Joe Wang, 301-451-0747, Wangh4@mail.nih.gov **06-AA-105 Monitoring the Blood Alcohol Concentration in the Magnetic Resonance (MR) Imaging Environment.** The understanding of alcohol's effects on brain function has benefited from the use of brain imaging technology such as magnetic resonance imaging (MRI). However, to determine more precisely the effects of alcohol on brain function (such as cerebral blood flow) and behavioral performance during brain imaging (such as working memory or a simulated driving task), it is necessary to know the exact blood alcohol level moment to moment over the ascending and descending portions of the alcohol curve. This will allow researchers to track changes in brain function and behavior and to directly relate them to the alcohol concentration in individual research subjects. But the MR imaging environment is sensitive to magnetic susceptibility artifacts that may be caused by the metal in instruments used to monitor alcohol concentration

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	when in close proximity to the MR scanner. This initiative seeks development of a MR-compatible device, validation of its use and determination of the effects of the instrument on the brain images acquired. The outcome, which is possible in two years with a directed effort, is the ability to continuously monitor the changes in blood alcohol concentration during brain imaging experiments. Contact: Dr. John Matochik, 301-451-7319, jmatochi@mail.nih.gov **06-AA-106 Technology Development for Analysis of Alcohol-Related Neural Circuits.** Technology has vastly expanded our understanding of neuroscience in the last decade. However, there are still limitations to our understanding of how neural circuits and neural plasticity integrate to produce complex behaviors. Multi-unit recordings, optogenetics and other sophisticated tools for neuroscience research have recently been developed, yet these tools have been relatively underutilized in neurobiological studies examining alcohol's effects on the brain. Studies using these or other novel techniques for neural circuit analysis in alcohol research would greatly increase our understanding of how various brain circuits and regions interact to influence alcohol consumption, withdrawal and relapse. The application of new technologies to determine the relative contribution of different brain circuits (e.g., cognitive, stress, homeostatic, and reward circuits) to stress-induced relapse will aid in the understanding of alcohol addiction and the development of new therapeutic targets for alcohol relapse. Contact: Dr. Tom Greenwell, 301-443-1192, greenwellt@mail.nih.gov **06-AA-107 Molecular Imaging of Dendritic Spines in Response to Alcohol Exposure.** Dendritic spines are the major postsynaptic compartments for excitatory synaptic transmission. Their structures and densities are dynamically influenced by synaptic activity, neurological and psychological disorders, and addictive drugs. Limited studies have demonstrated that acute and chronic alcohol exposure changes both the size and density of dendritic spines in various brain regions. However, little is known about the molecular dynamics that underlie these changes. Recent advances in live-cell imaging techniques, which combine fluorescent probes and optical recording methods, allow visualization of dynamic changes of dendritic spines and associated molecules in vitro and in vivo. Research applying advanced imaging techniques, combined with biochemical, functional, and behavioral analysis, provides an opportunity to improve our understanding of alcohol-induced alterations in the structure and density of dendritic spines. Contact: Dr. Changhai Cui, 301-443-1678, Changhai@mail.nih.gov **06-AA-108 Innovative Technologies for Drinking Pattern Analysis.** Most data on drinking patterns is based on self-reports of daily, weekly and/or monthly consumption. Studies are sought which utilize innovative methodologies/technologies such as ecological momentary assessment to obtain more detailed information about drinking patterns over the course of a day and how these patterns relate to physiology, context and other biological and environmental factors. Such data can also identify subgroups of individuals whose drinking patterns fall across the spectrum of alcohol use (e.g. initiation, escalation to harmful use, dependence). It can also be used to inform interventions. Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov **06-AG-101* Neuroscience Blueprint: Development of non-invasive imaging approaches or technologies that directly assess neural activity.** This could include research on imaging neuronal electrical currents, neurotransmitter changes and/or neuronal/glial cell responses to brain circuit activation. This scientific area could be advanced by improvements/refinements in existing imaging technology or use of emerging technology that could be developed in two years. The outcome of this challenge could

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	have high impact by connecting the system-level, large population view afforded by fMRI with the cellular processes and responses that contribute to the BOLD-fMRI signal. Two-year challenge projects could stimulate the development of human brain imaging techniques that link cell activity underlying neural communication to the structure and function of brain circuits, and could complement other brain connectivity imaging modalities. Contact: Dr. Bradley Wise, 301-496-9350, wiseb@nia.nih.gov; NIAAA Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov; NIBIB Contact: Dr. Yantian Zhang, 301-402-1373, yzhang@mail.nih.gov; NIMH Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov; NINDS Contact: Dr. Randy Stewart, 301-496-1917, rs416y@nih.gov **06-AG-102 Nanoreporters for health during aging.** With a few exceptions such as heart failure and prostate cancer, diagnostic biomarkers have been difficult to dissect from the thousands of physiological metabolites present in the circulation or secretions. State-of-the-art technologies using nanosensors have been developed in order to measure and report on specific disease states or conditions in real time. Biochemical compounds for specific metabolic pathways can be embedded in nanomaterials that can be recovered selectively, and the changes in these compounds can be determined by mass spectrometry or other analytical technologies. Nanosensors (nanoreporters) can be used in lieu of endogenous metabolites to assess metabolic function during aging and the metabolic syndrome. The selection of suitable compounds could be developed in model organisms as a function of aging or development of metabolic syndrome. In addition to their value as discovery tools, the outcomes could be "translated" rapidly for human use, contingent upon safety considerations. Contact: Dr. Bradley Wise, 301-496-9350, wiseb@nia.nih.gov **06-AG-103 Understanding the neural mechanisms responsible for tinnitus.** Millions of Americans suffer from chronic tinnitus, or the percept of ringing in one or both ears. The numerous mechanisms that underlie tinnitus are very poorly understood, and as a consequence, the known intervention strategies are ineffective for most affected individuals. The challenge is to understand the specific neural mechanisms giving rise to tinnitus and to develop novel intervention strategies. Contact: Dr. Wen Chen, 301-496-9350, ChenW@nia.nih.gov **06-AG-104 Development of new tools and technologies to interrogate human mitochondrial function *in vivo*.** These tools would include methods to manipulate human mitochondrial structure and activity, as well as novel imaging techniques to monitor and measure human mitochondrial function or dysfunction in healthy and diseased tissues. Contact: Dr. David Finkelstein, 301-496-7847, FinkelsD@nia.nih.gov **06-AG-105 Tools facilitating chemistry and biology collaborations.** Development of chemical probes, imaging agents, radiochemicals, and other tools for understanding biology through collaborations between a chemist(s) and a biologist(s). Contact: Dr. Jose Velazquez, 301-496-6428, Jvelazqu@mail.nih.gov **06-AG-106 New computational and statistical methods for the analysis of large data sets from genome-wide association studies (GWAS) and the use of next-generation sequencing technologies.** Develop new tools to enable the translation of vast amounts of genomic information into medical benefit to address large amounts of data generated (e.g., terabases of sequence) that overwhelm existing computational resources and analytic methods. These new approaches include very large-scale genotyping and sequencing studies, metagenomics, transcriptomics, and genetic network analysis.

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	Contact: Dr. Marilyn Miller, 301-496-9350, MillerM@nia.nih.gov **06-AG-107 Measuring the body burden of emerging contaminants: Biosensors and lab "on-chip" technology for measuring in vivo environmental agents.** New advances in biosensors and lab-on-chip technology create novel ways to measure the body burden and sub-clinical health effects of emerging contaminants in the environment in large study populations. Additional research funds would support field testing of the most promising sensors and analysis techniques through collaboration with existing epidemiologic studies taking advantage of both new and banked tissue specimens. Contact: Ms. Winifred Rossi, 301-496-3836, RossiW@mail.nih.gov **06-AG-108 Technologies for obtaining genomic, proteomic, and metabolomic data from individual viable cells in complex tissues.** Develop technologies that are able to use one or a small number of cells are needed to generate data to understand the molecular phenotype, or state, of a particular cell type and the role it plays in tissue and organ function in health and disease. Contact: Dr. Jose Velazquez, 301-496-6428, Jvelazqu@mail.nih.gov **06-AG-109 Brain imaging and higher order states.** Exploration of brain imaging technologies to provide insight into higher-order states such as awareness of self, focused attention, stress, meditative states, calm and other emotional states; utilize brain imaging to develop objective measures and rigorous, quantitative evaluation of subjective states. Contact: Dr. Molly Wagster, 301-496-9350, WagsterM@mail.nih.gov **06-AI-101 Development of novel ideas for diagnostic and assay platforms for use in clinical and field conditions.** Approaches may include microsampling and high-throughput cellular immune assays. Contact: Dr. Maria Giovanni, 301-496-1884, mgiovanni@mail.nih.gov **06-AR-101 Advanced Soft Tissue Imaging of Skin, Muscle, Tendons, Ligaments and Joint Tissues.** Advances in imaging approaches such as magnetic resonance and ultrasound are needed to improve detection and diagnosis, and to monitor regeneration of muscles and tendons damaged due to traumatic or repetitive strain injuries, acquired or inherited diseases. Emerging technologies offer opportunities for exploratory and more focused clinical research on imaging of soft tissues in rheumatic disease, including pre-diagnostic, and wound healing e.g., functional studies and non-invasive imaging to evaluate disease progression and response to treatment. Challenge grants offer support for studies to develop novel imaging techniques, standards and baseline data sets, approaches to integrate imaging data with other functional and physiological outcome measures. There is also interest on pilot studies of natural history of diseases and disorders of muscles and tendons, and on pilot studies on the use of soft tissue involvement for the evaluation of disease activity and clinical response in patients rheumatic and skin diseases. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **06-AR-102 Systems Biology for Musculoskeletal System Development, Function and Diseases**. Methodology is needed for integrated analysis of disease mechanisms in humans, combining GWAS, gene expression, microRNA, epigenetics studies, immunologic profiles and disease phenotype using existing databases. The goal is a better understanding of the regulatory networks involved in maintaining normal musculoskeletal tissues structure and function and the changes in these networks that correlate with musculoskeletal disease. Studies of gene expression, protein-DNA, protein-RNA, and

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	protein-protein, interactions and of regulatory micro-RNA have generated enormous amounts of relationship data (i.e., who controls whom). These data are being systematically curated to create computable databases by academic and commercial enterprises (e.g., Ingenuity Pathway Analysis software). This effort will eventually lead to the construction of a regulatory map. It is foreseeable that a map of the regulatory networks will provide a powerful tool for understanding all disease processes and for providing a guide for designing more effective therapies. Components include 1) Identify cohorts with valuable clinical and phenotypic data, cell and tissue samples, and existing data sets; 2) Address issues of consent for acquisition and use of resources, including post-mortem; 3) Address issues of data sharing; 4) Establish infrastructure and governance for widely accessible resource of data and analysis tools. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **06-AR-103 Systems Biology for Skin and Rheumatic Diseases.** Expansion of Merck's proposed Integrative Bionetwork Community to include skin biology and diseases and rheumatic diseases. Merck has proposed to make their database of phenotypic data and genetics available to the public. While it is not clear what this database currently contains, in the area of skin biology/diseases and rheumatic diseases, there are already efforts by several NIAMS-supported research groups to identify the genetic basis of several diseases (e.g. psoriasis, vitiligo, and alopecia areata) through GWAS and to link expression data with the genetics. Similar efforts are ongoing in rheumatic diseases. It would be useful to extend the dataset by the addition of genome-wide epigenetics data and a catalogue of microRNAs identified by high throughput sequencing technologies. The data could also be extended through the addition of more diseases as well as the effects of treatment. There may also be some benefit to include stages of skin development and epidermal differentiation. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **06-AT-101* Imaging correlates of brain states.** Exploration of brain imaging technologies to provide insight into higher-order states such as awareness of self, focused attention, stress, meditative states, calm and other emotional states; utilize brain imaging to develop objective measures and rigorous, quantitative evaluation of subjective states. Contact: Dr. Partap Khalsa, 301-594-3462, khalsap@mail.nih.gov; NIDA Contact: Dr. Steven Grant, 301-443-4877, sgrant@nida.nih.gov **06-CA-101 Enhancing Electronic Patient-Reported Outcomes Assessment in Clinical Research or Healthcare Delivery.** Provide support to enhance, and/or validate the use of electronic-based tools for the assessment of patient-reported outcomes, such as symptoms, functioning, or health-related quality of life, and/or health behaviors such as physical activity. Proposed research may include a variety of technologies including wireless, real-time data capture methods and other interactive tools that enhance patient feedback to facilitate patient centered care, intervention research, or behavior change or maintenance. Contact: Dr. Bryce Reeve, 301-594-6574, Bryce_reeve@nih.gov **06-CA-102 Transient molecular complexes in Cancer.** Aberrant molecular complex formation resulting in inappropriate biochemical pathway utilization is a hallmark of cancer. While highly accurate methods such as crystallography and NMR have revealed a great deal of information about molecular complexes, much remains to be understood. Detecting, identifying, and cataloguing transient molecular complexes (those that are too rapid or too unstable to be detected using methods like crystallography) is integral to understanding the aberrant reactions which characterize cancer. New methods for detecting and characterizing transient complexes both in vitro and in vivo are needed to

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	complete our understanding of molecular interactions in cancer. Contact: Dr. Randy Knowlton, 301-435-5226, knowltoj@mail.nih.gov **06-CA-103 Synthetic Biology.** As we increase our understanding of cancer we find ourselves in a unique position to re-engineer or manipulate fundamental cellular processes in an attempt to control and treat the disease. This type of approach would require an interdisciplinary effort between cancer biology and engineering principals to interrogate, target and integrate at subcellular and cellular levels to generate model synthetic biological systems. Contact: Dr. Dan Gallahan, 301-496-8636, gallahad@mail.nih.gov **06-CA-104 Quantum biology in Cancer Biology.** Cancer involves fundamental biological processes that involve the manipulation of chemical reactions in the transfer and conservation of energy, using fundamental physical and chemical principles. Quantum biology is an emerging and interdisciplinary field that seeks to apply quantum principles to macroscopic systems rather than the atomic or subatomic realms generally described by quantum theory. Biological interactions are modeled using mathematical computation and physical measurements in light of quantum mechanics effects. Exploratory work is needed to apply this novel field to cancer research. Contact: Dr. Dan Gallahan, 301-496-8636, gallahad@mail.nih.gov **06-CA-105 Structure Determination of Large Cancer-related Complexes.** Many of the fundamental cellular events utilize large molecular complexes assembled in a timely way for a specific function, such as DNA repair, RNA splicing, and apoptosis. Our understanding of the structures of these complexes is limited. Since structure often reveals information about function, new approaches need to be developed to determine the structures of these complexes. Contact: Dr. Randy Knowlton, 301-435-5226, knowltoj@mail.nih.gov **06-CA-106 Data integration and visualization methods and tools.** Cancer research is increasingly complex and data-rich. In order for biologists to view their data in the context of other similar data and to view it against the complex background of other data types, new data integration and visualization methods are needed. These can be in the form of software **modules** that can be plugged into existing portals or viewers and can include the adaptation of existing data visualization and integration methods now tailored to cancer research. Contact: Dr. Jennifer Couch, 301-435-5226, couchj@mail.nih.gov **06-CA-107 In vivo molecular profiling (spatial relationships) and Single cell Analysis.** A great deal of information has been gained through molecular profiling of cancer cells and specimens. But these profiles, patterns of gene or protein expression for example, have been identified by monitoring purified components. The context and timing of the expression of these molecules is also important and spatial changes in protein and other molecules are often important in the development of cancer. New methods for visualizing gene expression, proteins or other molecules in normal and cancer cells are needed. Methods for single molecule resolution and methodologies that can monitor expression over time in vivo are needed. Contact: Contact: Dr. Jennifer Couch, 301-435-5226, couchj@mail.nih.gov **06-CA-108 Nanotechnology-based Prevention, diagnostic, and Therapeutic Tools.** Nanotechnology is expected to radically change the way we diagnose, image, and treat cancer. Novel and multi-functional nanodevices will be capable of detecting cancer at its earliest stages, pinpointing its location within the body, delivering anticancer drugs specifically to malignant cells, and determining if these drugs are effective. Functionalized

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	nanoparticles would deliver multiple therapeutic agents to tumor sites in order to simultaneously attack multiple points in the pathways involved in cancer. Such nano-therapeutics is expected to increase the efficacy of drugs while dramatically reducing potential side effects. *In vivo* biosensors would have the capability of detecting tumors and metastatic lesions that are far smaller than those detectable using current, conventional technologies. Furthermore*, they will* provide rapid information on whether a given therapy is working as expected. Contact: Dr. Piotr Grodzinski, 301-496-1550, grodzinp@mail.nih.gov **06-CA-109 Advanced Tools to Study Mitochondria Energetics.** Development of new technologies for studying the role of mitochondrial respiration alterations (energetics and oxidative stress) in the context of cancer. This program will explore the working of a mitochondria from different cell and tissue types in different diseases to help understand essential differences that are present in physiological and pathological conditions and to discover new molecular target for drug development and therapeutic intervention. Contacts: Dr. Henry Rodriguez, 301-496-1550, rodriguezh@mail.nih.gov; Dr. Richard Aragon, 301-496-1550, raragon@mail.nih.gov **06-CA-110 In Silico Cancer Drug Medicine.** For years, researchers have explored the myriad wonders of the construction of virtual proteins based on gene and protein sequence alignments and the screening of virtual compounds against a database of drug targets. But as is so often the case in drug development, most of these virtual compounds fail to achieve their lofty goals when synthesized and exposed to the harshness of the real world and the complexity of the human body. This obstacle now negatively impacts translation of new chemical entities into the market. Today, an opportunity exists for the NIH to implement a concerted effort that develops transformative tools (virtual and physical) that test drugs in real-world scenarios, while still in the virtual phase of human physiology. Contact: Dr. Henry Rodriguez, 301-496-1550, rodriguezh@mail.nih.gov **06-CA-111 Integrative analysis of genomic data sets generated by TCGA and TARGET.** Methods for the unsupervised analysis of large and varied data sets that are predictive of cancer formation and can determine regulatory points in pathways and circuits. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **06-CA-112 Development of high throughput mechanisms for genomic analysis.** This includes methods to improve the throughput of next gen methods for genomic analysis. Methods could be either laboratory based or bioinformatics based improvements with the goal of decreasing the amount of time it takes to analyze a sample. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **06-CA-113 Pre-Clinical Diagnostic and Prognostic Technologies For the Early Detection of Cancer.** Technologies intended for pre-clinical cancer detection and diagnostics, prediction of progression from preneoplastic lesions to cancer, early detection of cancer, and technologies for risk assessment are badly needed to facilitate the early, effective, and more accurate detection of cancer. Specific technologies of interest include technologies and associated methods to significantly improve cancer biomarker discovery, multiplexing platforms to accurately measure low abundance biomarkers, including those from bodily fluids (serum, plasma, buffy coat cells, urine, sputum, saliva) or cells within these fluids, integrated technological platforms for enabling multiplexed biomarker assays, and cellular imaging technologies to detect preneoplastic lesions. Contact: Dr. Richard Aragon, 301-496-1550, raragon@mail.nih.gov

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	06-CA-114 Integrated Clinical Technologies. Novel devices, instrumentation, and tools intended for potential clinical application and those for the prediction of response to therapy or for therapy monitoring are needed to facilitate improved clinical outcomes. Such technologies include platforms for comprehensive, high throughput analysis of genomic or proteomic alterations of tumor tissue such as changes in epigenetic profiles, gene copy number, gene expression, post-translational modifications, and tumor-related changes in lipids and carbohydrates. Of particular utility will be the integration of varying technologies for the development of analytical or point of care devices, including microfluidics, nanotechnology, micro or nanofabrication devices, or the multiplexing thereof. Technologies designed for the targeted delivery and retention of anticancer agents or for the surveillance or monitoring of such agents are also needed to facilitate better interventions for cancer treatment and diagnosis. Contact: Dr. Richard Aragon, 301-496-1550, raragon@mail.nih.gov **06-CA-115 Molecular and Population Epidemiology and Health Disparities Reduction.** Advanced or significantly improved technologies are needed for high-throughput, non-invasive analysis and to help facilitate the movement of discoveries and improved technologies from the basic sciences arena to studies in human populations and the transfer of information from cancer-related health outcomes to practices in clinic and public health settings. Technologies applicable to cancer etiology, epidemiology, and health disparities reduction, including the novel identification and validation of functional or ancestral biomarkers for risk susceptibility in large or multiple populations with a high degree of specificity, sensitivity, cost-efficiency, predictive value, reproducibility and low variability are needed . Also sought are improved technologies in glycomics, proteomics, epigenetics, haplotyping and genotyping (both nuclear and mitochondrial), pharmacogenomics, toxicogenomics, and nanotechnology suitable for application to human populations, populations exhibiting differential health disparities, or in epidemiologic settings. Contact: Dr. Richard Aragon, 301-496-1550, raragon@mail.nih.gov **06-CA-116 Physical Sciences and Cellular Mechanics.** Technologies designed to elucidate, interrogate, and model the role of physical forces on varying cellular functions, including cellular metastasis, metastatic potential, or motility need to be developed in order to facilitate an increased understanding of the role that physical forces play in cancer pathology and metastasis. Of particular need are technologies to quantitatively and temporally model, monitor, track, and/or characterize changes that occur at the level of the cell, including the development of cell-based bio and nanosensors. Technologies for targeted measurements made at the level of the cell, including cell-cell adhesion, cellular motility, and/or cellular adherence properties are also of interest, as are technologies to quantitatively measure cytoskeletal changes and the impact of such changes on elements of metastatic potential, including increased/decreased motility, changes in intracellular mechanics, and ability of cells to interact with the environment. Contact: Dr. Jerry S. Lee, 301-496-1045, leejerry@mail.nih.gov **06-CA-117 Cancer Development, Pathology, and Pathological Progression.** Technologies that provide new tools and insights for basic research with increased speed, cost efficiency, sensitivity, selectivity, or the capability to create new avenues of research into the specific mechanisms can lead to a better understanding of the development and progression of cancer. Of interest are technologies for molecular, subcellular, cellular and extracellular structure/function studies; capture, separation, and characterization of biomolecules, molecular complexes, sub-cellular complexes, cells, and complex mixtures; and technologies to facilitate the development of more accurate in vitro and in vivo cancer models (especially mouse models for human cancers). Of specific interest are new

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	technologies that enhance understanding of the tumor microenvironment, cancer stem cells, complex pathways, and the role of pathogens in cancer development. Contact: Dr. Richard Aragon, 301-496-1550, raragon@mail.nih.gov **06-DA-101 Epigenome-Wide Association Studies (EWAS).** Given current technology, it would be prohibitively expensive to perform epigenome-wide association study in which epigenome-wide analysis is performed on thousands of cases and controls. This barrier significantly impedes our ability to identify epigenotypes important in common human diseases. The development of an approach enabling low cost EWAS scans would transform epigenomic investigations into diseases such as addiction. Contact: Dr. John Satterlee, 301-435-1020, satterleej@nida.nih.gov **06-DA-102 Tool Development for the Neurosciences.** Tools that unambiguously identify, manipulate, and report from neurons *in vivo* and *in vitro* are needed to help us understand interactions within neural circuits, to examine the functions of types of neurons that are derived from different brain regions, and to determine how selective and conditional silencing or activation of individual neurons or groups of similar neurons may alter functional outcomes, including behavior. This methodology can contribute greatly to the identification of real-time responses to drugs of abuse or to therapeutic interventions, and can play a key role in helping us understand endogenous neuroprotective mechanisms and the repair of frank brain damage or neural dysfunction as a result of drug abuse. Contact: Dr. Nancy Pilotte, 301-435-1317, npilotte@nih.gov **06-DA-103 Identification of chemical modulators of epigenetic regulators.** There are a limited number of pharmacological agents available to manipulate the in vivo activity of most epigenetic modifying enzymes, effector molecules, etc. High-throughput small-molecule screening strategies targeted at specific epigenetic regulatory molecules could identify chemical reagents targeting a broad range of epigenetic regulatory molecules. These high impact reagents have the potential to transform the way epigeneticists conduct in vivo disease research. Contact: Dr. John Satterlee, 301-435-1020, satterleej@nida.nih.gov **06-DA-104 Development of new technologies to change patient and provider behaviors to improve adherence.** New and innovative strategies to improve patient adherence to HIV/AIDS medical regimens and utilization of adherence-enhancing strategies in clinical practice would greatly enhance the health impact of efficacious treatments. This challenge invites the development of novel strategies to change patient and provider behaviors to enhance adherence to HIV/AIDS therapeutics among drug users. Contact: Dr. Jacques Normand, 301-443-1470, jnormand@nida.nih.gov **06-DA-105 Improving health through ICT/mobile technologies.** Enhancing patient compliance. ICT applications hold the prospect of dramatically improving patient health and treatment compliance in the US and abroad at greatly reduced cost. To realize these potentials, implementation research is required to identify behavior modification strategies at all levels (patient, provider and institutions) which will yield the most effective treatment outcomes using these technologies. Development and programming and feasibility testing of applications for computer and mobile devices will also be considered especially for evidence based therapies. Contact: Dr. Cecelia Spitznas, 301-402-1488, spitznasc@mail.nih.gov **06-DA-106 Predictive models of potential drug addiction treatment agents.** Develop predictive models of compound interactions with receptors and transporters

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	known to be involved in drug addiction or targets for drug addiction treatment. Models developed can be intended to predict various pharmacological properties (i.e., affinity, function, toxicity, etc.). Contact: Dr. Richard Kline, 301-443-8293, rkline@nida.nih.gov **06-DA-107 Measuring the body burden of emerging contaminants: Biosensors and lab "on-chip" technology for measuring *in vivo* environmental agents.** New advances in biosensors and lab-on-chip technology create novel ways to measure the sub-clinical health effects of second-hand and third-hand smoke in the environment. Development or field testing of the most promising environmental sensors that detect tobacco smoke combined with their use within existing epidemiologic studies are encouraged. Contact: Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **06-DA-108 Infrastructure for biomedical knowledge discovery.** Development of collaborative, research-community and concept based, integrated scientific knowledge environments to promote and accelerate articulation, discovery, exploration, discussion, testing, analysis, and sharing of hypotheses and the scientific evidence supporting them in basic neuroscience and behavioral addiction research. Contact: Dr. Karen Skinner, 301-435-0886, ks79x@nih.gov **06-DA-109 Developing new computational approaches to Information Retrieval.** Development of computational approaches which query multiple data sources and types relevant to basic neuroscience and behavioral addiction research, and which (1) employ or add to the Neurolex vocabulary (http://www.neurolex.org) of the NIH Blueprint Neuroscience Information Framework and (2) focus on enabling user-friendly complex queries based on concepts, anatomical coordinates, and other query parameters relevant to addiction research, that return source data elements directly within a format and context that makes them easily interpreted and accessible. Contact: Dr. Karen Skinner, 301-435-0886, ks79x@nih.gov **06-DC-101* Develop Improved Hearing Devices.** Approximately 36 million American adults report some degree of hearing loss and would benefit from hearing aid use. However, only approximately 20% of potential hearing aid candidates actually use these devices, owing to concerns about stigma, cosmesis, sound quality, and affordability. The Challenge is to develop improved hearing aids, both worn and implantable, for individuals with hearing loss. Contacts: Dr. Dan Sklare, 301-496-1804, sklared@nidcd.nih.gov; Dr. Gordon Hughes, 301-496-5061, hughesg@nidcd.nih.gov. **06-DC-102* Develop and Validate Methods for Delivery of Drugs and Molecules to the Inner Ear.** In order to capitalize on the new knowledge of the molecular basis for hearing impairment, better methods to deliver drugs and molecules to the inner ear need to be developed and validated. The Challenge is to identify methods of delivery that are robust, long lasting, and minimally toxic to the sensitive structures in the inner ear. Contacts: Dr. Nancy Freeman, 301-402-3458, freemann@nidcd.nih.gov; Dr. Amy Donahue, 301-402-3458, donahuea@nidcd.nih.gov. **06-DC-103* Understanding the Neural Mechanisms Responsible for Tinnitus.** Millions of Americans suffer from chronic tinnitus, or the percept of ringing in one or both ears. The numerous mechanisms that underlie tinnitus are very poorly understood, and as a consequence, the known intervention strategies are ineffective for most affected individuals. The Challenge is to understand the specific neural mechanisms giving rise to tinnitus and to develop novel intervention strategies. Contact: Dr. Roger Miller, 301-402-

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	3458, millerr@nidcd.nih.gov. **06-DE-101 Imaging of Oral Diseases.** High resolution imaging modalities with enhanced specificity and sensitivity can be powerful tools for early detection of oral diseases, and for monitoring of treatment outcome. Goal: Development, refinement or testing of novel imaging modalities for the early detection of oral and dental lesions, including but not limited to oral squamous cell carcinoma, demineralized tooth surface, or alveolar bone loss or necrosis. Development of non-invasive or minimally-invasive approaches for the early detection, diagnosis, and measurement of response to treatment of diseases that are currently difficult to diagnose, detect, or treat. Contact**:** Dr. Yasaman Shirazi, 301-594-4812, Yasaman.Shirazi@nih.gov **06-DE-102 Structural and Molecular Atlases of Craniofacial Development.** Craniofacial developmental processes are complex events that set up temporal and spatial tissue morphogenetic boundaries. Although much work has contributed to our knowledge base, a comprehensive high resolution map of the morphogenetic template has not been accomplished. Goal: Development of high resolution imaging of developmental processes and development of markers and probes to track normal and abnormal developmental processes at the single cell level for the construction of structural and molecular atlases of craniofacial development that will be shared through FaceBase. Contact: Dr. Lillian Shum, 301-594-0618, Lillian.Shum@nih.gov **06-DE-103 Novel Technologies for Cultivation of Oral Microbes.** Recent molecular studies reveal that nearly 800 taxa comprise the human oral microbiome. Initial identification of un-named phylotypes, and in many cases not-yet cultivated species or those incapable of *in vitro* growth, has been accomplished primarily through metagenomic studies. While metagenomics can indicate the presence of particular organisms, direct laboratory examination via cultivation ultimately will be needed. Goal: Development of new methods and technologies to allow for *in vitro* growth of organisms refractory to standard microbiological cultivation, including co-cultivation, domestication, and identification of host-derived nutrients for morphological analysis and classical biochemical and metabolic characterization. Contact: Dr. R. Dwayne Lunsford, 301-594-2421, lunsfordr@nidcr.nih.gov **06-DE-104 Click Chemistry for Oral, Dental and Craniofacial Applications.** "Click chemistry" was coined in 2001 by Barry Sharpless and colleagues to describe a synthetic chemical method to link simple organic molecules together through highly efficient, highly selective, and non-toxic reactions. Currently, the centerpiece of click chemistry is a reaction to connect building block molecules that can occur at physiological temperatures in aqueous medium. This reaction has proven useful for: developing reporters and tags for DNA, proteins, and carbohydrates *in vivo* through bioconjugation; developing protease inhibitors or a spectrum of anti-infective and anti-tumor agents; creating molecular libraries; synthesizing novel polymer materials; and functionalizing material surfaces for microarray, biosensor or microfluidic platforms. Goal: Application of "click chemistry" for oral, dental and craniofacial applications, including but not limited to the development of small molecules to disrupt oral biofilms or anti-infective agents for oral diseases, head and neck cancer detection agents and therapeutics, new dental materials, or novel *in vivo* molecular imaging modalities. Contact: Dr. Lillian Shum, 301-594-0618, Lillian.Shum@nih.gov **06-DE-105 Oral Fluid-based Point-of-care Diagnostic Platforms.** Cataloging the salivary proteome is a significant first step toward understanding how salivary protein levels and states may provide a profile of oral and systemic health and disease. Many of

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	these proteins already serve as biomarkers in lab-based bioassays of various bodily fluids. Goal: Using a targeted approach, development and validation of these bioassays for adaptation to oral fluid-based point-of-care diagnostic platforms. Contact: Dr. Lillian Shum, 301-594-0618, Lillian.Shum@nih.gov **06-DE-106 Real Time Feedback of Changing Conditions of Oral and Systemic Health.** Continuous measurement and monitoring of physiological variables face major challenges in the home setting for patients and especially for infants and the elderly. Non-invasive, non-restrictive health monitoring devices would allow continuous evaluation of an individual's current health to provide immediate patient awareness of changing conditions that could be corrected before entering a detrimental phase. Goal: Development of proof-of-concept biosensor wearable in the oral cavity for continuous and dynamic monitoring of changing conditions of oral and systemic health to allow immediate feedback. Contact: Dr. James A. Drummond, 301-402-4243, drummondj@nidcr.nih.gov **06-DE-107 Technologies to Facilitate Oral Health Behaviors.** New or adapted technologies provide opportunities to enhance oral health behavior, and allow for flexible delivery of evidence-based oral health behavioral interventions, without extensive staff time or training. Goal: Studies are encouraged that develop (or adapt) and test technologies to enable oral health behavior assessment, monitoring and/or intervention. Research is also encouraged that tests technologies to measure physiologic, behavioral, and social factors demonstrated to be important in oral health (e.g., novel measures of adherence to care-provider recommendations, remote monitoring of oral hygiene and nutrition practices, reliable and valid remote measures of tobacco use). Contact: Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov **06-DK-101* Development of cell-specific delivery systems for therapy and imaging.** Develop non-viral strategies for cell-specific delivery of pathway-interactors and molecular probes. These new molecular complexes could allow delivery of cell-penetrating agents for the study of disease pathways, the imaging of tissue mass and disease progression, or the development of tissue-specific therapeutics. Contact: Dr. Olivier Blondel, 301-451-7334, blondelol@mail.nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **06-DK-102* Mechanisms and measurement of human thermogenesis**. The unique mechanisms that alter the efficiency of energy utilization in various organ beds—white and brown fat, skeletal muscle, liver, gut—remain largely unknown. New technologies are needed that can quantify organ specific energy production, utilization and heat production in human subjects. Contact: Dr. Maren Laughlin, 301-594-8802, laughlinm@mail.nih.gov **06-DK-103 Enabling technologies in imaging.** Bioimaging technologies and systems can greatly improve diagnosis and treatment in both pre-clinical and clinical areas that fall within the scope of NIDDK's mission. Priority areas include, for example: Development of minimally invasive image-guided systems to improving biopsy sampling, safety of procedures, minimizing recovery time and complications of surgery; Development of bioimaging technologies and systems, especially those that enable robust, accurate and low cost point-of-care testing for relevant biomarkers; Development of advanced clinical phenotyping techniques for early detection, diagnosis and response to treatment of diseases that are currently difficult to diagnose, detect or treat. For example, development of imaging methods for beta cell mass as an outcome for studies of diabetes therapy; nephron number, related to kidney function; organ fibrosis related to loss of liver, biliary,

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	kidney or pancreas function; neuroimaging for appetite; and inflammation; and Enhancement of technologies for measuring the organ distribution of iron stores. Contact: Dr. Maren Laughlin, 301-594-8802, laughlinm@mail.nih.gov **06-DK-104 Enabling technology for the prevention and treatment of diseases within the NIDDK mission.** Priority areas include, for example: Development of better tools for minimally invasive surgical procedures, such as urologic surgeries, to minimize complications and shorten recovery; Development of technologies to improve medication delivery capitalizing on new understandings of the molecular basis of relevant diseases that are robust, long lasting, and minimally toxic to neighboring cells; Improvement of medical devices such as catheters, dialysis equipment, and lithotriptors to minimize complications of procedures; Creation of new or improved mechanical designs and control algorithms for devices or surgical techniques aimed at normalizing urologic function, focusing on technologies for improving bladder control and function; and Develop novel informatic methods, techniques, algorithms or tools. Contact: Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov **06-DK-105 Enabling technologies for cell biology and macromolecular analyses.** Priority areas for disease within the NIDDK mission include: Development of "proteostasis" (protein homeostasis) monitoring tools and reagents to visualize critical processes such as protein aggregation, the protein folding capacity/competence of various subcellular compartments, the redox state of protein processing compartments, protein degradation capacity and the Unfolded Protein Response; Improvement of technologies for obtaining genomic, proteomic, and metabolomic data from individual viable cells in NIDDK-relevant tissue types; and Development of new tools and technologies to interrogate human mitochondrial function *in vivo*, including methods to manipulate human mitochondrial structure and activity, as well as novel imaging techniques to monitor and measure human mitochondrial function or dysfunction in healthy and diseased tissues. Contact: Dr. Christian Ketchum, 301-594-7717, ketchumc@mail.nih.gov **06-DK-106 Identifying a standard anthropometric measure for pediatric central adiposity.** Identify reliable landmarks and methodology for pediatric abdominal circumference that correlate with total and intra-abdominal fat across the pediatric age, maturation, and total body adiposity range and are feasible in pediatric research studies in all settings, as well as clinical care. Such a measure could standardize phenotyping of pediatric research subjects and patients, and monitor response to intervention. Contact: Dr. Mary Horlick, 301-594-4726, horlickm@niddk.nih.gov **06-DK-107 New technologies for nutrition research.** Emerging technologies will be useful for further advances in studies of nutrient biomarkers, bioactive food components and strategies used for intervention efforts to reduce risk and complications of GI and liver disease. These include accelerator mass spectrometry, nanodevices, and new proteomics technologies. Further development of applications for nutrition research is needed. Contact: Dr. Michael (Ken) May, 301-594-8884, maym@mail.nih.gov **06-EB-101* Development of minimally invasive image-guided systems.** Target areas include (1) improving the accuracy of biopsy sampling / staging of disease such as in the evaluation for prostate cancer, (2) reducing the incidence of complications such as in improving prostate nerve bundle sparing, (3) reducing recovery time such as in thoracic cancer resection and (4) improving the safety of interventional procedures such as in lead placement in deep brain stimulation. Contact: Dr. John Haller, 301-451-3009,

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	hallerj@mail.nih.gov **06-EB-102*** **Development of biomedical technologies and systems.** Focus areas include: (1) providing immediate diagnostic information for multiple conditions at the point-of-care; (2) a robust, consistently accurate glucose sensor with extended functional lifetime, improved accuracy and low variability of readings; or (3) low cost diagnostic or therapeutic systems. Also, development of such devices engineered to work in low resource settings. Contact: Dr. William Heetderks, 301 451-6771, heetderw@mail.nih.gov **06-EB-103** **Development of Non-Invasive Therapies and Treatment Procedures.** Non-invasive ultrasound and RF techniques go one step further than minimally invasive technologies in eliminating invasive surgery. Also, nanotechnology-based therapies can be externally activated to deliver drugs to specific organs. NIH invites applications that will develop these (and other) non-invasive approaches for clinical applications. Contact: Dr. Hector Lopez, 301-451-4775, lopezh@mail.nih.gov **06-EB-104** **Fast MR Imaging for Routine Clinical Examinations.** Many MR imaging technologies hold substantial biomedical promise, but have not been translated into routine clinical applications because of the long exam times, which can cause problems with patient compliance and patient through-put. Two ways to decrease the exam time are (1) to use "parallel" imaging approaches, which simultaneously collect data from an array of "detectors", and (2) to use novel k-space sampling approaches. NIH invites applications that will significantly reduce the MRI exam times for routine clinical procedures, such as a "complete cardiac exam", using these approaches. Contact: Dr. Guoying Liu, 301 594-5220, liug@mail.nih.gov **06-EB-105** **Quantitative Molecular Imaging.** Many molecular imaging approaches have not been translated into routine clinical applications because of difficulties in quantitating the observed results. Examples could be quantitation of (1) the number of labeled immune cells "tracked" to target organs (e.g., the pancreas in type-1 diabetes), (2) gene expression of biochemical markers for disease, or (3) regional increases in cerebral oxygen consumption that occur during brain activation. NIH invites applications that will allow accurate and precise quantitation of molecular imaging approaches that can be used in clinical settings. Contact: Dr. Yantian Zhang, 301 402-1373, yzhang@mail.nih.gov **06-EB-106** **Optical Imaging of Internal Organs in Humans.** Due to the limited penetration of light in biological tissue, many optical microscopy and spectroscopy techniques that have shown exquisite tissue/cell contrast in basic biological research can not be easily translated to clinical applications. NIH invites applications that develop novel biomedical optical approaches that can overcome the light penetration depth limitation, and unleash the potential of optical imaging for clinical applications. Contact: Dr. Yantian Zhang, 301 402-1373, yzhang@mail.nih.gov **06-EB-107** **Point-of-Care Technologies.** Despite recent interest in advancing the field of point-of-care (POC) testing, major challenges remain in the development of new POC technologies, including a clinical needs-driven approach, appropriate clinical testing of prototype devices, and connectivity to health information systems. Multidisciplinary technology development efforts are required to facilitate device design that is appropriate for a given healthcare setting with the potential to significantly impact the delivery of healthcare in low-resource or remote settings. Contact: Dr. Brenda Korte, 301-341-4778, kortebr@mail.nih.gov

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	06-EB-108 Imaging of Drug and Gene Delivery Systems. Three major challenges in the field of drug and gene delivery are: targeting of therapies to tissues, cells, and intracellular compartments; monitoring exactly where the therapies localize after administration; and determining if the agents delivered are doing what they were intended to do. We encourage proposals to develop multifunctional systems that: 1) are capable of targeted delivery of drugs, proteins, genes, or nucleic acids to specific cells, or compartments within cells in vivo; and 2) possess imaging capabilities to track delivery, assess function, and determine therapeutic efficacy. Contact: Dr. Lori Henderson, 301-451-4778, hendersonlori@mail.nih.gov **06-EB-109 Model-driven Biomedical Technology Development.** Progress in the development of many biomedical technologies (e.g. neuroengineering technologies, drug and gene delivery systems, tissue engineering) could be greatly accelerated with the development of in silico modeling and simulation methods to drive hypothesis formation, experimental design, data collection, data analysis and synthesis, and re-formulation of the original hypothesis. In a systematic and robust manner, models should identify the gaps in knowledge and the limitations of the engineering design. Proposals that encourage the integration and translation of knowledge from in vitro to in vivo systems are being sought. Contact: Dr. Grace Peng, 301-451-4778, pengg@mail.nih.gov **06-EB-110 Methods for Assessment of Imaging Technologies.** Proposals to develop mathematical, statistical or computation models that can be used by technology developers to assess or calibrate their medical imaging technologies are encouraged. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov **06-EB-111 Validation of Image Analysis Methods.** Applications are sought that provide an infrastructure for the evaluation of image registration and segmentation algorithms. This infrastructure is expected to include a database of test images, a web-based interface with public access, consensus-driven evaluation metrics, and a system for storing and reporting measures associated with different algorithms. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov **06-EB-112 Large-scale Kinetics of Multiple Signaling Pathways**. Building upon successful efforts in detailed kinetic modeling of highly-complex chemical reactions (*e.g.,* turbulent combustion), large-scale kinetic models of multiple and integrated molecular signaling pathways are sought. This will help determine under which conditions particular pathways may dominate or interfere, and begin to form a predictive framework as new kinetic data and signaling molecules are identified. Construction of these models will highlight important kinetic information gaps and pave the way toward ultimately being able to perform *in-silico* simulations of inflammatory and immune response to new materials and engineered therapies. Contact: Dr. Albert Lee, 301-451-4781, alee@mail.nih.gov **06-EB-113 Bioprocess Sensors**. Concomitant with the increasing demand for protein-based therapeutics is the need for more sophisticated real-time monitoring of bioprocess cell culturing reactions, separations, end product characterization, and rapid detection of contaminants. Rapid assays and/or robust, on-line, sterilizable sensors are needed for: raw material characterization; quantifying feedstocks and cellular metabolites during fermentation; rapid proteomic analysis of fermentation intermediates; monitoring of separations, glycosylation and protein structure/folding; and rapid/standardized tests for endotoxin, mycoplasma, viral clearance and other contaminants. High throughput screening tools are also needed to optimize fermentation conditions and to help develop

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	improved process models. Contact: Dr. Albert Lee, 301-451-4781, alee@mail.nih.gov **06-ES-101* Measuring the body burden of emerging contaminants: Biosensors and lab "on-chip" technology for measuring *in vivo* environmental agents.** New advances in biosensors and lab-on-chip technology create novel ways to measure the body burden and sub-clinical health effects of emerging contaminants in the environment in large study populations. Additional research funds would support field testing of the most promising sensors and analysis techniques through collaboration with existing epidemiologic studies taking advantage of both new and banked tissue specimens. Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov **06-ES-102* 3-D or virtual models to reduce use of animals in research: Creation of miniature multi-cellular organs for high throughput screening for chemical toxicity testing.** Development of novel micro-scale systems of multiple cell types that replicate the macro-scale structure and function of major organ systems in response to environmental stressors linked with development of computational models of organ system function can accelerate testing of the multitude of chemicals in our environment for toxicity. Research which furthers the generation of 3-D biological models will provide new assays for rapid screening of toxicity in organs such as the lung and liver. Cell types, such as human stem cells, used in these systems would reduce the use of animals and improve our assessment of chemical hazards in the environment. Contact: Dr. David Balshaw, 919-541-2448, Balshaw@niehs.nih.gov **06-ES-103 Markers of DNA repair capacity and response.** Development of enabling technologies that will facilitate and stimulate translation of basic research in DNA damage and repair to human population and clinical studies are needed to facilitate improved studies of disease. The new tools should develop practical measures of global DNA repair capacity in individuals or responses in individual DNA repair pathways that are activated following DNA damaging exposures. These assays need to be scalable for use in clinical and population studies. Validation studies would also be deemed appropriate. Contact: Dr. Les Reinlib, 919-541-4998, Reinlib@niehs.nih.gov **06-GM-101* Structural analysis of macromolecular complexes.** Development of new approaches, technologies, and reagents that would facilitate functional and/or structural analysis of macromolecular complexes. Contacts: Dr. Ravi Basavappa, 301-594-0828, basavapr@nigms.nih.gov; Dr. Laurie Tompkins, 301-594-0943, tompkinl@nigms.nih.gov **06-GM-102* Chemist/biologist collaborations facilitating tool development.** Development of chemical probes, imaging agents, radiochemicals, and other tools for understanding biology through collaborations between a chemist(s) and a biologist(s). Contacts: Dr. James Deatherage, 301-594-0828, deatherj@nigms.nih.gov; Dr. Michael Rogers, 301-594-3827, rogersm@nigms.nih.gov **06-GM-103* Development of predictive methods for molecular structure, recognition, and ligand interaction.** Studies to more precisely predict molecular structure and interactions between molecules and ligands to lay the foundation for a new generation of therapeutics and drug design. Powerful predictive methods will require the acquisition of experimentally derived constraints and breakthrough computational methods. Reliable, high-throughput predictive methods would create a more comprehensive resource for understanding molecular interaction that would eventually replace the use of slower, empirical determinations. Contacts: Dr. Peter Preusch, 301-594-0828,

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	preuschp@nigms.nih.gov; Dr. Warren Jones, 301-594-3827, jonesw@nigms.nih.gov **06-GM-104 Dynamics of membrane structure and function**. Development of new technology to study the dynamics of membrane structure and function to better understand how membrane components change as they sense the environment, assemble, or bind metabolites. Contact: Dr. Jean Chin, 301-594-0828, chinj@nigms.nih.gov **06-GM-105 Small RNAs**. Identification and functional characterization of all classes of small RNAs, to elucidate their regulation and mechanism of action and to understand their evolutionary origin. Contact: Dr. Michael Bender, 301-594-0943, bendermt@nigms.nih.gov **06-GM-106 Subcellular imaging of metal ions**. Development of metallobiochemistry methods to image metal ions and metal ion species at the subcellular level. Contact: Dr. Vernon Anderson, 301-594-3827, andersonve@nigms.nih.gov **06-GM-107 Metal ion binding and function**. Development of high-throughput methods for the prediction of metal ion binding and function in proteins at the structural, redox, and/or catalytic levels. Contact: Dr. Vernon Anderson, 301-594-3827, andersonve@nigms.nih.gov **06-GM-108 Functions of glycan-binding proteins.** Creation of new, high-throughput methods for deciphering the biological functions of glycan-binding proteins. Contact: Dr. Pamela Marino, 301-594-3827, marinop@nigms.nih.gov **06-GM-109 Green chemistry and engineering for drug discovery, development, and production**. Development of chemical methodologies and tools to promote green chemistry and engineering innovation into drug discovery, development, and production. Contact: Dr. Miles Fabian, 301-594-3827, fabianm@nigms.nih.gov **06-GM-110 Synthesis, structure, and function of glycans**. Development of new approaches, technologies, reagents, and tools to facilitate understanding of the synthesis, structure, and function of glycans. Contact: Dr. Pamela Marino, 301-594-3827, marinop@nigms.nih.gov **06-GM-111 Natural products methodologies**. Development of novel, rapid methodologies for the detection, structural analysis, expression, and/or derivatization of natural products. Contact: Dr. John Schwab, 301-594-3827, schwabj@nigms.nih.gov **06-GM-112 Molecular and cellular dynamics technologies**. Development of tools, reagents, and technologies to better understand molecular and cellular dynamics *in vivo.* The goal is to develop the capability to characterize the abundance, location, composition, interactions, and turnover of individual molecules with high sensitivity and with little perturbation of the cellular environment. New methods, including those for single-molecule resolution, are needed for tracking and recording these changes *in vivo* at the subcellular level. Contact: Dr. Catherine Lewis, 301-594-0828, lewisc@nigms.nih.gov **06-GM-113 Structural analysis of large cellular components and organelles**. Development of hybrid methods to enable the structural analysis of large cellular components and organelles. This will enable the determination of structures that are not amenable to routine X-ray crystallography or NMR spectroscopy. The new methods will make use of combined, “hybrid” data from a variety of sources as well as computational methods to integrate data sources using a range of dimensions, scales, and formats.

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	Contact: Dr. Ravi Basavappa, 301-594-0828, basavapr@nigms.nih.gov **06-GM-114 Microbial sequence annotation**. Development of new approaches to the rapid and comprehensive annotation of microbial sequences resulting from metagenomics and other high-capacity outputs. Approaches may combine high-throughput experimental methods with innovative data mining algorithms and model building. Contact: Dr. James Anderson, 301-594-0943, andersoj@nigms.nih.gov **06-GM-115 High-end computing software**. Upgrading of biomedical computing software to high-end computing (HEC). This developmental effort will seek to expand the domain areas to the macromolecular, cell, tissue, organ, whole-organism, and population levels. The program would support grants to upgrade and port software to run and perform experiments on new generation HEC supercomputers. Contact: Dr. Peter Lyster, 301-594-3928, lysterp@mail.nih.gov **06-HD-101* Improved interfaces for prostheses to improve rehabilitation outcomes.** Mechanical design and control algorithms for prosthetic limbs have seen remarkable advances recently. Still lacking, however, are robust interfaces for these limbs to both the brain and the skeleton. The foci of this challenge will be to improve functional rehabilitation outcomes by 1) developing or refining control interfaces that can utilize signals from cerebral cortex to drive the latest generation of arm prostheses; 2) developing or refining methods for anchoring prosthetic arms directly into residual bone without risk of infection; and 3) incorporating these technologies into standard rehabilitation practices to improve patient quality of life. These improvements in prosthetic limbs could potentially provide enhanced functionality for recipients while reducing the time and cost of rehabilitation efforts. Contact: Dr. Michael Weinrich, 301-402-0832, weinricm@mail.nih.gov. **06-HD-102 Point of Care Diagnosis and Assessment.** Development of rapid point-of-care diagnosis could result in dramatic improvements in targeted therapy, outcomes, and cost of care. Research is needed to jumpstart the development and application of these techniques, particularly for newborn screening and diagnosis of serious conditions in infants. Examples of NICHD's interest in this area include: o Nanotechnologies and Microfluidics for Newborn Screening - Proof-of-concept projects are needed for new technologies, based on, but not limited to, micro- and nanofluidic and nanostring technologies, that pioneer reliable diagnostic approaches and tools for assessing 1) gene expression in small, well defined samples at specific developmental stages; 2). multiple analytes rapidly and efficiently with minimal-volume human specimens, pertaining to a broad range of early detectable developmental disabilities; and 3) sepsis in newborns. o Assessment of HIV and CD4 Counts in Infants - Diagnosis of HIV infection in infants involves direct assessment of the virus, and CD4 counts are needed for immune assessment in HIV; however, both require technology that does not lend itself to point of care assessment. New techniques need to be developed to facilitate early diagnosis and immediate treatment in infancy, particularly in low resource settings. o Hemoglobinopathies and thalassemias - Digital microfluidics technology offers the hope for quick diagnosis, assessment and monitoring of hemoglobinopathies and thalassemias, to speed infant, children and other patients' access to appropriate treatment. Contact: Dr. James Coulombe, 301-451-1390, CoulombeJ@mail.nih.gov; Dr. Tiina Urv, 301-402-7015, urvtiin@mail.nih.gov; Dr. Lynne Mofenson, 301-435-6870,

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	mofensol@mail.nih.gov; Dr. Tonse Raju, 301-402-1872, rajut@mail.nih.gov **06-HD-103 Novel Imaging Technologies to Determine Fetal Maturity.** There is an increasing trend for an elective delivery in the United States, resulting in more infants being delivered early and a concomitant increase in infant morbidities associated with a premature birth. Proof of concept studies are needed for developing novel imaging technologies to determine fetal maturity in utero. This would help physicians more accurately assess fetal maturity before scheduling elective deliveries. Contact: Dr. John V. Ilekis, 301-435-6895, ilekisj@mail.nih.gov **06-HD-104 Development of Catheters for Use in Newborns.** Intravascular catheters used in newborn infants can cause thrombus formation, leading to stagnation of blood flow, activation of platelets and formation of clots. Such clots can cause vascular obstruction, catheter malfunction, or life-threatening embolization. Research is needed to develop ultra-small (21 to 24 gauge) intravascular catheters coated with nitric oxide secreting polymers that function similar to vascular endothelium, producing nitric oxide locally, preventing biofilm, repelling platelets and preventing thrombus formation. Contact: Dr. Tonse Raju, 301-402-1872, rajut@mail.nih.gov **06-HD-105 Solid Oral Dosage Forms for Pediatric Medications.** There is a pressing medical need to develop technologies to produce solid oral dosage forms that allow the correct dosage to be administered (e.g., micro-pellets in small drug amounts) and that are orally dissolvable. These solid dosage forms would also be environmentally stable, could be measured for individualized dosing and administration, and could be administered orally for treatment of chronic childhood diseases such as asthma, seizure disorders, immunomodulation or antimicrobial therapy. Contact: Dr. Anne Zajicek, 301-435-6865, zajiceka@mail.nih.gov **06-HD-106 Imaging Techniques for Research on Early Development.** A current barrier to our understanding of normal (and abnormal) developmental processes is the lack of high resolution imaging techniques that limit our ability to visualize the dynamic molecular and cellular changes that occur at various developmental stages. Research is needed to develop, optimize, and/or validate advanced three-dimensional imaging techniques, including noninvasive approaches and high throughput analysis of images that will specifically allow researchers to visualize developmental processes in living embryos. Studies can be targeted to fundamental developmental events in animal models that can be easily translated into improved assessment of anatomic and genetic abnormalities associated with human structural birth defects. Contact: Dr. Mahua Mukhopadhyay, 301-435-6886, mukhopam@mail.nih.gov **06-HG-101* New computational and statistical methods for the analysis of large data sets from next-generation sequencing technologies.** The introduction of new methods for DNA sequencing has opened new avenues, including large-scale sequencing studies, metagenomics, transcriptomics, genetic network analysis, and determination of the relationship of sequence variation and phenotypes to disease, to address heretofore unapproachable problems in biomedical research. However, since the large amounts (terabases) of data generated overwhelm existing computational resources and analytic methods, urgent action is needed to enable the translation of this rich new source of genomic information into medical benefit. Contact: Dr. Lisa Brooks, 301 496-7531, brooksl@mail.nih.gov

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	06-HG-102* **Technologies for obtaining genomic, proteomic, and metabolomic data from individual viable cells in complex tissues.** Most existing technologies can only measure the properties of a population of cells and not the properties of individual cells. Technologies that are able to use one or a small number of cells are needed to generate data to understand the molecular phenotype, or state, of a particular cell type and the role it plays in tissue and organ function in health and disease. Contact: Dr. Brad Ozenberger, 301-496-7531, bozenberger@mail.nih.gov **06-HG-103*** **Methods to sequence highly variable, repeat-rich regions of complex genomes.** Variants in complex genomic regions, e.g. the MHC region, have implications for infectious and autoimmune diseases, yet these and many other highly repetitive and highly variable loci are often poorly represented in sequence assemblies using data from newer "short read" sequencing platforms, and are too expensive to sequence with older, Sanger-based platforms. Technology development is needed to sequence and assemble these regions efficiently and accurately or they will continue to be unexamined in large medical genomics studies. Contact: Dr. Adam Felsenfeld, 301 496-7531, felsenfa@mail.nih.gov **06-HG-104** **New technology and resources for personalized medicine.** To make personalized medicine a reality requires new technologies and resources, such as rapid point-of-care genotyping methods and more effective ways to use genetic testing results in conjunction with electronic medical records. Research on the effects that the utilization of such resources has on health costs and outcomes is also urgently needed to achieve the full integration of personalized medicine into current health care systems. NHGRI contact: Dr. Ebony Bookman, 919-541-0367, bookmane@mail.nih.gov **06-HL-101** **Develop technologies for assessment of aortic aneurysms prone to rupture or dissection**. Thoracic and abdominal aortic aneurysms (TAA and AAA, respectively) are life threatening conditions that together comprise the thirteenth leading cause of death in the U.S. The most common sources of mortality associated with aortic aneurysms are acute dissections (more common to TAA) and rupture (more common to AAA). For both TAAs and AAAs, close monitoring of aneurysm size is the only way currently available to determine when to intervene with elective surgery or endovascular repair to avoid dissection or rupture. However, size is not a reliable predictor so new technologies are needed, such as noninvasive imaging and biomarkers, that can reliably identify aneurysms that are prone to rupture or dissection. Contact: Dr. Eser Tolunay, 301-435-0560, tolunaye@mail.nih.gov **06-HL-102** **Develop high affinity/high specificity targeted molecular probes for molecular imaging of cardiovascular and pulmonary disease targets.** Clinical imaging currently provides primarily anatomical and functional information that does not address the underlying pathophysiology. Molecular imaging probes have the potential to provide additional information about the disease process itself by interrogating specific targets such as cell surface receptors and enzymes activity. By detecting specific markers expressed in physiological and pathophysiological states, molecular imaging probes can improve detection and staging of disease. The appearance or disappearance of specific probe targets in response to therapy is likely to provide information on therapeutic efficacy much faster than traditional imaging measurements based on anatomical and functional responses, helping to tailor therapies and dosage to individual patients. Contact: Dr. Denis Buxton, 301-435-0513, db225a@nih.gov

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	06-HL-103 Develop new imaging methodologies to track cells and measure accurately the chemical activities of enzymes and metabolites in intact cells, tissues, and organisms to improve basic understanding of cellular interactions, biological pathways, and their regulation. An improved ability to track cells in vivo will enhance our understanding of homing, engraftment, cell differentiation, and pathogenesis resulting from abnormal cells trafficking. Understanding the components and kinetics involved in biochemical reactions is key to evaluating and predicting the response of intact organisms to physiological and pathophysiological challenges and drug responses. Although our knowledge of the identity and quantity of proteins and complexes associated with reaction pathways in health and disease continues to advance, direct methods for imaging those reactions in intact systems are lacking. Development of appropriate tools to track cells, image the microvasculature, and image chemical activity in intact systems in real time will have broad applicability to many heart diseases, including myocardial ischemia and reperfusion injury, heart failure, and arrhythmias and lung diseases such as COPD, asthma, pulmonary hypertension, and sleep apnea. Similarly, new non-invasive cellular imaging modalities, capable of differentiating between normal and pathological states, would increase our understanding of the role of the microvasculature in sickle cell disease and thrombotic disorders. Contact: Dr. Lisa Schwartz Longacre, 301-402-5826, schwartzlongal@mail.nih.gov **06-HL-104 Develop nanotools for Pulmonary Medicine.** Pulmonary nanomedicine tools (mono- or multi-functional) would be of great value for inhalative delivery of encapsulated, controlled released payloads such as pharmaceuticals, gene therapy vectors, and bioactive molecules; detection of subclinical pathology; real-time, in vivo monitoring of injury/repair and treatment effects; and providing a scaffolding for engineered lung tissue. Targeted delivery methods made possible with nanotools should allow safer and more effective administration of life-prolonging drugs such as prostacyclines for pulmonary arterial hypertension, and nanotube-based scaffolds may allow reproduction of the complex microarchitecture required for regeneration of functional lung tissue. Contact: Dr. Robert Smith, 301-435-0202, smithra3@nhlbi.nih.gov **06-HL-105 Develop transgenic animal models that are informative for understanding chronic inflammation in humans**. Mouse models offer the advantage of being open to genetic manipulation and can provide data for hypothesis building and pilot intervention studies. Several complex models of inflammation relevant to heart, lung, and blood diseases have been developed, but their effect on the propensity to develop human diseases remains to be determined. Targeted research over short period of time in this area should lead to development of new animal models for chronic inflammation that are relevant to human pathology. Contact: Dr. Andrei Kindzelski, 301-402-0658, kindzelskial@mail.nih.gov **06-HL-106 Ensure a safe and adequate blood supply through the development of new processing technologies**. New technologies are needed to eliminate both the infectious and non-infectious complications of blood transfusion and thereby ensure a safe and adequate blood supply. Technologies such as pathogen inactivation/reduction should virtually eliminate transfusion risks from established threats such as HIV and hepatitis and most new or emerging infectious agents including bacterial contaminants. They should also reduce non-infectious complications such as transfusion-related immunomodulation. They and other approaches must be further developed for the treatment of all blood components and research is also needed to determine their safety and efficacy in ameliorating transfusion risks. Contact: Dr. Simone Glynn, 301-435-0078,

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	glynnsa@mail.nih.gov **06-HL-107 Develop new technologies to advance heart, lung, and blood research.** The development of new enabling technologies has the potential to significantly enhance diagnostics and therapeutics for heart, lung, and blood diseases. The delivery of drugs and nucleic acid-based therapeutics to disease targets can be significantly enhanced by strategies such as targeting to specific receptors, protection from nucleases and other enzymes, improvement of pharmacokinetics, and directing to the appropriate sub-cellular compartment. The ability to track cell delivery and survival to target tissues would facilitate the optimization of cell-based therapies. Improved surgical tools and procedures for minimally invasive surgery have the potential to decrease patient morbidity and mortality, and improve recovery time and quality of life for surgical patients. The ability to conduct quick and inexpensive assays of environmental risks would greatly enhance investigations of environmental causes of disease. Contact: Dr. Denis Buxton, 301-435-0513, db225a@nih.gov **06-HL-108 Develop new informatics techniques for integrative analysis of genomic and epigenomic data**. Much of the complex interplay between genetic and environmental risk factors for disease likely occurs through the interactive regulation of gene expression by both genotype and epigenetic markings of the genome. Epigenetic tags such as cytosine methylation and histone tail modifications, which modulate chromatin structure and function thereby affecting gene expression, are associated with environmental toxicities and are well documented. An integrated analysis of gene expression regulation, with simultaneous consideration of both genetic and epigenetic characteristics and of the interactions between these factors, is essential for understanding the complex pathobiology of chronic heart, lung, and blood diseases. New computational and informatics techniques are needed to allow such analyses. Contact: Dr. Robert Smith, 301-435-0202, smithra3@nhlbi.nih.gov **06-HL-109 Generate reagents for studying lung cell biology and disease progression**. Reagents for studying lung cell biology and disease progression are lacking. Examples include antibodies that recognize specific cells types, promoters that are expressed only in certain cell types and can be used in the generation of conditional knockout transgenic animals, and antibodies that recognize cell surface markers and can be used for FACS sorting different cell lineages in the airway. Such markers would be important not only for understanding the heterogeneity of lung cell types but are also for understanding cellular changes in the lung that emerge with lung disease. They may also be useful as surrogates for progression of lung disease and for dissecting cellular heterogeneity/function of lung cell types. Contact: Dr. Herbert Reynolds, 301-435-0222, hr72f@nih.gov **06-HL-110 Develop Lab on a Chip in Kit Form**. A sensitive nuclear magnetic resonance setup could easily take up a room. This challenge asks to build a small portable and automated device that can function as NMR by combining the NMR and MRI technology with all the advantages of the microfluidics chip. Such a device would enable the application of a metabolomics approach to many disease areas. Contact: Dr. Weiniu Gan, 301-435-0202, ganw2@nhlbi.nih.gov **06-HL-111 Develop devices and instruments for assessing and supporting assessment of pulmonary function in an ICU**. Despite major advances in biotechnology, research and development efforts directed at introducing new and innovative pediatric devices and instruments (of improving the existing ones) for use in

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	critically ill children have been limited. Technologies to assess tissue perfusion, pulmonary function (e.g., gas exchange, airway pressure, lung volumes, ventilation/perfusion ratios, and pulmonary arterial pressures) are needed. Also needing further development are improved systems for respiratory support of children, including non-invasive ventilation and nasal interface for nasal CPAP, improved methods of patient triggered ventilation and synchronization, and improved endotracheal and tracheostomy tubes to decrease nosocomial infection and reduce airleak and airway trauma. Contact: Dr. Carol Blaisdell, 301-435-0219, blaisdellcj@mail.nih.gov **06-LM-101*** **Intelligent Search Tool for Answering Clinical Questions.** Develop new computational approaches to information retrieval that would allow a clinician or clinical researcher to pose a single query that would result in search of multiple data sources to produce a coherent response that highlights key relevant information which may signal new insights for clinical research or patient care. Information that could help a clinician diagnose or manage a health condition, or help a clinical researcher explore the significance of issues that arise during a clinical trial, is scattered across many different types of resources, such as paper or electronic charts, trial protocols, published biomedical articles, or best-practice guidelines for care. Develop artificial intelligence and information retrieval approaches that allow a clinician or researcher confronting complex patient problems to pose a single query that will result in a search that appears to "understand" the question, a search that inspects multiple databases and brings findings together into a useful answer. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **06-LM-102*** **Self-documenting encounters**. Develop technologies, tools, and processes to achieve rapid and comprehensive electronic documentation of encounters with patients/research subjects. Clinicians & clinical researchers spend considerable time and effort in documenting clinical encounters (including using text to describe findings that are seen or heard) - often after the fact and with little immediate benefit to care of patients and clinical research subjects. Technologies and tools that could fully automate the capture of encounters and update electronic health records in real-time would support more effective and efficient health care and clinical research. Contact: Dr. Hua-Chuan Sim, 301-594-4882, simh@mail.nih.gov **06-MD-101*** **Development of Telehealth Tools to Promote Health and Connect At-Risk Youth to the Health System via Low-Cost, Mobile, and Wireless Technologies.** NCMHD is interested in the development of telehealth messages utilizing various forms of technology, aimed at high-risk youth as well as innovative culturally and linguistically appropriate media strategies for connecting at-risk youth with the healthcare system. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov; NIDA Contact: Dr. Jacqueline Lloyd, 301-443-8892, lloydj2@nida.nih.gov **06-MH-101** **Non-invasive technologies to map trajectories of axon bundles in the human brain.** Develop non-invasive technologies to demonstrate the locations and trajectories of axonal bundles in the living human brain. Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov **06-MH-102** **Technologies to study neuronal signaling, plasticity, and neurodevelopment.** Develop tools and technologies to study neuronal signaling, plasticity, and neurodevelopment. These can include new approaches, technologies, and reagents for structural and/or functional analysis of molecules and macromolecular complexes within brain cells at the resolution of single cells or sub-cellular components

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	(e.g. synapses, dendrites, nuclei). Priority given to new technologies that allow for repeated imaging of neuronal structure and/or function (e.g. dendritic spines, synaptogenesis, and axonal projections) in longitudinal, developmental studies and to non-invasive imaging approaches or technologies that directly assess neural activity, including imaging neuronal electrical currents, neurotransmitter changes and neuronal/glial cell responses to brain circuit activation. Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov **06-MH-103 New technologies for neuroscience research.** Develop technologies for neuroscience research that are software-based, (e.g., informatics tools, implementation of data analytic algorithms), hardware-based (e.g., instrumentation or devices), or biology-based (e.g., driven by conditional gene expression or bioactive agents). Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov **06-MH-104 Linking data resources with NIH's National Database for Autism Research (NDAR).** Link existing, significant data resources related to autism spectrum disorder with the NIH's National Database for Autism Research (NDAR). Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov **06-NS-101 Developing minimally invasive measures of neural activity.** Research in the nervous system is often limited by the inability to access the critical pathology. Major neurobiological breakthroughs have come on the back of technological advances. New technologies that enable neuroscientists to study important, but previously unmeasurable, aspects of neural activity and anatomy, gene expression, metabolism, protein distribution, specific cell-type distribution, etc. could lead to quantum leaps in neuroscience. Contact: Dr. Randy Stewart, 301-496-1917, rs416y@nih.gov **06-NS-102 Minimally invasive diagnostic and treatment tools.** Treatment and diagnosis of patients with neurological disorders is often limited by access to the neuro-pathology. Minimally invasive procedures that allow access to neuro-pathology for diagnostic, monitoring, or treatment with greater efficacy and decreased morbidity could significantly enhance neurological health. Contact: Dr. Joe Pancrazio, 301-496-1447, jp439m@nih.gov **06-NS-103 Breakthrough technologies for neuroscience.** Advances in basic neuroscience are often catalyzed by the development of breakthrough technologies that allow interrogation of nervous system function (e.g. patch clamp recording from single cells, optical imaging, multi-channel recording arrays, fluorescent dyes to image cell types and intracellular processes, etc.). The challenge is to develop new technologies with the potential to enable basic neuroscientists to make future quantum leaps in understanding nervous system development and function. Contact: Dr. Edmund Talley, 301-496-1917, talleye@ninds.nih.gov **06-NS-104 Developing and validating assistive neuro-technologies.** The burden of illness of neurological disorders could be reduced by enabling technologies that reduce functional disability in patients with severe motor or sensory loss. For example, these would include technologies that improve ambulation, upper extremity dexterity, swallowing, or neural control of prostheses. Contact: Dr. Naomi Kleitman, 301-496-1447, nk85q@nih.gov **06-NS-105 Importing important technologies into neuroscience.** The challenge is to capitalize on existing knowledge and technologies from other scientific disciplines (e.g.

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	applied physics, nanotechnology, cancer biology, and immunology) to catalyze progress in basic and clinical neuroscience (e.g. cell signaling or cell cycle control mechanisms in neurodegeneration, inflammation in neurological disease, epigenetics in neural development, etc.). Proposals will also be considered that seek to validate, in neurological systems, technologies originally developed for use in other biological systems. Contact: Dr. Joe Pancrazio, 301-496-1447, jp439m@nih.gov **06-NS-106 Validating new methods to study brain connectivity.** More complete understanding of the structure and function of human brain networks will be critical for answering many longstanding questions in neuroscience research. Toward this end, applications are invited for research efforts that will contribute to or facilitate coordinated approaches to map mammalian brain connectivity, including research to develop experimental, analytical or computational tools and methods. Contact: Dr. Edmund Talley, 301-496-1917, talleye@ninds.nih.gov **06-NS-107 Sensors to monitor neurologic function.** Clinical neuroscience research is often based on a small number of repeated assessments of neurological function, deterioration of which is associated with disease progression and functional disability. New sensor technologies that directly monitor and integrate patient function in real life, e.g. daily ambulation distance and speed, sway and falls, tremor, chorea, dysarthria, speech quality and output, sleep and drowsiness, absence seizures, would offer a completely new method of evaluating disease burden, response to therapeutic intervention, and adverse events. Contact: Dr. Debra Babcock and Dr. James Gnadt, 301-496-9964, dbabcock@ninds.nih.gov and gnadtjw@mail.nih.gov **06-OD(OBSSR)-101* Using new technologies to improve or measure adherence.** New and innovative technologies to improve and/or measure patient adherence to prescribed medical regimens and utilization of adherence-enhancing strategies in clinical practice would greatly enhance the health impact of efficacious treatments and preventive regimens. This challenge invites the development of new technologies to measure or improve patient adherence. Contact: Dr. Lynn Bosco, 301-451-4286, boscol@od.nih.gov; NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NHLBI Contact: Dr. Susan Czajkowski, 301-435-0406, czajkowskis@nhlbi.nih.gov; FIC Contact: Dr. Xingzhu Liu, 301-496-1653, liuxing@mail.nih.gov **06-OD-101* Development of new tools and technologies to interrogate human mitochondrial function *in vivo.*** These tools would include methods to manipulate human mitochondrial structure and activity, as well as novel imaging techniques to monitor and measure human mitochondrial function or dysfunction in healthy and diseased tissues. Contact: Dr. Phil Smith (NIDDK), 301-594-8816, smithp@mail.nih.gov; NIAAA Contact Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov **06-OD-102 Characterizing metabolites of microbes as a way to analyze how changes in microbiome relate to health and disease.** One of the aims of the NIH HMP is to find out how microbiome relates to health and disease. In addition to understanding the content of human microbiome, such as the microbial genes that encode the pathways of metabolites, it is important to understand the microbial metabolites both from dietary factors and endogenously produced substances and their relationship to disease. Additionally it will be important to understand how an individual's microbiome influences the metabolites that are formed. Contact: Dr. Jane Peterson (NHGRI), 301-496-7531, petersoj@mail.nih.gov.

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	06-OD-103 High throughput methods for growing unculturable microbes by providing nutritional requirements. Growing large quantities of microorganisms that are isolated from human bodies will enable further analyses in vitro. However some microorganisms are hard to grow *in vitro*. Identifying and then providing nutritional requirements is a way to grow these organisms. This will allow high throughput culturing of microorganisms. There have been a small number of preliminary research efforts in this area. A more focused effort in the next two years would facilitate human microbiome research and infectious diseases research. Contact: Dr. Jane Peterson (NHGRI), 301-496-7531, petersoj@mail.nih.gov **06-OD-104 Reconstituting metabolic pathways *in vitro.*** This will provide an in vitro system to understand how microbial metabolites affect human health. Contact: Dr. Jane Peterson (NHGRI), 301-496-7531, petersoj@mail.nih.gov **06-OD-105 Identification of chemical modulators of epigenetic regulators.** There are a limited number of pharmacological agents available to manipulate the *in vivo* activity of most epigenetic modifying enzymes, effector molecules, etc. High-throughput small-molecule screening strategies targeted at specific epigenetic regulatory molecules could identify chemical reagents targeting a broad range of epigenetic regulatory molecules. These high impact reagents have the potential to transform the way epigeneticists conduct *in vivo* disease research. Contact: Dr. Olivier Blondel (NIDDK), 301-451-7334, blondelol@mail.nih.gov **06-OD-106 Renewable affinity reagents for epigenomic research.** Chromatin immunoprecipitation (ChIP) and related techniques are dependent upon high quality polyclonal antibodies. A major challenge is that these reagents are available in finite quantity and are non-renewable. The development of recombinant affinity reagents specific for post-transcriptional histone modifications and/or epigenetic regulatory proteins would provide a renewable supply of these high-impact reagents sufficient to allow researchers across the country to standardize their ChIP experiments using identical affinity reagents. Contact: Dr. John Satterlee (NIDA), 301-435-1020, satterleej@mail.nih.gov **06-OD-107 Functional manipulation of epigenomic modifications.** Epigenomic analyses can reveal interesting differences between normal and diseased cell types. However a major challenge that remains is our limited ability to manipulate epigenetic modifications at a particular gene locus to prove that an epigenetic change leads to a functional change in chromatin structure and long term gene expression potential. The adaptation of existing technologies to enable functional manipulation of epigenetic changes would be a major advance in this area and have widespread implications for improving our understanding of epigenetic regulation. Contact: Dr. John Satterlee (NIDA), 301-435-1020, satterleej@mail.nih.gov **06-OD-108 *In vivo* Epigenetic Imaging Reagents.** Although epigenomic changes appear to be important in many diseases, disease diagnosis may be quite challenging if epigenomic analysis of tissues that are not readily accessible (brain, heart, etc) is required. The development of compounds that would allow in vivo imaging of epigenetic modifying enzymes, effector molecules, epigenetic marks, etc. could lead to the development of entirely new non-invasive diagnostic strategies. Contact: Dr. John Satterlee (NIDA), 301-435-1020, satterleej@mail.nih.gov **06-OD-109 3D Tissue High Throughput Screening Platforms.** Engineered three-dimensional human tissue models are needed to rapidly evaluate, with high fidelity, the

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	safety and efficacy of drug candidates in a cost-effective manner. A critical challenge is to make a modular three dimensional tissue system that can accommodate multiple tissue types compatible with high throughput screening platforms. Contact: Dr. Rosemarie Hunziker (NIBIB), 301-451-1609, hunzikerr@mail.nih.gov **06-OD-110 Protein Capture Reagents.** The challenge is to generate diverse small molecules that specifically or selectively recognize, bind and "capture" human proteins or that distinguish among the natural variants [splice variants, co-and post translational modifications (by glycosylation, phosphorylation, acylation, oxidation, etc.] of a single protein. Contact: Dr. Dan Gallahan (NCI), 301-496-8636, gallahad@mail.nih.gov **06-OD-111 Mathematical and/or computational models of health-relevant behaviors.** The challenge is to bridge mathematical and computational science with behavioral/social science and health to model changes in health relevant behaviors or social processes that occur over time. Projects could focus on individual or groups, healthy individuals or populations who later become ill, health care providers, or organizations. Contact: Dr. Lisa Onken (NIDA), 301-443-2235, lonken@mail.nih.gov **06-OD-112 Novel technologies to enable simultaneous measurement of behavioral and biological variables.** Existing technologies such as imaging probes, noninvasive techniques, or robotics may be adapted for this purpose. These technologies will foster interdisciplinary approaches to the analysis of the interaction between health and behavior. Contact: Dr. Lisa Onken (NIDA), 301-443-2235, lonken@mail.nih.gov **06-OD-113 New technologies to measure, diagnose, or predict behavioral or psychiatric disorders.** The challenge is to improve measures and/or diagnostic indicators of behavioral phenotypes that combine behavioral, emotional, cognitive, or social indices with biological markers. These tools are necessary for interdisciplinary analyses of the biological basis of behavioral/psychiatric disorders. Contact: Dr. Lisa Onken (NIDA), 301-443-2235, lonken@mail.nih.gov **06-OD-114 Technology to integrate video data with large scale survey data.** These technologies must protect participant confidentiality and permit qualified parties to analyze the data. These technologies will require collaboration between experts in social/behavioral sciences, information technologists, computer engineers, and videographers. Contact: Dr. Lisa Onken (NIDA), 301-443-2235, lonken@mail.nih.gov **06-RR-101* Virtual environments for multidisciplinary and translational research.** Virtual networking environments like Science Commons, Facebook, and Second Life, create platforms that can eliminate many barriers in scientific collaborations. These environments integrate fragmented information sources, enable "one-click" access to research resources, and assist in re-use of scientific workflows. Funded projects would develop and implement virtual collaborative environments to facilitate biomedical and translational research, e.g. addressing issues of privacy, technology transfers, and sharing resources. Contact: Dr. Olga Brazhnik, 301-435-0758, brazhnik@mail.nih.gov; NIDA Contact: Dr. David Thomas, 301-435-1313, dthomas1@nida.nih.gov **06-RR-102* Infrastructure for biomedical knowledge discovery.** Biomedical research depends on heterogeneous data of varying reliability that are increasingly multimedia and high-dimensional. Recent advances in web technologies enable discovery and aggregation of disparate data on specified topics, visualization and navigation of complex and abundant data, extraction of concepts from text, and detection of

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	associations. Funded projects would coalesce the most effective information technologies with domain specific knowledge structures and data processing and to create computational infrastructures for integrated, customizable access to biomedical data. Contact: Dr. Olga Brazhnik, 301-435-0758, brazhnik@mail.nih.gov

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(07) Enhancing Clinical Trials	**07-AG-101 Validating NIH Neuroscience Blueprint Toolbox assessments.** Validation of NIH Toolbox assessments in multiple clinical populations (AD, ADHD, PD etc.) by leveraging currently funded NIH clinical studies. Contact: Dr. Molly Wagster, 301-496-9350, WagsterM@mail.nih.gov **07-AG-102 Biological samples in the NIH Neuroscience Blueprint Toolbox.** Collection, genotyping and archiving of biological samples in n=5800 national random sample (ages 3 - 85 years) used in the NIH Toolbox assessment norming, including a 12 month longitudinal reassessment of the national sample. Contact: Dr. Molly Wagster, 301-496-9350, WagsterM@mail.nih.gov **07-AG-103 Development of methodologies and scientific tools for improving and/or assessing the external validity of randomized clinical trial (RCT) results to known populations.** The practice of conducting RCTs with volunteer samples recruited from patients in clinical or community settings limits the generalizability of results, a critical problem for comparative effectiveness research. Research is needed to develop scientific tools for improving and/or assessing the external validity of RCT results to known populations, including methods for applying probability sampling in the identification and recruitment of RCT participants, measuring biases in RCT participant pools, and accounting for such biases in the analysis of RCT results. Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **07-AG-104 New and innovative technologies to monitor patient behaviors and clinical status in clinical trials.** Develop and test new affordable, technologies to enable remote, centralized monitoring of physiologic, behavioral and neurologic indices as well as study medication compliance, and adverse effects in clinical trials. These technologies should provide opportunities to enhance efficiency in clinical trials, as well as to collect more “real life” data. Contact: Dr. Sergei Romashkan, 301-435-3047, romashks@nia.nih.gov **07-AR-101 Modeling Clinical Trials in Rheumatic, Skin and Musculoskeletal Diseases**. Promote the development of computer models to assess the influence of prevention and treatment strategies on outcomes and cost effectiveness in common chronic diseases (e.g., osteoarthritis, psoriasis, rheumatoid arthritis and osteoporosis). Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-AR-102 Expanding the Use of Alternative Trial Design in Clinical Trials of Rare Diseases of Connective Tissue, Muscle, Skin and Bone.** Owing to the unique nature and limited availability of patients with rare diseases, large traditional clinical trials are often not possible. The objective is to propose novel trial designs that not only capture the scientific and statistical rigor necessary to draw meaningful conclusions from the trial once complete, but are able to accommodate and adapt as necessary to the challenges posed by the study of patients with these diseases. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-AR-103 Expand The Involvement Of Clinical Practice Physicians In Community Settings, In Large-Scale Trials in Chronic Musculoskeletal and Skin Diseases**. Efficacy and Effectiveness studies in common chronic diseases often require a large number of patients that are not always followed at large clinical centers. Rare diseases are often hampered by the difficulty in recruiting patients in a timely and cost effective way. The objective is to develop mechanisms that facilitate and accelerate the

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	integration of clinical practices in the organization and implementation of clinical and community based interventions and prevention programs. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-AR-104 Develop Central IRB Approval Processes For Existing Clinical Research Networks.** An IRB managed by one institution which reviews all multicenter trials conducted by a collaborating network could potentially provide a higher standard of review with greater efficiency and shorter turn around times. This can potentially decrease trial costs and duration significantly. The goal is to develop stringent but dynamic Central IRB policies and procedures and standardize their deployment for clinical studies in chronic skin, rheumatic and musculoskeletal diseases conducted by established networks. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-CA-101* Novel Agents for Cancer Treatment.** Initiate early phase clinical trials of novel agents in three areas: 1) targeting the tumor stem cell by evaluating the sonic hedgehog smoothened antagonist, GDC-0449, and the pan-notch inhibitor, RO4929097, in collaboration with Genentech and Roche, respectively, in trials of breast, lung, colon, leukemia and ovarian cancer; 2) testing Anti-IGFR-1 Monoclonal Antibody IMC-A12 (ImClone) in pediatric tumors such as rhabdomyosarcoma, osteosarcoma, and neuroblastoma, as well as studies in breast, small cell lung, adrenocortical and pancreatic cancer; and 3) testing PARP inhibitor ABT-888 in breast, ovarian, and pancreatic cancer. Contact: Dr. Jeff Abrams, 301-496-2522, abramsj@mail.nih.gov **07-DA-101 Enhancing medications development for drug addiction treatment by addressing the increasing complexity of designs, increasing costs, and regulatory hurdles of clinical trials.** NIDA is soliciting grant applications focusing on strategies to enhance the success of clinical trials of medications for the treatment of drug addiction. Applications may focus on improving the design, implementation, data management, data analysis, and/or treatment outcomes to increase the chances of obtaining NDA approvals. Approaches and goals may involve but shall not be limited to the use of new technologies, electronic data capture, web-base data transmission, real-time data collection, biomarker electronic monitoring, adaptive clinical trial designs, early identification and management of safety concerns, and improvement of subject recruitment and retention in clinical trials. Contact: Dr. Ivan D. Montoya, 301-443-8639, Imontoya@mail.nih.gov **07-DA-102 Development of methodologies and scientific tools for improving and/or assessing the external validity of randomized clinical trial (RCT) results to known populations.** Typically, participants in NIDA's RCTs are volunteer patients with substance abuse disorders who are seeking treatment. The fact that these patients are not randomly selected, and are recruited from non-randomly selected clinical or community settings limits the generalizability of results, a critical problem for comparative effectiveness research. Research is needed to develop scientific tools for improving and/or assessing the external validity of RCT results to known populations, including methods for applying probability sampling in the identification and recruitment of RCT participants, measuring biases in RCT participant pools, and accounting for such biases in the analysis of RCT results. Contact: Dr. Paul G. Wakim, 301-402-3057, pwakim@nida.nih.gov and Ms. Debbie Grossman, 301-443-2249, Dg79a@nih.gov and Dr. Belinda Sims, 301-402-1533, bsims@nida.nih.gov **07-DA-103 Development of methodologies and scientific tools for improving and or assessing the external validity of randomized clinical trial (RCT) results to known**

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	populations. Develop a strategy utilizing existing data from substance abuse clinical trials to identify and compare the evaluation period and methodology utilized for measuring primary outcome success. Consideration should be given to both the achievement and duration of success and the optimal measurement strategy for treatment success. Explore long-term outcomes of study participants and patients in treatment to determine how the short term outcome correlates to long term results. Contact: Ms. Michele M. Straus, 301-443-8888, mstraus@nida.nih.gov **07-DA-104 Development of methodologies and scientific tools for improving and/or assessing the external validity of randomized clinical trial (RCT) results to known populations.** Often in substance abuse and HIV/AIDS research, potential participants are involved with the criminal justice system and minority groups are overrepresented; frequently they are either excluded from the studies or included in such a way that their data cannot be collected in a systematic manner. Research is needed for assessing the impact of exclusion/missing data and the external validity of RCT results to this important group of individuals with substance abuse problems and criminal justice involvement. Contact: Carmen L. Rosa, M.S., 301-443-9830, crosa@nida.nih.gov **07-DA-105 Enhanced Technologies to Monitor Illicit Drug Use Behaviors in Clinical Trials.** To develop and validate new and innovative technologies that may improve the validity and reliability of data collected on illicit drug use behaviors in clinical trials. Applications may involve but are not limited to the use of technologies to enhance the quality of the report of illicit drugs and associated behaviors such as drug craving and withdrawal as well as adverse events and concomitant use of medications by participants in clinical trials. Contact: Dr. Ivan Montoya, 301-443-8639, imontoya@mail.nih.gov **07-DA-106 Impact of drug abuse treatments on quality of life.** Research to determine the impact on quality-of-life of medications and other interventions employed to treat drug abuse, particularly in the stimulant abuse area. Validation of existing measures and techniques, and to encourage the development, improvement and/or adaptation of instruments that measure quality-of-life and cost-effectiveness of treatments employed in drug abuse research. Contact: Dr. Ivan Montoya, 301-443-8639, imontoya@mail.nih.gov **07-DE-101 Enhancing Clinical Trials:** Data capture in clinical trials is costly and time-consuming, and subject adherence can be difficult to monitor. **Goal**: Improvement of methods to enhance automated full capture of oral health status and dentist-patient interactions would greatly benefit clinical trials for oral diseases, oral health research and practice-based research conducted in private dental practice settings. This would include affordable technologies to enable: remote capture of oral health measures, study medication compliance and adverse event monitoring. Contact: Dr. Jane Atkinson, 301-435-7908, Jane.Atkinson@nih.gov **07-DK-101 Enhancing clinical trials in diabetes, obesity, and metabolic, endocrine, digestive, liver, renal and urological diseases.** Translation of new research developments from the laboratory into clinical practice requires the development of tools to facilitate the conduct of phase 3 clinical trials. This could include, but is not limited to, the development of 1) new statistical methodologies, including computer programs, to enhance data analysis and evaluate cost-effectiveness; 2) computer simulations to design trials and evaluate the implications of different designs; 3) predictive alogorithms or markers of disease development or progression, or response to therapy; 4) improved, non-invasive imaging tests; 5) instruments to assess behavior, adherence, processes of care and quality of life; and 6) registries or other infrastructure to enhance recruitment and retention of

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	subjects. Proposals to develop resources should include a long-term plan for sustainability of the resource once funding has ended. Contact: Dr. Elizabeth Wright, 301-402-8729, wrightel@mail.nih.gov **07-DK-102 New and innovative technologies to monitor patient adherence in clinical trials of NIDDK interest.** Develop and test new affordable, technologies to enable remote, centralized monitoring of physiologic and behavioral indices, as well as study medication adherence, and adverse effects in clinical trials. These technologies should provide opportunities to enhance efficiency in clinical trials. They should also be useful for future applicability to medical care in a non-trial setting, and may lead to enhanced chronic disease self-management. Contact: Dr. Marva Moxey-Mims, 301-594-7717, moxeymimsm@mail.nih.gov **07-DK-103 Support for Registries.** Develop an infrastructure for rare disease registries in areas of NIDDK mission, showing the feasibility of populating such a registry, and developing a long-term plan for sustainability of the registry beyond the 2 year funding period. Establishment of comprehensive registries with well-characterized patients, that may include samples of urine, serum, biopsy / surgical tissue, radiographs. Contact: Dr. Marva Moxey-Mims, 301-594-7717, moxeymimsm@mail.nih.gov. **07-DK-104 Assessing cost effectiveness of discrete interventions in clinical trials of diseases in NIDDK mission.** Develop methods for incorporating data regarding health care utilization of enrolled subjects into study data sets such that analyses of cost effectiveness of interventions can be undertaken. Such an approach can be undertaken in existing multi center trials by incorporating new projects that would rigorously collect all healthcare utilization data on enrolled participants. Contact: Dr. Marva Moxey-Mims, 301-594-7717, moxeymimsm@mail.nih.gov **07-DK-105 Develop innovative technology for the diagnosis and treatment of diseases of NIDDK interest, including luminal disease of the alimentary system.** Examples include: Develop and validate a method to perform “molecular” biopsy of luminal abnormalities in real time; Develop improved instrumentation for therapeutic endoscopy; Develop improved virtual endoscopy technology to access the luminal space of the GI tract; Develop new PET tracers for clinical use, including markers of proliferation, tumor-specific antigens, and markers of apoptosis and inflammation; Develop intraoperative high-energy gamma and beta detectors to enhance intraoperative localization; Develop energy delivery and real-time tracking devices to optimize local image-guided interventions; Develop improved devices for facilitating single port laparoscopic procedures, intraluminal procedures, natural orifice surgeries, and robotically assisted procedures. Contact: Dr. Frank Hamilton, 301-594-8877, hamiltonf@mail.nih.gov **07-EB-101 Enhancing Multi-Site MR Imaging Studies.** Translating the full potential of MRI/MRS into future benefits for multi-site clinical trials requires a framework that standardizes data acquisition and data processing across imaging platforms and centers. The NIH invites proposals that develop novel approaches for standardizing MRI approaches used in multi-site clinical studies. Contact: Dr. Guoying Liu; 301-594-5220; liug@mail.nih.gov. **07-EY-101* Cost Effectiveness/Quality of Life: Tools to assess the impact of interventions on quality-of-life and cost effectiveness of ophthalmic treatments.** Fostering interdisciplinary collaboration with specialties such as health outcomes, economics, genetics, statistics, and clinical and bench science is needed to develop and

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	improve instruments that measure the effect of ophthalmic treatments on the patient's quality-of-life and cost-effectiveness. Such teams could be used develop tools to evaluate and influence patient adherence with effective treatments in order to improve outcomes. Contact: Dr. Natalie Kurinij, 301-451-2020, kurinijn@mail.nih.gov **07-NS-101* Developing technology to increase efficiency and decrease cost of clinical trials.** Clinical trials are becoming increasingly expensive, and many US patients are unwilling to enroll, which has led to delays in trial completion and further cost increases. The challenge is to develop and test affordable, technologies to enable remote, centralized monitoring of physiologic, behavioral and neurologic indices as well as study medication compliance, and adverse effects in clinical trials. These technologies should provide opportunities to enhance efficiency in clinical trials, as well as to collect more "real life" data. Contact: Dr. Emmeline Edwards, 301-496-9248, ee48r@nih.gov; NIAAA Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **07-OD(OBSSR)-101* Improving and/or assessing external validity in randomized clinical trials (RCTs).** The practice of conducting RCTs with volunteer samples recruited from patients in clinical or community settings limits the generalizability of results, a critical problem for comparative effectiveness research. Research is needed to develop scientific tools for improving and/or assessing the external validity of RCT results to known populations, including methods for applying probability sampling in the identification and recruitment of RCT participants, measuring biases in RCT participant pools, and accounting for such biases in the analysis of RCT results. Contact: Dr. Ronald Abeles, 301-496-7859, abelesr@od.nih.gov; NIAAA Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov; NHLBI Contact: Dr. Peter Kaufmann, 301-435-2467, kaufmannp@nhlbi.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055,NIAMShelp-NIHChallengeGrants@mail.nih.gov **07-OD(ORDR)-101* Library of standardized patient registry questions.** Develop standardized questions and data elements that can be used when developing rare diseases patient registries. Having a standardized library of data elements will enable cross-indication analyses of patient populations, speed the development and deployment of patient registries, and allow registries to exchange and aggregate patient registry data. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov **07-OD(ORDR)-102* Rare disease genetic patient registry.** Support for an efficient infrastructure and expert staff in developing a registry capable of asking for rare-disease-specific information and capturing genetic results across any number of rare diseases, thereby ensuring patients are identified for trials as treatments become available. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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(08) Genomics	**08-AA-101 Inflammation and Alcoholic Liver Disease.** Research is sought to study the relationship between alcoholic liver disease and gene polymorphisms affecting theTLR4 signaling complex (e.g., TLR4, MD2, and LBP) and pro- and anti-inflammatory cytokines, chemokines and their receptors. Understanding of genetic variations of these key inflammatory factors and their association to the susceptibility to alcohol-related diseases will provide a basis for better diagnosis and optimal design of treatment options. Contact: Dr. Joe Wang, 301-451-0747, Wangh4@mail.nih.gov **08-AA-102 Genome Wide Association Studies of Alcohol Dependence.** The genetic contribution to the development of alcohol dependence has been established by twin, adoption and family studies. In addition, environmental factors play a major role in the development of this disorder. Genome Wide Association Studies (GWAS) provide a powerful approach to pinpointing the genes or gene variants that contribute to risk for developing the disorder. However, GWAS requires a large and well-characterized sample. This initiative will provide two-year funding for genotyping and data analysis of existing samples of complex behavioral disorders, including alcohol dependent subjects and matched controls that are suitable for GWAS. Contact: Dr. Abbas Parsian, 301-443-5733, parsiana@mail.nih.gov **08-AA-103 Collaborative Cross for Phenotyping of Behaviors.** The impact of genes on behavior has been established and shown to significantly influence susceptibility to mental health disorders and other behaviors such as those that influence risk for alcohol dependence. Current approaches have localized chromosome regions, or quantitative trait loci (QTL), that are associated with increased risk for alcohol dependence. However, within these QTLs there are numerous potential genes and it remains unclear which ones(s) is responsible. Research is sought to develop mouse lines with increased genetic variability and complexity, more similar to humans, and to perform behavioral phenotyping on these animals to identify the specific genes contributing to physiological or behavioral disorders, including those associated with risk for alcoholism. Contact person: Dr. Lindsey Grandison, 301-443-0606, lgrandis@mail.nih.gov **08-AA-104 Regional Central Nervous System (CNS) Gene Expression.** Response to an environmental challenge or to alcohol exposure results in significant changes in gene expression that leads to neuroadaptation. Recent advances in microarray technology allow rapid and widespread characterization of regional changes in gene expression in brain areas such as the Bed Nuclei of the Stria Terminalis (BNST), prefrontal cortex, raphe nucleus, as well as CNS areas commonly involved in alcohol abuse. Research is needed to fully characterize the gene expression profile in response to stress or alcohol to permit identification of responsive gene networks that mediate the change in behavior. Such studies would be a valuable resource for determining the impact of stress on alcohol related behaviors, reward sensitivity and neurocircuitry of consumption. Subsequent gene network analysis would permit identification of the genes involved in orchestrating behavioral response. Contact: Dr. Lindsey Grandison, 301-443-0606, lgrandis@mail.nih.gov **08-AA-105 Epigenetic regulation of synaptic adaptation in alcohol dependence, withdrawal and relapse.** Alcohol dependence involves complex synaptic remodeling with associated changes in receptor trafficking, local mRNA translation, protein turnover, and gene expression. Increasing evidence suggests that stable gene expression and synaptic structure and function changes associated with drug and alcohol addiction are mediated in part by epigenetic mechanisms. This initiative encourages 2-year projects to: 1) determine the role of epigenetic factors in regulating synaptic plasticity and adaptation; and 2) identify

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	genes under epigenetic control in acute and chronic alcohol exposure. Such research is expected to reveal molecular substrates mediating long-term synaptic changes in the brain that underlie alcohol addiction and relapse, and inform potential therapeutic targets to block the transition to, or even reverse, the alcohol dependent state. Contact: Dr. Qi-Ying Liu, 301 443-2678, liuqiy@mail.nih.gov **08-AA-106 Genome Wide Association Studies of Drinking Patterns and the Etiology of Alcohol Problems.** There are many well-characterized populations from studies which have or are still collecting information about drinking patterns and the etiology of alcohol problems including abuse and dependence. These studies include both prospective studies with children and adolescents as well as studies of adults that have been followed for many years. Projects could collect DNA from individuals in these studies and conduct gene association studies among subgroups of these individuals to expand understanding of genetic and environmental contribution to drinking patterns. Contact: Dr. Marcia Scott, 301-402-6328, mscott@mail.nih.gov **08-AG-101* Genetic factors affecting rates of change in disease risk factors with age.** Human aging is associated with an increase in the levels of numerous chronic disease risk factors, but the rates at which these factors increase with age varies considerably among persons. There is evidence that genetic factors influence rates of age-related change, but there have been few studies to identify specific factors. The identification of genetic factors which protect against such adverse aging changes could contribute significantly to the development of interventions for healthier aging. The recent acquisition of genome-wide SNP data from several large long-term longitudinal studies provides the opportunity to identify genes affecting rates of change of important risk factors efficiently by analyzing phenotype data collected on individuals over decades, combined with information from the SNP scans. Such genes could also be identified by other approaches, such as linkage analyses and studies of rare variants in candidate genes. Proposals for analyses to identify relationships of specific genetic factors to rates of change with age in phenotypes measured in longitudinal studies of young, middle-aged, or older populations are encouraged. Contact: Ms. Winifred Rossi, 301-496-3836, rossiw@mail.nih.gov **08-AG-102 Epigenetic changes**. Identification of epigenetic changes that are specifically associated with age-related neurodegenerative diseases. Contact: Dr. Suzana Petanceska, 301-496-9350, PetanceskaS@mail.nih.gov **08-AG-103 Environmental factors**. Identification of environmental factors that are associated with age-related neurodegenerative diseases and disorders and the influence of these environmental factors on the properties and function of the relevant nervous system. Contact: Dr. Suzana Petanceska, 301-496-9350, PetanceskaS@mail.nih.gov **08-AG-104 Genetic and epigenetic predictors of symptom severity.** Support research on the genetic underpinnings of symptom severity, and identify individuals at greatest risk for symptoms from both acute and chronic conditions. Design individualized interventions that will maximize symptom management. Contact: Dr. Susan Nayfield, 301-496-6949, NayfielS@mail.nih.gov **08-AG-105 Approaches to study the interactions among individual behaviors, social and physical environments, and genetic/epigenetic processes during critical developmental periods.** Research is needed to develop analytic methods, systems science approaches, or computational models designed to address the interactions among

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	individual behaviors, social and physical environments and genetic/epigenetic processes during critical developmental periods and over time. Contact: Dr. John Haaga, 301-496-3131, haagaj@mail.nih.gov **08-AG-106 Cross-disease research to identify commonly targeted pathways or mechanisms between low incidence, neurogenetic disorders with high incidence, population-based disease.** Progress in treating many common neurological and neurobehavioral disorders has been hindered by the complex genetics and heterogeneous etiologies of these disorders. However, analyzing related or clinically overlapping Mendelian disorders or studying rare genetic variants of large effect can yield unique biological insight into the mechanisms underlying common disease. Focus on studies that dissect pathways common to simple and complex genetic disorders, with the goal of identifying potential therapeutic targets. Contact: Dr. Steven Snyder, 301-496-9350, snyderd@mail.nih.gov **08-AG-107 Approaches to study the interactions among individual behaviors, social and physical environments, and genetic/epigenetic processes during critical developmental periods.** Research is needed to develop analytic methods, systems science approaches, or computational models designed to address the interactions among individual behaviors, social and physical environments and genetic/epigenetic processes during critical developmental periods and over time. Contact: John Haaga, 301-496-3131, haagaj@mail.nih.gov **08-AG-108 Technology and resources for high-throughput functional analysis of functional elements in genomic sequences.** Develop robust, high-throughput methods to carry out functional assays to determine whether and how putative functional elements (e.g., genes and regulatory sequences) operate to determine cell states in development, health, and disease. Such new methods should include both cellular and whole organism methods to allow systematic analysis of the effects of both genetic (normal variation and mutation) and environmental perturbations, and should include methods for both molecular (transcriptomic, proteomic) analysis and high-throughput phenotyping. Contact: Dr. Anna McCormick, 301-496-6402, mccormia@nia.nih.gov **08-AG-109 Identifying causal genetic variants associated with heart, lung, and blood diseases.** Utilize application of targeted DNA capture and massively parallel sequencing technologies followed by selective genotyping of DNA samples from large well-phenotyped populations. Two applications of this approach are needed: (a) targeted resequencing of entire chromosomal regions already known from GWAS findings to be strongly associated with disease, and (b) disease or other clinical trait-based exome-wide resequencing for the unbiased discovery of rare variants having large effects. Contact: Ms. Winifred Rossi, 301-496-3836, rossiw@mail.nih.gov **08-AI-101 Explore the utilization and integration of available "omic" datasets to assess pathogen-host biological networks:** Challenge Grant studies in this area can facilitate alternative and innovative approaches for the development of new prevention and therapeutic options. Contact: Dr. Valentina Di Francesco, 301-496-1888, difrancesco@mail.nih.gov **08-AR-101 Genotyping of Existing Cohorts in Rheumatic, Skin, and Musculoskeletal Diseases**. These studies will utilize existing clinical cohorts to add to the broadly shared data resources available to genetic researchers. The immediate result of the work will be the submission of large genotype-phenotype datasets to the database of

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	Genotypes and Phenotypes (dbGaP) (http://www.ncbi.nlm.nih.gov/sites/entrez?db=gap). This is expected to allow the submitting investigators and others to pursue analytical projects that will identify genetic loci contributing to disease risk. The datasets will also provide a testing ground for new methodological approaches for the identification of genetic risk factors. Medical sequencing and replications studies are included, but recruitment of new cohorts is not**.** Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **08-AR-102 Gene Environment Interactions in Autoimmune Disease**. Explore the contribution and mechanisms mediating the contribution of gene-environment interactions in autoimmune disease onset and progression. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **08-CA-101* Augmenting Genome-Wide Association Studies.** Genome-wide association studies (GWAS) represent the starting point for a variety of experimental and epidemiological approaches designed to identify the functional gene variants and gene-environment interactions that increase or decrease the risk of cancer, and may thus provide new insights into risk prediction as well as preventive and therapeutic interventions. Linking genomic and molecular alterations within tumors (the Applied Molecular Pathology Lab and the Cancer Genome Atlas) with the germline variants uncovered by GWAS will further catalyze downstream biological research, and speed the translation of genomic discoveries into clinical practice. Furthermore, studies of the "dark matter" in the human genome that are not captured by the SNP-based GWAS (e.g., structural and rare gene variants, micro-RNAs, and epigenetics) are needed to fully understand the inherited component to cancer. Contact: Dr. Daniela Gerhard, 301-451-8027, Daniela.Gerhard@nih.hhs.gov **08-CA-102 The Role of Gene-Environment Interactions in Cancer Health Disparities Research.** Minority and underserved communities usually depict higher incidence and mortality rates for a number of different cancers (e.g. breast and prostate). Most research in this area have focused on the social factors that lead to these disparities, however, racial or ethnic disparities in cancer cannot be explained by poverty, access to healthcare or behavior alone. Understanding the etiology of cancer requires the knowledge of how the social and physical environments affect biological pathways/processes at a molecular level. This presents one of the most challenging issues in health disparity research. Studies are needed to delineate how the social/physical environment interplay with biology to affect genetic pathways or mechanisms that contribute to cancer disparities and to help create interventions that would eliminate/reduce them. Contact: Dr. Damali Martin, 301-451-1956, Damali_martin@nih.gov **08-CA-103 Micro-RNAs in Cancer.** MicroRNAs are recently identified small non-coding RNAs that have been shown to be both ubiquitous in the mammalian genome but also exerting control over many cancer genes and processes. New technologies and informatics tools are needed to survey the micro-RNAs in cancer and their role in its development. Contact: Dr. Chamelli Jhappan, 301-435-1878, jhappanc@mail.nih.gov **08-CA-104 Regulatory functions of small RNAs.** Recent genome wide expression studies have revealed the existence of small RNAs, transcribed from nearly all genes in both the sense and antisense orientation from promoters. The role of these small RNAs in normal and aberrant gene regulation remains is not known. Research is needed to understand their control and function in normal and cancer cells. Contact: Dr. Chamelli

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	Jhappan, 301-435-1878, jhappanc@mail.nih.gov **08-CA-105 Development of a project that evaluates tumors that do not qualify for TCGA or TARGET.** This includes the expansion of TCGA and TARGET to include tumors that are either too small (physically) to make it possible to isolate sufficient RNA and DNA for analysis or are so rare that a statistically significant number of samples can be obtained for characterization under these programs. These "orphan tumors" will miss the genomic revolution as it is applied to other cancers. Methods for the genomic characterization of these tumors exists however, there is no funding to include them in these projects. Expansion of TCGA and TARGET to include these is critical to a comprehensive identification of diagnostic and therapeutic targets as well as understanding the basic biology of these tumors. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **08-CA-106 Development of methods for the validation of gene discoveries as they relate to cancer.** This includes high throughput methods for validation of targets and the analysis of these data. This may be cellular based approaches to validation. The key is high throughput capacity. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **08-CA-107 Bioinformatic pipeline for rapid genomic analysis.** Development of bioinformatics tools and analytical pipelines that will significantly decrease the amount of time it takes to analyze data from TCGA, TARGET and other high throughput projects. Contact: Dr. Joseph Vockley, 301-435-3881, vockleyj@mail.nih.gov **08-CA-108 Genomic changes introduced by Biospecimen Pre-Analytical Variables.** Normal human tissues are needed for studies that seek to understand early development of disease. The human biospecimens that form the basis of medical research are collected, processed and stored under very different, non-standardized methods in multiple institutional settings. The molecular changes induced by these pre-analytical biospecimen variables can significantly confound research studies. New biospecimen research is needed to better understand the contribution of biospecimen pre-analytical variables to molecular profiles. Potential topics may include: 1) How do differences in methods for obtaining normal human tissues affect resulting molecular profiles?; 2) How does post-mortem interval affect the molecular integrity of different tissues?; 3) How do differences in methods for obtaining normal human tissues affect resulting molecular profiles?; 4) How does post-mortem interval affect the molecular integrity of different tissues? Contact: Dr. Helen M. Moore, 301-496-0206, moorehe@mail.nih.gov **08-CA-109 Genome-wide Association Studies in Cancer Prevention.** The multi-step, multi-factorial process of carcinogenesis involves mutations in oncogenes, or tumor suppressor genes, as well as the influence of environmental factors. In addition, common DNA polymorphisms in low penetrance genes have also emerged as genetic factors that seem to modulate an individual's susceptibility to malignancy. Genetic studies, which lead to a true association, are expected to increase understanding of the pathogenesis of each malignancy and to be a powerful tool for prevention and prognosis in the future. Here, we propose integrating such genomic approaches in existing clinical and translational research portfolio and utilization of existing DCP biospecimen resources to promote genome wide association and also gene-environment interactions as they apply to prognostic and diagnostic opportunities in cancer prevention research. Contact: Dr. Asad Umar, 301-594-7671, Asad.Umar@nih.gov

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	08-CA-110 Human Proteome Atlas (HPA). This genomic-centric approach will focus on chromosomes that have been fully mapped and implicated in diseases. This way the proteomic mapping of known genomic aberrations will be able to lead the development of functional assays that could be employed in disease detection. Contact: Dr. Sudhir Srivastava, 301-435-1594, srivasts@mail.nih.gov **08-CA-111 Proteomics programs for Cancer Prevention and Early Detection.** Foster new technology to rapidly detect proteins in the serum, urine, saliva, and other accessible fluids/cells for the purpose of identifying high risk cohorts for prevention trials and possible surrogate endpoints for Phase II Trials. It would also fund some back validation from trials where samples are available and outcomes known. Contact: Dr. Vernon Steele, 301-594-0420, vs1y@nih.gov **08-CA-112 Identifying Noncoding RNA Targets for Cancer Early Detection and Prevention.** The objective of this funding opportunity is to promote research on microRNAs (miRNAs) and other small noncoding RNAs (ncRNAs) in preneoplastic lesions, examine the usefulness of these RNAs to predict progression to cancer and determine whether ncRNAs in body fluids can be used for early cancer detection. The purpose of this initiative is to promote research on the discovery and characterization of ncRNAs in preneoplasias and early stage cancers to (1) improve early cancer detection, intervention, and prevention, (2) predict risk of progression from preneoplasia to cancer, and (3) distinguish benign lesions from precancerous lesions. Contact: Dr. Sudhir Srivastava, 301-435-1594, srivasts@mail.nih.gov **08-CA-113 Enhance genomic studies with social determinants of disparities.** Genomic studies to study disparities need to include social determinants of disparities, such as SES, access to care, cultural issues, and environmental data, to give context to the genetic factors for disease. Using multidisciplinary teams within a community-based participatory research framework, these studies will integrate the genomic data with the social determinants to gain a fuller understanding of how these factors can affect cancer health disparities. Contact: Dr. Ken Chu, 301-435-9213, chuk@dcpcepn.nci.nih.gov **08-CA-114 Genomics Research targeting Minority Populations.** Support epigenetic and gene-environment interaction research targeting specific communities with an excess burden of disease. Projects should collaborate with other Federal programs in the targeted community, including HRSA centers, CDC, NCI and NIH community-based programs to improve outreach and education efforts, provide updates, etc. Community leaders/representatives should be a part of the ancillary research support team. New jobs needed at community level to manage and monitor community education and outreach programs, e.g., patient navigation programs. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **08-DA-101 An Epigenomic "Neurochip".** Individual genomic variation is likely to influence epigenomic variation significantly. One solution to the challenge of conducting epigenomic investigations into neuropsychiatric disorders could thus be to computationally identify genomic regions or single nucleotide polymorphisms in known or suspected regions of epigenomic variation. This composite data could be used to develop a "neurochip" for use in case and control studies to identify gene variants (and corresponding epigenotypic variants) important in neuropsychiatric disorders such as addiction Contact: Dr. John Satterlee, 301-435-1020, satterleej@nida.nih.gov

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	08-DA-102 Improved Bioinformatics Analysis for Deep Sequencing. The current estimate of sequencing an entire human genome is $5000 and can be accomplished in a few months. However, current bioinformatic and analytic capabilities are inadequate to analyze the volumes of data that would be generated by deep sequencing many individuals. Specifically, RC1 applications are sought to (1) optimize base calls from next-generation sequencing machines, (2) develop and improve optimal alignment/mapping methods that tackle uncertainty and multiple potential placements, (3) identify methods for SNP calling from multiple reads and multiple samples, (4) identify copy-number variation calling from next-generation sequencing data, and (5) develop automated methods for searching sequence databases that could be used to give probabilities that a variant is real. Contact: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov **08-DA-103 Genetic and epigenetic predictors of symptom severity.** Research on the genetic and epigenetic underpinnings of symptom severity in acute or chronic HIV-associated neurological and neurocognitive impairment, and identify individuals at greatest risk for these symptoms. Individuals with a history of substance abuse or current substance users, or SIV models incorporating substances of abuse, must be included in the analyses. Dr. Diane Lawrence, 301-443-1470, lawrencedi@nida.nih.gov **08-DA-104 Cross-disease research to identify commonly targeted pathways or mechanisms between low incidence, neurogenetic disorders with high incidence, population-based disease.** Progress in treating drug addiction and related disorders has been hindered by the complex genetics and heterogeneous etiologies of these disorders. Analyzing related or clinically overlapping disorders (e.g., smoking and schizophrenia, substance abuse and conduct disorder, or poly-substance abuse) or studying rare genetic variants of large effect can yield unique biological insight into the mechanisms of underlying common diseases. Dissecting pathways common to complex genetic disorders of addiction and other neurobehavioral comorbidities will help identify potential therapeutic targets. Contact: Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **08-DA-105 Beyond GWAS: Deep sequencing of mental disorders.** Over the past few years, genotyping studies have identified several candidate risk genes for addiction and related disorders. Exploit new sequencing technologies that move beyond genotyping to identify rare and/or structural variants and novel risk genes for these disorders in existing DNA samples. Contact: Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **08-DA-106 Technology and resources for high-throughput functional analysis of functional elements in genomic sequences.** Develop robust, high-throughput methods to carry out functional assays to determine whether and how putative functional elements (e.g., genes and regulatory sequences) operate to determine cell states in development, health, the addicted states, and response to abused drugs. Such new methods should include both cellular and whole organism methods to allow systematic analysis of the effects of both genetic (normal variation and mutation) and environmental perturbations, and should include methods for both molecular (transcriptomic, proteomic) analysis and high-throughput phenotyping. Contact: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov **08-DE-101* Planning Grants for Genome-wide Studies of Understudied Oral and Craniofacial Diseases and Disorders [Temporomandibular Joint Disorder, Oral Cancer, Sjögren's Syndrome, Periodontal Disease**]. Genome-wide studies have yielded significant insights into the genetic etiologies of many common complex diseases, but this approach has not been widely adopted for highly complex oral and craniofacial

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	diseases such as TMJ disorder, oral cancer, Sjögren's syndrome, or periodontal disease. **Goal**: Assessment of the adequacy and consistency of clinical, risk factor, endophenotype, behavioral and demographic data of participants from different research groups; adequacy of tissue specimens for genome-wide technologies; and feasibility of the initial genome-wide study and follow-up studies. [High Priority Topic for NIDCR.] Contact**:** Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov **08-DE-102 Measurement of Behavioral and/or Social Factors in GEI Studies.** The quality of Gene-by-Environment Interaction Studies (GEI) depends in large part on the quality of measures of the environmental influences on health. **Goal**: Studies are encouraged that develop measures, assessments and/or methods that capture the environmental factors (e.g., behavioral, social) hypothesized to interact with genetic influences on oral health or craniofacial disorders. Contact: Dr. Melissa Riddle, 301-451-3888, riddleme@mail.nih.gov **08-DE-103 Epigenomics and Epigenetics of Oral Health and Disease.** The maintenance of health and susceptibility to disease are, in part, the result of epigenetic regulation of the genetic blueprint. Epigenetic/epigenomic regulation of gene transcription is an emerging frontier of science that directs functional processes in development across the lifespan as well as in disease states. **Goal**: Elucidation of the epigenetics/epigenomics basis and environmental influences on the molecular mechanisms underlying the susceptibility, development, progression and resolution of oral, dental and craniofacial diseases and conditions, including but not limited to craniofacial disorders, head and neck cancer, periodontal disease, Sjögren's syndrome, orofacial pain; elucidation of the epigenetic/epigenomic regulation of orofacial stem and progenitor cells; production of epigenome-wide information for the identification and characterization of therapeutic targets and predictive biomarkers. Contact**:** Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov **08-DE-104 Genotyping of Existing Cohorts in Craniofacial, Dental, and Oral Conditions**. These studies will utilize existing clinical cohorts to add to the broadly shared data resources available to genetic researchers. The immediate result of the work will be the submission of large genotype-phenotype datasets to the database of Genotypes and Phenotypes (dbGaP) (http://www.ncbi.nlm.nih.gov/sites/entrez?db=gap). This is expected to allow the submitting investigators and others to pursue analytical projects that will identify genetic loci contributing to disease risk. The datasets will also provide a testing ground for new methodological approaches for the identification of genetic risk factors. Medical sequencing, fine-mapping, and replication studies are included, but recruitment of new cohorts is not. Contact: Dr. Emily Harris, 301-594-4846, harrisel@nidcr.nih.gov **08-DK-101 Develop an individualized approach to risk evaluation and management based on genetic susceptibility in diseases of interest to NIDDK.** Examples include: Complete identification of risk susceptibility genes among diverse patient populations; Determine the functional role of NIDDK disease-associated gene variants in pathophysiologic pathways leading to NIDDK diseases; Determine the impact of environmental factors on disease-associated genetic variants; Define genetic subset/phenotype-genotype correlations, Identify and assess relevant pharmacogenetic variations; Correlate genotype (disease susceptibility and pharmacogenetics) with response to therapy and incorporate genotypes into clinical trials; Use genotypic variations to define disease risk. Contact**:** Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@mail.nih.gov

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	08-DK-102 Beyond GWAS. Use methods such as 'deep' sequencing, exon sequencing, high-throughput genotyping and comparative genome hybridization to identify structural variations to pinpoint causal variants associated with NIDDK-relevant diseases or phenotypes, especially those identified in GWAS. Contact**:** Dr. Rebekah Rasooly, 301-594-6007, rasoolyr@mail.nih.gov **08-DK-103 Genetic interactions for complex diseases.** Develop and apply new approaches to study gene-gene and gene-environment interactions and epigenetic processes affecting the development of NIDDK-relevant diseases or phenotypes, especially using genes identified through GWAS. Contact**:** Dr. Paul Kimmel, 301-594-7713, kimmelp@mail.nih.gov. **08-DK-104 Genome wide genetic studies.** Carry out genome-wide studies of understudied diseases and phenotypes within the NIDDK mission, especially in minority populations, to identify associated loci and genes. Contact**:** Dr. Catherine McKeon, 301-594-8810, mckeonc@mail.nih.gov **08-DK-105 Modifier loci.** Use genetic and genomic technologies to identify modifier loci, genes and specific variants influencing the phenotype of Mendelian diseases within the NIDDK portfolio. Contact**:** Dr. Catherine McKeon, 301-594-8810, mckeonc@mail.nih.gov **08-DK-106 Genomics of complex diseases.** Develop and use new methods to integrate data such as pathway analysis, gene interactions and expression data to better understand the pathophysiology of complex diseases, such as obesity, diabetes, Inflammatory Bowel Disease (IBD), and diabetic complications. Contact**:** Dr. Robert Karp, 301-451-8875, karpr@mail.nih.gov **08-DK-107 Nuclear Receptor mediated assembly of functional transcriptional units.** Recent studies have revealed that Nuclear Receptors, particularly in response to ligands, seed the formation of transcriptional complexes both at proximal promoters and distal enhancers. Recruitment of coregulators with enzyme activities essential to cofactor exchange, chromatin remodeling, transcriptional activation, and RNA processing follows may be mimicked by agonists and small molecule compounds with drug-like activities. The application of genome-wide analyses of response element occupancy has the potential to rapidly and comprehensively reveal novel mechanisms of gene regulation. When applied to models of disease, including mouse models of diabetes and obesity, and human tissue samples, new insights into mechanisms of disease will be obtained. Contact**:** Dr. Ronald Margolis, 301-594-8819, margolisr@mail.nih.gov **08-DK-108 Bioactive food components.** Identification and characterization of sites of action of specific bioactive food components, as well as interactions of bioactive components, will be important in understanding how such sites relate to disease intervention. Further work is needed at the genetic, epigenetic and post-translational levels, all of which have now been shown to be affected by a number of bioactive food components. Contact**:** Dr. Michael (Ken) May, 301-594-8884, maym@mail.nih.gov. **08-DK-109 Characterization of polymorphisms associated with nutrition.** Single polynuclear polymorphisms (SNP) are now recognized as factors which can affect responses to specific nutrients at sites of action, absorption, and metabolism. Such have already been identified for vitamin D, folate and amino acid metabolism. Further work on identification and characterization of SNP-nutrient responses should explain individual

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	variations in nutrient status and responses to dietary treatments. Contact**:** Dr. Michael (Ken) May, 301-594-8884, maym@mail.nih.gov. **08-ES-101 Replication of GWAS findings in populations with known environmental exposures.** Conduct replication studies in populations with known levels of environmentally relevant exposures to validate GWAS studies or to discover gene x environment interactions that were not apparent from GWAS methods. Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov **08-ES-102 Explore the functional analysis of environmentally-responsive genes through high-throughput approaches.** The value of the existing epidemiologic and genotyping data for investigation of gene-environment interactions will be increased substantially by understanding and characterizing functional mechanisms caused by the genetic variants that are currently being identified through GWAS studies and other gene discovery methods. The goal of this proposal would be to develop or refine high-throughput tests (e.g. yeast, C. elegans, cell culture systems, or computational approaches) to look at different aspects of variant function in environmentally-responsive genes. Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov **08-ES-103 Statistical tools for GxE analysis.** Develop new statistical tools and software to design and analyze data from studies which can tease out the role of genes which are involved in garnering susceptibility to environmental agents which would not be found using traditional GWAS methods. Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov **08-ES-104 Identification of alterations in epigenetic marks related to environmental exposures.** Recent data show the environmental exposures can alter epigenetic marks on chromosomes, but there is still a strong need to investigate the epigenetic status of specific genes associated with environmental exposures. The NIH Roadmap sponsors research to identify epigenome-wide changes related to diseases or exposures, but research to identify epigenetic changes in genes or chromosomal regions known or suspected to be associated with responses to environmental exposures is also needed. Proposals can address epigenetic changes over the entire lifespan of experimental animals including prenatal exposures leading to developmental changes or increased risk in adult life, as well as epigenetic changes that persist across multiple generations causing increased disease risk in subsequent generations. Contact: Dr. Fred Tyson, 919-541-0176, tyson2@niehs.nih.gov **08-ES-105 Demonstration of the functional consequences of changes in epigenetic marks resulting from environmental exposures.** Functional consequences of environmental exposure induced alterations in epigenetic marks or profiles may include changes in transcription which can consist of unscheduled transcription, alternative transcription resulting in transcripts with varying length and function, gene silencing or elevated/repressed levels of transcription. Studies may focus on specific genes or more globally with genome wide studies and may utilize model systems, e.g., yeast, C. elegans, in vitro, in vivo or in silica models. Contact: Dr. Fred Tyson, 919-541-0176, tyson2@niehs.nih.gov **08-ES-106 The role of environmental exposure in copy number variation (CNV**). Microscopic deletions and replications of the genome have attracted increasing attention for their potential role in many complex human diseases. Of particular interest are spontaneous CNVs, defined as those present in an affected individual, but absent in both

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	parents. There is limited understanding of how spontaneous CNVs arise. Studies are needed that will determine whether environmental exposures can affect risk for copy number variation and other structural variations that have been implicated in complex diseases. Given the early stage of this research area, studies should focus on changes in cells exposed in vitro. Contact: Dr. Cindy Lawler, 919-316-4671, lawler@niehs.nih.gov **08-ES-107 Integrated analysis of epigenetic and genetics alterations in human disease.** Recent analysis of environmentally altered epigenetic profiles suggest that both genetic and epigenetic regulation of the genome is important for complex disease pathogenesis. The integration of genomic sequence data in cis or in trans with epigenetic marks in existing data sets or the overlaying of epigenetic data in existing human population studies with extensive whole genome analysis is necessary to understand the mechanisms of complex biological networks implicated in diseases with environmental risk factors. This computational analysis of integrating existing genetic and epigenetic datasets can be completed in two years and will be critically important to further enhance our understanding of gene-environment interactions in complex human diseases. Contact: Dr. Kimberly McAllister, 919-541-4528, mcalis2@niehs.nih.gov; Dr. Fred Tyson, 919-541-0176, tyson2@niehs.nih.gov **08-EY-101* Genomics of complex eye diseases.** Opportunities exist to make scientific inroads into complex, but common eye diseases such as cataract, diabetic retinopathy, macular degeneration and primary open angle glaucoma. One approach would be to use comprehensive genomic profiling of ocular cell types in normal and disease states by using high throughput expression analysis methods (e.g., sequencing and exon arrays, methylation sequencing) Contact: Dr. Hemin Chin, 301-451-2020, chinh@mail.nih.gov **08-HD-101 Genetic and Environmental Exposures and Autism Spectrum Disorders.** It is generally agreed that both genetic and environmental factors contribute to the causes of autism spectrum disorders (ASD), and it is well known that infant siblings of individuals with ASD have significantly greater probability to develop ASD than the general population. Additional pilot studies are needed to determine the contributions of specific genetic variations (such as mutations or structural genetic variations, either inherited or de novo) and environmental exposures (such as prenatal or perinatal exposure to pollutants, pesticides, or viruses), or their interactions, to the development of ASD in high-risk populations. Contact: Dr. Alice Kau, 301-496-1385, kaua@mail.nih.gov **08-HD-102 GWAS research** may help scientists achieve greater understanding of pediatric and reproductive health conditions. Areas of special interest to the NICHD include: o Learning Disabilities: Estimates for learning disabilities range from 5-20% of the school age population, yet the relationship between observed learning disabilities and possible genetic predispositions is poorly understood. Exploratory research is needed to identify associations across the genome for individuals identified with one or more learning disabilities, with or without comorbid conditions such as ADHD, using pre-existing, well-characterized samples of genetic materials. Collection of genetic material from individuals, and family members, to compliment previous and ongoing data collection efforts is also encouraged. o Bone Mineral Accretion During Childhood: Exploratory GWAS research could take advantage of the public use data now available from the NICHD Bone Mineral Density in Childhood Study, a population-based study that involves 2000 children and

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	adolescents. Focus is needed on the genetic variants associated with impaired acquisition of bone particularly during childhood and adolescence, to help identify genetic regulatory mechanisms that can ultimately help to prevent osteoporosis. o Reproductive Diseases and Disorders: Studies are needed in reproductive diseases and disorders that have been shown to have a hereditary component (i.e., polycystic ovarian syndrome, endometriosis, and premature ovarian insufficiency). Identifying phenotypes for control and affected populations would yield valuable data, as would conducting SNP analyses of available DNA samples and/or studying regions of the human genome not captured by SNP-based GWAS analysis. Contact: Dr. Brett Miller, 301-496-9849, brett.miller@nih.gov; Dr. Susan Taymans, 301-496-6517, st56q@nih.gov; Dr. Karen Winer, 301-435-6877, winerk@mail.nih.gov **08-HG-101* Technology and resources for high-throughput functional analysis of functional elements in genomic sequences.** Computational and experimental research programs are currently identifying thousands of putative functional elements (e.g., genes and regulatory sequences) based on their sequence properties; however, new, robust, high-throughput methods are needed to carry out functional assays to determine whether and how these elements operate to determine cell states, in development, and in health and disease. Such new methods should include both cellular and whole organism methods to allow systematic analysis of the effects of both genetic (normal variation and mutation) and environmental perturbations, and should include methods for both molecular (transcriptomic, proteomic) analysis and high-throughput phenotyping. Contact: Dr. Elise Feingold, 301-496-7531, elise_feingold@nih.gov **08-HL-101* Identify causal genetic variants associated with heart, lung, and blood diseases by application of targeted DNA capture and massively parallel sequencing technologies followed by selective genotyping of DNA samples from large well-phenotyped populations**. Genome-wide association studies (GWAS) have been successful in identifying high frequency genetic variants of modest effect that are associated with numerous common diseases, but identifying actual disease-causing genetic variants will require large-scale DNA sequencing of individuals from well-phenotyped populations. Two applications of this approach are needed: (a) targeted resequencing of entire chromosomal regions already known from GWAS findings to be strongly associated with disease, and (b) disease or other clinical trait-based exome-wide resequencing for the unbiased discovery of rare variants having large effects. Validation/replication of newly discovered genetic variants from both experimental designs would then have to be undertaken by selective genotyping of well-phenotyped populations, particularly from existing large consortia. This sequential strategy is needed to characterize the complete set of causal variants contributing to disease heritability and etiology. Contact: Dr. Alan Michelson, 301-594-5353, michelsonam@nhlbi.nih.gov **08-HL-102 Develop methods to integrate and analyze data from two or more different 'omics approaches (e.g., GWAS, sequencing, epigenetics, metabolomics, transcriptomics) to capitalize on existing heart, lung, and blood data sets.** Considerable resources have been expended in developing 'omics technologies and applying them to heart, lung, and blood studies. However, the diverse 'omics technologies each generate multiple data types. Limitations in our ability to combine and analyze data across various 'omics studies have constrained their use in efforts to elucidate the molecular mechanisms underlying heart, lung, and blood disorders. To obtain full value from those data will require new and improved tools to: ▪ Integrate data across two or more 'omics data sets.

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	▪ Analyze integrated data sets using improved statistical tools and approaches necessary to handle the challenges inherent in the complex integrated data sets. Contact: Dr. Deborah Applebaum-Bowden, 301-435-0513, applebad@nhlbi.nih.gov **08-HL-103 Perform Genome-Wide Association and Exon Sequencing Studies for Rare Lung Diseases**. Genome-wide association studies (GWAS) have emerged as a powerful tool for identifying genetic variants related to rare diseases such as age-related macular degeneration and Type I diabetes. The emerging all-exon sequencing approach (exome) may also be a useful approach for GWAS of rare diseases. Both GWAS and exome approaches are needed to gain further insight into rare lung diseases. Analysis of well defined clinical phenotypes, especially of the most severe forms of rare lung diseases, should make it possible to reach sufficient statistical power using the existing database and biological samples collections. Case-control, population, cohort, clinical, and family studies for which detailed phenotypic data and DNA samples have already been acquired are all needed. Contact: Dr. Sandra Hatch, 301-435-0222, hatchs@nhlbi.nih.gov **08-HL-104 Assess genetic variation in African Americans and determine its effect on disease**. Resources are lacking for imputation of existing SNPs (single nucleotide polymorphisms) or for the assessment of CNVs (copy number variants) and their relation to disease in individuals of African ancestry. Existing statistical software and models involved in SNP imputation should be assessed by examining genotype data for African Americans, creating imputed maps, and genotyping or sequencing the regions of interest that will help to refine both the resulting imputed map and the statistical models used in imputing. Also needed are efforts to identify meaningful CNVs, i.e., CNP (Copy Number Polymorphisms), by accurately measuring copy level, location, and frequencies in established African-American cohort(s). An examination of the association of discovered CNPs between affected and unaffected individuals for a disease measure within a cohort will greatly aid investigators in their understanding of CNVs and their subsequent impact on human disease. Contact: Dr. Paul Sorlie, 301-435-0456, sorliep@nhlbi.nih.gov **08-HL105 Multidisciplinary consortia to stimulate in-depth analysis and gene discovery in existing GWAS**. Genome-wide association studies (GWAS) of large population sample sizes have been successful in identifying a number of genetic variants of moderate effect for complex diseases; even larger sample sizes will be needed to discover genes of small effect or to assess gene by gene and gene by environment interactions. To meet this challenge, the NHLBI proposes to support infrastructure and logistics of consortia of over one hundred thousand research participants focused on in-depth analysis and data mining coupled with highly focused follow-up genotyping and resequencing in specific domains (e.g., cardiovascular, pulmonary, sleep, blood disease, obesity, metabolic syndrome). Consortia would have expertise in phenotyping, genotyping, sequencing and analysis, would leverage our investment in GWAS and maximize scientific output from shared data sets. Contact: Dr. Paul Sorlie, 301-435-0456, sorliep@nhlbi.nih.gov **08-MH-101* Beyond GWAS: Deep sequencing of mental disorders.** Over the past 3 years, genotyping studies have identified several candidate risk genes for autism, schizophrenia, and bipolar disorder. Exploit new sequencing technologies that move beyond genotyping to identify rare variants and novel risk genes for these disorders in repository DNA samples. Contact: Dr. Thomas Lehner, 301-443-9869, tlehner@mail.nih.gov

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	08-MH-102* **Schizophrenia interactome.** Explore candidate genes for schizophrenia and other major mental disorders and their relationship and expression patterns. Jumpstart the move from genomics to biology by identifying the patterns of gene expression in post-mortem brain from individuals with various candidate genes. Elucidate the complex functional interactions of their protein products. Contact: Dr. Douglas L. Meinecke, 301-443-1692, dmeineck@mail.nih **08-MH-103** **Understanding the genomic risk architecture of mental disorders.** Use model systems (or human postmortem tissue) to profile regional changes in gene expression across development and/or to identify epigenetic risk markers to build an understanding of the genomic risk architecture associated with mental disorders. Contact: Dr. Andrea Beckel-Mitchener, 301-443-3825, amitchen@mail.nih.gov **08-MH-104** **Technologies to analyze functional elements in genomic sequences implicated in mental disorders.** Develop and/or apply technologies for high-throughput analyses of functional elements in genomic sequences implicated in mental disorders, including both cellular and whole organism methods to address affects on brain function and behavior. Contact: Dr. Thomas Lehner, 301-443-9869, tlehner@mail.nih.gov **08-NR-101*** **Genetic and Epigenetic Predictors of Symptom Severity.** This initiative will support research on the genetic underpinnings of symptom severity. The findings from this research will identify individuals at greatest risk for symptoms from both acute and chronic conditions and design individualized interventions that will maximize symptom management. Contact: Dr. Joan Wasserman, 301-594-5971, wassermanje@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; NIDA Contact: Dr. John Satterlee, 301-435-1010, satterleej@mail.nih.gov **08-NS-101*** **Cross-disease research to identify mechanisms common to Mendelian disorders of low incidence and genetically complex, high incidence disorders.** Progress in treating many common neurological and neurobehavioral disorders has been hindered by the complex genetics and heterogeneous etiologies of these disorders. However, analyzing related or clinically overlapping Mendelian disorders or studying rare genetic variants of large effect can yield unique biological insight into the mechanisms underlying common disease. This challenge encourages studies that dissect pathways common to simple and complex genetic disorders, with the goal of identifying potential therapeutic targets. Contact: Dr. Jane Fountain, 301-496-1431, fountai@ninds.nih.gov **08-OD-101** **Computational approaches for epigenomic analysis.** Technologies such as ultra-high-throughput sequencing allow one to perform epigenomic analyses that were previously impossible. However one of the major remaining challenges is the lack of effective tools for the analysis and integration of epigenomic data. The development of computational or statistical tools to analyze epigenomic data and integrate it with other data types (multiple epigenetic marks, gene expression data, DNA sequence, comparison to diseased cell types etc) would allow epigeneticists to overcome this challenge and make it significantly easier for researchers to investigate the epigenomic basis of disease states. Contact: Dr. Joni Rutter (NIDA), 301-435-0298, jrutter@mail.nih.gov. **08-OD-102** **Integrated Analysis of Epigenetic and Genetics Alterations in Environment-Induced Human Disease.** Both genetic and epigenetic approaches are yielding exciting insights into mechanisms of environmental disease pathogenesis and

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	ultimately suggesting novel therapeutic targets and strategies. The integration of epigenetic and genetic data will be necessary to understand gene-environment interactions in complex human diseases. Applicants may consider using existing human biological samples in existing cohorts. Contact: Dr. Kim McAllister (NIEHS), 919-541-4528, mcallis2@mail.nih.gov

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(09) Health Disparities	**09-AA-101 Factors Influencing Effectiveness of Alcohol Treatment Among Minorit Populations.** Despite the increased awareness of the diversity of individuals with alcohol use disorders, research has tended to focus more on differences in socioeconomic status and insurance coverage as it impacts access to care. Even apart from access, little is known about the relative effectiveness of treatment among minority and at-risk populations. A shift in focus is needed to one that examines diversity within groups and how that may influence disparity (Thurman & Edwards, 2007). The initial priority then is to examine the extent to which socioeconomic status interacts with race, ethnicity, gender, sexual orientation, age, and physical and mental disabilities and to determine the impact that these factors have on help seeking, availability and access, and the quality and appropriateness of care. For example, the Hispanic population is rapidly growing, and in some areas of the country constitutes a majority. Yet there are few if any studies about treatment and provision specifically to this population. Other groups not well studied are those who are physically impaired (such as deaf or hearing impaired), gay-lesbian, brain-injured, suffer chronic pain, etc. As a key component of this plan, research is needed on consumer preferences and needs. Too often, untested assumptions form the basis for decisions about research questions or care provision. New models of care need to be developed and tested in order to more completely address disparities. Contact: Dr. Mark Willenbring, 301-443-1208, mlw@niaaa.nih.gov **09-AG-101* Geographic Disparities in Medicare Usage and Cost.** It is well documented that there are major geographic differences across the U.S. in quality of care and clinical outcomes for older adult populations. Moreover, these differences are not correlated with the extent and cost of Medicare usage. Research is needed to (1) foster evidence-based approaches to financing, staffing, public health programs, and clinical practice to reduce these disparities and (2) develop interventions to reduce disparities in one or multiple categories of health determinants − e.g., geography, socioeconomic status, race/ethnicity − using techniques that can be duplicated in a variety of community settings. Contact: Dr. Sidney Stahl, 301-402.4156, StahlS@mail.nih.gov **09-AG-102 Creating transformational approaches to address rural health disparities.** Research will focus on approaches, partnerships, and technologies for improving rural health outcomes. Additional focus on innovative outreach strategies that involve collaboration among traditional and non-traditional groups including new categories of community health workers, non-traditional occupations and settings. Contact: Sidney Stahl, 301-402.4156, StahlS@mail.nih.gov **09-AG-103 Trans-disciplinary research to integrate the biological and non-biological determinants of health to address health disparities.** Research interests include trans-disciplinary approaches to address health disparities through collaborative efforts and sustained partnerships with social scientists, policy researchers, health researchers, environmental scientists, and behavioral scientists, among others. Strategies that develop community infrastructure and networks, including non-traditional partnerships are also of interest. Contact: Sidney Stahl, 301-402.4156, StahlS@mail.nih.gov **09-AR-101 Define The Biologic Mechanisms Underlying Increased Susceptibility To And Severity Of Lupus Among Ethnic Groups**. People of all races can have lupus; however, African American women have a three times higher incidence (number of new cases) and mortality than white women, develop the disease at a younger age and have more serious complications. Lupus it is also more common in women of Hispanic, Asian, and Native American descent. The goals are to define the biologic mechanisms underlying increased susceptibility to and severity of lupus among ethnic groups, foster research to

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	identify strategies to reduce health disparities in lupus patient populations, promote research on the relationships between socioeconomic status factors and disease outcomes (i.e. self-efficacy, literacy, patient preferences, access,), and explore new strategies that improve participation of disproportionately affected lupus groups in patient-oriented research. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-AR-102 Prevention Strategies that Target Disproportionately Affected Lupus and Scleroderma Patient Populations**. Basic and epidemiologic research provides the knowledge base to design effective strategies for biologic prevention of disease onset. The goal is to develop reagents and methods to identify populations at risk for disease onset and organ-specific clinical manifestations. This includes the development of new technologies, such as chip technology to identify populations at risk, diagnose disease, assess tissue damage and monitor responses to therapy. Chip technology allows for high-density, comprehensive gene expression analysis, and for measuring the expression of thousands of genes at a time, producing a very detailed picture of how one cell differs from other cells. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-AR-103 Reduce Racial Disparities In Total Joint Replacement.** Total joint replacement is a successful procedure for end-stage arthritis of the major weight-bearing joints. More than 500,000 hip and knee replacements are done annually in the United States. For reasons that are not fully understood, more of these procedures are performed in whites than in African Americans. Observed differences in the rate of total hip replacement by race may reflect a disparity in access, referral for care, or patient knowledge and preferences for African Americans. The focus is on new refined methods to further analyze the underlying reasons for the disparate ratio of total joint replacement utilization. In this way, the benefits of total joint replacement can be extended to a segment of the population that may benefit, but appears to have limited utilization. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-AR-104 Understanding Vitiligo.** Vitiligo is a disease of the skin characterized by a loss of pigment in all people who are affected. The psychological and social consequences are particularly profound in people of color who are affected. The goal is to discover the genes that cause vitiligo and once the gene(s) are identified characterize the gene defects, protein abnormalities, and determine how these changes result in the disease itself. Utilize this information to design predictive, diagnostic and treatment approaches. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-AR-105 Keloids.** Keloids are an abnormal exuberant form of wound healing in which excessive connective tissue is laid down at the wound site, and is not remodeled normally (as distinguished from hypertrophic scars in which there is excess connective tissue initially, but remodeling takes place over time). Keloids are seen predominantly in African American individuals. The goals are to identify the gene(s) for keloid formation and how these abnormalities produce disease and the use this information to design predictive, diagnostic, and treatment strategies. The focus is also on studies of collagen deposition and remodeling, fibroblast growth and metabolism and its control and on new experimental model systems for keloids to evaluate potential new therapies. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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	09-CA-101 The Basis for Differences in Cancer Incidence. There is profound difference in the incidence and outcomes of cancer in various populations. This is also reflected in gender and age demographics. Efforts are needed to better understand the genetic and environmental mechanisms behind these differences so that they can be prevented and more effectively treated. Contact: Dr. Phil Daschner, 301-496-1951, daschnep@mail.nih.gov **09-CA-102 Building Transdisciplinary Regional Capacity in Cancer Health Disparities Research and Training.** Eliminating cancer health disparities can be accelerated through enhanced cooperation, collaborations and partnerships across the cancer research enterprise. Provide support to stimulate transdisciplinary planning for the creation of state-of-the-art regional networks of scientists working in cancer health disparities research and care. An initial phase will encourage information sharing and gathering on region-based cancer epidemiology, existing cancer research, diversity training, and resources, and begin to establish the capacity and infrastructure needed to support region-specific pilot research programs in one of the following areas: clinical trials, bioinformatics, minority biospecimens or biobanking, and emerging or advanced technologies, and establish new transdisciplinary research partnerships. Contact: Dr. Mary Ann S. Van Duyn, 301-451-4284, vanduynm@mail.nih.gov **09-CA-103 Communication, Bio-Behavior and the Physical Environment: Exploring Interactions to Address Health Disparities.** Disparities in cancer outcomes continue to grow despite interventions to increase screening, access to treatment, and preventive strategies. Contributing factors include constraints within the built environment. Recent studies show that we can increase the reach and effectiveness of health information through the identification of optimal settings, improved connections and enrichment of the information and physical environment, and that multi-factor, biobehavioral interventions can positively impact cancer patients. Further studies and new approaches that consider multiple levels of factors that contribute to disparities need to be tested among multi-ethnic cancer patients whose physical environment contributes to health disparities. Contact: Dr. Mary Ann S. Van Duyn, 301-451-4284, vanduynm@mail.nih.gov **09-CA-104 Basic cancer research in cancer health disparities.** The role of biological factors in cancer health disparities is now a reality with studies that show that genetic risks to cancer varies by racial/ethnic groups. Basic research is needed in cancer cell biology, cancer etiology, cancer immunology and hematology, DNA and chromosome aberrations, structural biology, and the tumor microenvironment to examine variation among racial/ethnic groups. This will create the knowledge base for understanding the role of basic cancer mechanisms in cancer health disparities. Contact: Dr. Ken Chu, 301-435-9213, chuk@dcpcepn.nci.nih.gov **09-CA-105 Cost effectiveness analysis of patient navigation.** The Patient Navigation Research Program (PNRP) has developed models for determining the cost-effectiveness of patient navigation within that program. Further studies will allow a formal cost-effectiveness analysis of the PNRP to be undertaken. This research will allow various patient navigation models, such as the use of lay navigators, nurse navigators and social work navigators, to be compared both in effectiveness and cost. This cost-effectiveness analysis will occur among the 8 PNRP sites. Contact: Dr. Martha L. Hare, 301-594-1908, Martha.hare@nih.gov

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	09-CA-106 Designing a systems approach to address health disparities. Support interdisciplinary research projects in targeted community settings where disparities exist. Projects should demonstrate a clear systems approach to the research design that weaves education and outreach into the research intervention, and where formal partnerships across the current network of community-based participatory research programs supported by NIH Institutes and Centers and among a wide range of Federal departments and agencies are developed. Contact: Ms. Jane L. MacDonald-Daye, 301-594-5946, dayej@od.nci.nih.gov **09-DE-101 Behavioral and Social Sciences to Reduce Oral Health Disparities.** Many ongoing studies seek to determine if behavioral and social science approaches can reduce health disparities in the U. S. population. These projects often test interdisciplinary approaches to change health behaviors. Oral health messages could be incorporated into these programs. **Goal**: Basic behavioral and/or social sciences research is encouraged that identifies specific, mutable, causal factors responsible for disparate oral disease or oral health outcomes in specific populations. Applied behavioral and/or social sciences research is encouraged that develops or adapts and tests interventions to reduce hypothesized causes of oral health disparities in specific populations. For intervention studies, applicants need to provide a strong justification for the need to develop a new behavioral or social intervention, e.g., providing evidence that an existing intervention is not adequate for the target population, or providing a compelling rationale for why an existing intervention does not address the causes of oral health disparities. Populations of particular interest include racial or ethnic minority populations, economically disadvantaged communities, those in rural geographic areas, older adults with complex medical conditions, institutionalized individuals, etc. Contact: Dr. Ruth Nowjack-Raymer, 301-594-5394, ruth.nowjack-raymer@nih.gov **09-DK-101 Identifying factors that influence health disparities in NIDDK Diseases.** Clearly, health disparities in the United States are related to a complex set of issues that includes social and economic factors. Access to care is a particularly strong predictor but, even when access is adequate, health disparities often remain. The reason for continued disparities within healthcare systems is not well understood and may be related to healthcare practices, system or provider level biases, environmental factors, patient level factors such as age, gender, genetics, cultural beliefs, trust, and behavioral norms, or an interaction between these various factors. Exploratory research is sought to identify factors, other than access to care, that influence and can potentially mitigate health disparities in NIDDK diseases. Contact**:** Dr. Peter Savage, 301 594-8858, savagep@niddk.nih.gov **09-DK-102 Identifying causes of health disparities in patients with NIDDK diseases.** The prevalence and both acute and chronic complications of diabetes (type 1 and 2) are higher and life expectancy is generally lower in U.S. minority patients with diabetes. The prevalence of chronic kidney disease does not vary greatly by demographics (race and gender); however, progression (as measured by end stage renal disease) is much greater for minorities and for males. Access to transplantation differs greatly by race despite a national system to promote equal access; African Americans also have poorer long term renal allograft survival. Minorities have a higher incidence of certain glomerular disease (FSGS, lupus nephritis), and of arteriovenous access failure. Additional studies to understand basis of these differences are needed to help to identify focused interventions targeted to the vulnerability of a group. Examples include: identify factors responsible for differences in incidence, complication rates, or response to treatment regimens between in subgroups of the U.S. population; and development of methods to remove barriers and

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	improve outcomes. Studies might be performed in small populations with unique characteristics, or using existing data or samples from clinical trials and epidemiologic studies. Contact**:** Dr. Peter Savage, 301 594-8858, savagep@niddk.nih.gov. **09-DK-103 Evaluating the efficacy of educational outreach to under-served communities.** Many NIDDK relevant diseases disproportionately affect minority populations. Develop and evaluate improved effective educational materials and outreach approaches to these communities. Contact**:** Dr. Andrew Narva, 301-594-8864, narvaa@mail.nih.gov. **09-EB-101 Health Disparities.** Health disparities result in more than 80,000 premature deaths each year from a variety of diseases including heart disease, HIV/AIDS, infant mortality, diabetes, and breast cancer. New, affordable and appropriate diagnostic devices and treatments are needed that address health disparities in low-resource settings. Contact: Dr. John Haller; 301 594-3009; hallerj@mail.nih.gov. **09-ES-101* Building trust between researchers and communities through capacity building in Environmental Public Health.** Building partnerships between researchers and community members is essential to conduct research which is responsive to the needs of communities for public health changes to protect human health. Two years of support will nurture newly evolving partnerships focusing on building trust and creating a common vocabulary with which to discuss community concerns arising from exposures to hazardous agents, needs to adapt to climate change, barriers to health care and services, and food insecurity. Building knowledge about health promotion behaviors will provide a new source of jobs to communities. Contact: Mr. Liam O'Fallon, 919-541-7733. Ofallon@niehs.nih.gov **09-ES-102 Environmental justice and public health.** Conduct studies to understand the environmental justice concerns of communities regarding emerging exposures such as the impact of climate change, levels of brominated flame retardants such as PBDEs and perfluorinated chemicals such as PFOAs by creating multidisciplinary teams of environmental scientists and community members. Contact: Dr. Caroline Dilworth, 919-541-7727, dilworthch@niehs.nih.gov **09-ES-103 Improving Environmental Health literacy.** Improve health literacy by creating outreach and education materials on emerging environmental health concerns in order to raise awareness of these issues in affected communities. Partnerships involving community members are encouraged. Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov **09-GM-101 Mathematical and computational models for health disparities studies.** Development of mathematical and computational models of the causes of, and potential interventions related to, health disparities. Contact: Dr. Irene Eckstrand, 301-594-0943, eckstrai@nigms.nih.gov **09-HD-101 Youth Violence.** Having direct exposure to and being a victim of violence have profound long-term effects, both physiologically and psychologically, and are especially pervasive in underserved and low- income communities. Interventions are needed that build on and strengthen community resources to specifically target these issues and hasten progress in preventing negative impacts on child and adolescent development. Investigators should propose intensive two-year pilot studies of acute pharmacologic and behavioral interventions to prevent and ameliorate the psychological

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	consequences of exposure to violence, including the development of collaborative community research protocols that could heighten the comparability of results across communities. Contact: Dr. Valerie Malhomes, 301-496-1514, maholmev@mail.nih.gov **09-HD-102 Telehealth in rural areas.** Compared with urban areas, children living in rural areas have higher poverty rates, tend to be in poorer health, and have fewer doctors, hospitals, and other health resources available to them. Pilot telemedicine interventions offer a great opportunity to improve health access and care for children living in rural communities. Studies are needed to evaluate and document feasibility and reliability of pediatric applications of telehealth in rural communities. Contact: Dr. Regina James, 301-435-2692, rjames@mail.nih.gov **09-HD-103 Disparities in Adolescent Obesity.** In the United States, it is estimated that 14 percent of adolescents age twelve to nineteen years are at risk or are already overweight. African-American, Hispanic, Native American/Alaskan Native and Pacific Islander teens are more likely to be at risk or over-weight when compared to their White counterparts. Pilot intervention studies are needed to address this epidemic in African American, Hispanic, Native American and Pacific Islander teens, capitalizing on the utilization of communication technologies (e.g. websites, cellular telephones, wireless PDA's) as a tool to monitor and modify behaviors associated with food intake, physical activity and adherence to recommended treatment. Contact: Dr. Regina James, 301-435-2692, rjames@mail.nih.gov **09-HD-104 HIV in Minority Female Youth.** Currently, HIV incidence in the U.S. is concentrated among minority youth; however, identifying female youth of color with behaviorally acquired undiagnosed HIV infection poses a daunting challenge for adolescent healthcare providers. To combat the rising incidence of HIV among this population, research is urgently needed to develop novel clinical and epidemiologic strategies aimed at identifying such youth and their subsequent linkage to health care services, and/or to implement these approaches using feasibility and acceptability studies. Contact: Dr. Bill Kapogiannis, 301-402-0698, kapogiannisb@mail.nih.gov **09-HL-101 Develop tools to detect early indicators of health disparities, and to test collaborative interventions to reduce differential health care or outcomes for heart, lung, and blood diseases**. The purpose of this challenge is twofold: first, to develop new measures of early determinants of disparities; and second, to develop and test interventions to reduce health and healthcare disparities. Multidisciplinary research studies across entities such as healthcare, education, and housing to improve built environment, neighborhood structures, and health education, for example, would create unique opportunities to mitigate differences in health outcomes at the population level. The focus of both should be on the patient, social and community context as well as the healthcare setting and provider characteristics. Contact: Dr. Lawrence Fine, 301-435-0305, lf128x@nih.gov **09-MD-101* Creating Transformational Approaches to Address Rural Health Disparities.** Research will focus on approaches, partnerships, and technologies for improving rural health outcomes. In addition, NCMHD is interested in proposals that utilize innovative outreach strategies that involve collaboration among traditional and non-traditional groups including new categories of community health workers, non-traditional occupations and settings. Contact: Dr. Nathaniel Stinson, 301-402-1366, stinsonn@mail.nih.gov; NIDA Contact: Dr. Lula Beatty, 301-443-0441,

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	lbeatty@nida.nih.gov **09-MD-102* Trans-disciplinary Research to Integrate the Biological and Non-biological Determinants of Health to Address Health Disparities.** Research interests include trans-disciplinary approaches to address health disparities through collaborative efforts and sustained partnerships with social scientists, policy researchers, health researchers, environmental scientists, and behavioral scientists, for example. Strategies that develop community infrastructure and networks, including non-traditional partnerships are also of interest. Contact: Dr. Kyu Rhee, 301-402-1366, rheekb@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **09-MD-103* Initiating Innovative Interventions to Prevent Family Violence.** NCMHD will focus on strategies to prevent family violence including domestic and intimate partner violence and enhance behavioral research efforts that build workforce infrastructure. The development of culturally and linguistically appropriate messages and tools, the use of non-traditional methods, along with marketing strategies are also of interest. Contact: Dr. Robert Nettey 301-402-1366, netteyr@mail.nih.gov; NIAAA Contact: Dr. Ralph Hingson, 301-443-1274, hingson@mail.nih.gov **09-MH-101 Validating models of community re-entry programs for prisoners with mental disorders.** Harmonize administrative databases and analysis data to validate the effectiveness of existing models of community re-entry programs for released prisoners with mental illness. Contact: Dr. Denise M. Juliano-Bult, 301-443-3364, djuliano@mail.nih.gov **09-MH-102 Improving the quality of care of racially and ethnically diverse severely mentally ill populations.** Conduct pilot studies focusing on the improvement of quality of care of racially and ethnically diverse severely mentally ill populations served in the public sector, to prepare for the development of a disparity index and assist in identifying targets to reduce disparities in quality of care. Contact: Dr. Agnes Rupp, 301-443-3364, arupp@mail.nih.gov **09-NS-101 Improving representation of African American, Hispanic Americans and Native Americans in clinical research.** Current data indicate that African Americans, Native Americans and Hispanic Americans are underrepresented in NINDS clinical research. NINDS supported clinical research would be greatly enhanced by testing of new methods, or use of previously proven methods, to ensure that the diversity in enrolled patients better represents the US population. Contact: Dr. Salina Waddy, 301-496-3102, waddysp@ninds.nih.gov

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(10) Information Technology for Processing Health Care Data	**10-AG-101 Adapt existing genetic and clinical databases to make them interoperable for pharmacogenomics studies.** In order for personalized approaches to drug therapy to be developed, genetic data and clinical data need to be superimposed. Analysis of the superimposed data will generate hypotheses concerning genetic control of drug efficacy. Contact: Dr. Susan Nayfield, 301-496-6949, NayfielS@mail.nih.gov **10-AG-102 Information technology demonstration projects facilitating secondary use of healthcare data for facilitating secondary use of healthcare data for research.** Determine potential benefit of the analysis of enormous amounts of aggregate, anonymous, healthcare data for obtaining evidence for best practices and identifying promising areas for additional research. Develop policies and technology to ensure stringent protection of individual privacy for aggregate anonymous data used for research. Examples of responsive topics include, but are not limited to: multi-institutional data repository research querying projects; vocabulary and ontology standards in data repositories; policies, process, and governance of data repositories; Extract, Transform, Load (ETL) procedures for data for uses for data for clinical data research repositories. Contact: Dr. John Phillips, 301-496-3138, phillipsj2@mail.nih.gov **10-CA-101* Cyber-Infrastructure for Health: Building Technologies to Support Data Coordination and Computational Thinking.** The National Science Foundation has identified research based on "*cyberinfrastructure*" as the single most important challenge confronting the nation's science laboratories (http://www.nsf.gov/news/special_reports/cyber/index.jsp). The challenge is based on a "grand convergence" of three trends: (a) maturation of the Internet as connective data technology; (b) ubiquity of microchips in computers, appliances, and sensors; and (c) an explosion of data from the research enterprise. The NIH, for example, has invested millions within its Genes, Environment, and Health Initiative (GEI) to develop new technologies for measuring environmental exposure to accompany the millions already spent on data from Genome Wide Association studies. The DHHS is spending millions to catalyze the deployment of interoperable electronic health records as a springboard for research (i.e., in the "learning health system"). Relatively little has been spent on accommodating the *petabytes* (i.e., 10^{15} bytes of data) of data expected from these investments. What is needed is a focused concentration of resources to stimulate the creation of new technologies to accommodate these data and accelerate knowledge discovery through computational means. Such a stimulus should help bootstrap a new sector of the knowledge economy, one that is dedicated to accelerating the pace by which data are turned into population health benefits. Contact: Dr. Bradford Hesse, 301-594-9904, hesseb@mail.nih.gov **10-CA-102 Predictive Mathematical Models of Normal and Cancer Processes.** Develop and verify mathematical models or computer simulations of cancer processes towards integration into basic and translational research. Contact: Dr. Jerry Li, 301-435-5226, jiayinli@mail.nih.gov **10-CA-103 Cell Behavior Ontology.** Descriptions of various processes and behaviors of cells are still crudely described and quantified. This type of description makes it difficult to compare and integrate this type of research into various aspects of biological research. Approaches and nomenclatures are desperately needed to better understand, describe, and utilize the vast amount of information about these critical processes in the transforming environment. Contact: Dr. Jerry Li, 301-435-5226, jiayinli@mail.nih.gov

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	10-CA-104 Infrastructure for the Application of *In Silico* Models in Cancer. As mathematical models of biological functions begin to populate the literature there is a need for a bio-informatics infrastructure to promote and enhance their usage. Components of this can be a repository, web based tools and annotation features. Contact: Dr. Jerry Li, 301-435-5226, jiayinli@mail.nih.gov **10-CA-105 Databases for Shared Nanomaterials Characterization.** Nanotechnology is rapidly developing tools and materials for novel therapeutic applications. Since it is new and emerging field, several solutions are available, with most of them being developed in university laboratories. The information sharing through the development of common databases and portals enabling the selection of most appropriate and useful constructs is critical for the progression of this field. Contact: Dr. Piotr Grodzinski, 301-496-1550, grodzinp@mail.nih.gov **10-CA-106 National Cancer Database Integration**. The American College of Surgeons Commission on Cancer (CoC) and its empirical arm, the National Cancer Data Base (NCDB), have been identified as a key resource from which to obtain demographic characteristics of the patient and information describing the clinical management of a patient's disease and the outcomes associated with that patient. These data are a critical piece in adequately describing biospecimens used in molecular studies. Contact: Dr. Helen M. Moore, 301-496-0206, moorehe@mail.nih.gov **10-CA-107 Expand Spectrum of Cancer Surveillance through Informatics Approaches.** Initiate projects using informatics approaches to facilitate electronic transmission of clinical, EMR, administrative and claims data to facilitate cancer surveillance. Data may originate at physician offices, hospitals, HMOs, third party payers, radiology facilities, pathology facilities, laboratories, etc. Use of data linkage and natural language processing to auto-populate data fields taking into account data coding schemes and quality assurance measures is highly encouraged. Treatment and co-morbidity data are high priorities. Collaboration among epidemiologists, bioinformaticians, health services researchers, etc is necessary to achieve these goals. Projects that develop caBIG compliant tools that can be deployed on the caGRID are especially welcome. The overall goal is to increase the spectrum of data elements routinely used for cancer surveillance in an efficient, cost effective, state of the art fashion. Contact: Dr. Marsha Reichman, 301-594-6776, Marsha.reichman@nih.gov **10-DA-101 Dynamic Simulations of Drug Abuse.** Dynamic Simulation Models are being used in many fields to reduce the resource burden of research, to maximize the use of collected data, and to combine and consider the interaction of findings from multiple sources. The development of drug abuse simulations may be useful in a wide variety of situations including the screening of pharmacological compounds, the development of enhanced computational algorithms to increase the predictive validity of animal models, for facilitating the adoption of interventions, to more effectively tailor interventions for special populations and newly emerging abusable drugs and drug use patterns, for the exploration of the impact of policy changes, cultural and public health developments, and to improve the anticipation of epidemiological trends. Contact: Dr. Tom Hilton, 301-435-0808, thilton@nida.nih.gov **10-DA-102 Development of innovative information and communication technology (ICT) to enhance capabilities of U.S. institutions in global health research and research training.** Drug use is a global problem and driving the HIV epidemic in many developing and transitional countries. Widespread implementation of

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	effective drug treatments and HIV risk reduction interventions targeting drug users is an urgent priority. This initiative encourages the development of innovative strategies for rapid refinement, dissemination, and expansion of drug treatment and HIV risk reduction interventions using ICT targeting the specific local circumstances and cultures of drug users in developing and transitional countries. Contact: Dr. Jacques Normand, 301-443-1470, jnormand@nida.nih.gov **10-DA-103 Data warehouse of drug abuse pharmacotherapy clinical trials.** Creation of a database system for entry of efficacy as well as safety data from drug abuse clinical trials that will facilitate the analysis of data across multiple clinical trials that have evaluated multiple medications. Contact: Dr. Ivan Montoya, 301-4435-8631 imontoya@mail.nih.gov **10-DK-101 Virtual biosample/data catalogue.** Develop information technology to create a virtual biosample/data cataologue of available biosamples/data contained in the NIDDK repository or other large collections relevant to NIDDK research. By collecting inventory data using standardized language and descriptors, with common variables, researchers will be able to search across many different repositories to find biosamples of interest. Contact**:** Dr. Paul Eggers, 301 594-8305, eggersp@extra.niddk.nih.gov. **10-DK-102 Accessing CMS part D (pharmaceutical data) for drug comparative effectiveness research studies in areas of NIDDK mission.** Contact**:** Dr. Paul Eggers, 301 594-8305, eggersp@extra.niddk.nih.gov. **10-DK-103 Use of NIDDK repository data or USRDS/UDA data for outcome studies in NIDDK disease areas.** Contact**:** Dr. Paul Eggers, 301 594-8305, eggersp@extra.niddk.nih.gov **10-EB-101* Engineering improved quality of health care at a reduced cost.** Target areas include: (1) developing informatics systems for electronic records that integrate image data with clinical data for more efficient health care decision support; or (2) developing a “universal interface” to effect transmission of image data across institutions/hospitals to reduce duplication. Dr. William Heetderks, 301 451-6771, heetderw@mail.nih.gov **10-EB-102 User-friendly computing infrastructures for biomedical researchers and clinicians.** Openly available computing infrastructures that link to shared research and clinical databases as well robust analysis and visualization tools need to be available to users who do not have prior computing expertise. Rather than spending time on understanding how to use the tools, these infrastructures will allow researcher to focus on synthesizing knowledge. The infrastructures should be seamlessly integrated in the research and clinical environment and provide optimal usability for all researchers. Projects should focus on linking existing databases, models, algorithms, visualization tools and developing the user-friendly interface environment. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov **10-EB-103 Content-Based Image Retrieval.** Develop and validate automated methods for retrieving images from a database based on quantitative features of the images. Such techniques will have a directly improve clinical decision-making and will have far-reaching applications in alleviating the burden of image data overload in the clinical setting. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov

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	10-EB-104 Medical Image Compression. Develop and validate image compression protocols to enable storage within an electronic health record and fast transmission of image data. Protocols should be intelligent in that different sections of the image will be compressed to different extents based on automatic assessment of image content. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov **10-EB-105 Intelligent Systems for Enhancing Patient Safety and Avoiding Errors in the Clinical Setting.** Develop an interface between medical devices or an embedded system within a medical device to analyze clinical data and recognize dangerous conditions. Such a system may provide alerts or directly control the device in question to address the concern. Contact: Dr. Zohara Cohen, 301-451-4778, zcohen@mail.nih.gov **10-HD-101 Monitoring Rehabilitation Outcomes.** Computerized systems are needed to monitor rehabilitation outcomes across diverse health care environments (such as hospital, rehabilitation facility, nursing facilities, or home care) to help determine the most effective strategies for treating chronic illness, reducing disability and secondary conditions, improving health outcomes, and reducing health-care burden. Researchers are encouraged to build on existing research networks, databases, and innovative platform technologies to identify positive trends and successful strategies. Contact: Dr. Louis Quatrano, 301-402- 4221, Quatranl@mail.nih.gov **10-HD-102 Data Archiving and Dissemination.** Additional research is needed to develop technologies, methods, and practices for archiving and disseminating demographic and behavioral data sets that ensure stringent protection of individual privacy while enhancing usability. Developing methods of archiving and disseminating multi-level and/or multi-method data sets are particularly encouraged. Contact: Dr. V. Jeffrey Evans, 301-496-1176, evansvj@mail.nih.gov **10-HG-101 New information technology and resources for disease prevention and personalized medicine.** Family history information forms a cornerstone for the delivery of preventive health care and the future of personalized medicine. The open-source electronic family history collection tool My Family Health Portrait (MFHP) created by the U.S. Office of the Surgeon General offers interoperability with both personal health record and electronic health record systems. MFHP provides a starting point for the development, validation, and study of compatible, open-source, electronic risk - assessment tools for preventable common chronic conditions in the context of existing health information technology systems. Much needed research on developed tools could include: qualitative and quantitative investigations of patient, provider and health system uptake, satisfaction, and utilization of such tools; qualitative and quantitative investigations of the effects such tools have on patient and provider behavior or health outcomes; or the effect such tools have on the appropriate utilization of downstream health care services. Such studies will provide a paradigm for future studies of risk assessment tools that make use of personal genomic information. Contact: Dr. Ebony Bookman, 919-541-0367, bookmane@mail.nih.gov **10-HL-101* Develop data sharing and analytic approaches to obtain from large-scale observational data, especially those derived from electronic health records, reliable estimates of comparative treatment effects and outcomes of cardiovascular, lung, and blood diseases.** Advances in this area will address two important barriers to research on comparative treatment effects: ▪ inability to link data across disparate data platforms and health care settings

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	▪ inability to address confounding and on-treatment biases in observational studies based on data from clinical practice. The first could be addressed by creating an interoperable electronic health record (EHR)-based research platform that assures privacy and confidentiality while allowing questions to be addressed that could not be by using data from only one clinical practice, health plan, or health system; the second by developing new methods to address confounding when attempting to use observational data to compare treatment effects, e.g., instrumental variables, innovative quasi-experimental designs, facilitating ecologic analyses of clinical data using linkages of geographic and clinical data. Such approaches would increase the credibility and value of observational analyses of huge integrated EHR databases in identifying optimal treatment practices for cardiovascular, lung, and blood diseases with multiple available treatment options. Contact: Dr. Michael Lauer, 301-435-0422, ml580m@nih.gov **10-LM-101*** **Informatics for post-marketing surveillance**. Use computational data mining (artificial intelligence and natural language processing, among other techniques) of a large longitudinal medical records database to perform post-marketing surveillance (Phase 4 Clinical Trial). Large clinical data repositories exist that contain longitudinal health records for millions of people. Advanced computational techniques can be used to mine clinical notes, test data and abnormal images to undertake an *in silico* Phase 4 Clinical Trial, by searching for possible adverse drug events and side effects of drugs already in use. Contact: Dr. Milton Corn, 301-496-4621, cornm@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **10-LM-102*** **Advanced decision support for complex clinical decisions**. Use artificial intelligence techniques to provide practical support for complex decision making in health care and clinical research contexts. Most electronic data about patients and clinical research subjects exists at the level of raw data, individual test results and observations, and individual encounters. This mass of data obscures the view of the patient as a whole, hides key facts that deserve attention, and complicates the delivery of relevant electronic knowledge to improve decisions or identify candidate research subjects. Advanced computational techniques should be useful in generating a higher level picture of the patient that can support more effective clinical decision support. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **10-MH-101** **Technologies to improve treatment adherence for mental disorders and HIV/AIDS.** Develop new technologies to change patient and provider behaviors to improve adherence. This might include technologies such as automated reminder systems for patients and web-based systems that link providers, patient medical records and pharmacies to allow rapid identification of non-adherence. Contact: Dr. William Riley, 301-435-0301, wiriley@mail.nih.gov **10-NS-101** **Neuroepidemiologic research from large existent databases.** The evidence-base that supports the incidence and prevalence of many neurological disorders in the United States is often weak or lacking. Creative strategies to better define or answer neuroepidemiologic questions from large health care databases could enhance knowledge of the impact of neurological disorders in the US population. Contact: Dr. Deborah Hirtz, 301-496-5821, dh83f@nih.gov **10-OD-101*** **Adapt existing genetic and clinical databases to make them interoperable for pharmacogenomics studies.** In order for personalized approaches to

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	drug therapy to be developed, genetic data and clinical data need to be superimposed. Analysis of the superimposed data will generate hypotheses concerning genetic control of drug efficacy. Contact: Dr. Joni Rutter (NIDA), 301-435-0298, jrutter@mail.nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **10-RR-101* Information Technology Demonstration Projects Facilitating Secondary Use of Healthcare Data for Research.** Analysis of enormous amounts of aggregate, anonymous, healthcare data has potential to provide evidence for best practices and to identify promising areas for additional research. The increasing adoption of health information technology in the United States offers a source of large amounts of data. This initiative would fund development of policies and technology to ensure stringent protection of individual privacy for aggregate anonymous data used for research. Examples of responsive topics include, but are not limited to: multi-institutional data repository research querying projects; vocabulary and ontology standards in data repositories; policies, process, and governance of data repositories; Extract, Transform, Load (ETL) procedures for data for clinical data research repositories. Contact: Dr. Elaine Collier, 301-435-0794, colliere@mail.nih.gov **10-TW-101* Innovative information and communication technologies to enhance capabilities of U.S. institutions in global health research and research training.** Develop culturally adaptive, interoperable data management, long-distance communication, and distance learning applications that can enhance productivity and quality of active U.S.-international research and research training collaborations. Contact: Dr. Flora Katz, 301-496-1653, katzf@mail.nih.gov

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(11) Regenerative Medicine	**11-AA-101 The Role of Circadian Rhythms in Alcohol-induced Organ Damage.** Acute and chronic alcohol intake can affect circadian rhythms, impacting physiological, endocrine, and behavioral functions. Alcohol may also affect liver oscillators by altering the redox state of the cell. Recent advances in understanding the molecular mechanisms that regulate the circadian system, particularly their connection with metabolism and metabolic disorders, have provided us new perspectives in understanding the underlying mechanisms of alcohol-induced organ damage. Further investigation is warranted. Contact: Dr. Max Guo, 301-443-0639, qmguo@mail.nih.gov **11-AA-102 Roles of Cellular Organelles and the Cytoskeleton in Alcohol-induced Organ Damage.** Whereas molecular mechanisms by which mitochondria contribute to alcohol-induced tissue injury have been studied to some extent, the role of other cellular organelles is largely unknown. Elucidating the role of mitochondria and other cellular organelles, including cytoskeleton, is crucial for understanding the underlying mechanisms of alcohol-induced disorders. Contact: Dr. Max Guo, 301-443-0639, qmguo@mail.nih.gov **11-AA-103 Traumatic Brain Injury.** The increasing incidence of traumatic brain injury (TBI) in soldiers returning from war zones presents an emerging health-care challenge. In general, alcohol consumption negatively impacts recovery from trauma, e.g. hemorrhagic shock. However, a limited preliminary epidemiological study suggests a mild protective effect for alcohol during recovery from TBI. Studies are sought to determine the beneficial and/or harmful effects of alcohol during recovery from neurological damage or other trauma. Contact: Dr. Kathy Jung, 301-443-8744, jungma@mail.nih.gov **11-AA-104 The Endocannabinoid System and Alcohol Pathology.** The Endocannabinoid System (ECS) is central to the development of alcohol dependence and its pathological consequences, including organ damage. The brain and liver are key targets for alcohol-induced damage, and both are sites of ECS expression and targets of its action. Therefore, studies that explore modulation of the ECS as potential new avenues for treating alcoholism, metabolic syndrome and alcoholic liver disease and its complications are encouraged. Contact: Dr. Svetlana Radaeva, 301-443-1189, sradaeva@mail.nih.gov **11-AG-101 Musculoskeletal and skin tissue regeneration.** Define the molecular pathways that regulate the integration of muscle, tendon, and bone into functional units. Develop applicable animal models for regeneration of musculoskeletal or skin tissues. Define outcome measures, such as non-invasive analysis of disease, injury, and repair. Contact: Dr. John Williams, 301-496-6402, williamsj6@mail.nih.gov **11-AG-102 Hair cell regeneration and maintenance in the ear.** Develop and validate methods to regenerate and maintain hair cells in animal model systems with the eventual goal of successful translation to human treatments. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **11-AR-101* Musculoskeletal And Skin Tissue Regeneration.** Define the molecular pathways that regulate the integration of muscle, tendon, and bone into functional units. Develop applicable animal models for regeneration of musculoskeletal or skin tissues. Define outcome measures, such as non-invasive analysis of disease, injury, and repair. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, 301-402-1770, jevajiip@od.nih.gov

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	11-AR-102 Basic Studies on Regenerative Medicine/Tissue Engineering and Wound Repair. The objectives are to define differences in molecular pathways in healing versus non-healing wounds, in acute versus chronic tissue (skin, joint) damage, and in the pathways that regulate the integration of muscle, tendon and bone into functional units. NIAMS Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **11-DC-101* Hair Cell Regeneration and Maintenance.** One common cause of hearing impairment in humans is the progressive loss of the auditory transduction cells, or hair cells, in the inner ear. A similar loss of motion transduction cells in the vestibular organ is a probable cause of balance disorders. Once lost, these cells cannot be spontaneously regenerated in mammals. The Challenge is to develop and validate methods to regenerate and maintain hair cells in animal model systems with the eventual goal of successful translation to human treatments. Contact: Dr. Nancy Freeman, 301-402-3458, freemann@nidcd.nih.gov **11-DE-101 Craniofacial Tissue Regeneration.** Every hour, a baby is born with a craniofacial birth defect that requires complex surgical correction. In addition, numerous procedures are performed each year for maxillofacial reconstruction following head and neck cancer surgery, and trauma and injuries from accidents, violence, and, more recently, combat. Technological advances present the timely research opportunity to promote craniofacial tissue regeneration using bioengineering and biomimetic approaches. **Goal**: Design of strategies to promote craniofacial tissue regeneration using bioengineering and biomimetic approaches, including the development of novel biomaterials and scaffolds, directed differentiation of stem and progenitor cells, modulation of mechanical and other physical properties of tissues to guide their morphogenesis, control of the wound healing microenvironment, tissue printing and local delivery of therapies. Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov **11-DK-101 P**romote regeneration and repair in the digestive system, liver, pancreas, kidneys, Hematologic, and urological system.** Develop the knowledge base or research tools to understand normal repair processes and their alteration during disease or infection; define the molecular pathways that regulate the integration of different cell types into a functional tissue; or facilitate engineering of functional tissues or artificial organs in vitro for transplantation or to foster tissue regeneration directly in vivo. May study tissues from humans, experimental animals, or model systems. Contact**:** Dr. Deborah Hoshizaki, 301-594-7712, hoshizakid@mail.nih.gov **11-DK-102 Vascular network in engineered or regenerated tissues.** Research on the design, optimization, and formation of a complete vascular network capable of delivering oxygen and nutrients and removing waste products in NIDDK relevant engineered or regenerated tissues. Contact**:** Dr. Deborah Hoshizaki, 301-594-7712, hoshizakid@mail.nih.gov **11-DK-103 Organ innervation.** Develop a basic cellular, molecular, and genetic understanding of the biology of organ innervation during development, disease progression, repair following injury, and engraftment of transplanted organs. Examples include: the developmental mechanisms underlying neural crest fate specification and migration to NIDDK relevant organs as well as factors that guide these processes and regulate neural survival; mechanisms of neural repair and autonomic plasticity to restore innervation of -NIDDK relevant organs in the aftermath of organ disease, injury, or

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	transplantation. Contact**:** Dr. Deborah Hoshizaki, 301-594-7712, hoshizakid@mail.nih.gov **11-DK-104 Use of Hematopoietic Stem Cells (HSC) to regenerate or repair mesenchymal tissues.** Examples include: Develop and validate methods and reagents that induce HSCs to develop or trans-differentiate into different mesenchymal cell and tissue types; Develop and validate methods and reagents that allow HSCs to be propagated in vitro without loss of self-renewal potential. Contact: Dr. Terry Bishop, 301-594-7726, bishopt@mail.nih.gov **11-DK-105 Transdifferentiation or directed reprogramming of one cell fate to another (e.g., a pancreatic exocrine cell to a pancreatic beta cell).** Recent evidence has demonstrated that is possible to directly reprogram a fully committed differentiated cell from one lineage into another, thereby bypassing steps of either de-differentiation or reversion to a pluripotent state. Examples include: Identify and use of small molecules rather than viral reprogramming inducers to achieve direct reprogramming; Explore strategies for the in vivo programming of cell fates. Contact**:** Dr. Sheryl Sato, 301-594-8811, smsato@mail.nih.gov **11-DK-106 Enhancing beta cell replication or beta cell mass.** There is emerging evidence in rodents and humans that pancreatic beta cells may have significant regenerative potential, but that this potential is dampened by ongoing autoimmune attack in type 1 diabetes and by the loss and dysfunction of beta cells in type 2 diabetes. Examples include: Identify small molecules and factors that promote expansion of beta cell mass; Determine the regenerative capacity of human islets in a variety of pathophysiological settings (hyperglycemia, inflammation, etc.). Contact**:** Dr. Sheryl Sato, 301-594-8811, smsato@mail.nih.gov **11-DK-107 Directed replication and differentiation of replacement cells from adult stem cells in situ**. Research to identify key endogenous or exogenous factors that can be used to direct digestive system stem cell replication and daughter cell differentiation in situ in order to speed healing under conditions of tissue damage and disease. Contact: Dr. Jill Carrington, 301-402-0671, carringj@mail.nih.gov **11-EB-101* Vascular networks in engineered tissues.** Research on the design, optimization, and formation of a complete vascular network capable of delivering oxygen and nutrients and removing waste products in engineered tissues (i.e., vascularization of engineered tissue constructs). Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **11-EB-102 Advanced Biomaterials to Support Engineered Tissues.** The critical role of cell-matrix interactions in designing functional engineered tissues is increasingly appreciated. Scaffolds need to be: biocompatible (i.e. non-immunogenic, non-toxic, able to fully integrate with existing structures), biomechanically robust (i.e. capable of withstanding a wide array of stresses and strains), biomimetic (i.e. approximating the function of a target tissue as well as the native structure—at the nano- through macro- scales), complex (i.e. incorporating spatial-temporal-structural gradients as needed), and appropriately biodegradable (i.e. decomposing into non-toxic component parts as host remodeling occurs). Proposals addressing novel structural aspects of known materials, or the development of new synthetic or natural materials are encouraged. Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov

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	11-EB-103 Modular Platforms for Regeneration and Development. Current state-of-the-art for assessing the developmental/differentiation potential of a stem cell involves transplantation to an animal, waiting, and a full histological and physiological analysis upon autopsy. This process is slow, cumbersome, costly, and unwieldy. In vitro tissue models offer a more reliable system with tighter control, greater access to spatio-temporal variables, and many other advantages. Stem cells can be introduced into the basic tissue model platform to study development and how specific interventions affect outcomes becomes more accessible. Such surrogate developmental assays can establish a new toolkit for "tissueomics"—the collection and analysis of complex, multi-scale, rigorous, structured, quantitative data at the tissue level. Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **11-EB-104 Living Human Tissue Microarrays.** Prototypes of vitro tissue models of target organs (e.g. skin, liver, lung, muscle) currently exist. However, these systems are not user-friendly, robust, or flexible—preventing their use for high throughput assays that would underlie the next generation of drug/toxicity screening systems for predicting human tissue responses. Proposals are invited to Generate organotypic platforms that are complex yet modular, hardened, standardized, simplified, and validated against traditional animal models. Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **11-EB-105 Advanced Imaging Systems for Tissue Engineering.** The ability to monitor complex cell-cell and cell-matrix interactions in engineered tissues in vitro and in vivo is critically important. The imaging needs to be *functional*—able to assess meaningful changes non-destructively and non-invasively; *intrinsic*—using inherent signatures of normal biological processes (e.g. intermediates of energy metabolism, conformationally-based changes in light scattering); and *dynamic*—monitoring events as they are occurring. Proposals to develop tools for characterizing engineered tissues in vitro and in vivo are encouraged. Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **11-EB-106 Technologies for Expanding Stem Cells and Producing Engineered Tissue**. Tissue engineering and regenerative medicine is a rapidly evolving field, but current production and manufacturing technologies are confined to the laboratory scale and grossly inadequate to ensure sufficient quantity and quality on an industrial scale. New measurement tools, and engineering methods and design principles that can model, monitor, and influence the interaction of cells and their environment at the molecular and organelle level are urgently needed. Projects are sought to develop scaleable bioreactors to precisely control the chemical and mechanical environment for functional 3D tissue growth or for rapidly expanding stem cells; quantitative, non-invasive tools to monitor structure, composition, quorum sensing, and function of heterogeneous tissues in real time; and technologies for preservation, sterilization, packaging, transport, and ensuring cell and tissue health and phenotypic stability. Contact: Dr. Albert Lee, 301-451-4781, alee@mail.nih.gov **11-GM-101 Establishment of regenerative capabilities**. Development of approaches and technologies to establish regenerative capabilities in adult cells to repair or replace damaged tissues and organs *in situ* and to improve wound healing and reduce scarring in human and animal models. Contacts: Dr. Susan Haynes, 301-594-0943, hayness@nigms.nih.gov, Dr. Richard Ikeda, 301-594-3827, ikedar@nigms.nih.gov **11-HL-101* Develop cell-based therapies for cardiovascular, lung, and blood diseases.** Cell-based therapies for cardiovascular, lung, and blood diseases offer a new paradigm for advancing and transforming patient care. Translational and early-phase

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	clinical research has demonstrated that cell-based therapies may improve left ventricular function, reduce myocardial ischemia, and lead to improved lung function. Reconstitution of normal hematopoeisis using modified stem cell graft sources has great potential for treating specific genetic blood disorders. However, a number of significant challenges and barriers must be overcome to move the field forward toward broad clinical application. We encourage further research to determine the characteristics of the most promising target patient population, the best cell type and number of cells to use, the optimal methods and timing of delivery, and other preclinical parameters. Contact: Dr. Sonia Skarlatos, 301-435-0477, skarlats@nhlbi.nih.gov **11-NS-101 Imaging neural plasticity.** New methods to identify and track important processes related to human neural development and repair in the nervous system would open entire new fields of study in a variety of neurological disorders. Contact: Dr. Naomi Kleitman, 301-496-1447, nk85q@nih.gov

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(12) Science, Technology, Engineering and Mathematics Education (STEM)	**12-AG-101 Efficacy of educational approaches toward promoting STEM competencies.** Research on efficacy testing of educational pedagogy, tools, and curricula (both classroom and non-classroom approaches) that are targeted at improving student understanding of science, technology, engineering, and math (STEM) concepts. Contact: Dr. Chyren Hunter, 301-496-9322, hunter@mail.nih.gov **12-CA-101 Cross Science Training in Cancer.** Joint projects in STEM disciplines and cancer biology. Contact: Dr. Jennifer Couch, 301-435-5226, couchj@mail.nih.gov **12-CA-102 Bringing New Mathematical Methods into Cancer Biology.** Cancer is inherently a complex system involving many types of interactions and many scales both spatial and temporal. Mathematical methods for modeling, analyzing and understanding complex systems are applied across a wide range of complex systems from transit networks to social systems. Some of these methods have been adapted and applied to the study of cancer risk, initiation and progression. However many cancer processes remain difficult to model and analyze; new methods and methods adapted from the studies of other complex systems analysis are needed to better model cancer processes. Contact: Dr. Jennifer Couch, 301-435-5226, couchj@mail.nih.gov **12-CA-103 Modeling and Predictive Tools for Development and Testing of Nanotechnology-based Diagnostics and Therapeutics.** Accurate predictive modeling tools can aid researchers in designing and deciding future experiments, thereby saving valuable time and resources. Such tools have been successfully developed in several industries (e.g., semiconductor device fabrication) and have become indispensable to accelerate the design process as well as provide standardization to the developments for different companies. The development of such predictive and modeling tools can make a major impact on the nanobiotechnology efforts to recommend suitable surface functionalization and structural improvements, which can then be incorporated into the design of nanomaterials. As a result, the nanoparticle circulation times, non-specific binding, aggregation, and cellular uptake can be assessed and optimized prior to the development of the actual material and ultimately lead to the optimization of the diagnostic and/or therapeutic nanotechnology-based tool. Contact: Dr. Piotr Grodzinski, 301-496-1550, grodzinp@mail.nih.gov **12-CA-104 Developing the Workforce in Emerging Technologies CURE.** The overarching goals of the Emerging Technologies Continuing Umbrella of Research Experiences (ET CURE) initiative are to: 1) Create a pipeline of underserved students and investigators in the fields of emerging and advanced technologies; 2) Increase the number of scientists from underserved populations with training in the elective disciplines of focus, such as nanotechnology, clinical proteomics, bioinformatics, biophotonics and cancer health disparities across the cancer research continuum; 3) Enhance the application of emerging technologies to cancer research through increased training and educational opportunities; and 4) Foster academic, scientific and multi-disciplinary research excellence. This training program provides employment opportunities for the public health sector, academic institutions and the next generation of clinicians and scientists. The program is comprehensive and can be augmented at training sites nationwide and has a steadfast commitment to diversity and to the underserved populations that are impacted. It is paramount that we enhance the application of emerging technologies to cancer research through increased training and educational opportunities and increase the number of individuals with diversity in the pool of future investigators, by the creation of training and employment opportunities such as ET CURE. It is believed that the provision of resources, the joining of committed partners and the utilization of the above opportunities in concert

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	will bring to fruition a positive impact on diversity in the areas of advanced and emerging technologies and reduce cancer health disparities. Contact: Dr. LeeAnn Bailey, 301-496-7344, BaileyL@mail.nih.gov **12-DK-101 Increasing involvement of surgical sub-specialties in biomedical research.** The surgical sub-specialist is under-represented in the NIDDK research portfolio, however; it is vitally important to increase their participation in basic and clinical research to better translate research developments into improved surgical and clinical practice. Responsive research topics in areas of NIDDK research mission include: identifying causal factors that preclude surgeons from a career in research; piloting interventions that facilitate research participation of surgeons. Contact**:** Dr. Debuene Chang, 301-594-7717, changtd@mail.nih.gov **12-DK-102 Expanding Biomedical Research Opportunities at the Undergraduate Level.** Undergraduate college students are provided little opportunity to experience biomedical laboratory research in a mentored environment. It is important to increase the participation of college students, especially those who have not yet made biomedical career decisions, in laboratories conducting biomedical research and to develop effective mentoring programs. Contact**:** Dr. Tracy Rankin, 301-594-4748, rankint@mail.nih.gov **12-DK-103 Evaluating the efficacy of mentoring training in STEM fields.** Effective mentoring early in the biomedical career path is important to maintaining interested individuals in biomedical careers. Research that evaluates and designs effective programs to "mentor the mentor" in areas of NIDDK research mission will be responsive. Contact**:** Dr. Tracy Rankin, 301-594-4748, rankint@mail.nih.gov **12-DK-104 Increasing participation of mathematicians, engineers and computational specialists in biomedical research.** Today's research environment demands the involvement of inter-disciplinary teams to further the translation of basic science advances into improved public health. Responsive research topics in areas of NIDDK research mission include: evaluating the efficacy of current STEM curricula and training programs to attract these specialists to biomedical research. Contact**:** Dr. Tracy Rankin, 301-594-4748, rankint@mail.nih.gov **12-ES-101 Material Development for Environmental Health curriculum.** Develop education curriculum materials for grades K-12 in the area of the causes of environmentally related diseases such as asthma, autism, cancer, and Parkinson's disease. Use of new technologies is encouraged – Web-based simulations, social media, computer/video games, etc. – as well as use of innovative delivery methods – (e.g., mobile labs/buses, mobile communications devices). Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov **12-ES-102 Professional development in issues in Environmental Health.** Establish programs to support effective STEM teaching which include in-service professional development of STEM teachers, pre-service programs for future STEM teachers, and summer research opportunities for teachers in research laboratories in order to understand contemporary and emerging issues in environmental health. Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov **12-ES-103 Engagement of scientists in Environmental Health science education.** Develop programs that encourage environmental health scientists to become advocates for better science education in their local communities, assist scientists in

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	translating/communicating research to teachers and students, provide tools and resources for scientists to increase their effectiveness when they engage with school systems, and seek ways to remove barriers to participation and reward scientists for engaging in K-12 activities. Contact: Mr. Liam O'Fallon, 919-541-7733, Ofallon@niehs.nih.gov **12-GM-101 Novel interventions to improve development of research scientists from underrepresented groups**. Development and testing of novel interventions based on recent, theoretically grounded research from the behavioral and social sciences that will enhance the development of creative research scientists from underrepresented groups. Contact: Dr. Shiva Singh, 301-594-3900, singhs@nigms.nih.gov **12-HD-101 Educational Interventions to Increase Science Literacy.** Development and/or testing of educational interventions appropriate for different age groups designed to increase science literacy are urgently needed to: (1) increase a consumer's ability to synthesize, evaluate and act on information from various sources (e.g., television, newspapers, word-of-mouth) related to health topics such as diet and nutrition, effects of violent television and video games, the risks/benefits of immunizations, etc.; and (2) reduce harmful effects of making decisions based on information that has no scientific basis (e.g., fad diets, untested "miracle" cures, medical noncompliance). Development and/or testing of educational interventions that work on multiple levels (e.g., the individual, family, school, community) to promote science literacy are encouraged. Contact: Dr. James Griffin, 301-435-2307, james.griffin@nih.gov **12-HD-102 Optimal Environments and Techniques for Science Learning.** Little is known about the optimal learning environments for elementary and middle school children learning science concepts, although we do know that they should be taught these concepts earlier than is current practice in schools to help prevent misconceptions from forming, which must then be "unlearned" as correct concepts are taught. Research is needed to test optimal methods for presenting science concepts at various ages to maximize science learning, such as using oral vs. written presentation of information, hands-on experiential learning vs. use of static or animated graphic representations, and direct instruction vs. discovery learning approaches. Contact: Dr. Kathy Mann Koepke, 301-451-5650, kmk@nih.gov **12-MH-101 Models for national mentoring networks for individuals from diverse backgrounds.** Develop and pilot innovative models for national mentoring networks for individuals from diverse backgrounds (individual from under-represented racial and ethnic groups, individuals from disadvantaged backgrounds and individuals with disabilities) with interest in mental health research. Contact: Dr. Nancy Desmond, 301-443-3107, ndesmond@mail.nih.gov **12-OD-101* Efficacy of educational approaches toward promoting STEM competencies.** Research on efficacy testing of educational pedagogy, tools, and curricula (both classroom and non-classroom approaches) that are targeted at improving student understanding of science, technology, engineering, and math (STEM) concepts. Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov **12-OD-102 Teacher preparation development programs to support effective STEM teaching.** In-service professional development of STEM teachers. Pre-service programs for future STEM teachers. Use of Web technologies to engage and support a diverse array of teachers. Summer research opportunities for teachers in research

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	laboratories. Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov **12-OD-103 Informal Science Education.** Museums, radio, TV, film, traveling exhibits, community approaches. Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov **12-OD-104 Innovative approaches to STEM education.** New technologies – Web-based simulations, social media, computer/video games, etc. Innovative delivery methods – (e.g., Mobile labs/buses; mobile communications devices). Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov **12-OD-105 Identification of practices that overcome equity issues in STEM learning.** Developing and maintaining interest in STEM among girls as they progress through school. Encouraging diversity within the population of students interested in STEM careers. Efficacy and effectiveness of specific approaches (e.g., role models, mentors, tutoring, etc.) that aim to increase diversity in the STEM workforce. Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov **12-OD-106 Engaging Scientists in Science Education.** Programs to encourage scientists to become advocates for better science education in their local communities. Programs that assist scientists in translating/communicating research to teachers and students. Programs that provide tools and resources for scientists to increase their effectiveness when they engage with school systems. Programs that seek ways to remove barriers to participation and reward scientists for engaging in K-12 activities. Contact: Dr. Bruce Fuchs (OD/OSE), 301-402-5225, fuchsb@mail.nih.gov

Broad Challenge Area	Specific Challenge Topic
(13) Smart Biomaterials - Theranostics	**13-AG-101 Theranostics: Combined delivery of diagnostic and therapeutic agents.** Development of novel approaches to deliver combined diagnostic and therapeutic agents to appropriate sites with high specificity and in adequate concentrations to realize the promise of combined diagnosis and treatment of diseases in a single sitting ("theranostics"). Contact: Dr. Susan Nayfield, 301-496-6949, NayfielS@mail.nih.gov **13-AG-102 Novel self-healing smart dental and bio-restorative materials.** Dental materials and other biomaterials have limited survival when placed in the human body. Develop a new generation of "self-healing" and "smart" dental and bio-restorative materials that can diagnose structural failure and repair themselves to minimize the loss of natural structures associated with materials failure. Contact: Ms. Winifred Rossi, 301-496-3836, RossiW@mail.nih.gov **13-AG-103 Methods to evaluate the health and safety of nanomaterials.** Develop novel tools and approaches to determine the impact on biological systems and health outcomes of an array of engineered nanomaterials. Conduct biological, physical and chemical characterization of selected nanomaterials to aid in setting standards for health and safety, and developing computational models for the prediction of long term secondary effects. Contact: Dr. Ron Kohanski, 301-496-6402, KohanskiR@mail.nih.gov **13-AR-101 Biomaterials for Wound Healing**. The inability of chronic wounds to heal is a major health problem in the United States, and the problem will increase in magnitude as the population ages. Understanding and controlling the regenerative process is essential; the natural wound healing response is "over-exuberant" and can create additional morbidity in the form of hypertrophic scarring and fibrosis. There is tremendous interest in developing methods to attract endogenous cells to the wound site to mediate the healing processes; to conduct exploratory work to evaluate new scaffolds and biomaterials that may allow identification of cell populations migrating to the wound edge, and enhance homing and residency of endogenous cells. Other studies of interest include investigation of materials to deliver cells, growth factors, cytokines, or other agents and the use functional bonds to regulate release of these factors. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **13-CA-101 Cellular mechanics.** A great deal of information about cancer has come to light through the generation of molecular data, including gene and protein expression data that differs between cancer and normal cells. But also of critical importance is the mechanics of the cells themselves: adhesion strength, motility, and shape deformation changes have all been identified in cancer cells compared to normal. High throughput methods for capturing the physical properties of cells are needed to help complete our understanding of cancer processes. Contact: Dr. Randy Knowlton, 301-435-5226, knowltoj@mail.nih.gov **13-CA-102 Nanotechnology-based multi-functional materials for theranostic applications.** Nanotechnology provides a unique opportunity to develop multi-functional constructs carrying targeting moiety, therapeutic construct, and imaging agent. Such constructs will enable entirely new category of clinical solutions which permit early recognition of the disease through the use of novel contrast agents combined with one of the existing imaging modalities (MRI, ultrasound, optical imaging) followed through tailored release of the therapeutic. This new category of solutions – theranostic will provide a path for personalized medicine in oncology. Contact: Dr. Piotr Grodzinski, 301-496-1550, grodzinp@mail.nih.gov

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	13-CA-103 Chemoprevention Using Pharmacogenomic Profiles. Studies that focus on chemopreventive interventions based on pharmacogenomics profiles are sought. Examples include: chemoprevention clinical trials that utilize specific genomic polymorphisms or proposals that will obtain this information as part of their secondary objectives. Contact: Dr. Asad Umar, 301-594-7671, Asad.Umar@nih.gov **13-DA-101 Theranostics: Combined delivery of diagnostic and therapeutic agents for drug abuse/HIV research/treatment.** Development of novel, nanotechnologically-based multimodal imaging approaches (e.g. optical, MR) to deliver combined diagnostic and therapeutic agents to (appropriate) targeted sites with high specificity and in adequate concentrations to realize the promise of combined diagnosis and treatment of drug abuse and HIV/AIDS in a single sitting ("theranostics"). Contact: Dr. Thomas Aigner, 301-435-1314, taigner@nida.nih.gov **13-DA-102 Methods to evaluate the health and safety of nanomaterials.** Develop novel tools and approaches to determine the impact on biological systems and health outcomes of an array of engineered nanomaterials *used to study drug abuse and HIV/AIDS*. Conduct biological, physical and chemical characterization of selected nanomaterials to aid in setting standards for health and safety, and developing computational models for the prediction of long-term secondary effects. Contact: Dr. Thomas Aigner, 301-435-1314, taigner@nida.nih.gov **13-DE-101* Novel Self-Healing Smart Dental and Bio-Restorative Materials.** Dental materials and other biomaterials have limited survival when placed in the human body. Goal: Development of a new generation of "self-healing" and "smart" dental and bio-restorative materials that can diagnose structural failure and repair themselves to minimize the loss of natural structures associated with materials failure. These new materials can also be designed with properties to survive in extreme and adverse conditions, such as in patients with xerostomia. Contact: Dr. James A. Drummond, 301-402-4243, drummondj@nidcr.nih.gov **13-DE-102 Dental Resin Composites and Caries.** Half of all dental restorations fail within 10 years, and replacing them consumes 60% of the average dentist's practice time. Dental materials are challenged by the harsh mechanical and chemical environment of the oral cavity with secondary decay being the major cause of failure. Goal: Development of stronger and longer-lasting biocompatible dental restorations by engineering novel dental materials or new resin systems, enhancing existing materials, and incorporating bioactive agents in materials to combat microbial destruction and to sustain the harsh mechanical and chemical environment of the oral cavity. Contact: Dr. James A. Drummond, 301-402-4243, drummondj@nidcr.nih.gov **13-DK-101 Theranostics.** Examples: Development of novel approaches and technologies relevant to the NIDDK mission including agents with combined diagnostic/therapeutics properties or drug-biomarker combinations useful in Phase 0 studies. These might allow for a more precise diagnosis, assessment of the effectiveness of therapeutic interventions, prediction of individual susceptibility/responsiveness to therapeutic intervention, and optimized personalized therapeutic strategies. Contact**:** Dr. Guillermo Arreaza, 301-594-4724, arreazag@mail.nih.gov. **13-DK-102 Glucose sensing and insulin delivery devices.** Application of nanotechnology and microfabrication advances combined with smart biomaterials to the design of new glucose sensing and insulin delivery devices/platforms. Contact**:** Dr.

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	Guillermo Arreaza, 301-594-4724, arreazag@mail.nih.gov. **13-DK-103 Scaffolds, biomatrices, smart materials.** Examples: Development of novel biomaterials, scaffolds, and biomatrices that may modulate cellular behavior, differentiation, and engraftment to optimize cellular replacement therapies and tissue engineering; Development of smart biomaterials, implantable biohybrids matrices or membranes that may release bioactive agents that promote vascularization, innervation, or inhibit the inflammatory/fibrotic response thus improving biocompatibility and durability. Contact**:** Dr. Guillermo Arreaza, 301-594-4724, arreazag@mail.nih.gov. **13-DK-104 Islet encapsulation.** Development of novel islet encapsulation technologies/biomaterials for the optimization of a bioartificial pancreas. Contact: Dr. Guillermo Arreaza, 301-594-4724, arreazag@mail.nih.gov. **13-EB-101* Theranostics: Combined delivery of diagnostic and therapeutic agents.** Development of novel approaches to deliver combined diagnostic and therapeutic agents to appropriate sites with high specificity and in adequate concentrations to realize the promise of combined diagnosis and treatment of diseases in a single sitting ("theranostics"). Contact: Dr. Lori Henderson, 301-451-4778, hendersonlori@mail.nih.gov ; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **13-EB-102 Non-viral Gene Delivery Systems.** The major barrier to success of gene therapy in the clinic is the lack of safe and efficient DNA delivery methods. Although viral delivery systems allow efficient and long-term gene expression, they generally do not permit targeted delivery to particular cells and tissues and pose problems with regard to immune response. Proposals are invited to develop novel, safe, and targeted, synthetic or viral mimetic vectors for gene delivery including quantitative studies that relate their structure and properties to function. Contact: Dr. Lori Henderson, 301-451-4778, hendersonlori@mail.nih.gov **13-EB-103 Feedback-controlled Drug Delivery Systems**. Current drug delivery technologies allow controlled dosing but are limited in that they don't respond to actual biological status so there is no feedback loop. To address this, a transformation that shifts the current controlled release paradigm from passive (one drug at a single dose over time) to a "smart" active delivery system that includes sensing and biofeedback is needed. Proposals are sought to create smart, active biomaterials that respond to physiological/pathological stimuli by delivering a drug only when necessary and that can be turned off when the stimulus changes with the overall goal of optimizing treatment outcomes. Contact: Dr. Lori Henderson, 301-451-4778, hendersonlori@mail.nih.gov **13-EB-104 Active Biomaterials.** Atomic-level control and production methods have the potential to usher in a new generation of active biomaterials with unprecedented capabilities and applications. New materials are sought with highly-specific molecular recognition capabilities that can undergo drastic changes in conformation and/or chemical functionality when bound to a target. Advanced materials are also sought that can actively adapt to their surrounding environment. This includes materials that can modify their behavior or properties to perform new functions in response to changing conditions, or materials that can sense damaged or malfunctioning portions and initiate repair or restoration. Contact: Dr. Albert Lee, 301-451-4781, alee@mail.nih.gov

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	13-ES-101* **Methods to evaluate the health and safety of nanomaterials.** Evaluation of the health and safety risks of nanoscale products is critical as nanomaterials are being used in applications as diverse as medical devices, drug delivery, cosmetics, and textiles. The development of novel tools and approaches to determine the impact on biological systems and health outcomes of an array of engineered nanomaterials is necessary to protect human health. Biological, physical and chemical characterization of selected nanomaterials will be conducted to aid in setting standards for health and safety and developing computational models for the prediction of long term secondary effects. Contact: Dr. Sri Nadadur, 919-541-5327, Nadadurs@niehs.nih.gov **13-NS-101** **Developing novel biomaterials to interfaces with neural activity.** The burden of neurological illness could be advanced by development of smart biomaterials that enable interfacing with the nervous system to restore function and decrease disability. These might include biomaterials that allow more effective neural-computer interfaces, scaffolds to improve repair of injured nerve or spinal cord as well as neurotransmission across damage nerve or cord. Contact: Dr. Joe Pancrazio, 301-496-1447, jp439m@nih.gov **13-NS-102** **Theranostics in neurological disorders.** Personalized therapy for a large number of neurological disorders is impeded by inability to risk stratify patients. This is especially vexing in conditions in which there is an identifiable anatomic or functional abnormality that is known to be linked to a disabling condition but the risk in the overall population with the abnormality is low; i.e. unruptured intracranial aneurysm or arteriovenous malformation, asymptomatic internal carotid or vertebral artery atherosclerotic stenosis, impaired smell discrimination in Parkinson's disease, first seizure, febrile seizure, etc. Methods to identify those at highest risk, or extremely low risk of disabling event would enhance neurological outcomes, minimize risk of interventions, and improve cost-effectiveness. Contact: Dr. Wendy Galpern, 301-496-9135, wg71m@nih.gov

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(14) Stem Cells	**14-AA-101 Mechanisms of Stem Cell Dysregulation by Alcohol.** The ability to isolate human cord blood stem cells, animal embryonic stem cells and human/animal tissue-specific stem cells, and to manipulate and assess them using commercially available reagents provides an opportunity to examine the effects of alcohol on stem cell survival and differentiation in vitro. Examples of appropriate studies in this area include, but are not limited to: (1) Understand how alcohol-induced changes in mitochondrial metabolism, biogenesis, death pathways, etc. affect stem cell survival and maturation; (2) Determine epigenetic changes due to alcohol exposure in stem cells and their functional consequences; and (3) Identify alterations due to alcohol in stromal cells that support stem cells and determine how these changes influence stem cell fate. Contact: Dr. Svetlana Radaeva, 301-443-1189, sradaeva@mail.nih.gov **14-AA-102 Alcohol's Effects on Endogenous Stem Cells.** Heavy alcohol binges reduce the amount of endogenous stem cells in the brain, especially in the hippocampus. However, it is not well understood how alcohol inhibits neural stem cell proliferation in the brain and how these effects alter function and/or behavior. Research examining the effects of alcohol on neural stem cells may shed light on alcohol's neurodegenerative effects on the brain and the regenerative capacity of these cells. This initiative solicits projects to examine mechanisms of alcohol's effects on neural stem cells, the impact of alcohol on stem cells in other areas of the brain such as the subventricular zone, and an examination of functional and behavioral outcomes of reduced stem cell proliferation as a result of heavy alcohol exposure. Contact: Dr. Tom Greenwell, 301-443-1192, greenwellt@mail.nih.gov **14-AG-101* Induced Pluripotent Stem (iPS) Cells for Aging and Neurodegeneration Research**. Studies have shown that human skin cells can be reprogrammed to become pluripotent stem cells and that such iPS cells act like embryonic stem cells in that they can develop into different cell types. Generating tissue-specific differentiated cells from iPS cells could allow studies on the molecular and cellular changes that characterize aging and neurodegenerative processes. Studies on iPS cells could determine whether they can be used as cell-based models of aging and disease, such as Alzheimer's disease. Two year challenge projects could stimulate the development of, and biological studies on, iPS cells derived from human tissue of different ages and disease states, and could lead to novel drug screening approaches and open up the possibility of individualized cell therapy. Understanding the differentiation of skin-derived iPS cells. Contact: Dr. Bradley Wise, 301-496-9350, wiseb@nia.nih.gov or Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AG-102 Development of stem cell treatment for degenerative diseases of the eye.** Identify biomarkers that can define stem cells and the end-stage cells, as well as reproducible protocols for the generation and purification of viable terminally differentiated cells. The restorative properties of stem cells hold the promise in the treatment of degenerative eye diseases such as macular degeneration, diabetic retinopathy, retinitis pigmentosa and glaucoma, and diseases of the ocular surfaces. Contact: Dr. Wen Chen, 301.496.9350, ChenW@mail.nih.gov **14-AG-103 Induced pluripotent stem cells: Cellular and humanized mouse models of disease.** Somatic cells, such as fibroblasts, from patients with diseases can be used to create cell lines, tissues and, perhaps, organ systems, through induced Pluripotent Stem Cell (iPSC) technology. Such models could be used to elucidate underlying pathology of disease or screen for agents that could be used therapeutically. Combining this approach with mouse strains able to accept multiple human tissues without rejection

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	could provide the microenvironmental milieu to support the tissue's physiological function within the context of the whole organism, enabling greater understanding of disease pathogenesis and providing a platform for preclinical testing of drug candidates. Contact: Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AG-104 Delineate factors that control the differentiation of pluripotent stem cells in the skin and musculoskeletal system into different lineages.** Define the cells' phenotypes as they differentiate along these pathways. Develop a common vocabulary for stem cell differentiation states. Contact: Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AG-105 Exploratory studies of induced pluripotent stem (iPS) cells from healthy individuals and patients with mental/nervous system disorders.** This is an effort to reverse-engineer human disease study by generating and characterizing iPSCs from human control and patient populations. Research topics can include maximizing derivation efficiency, maintenance, or reproducibility, studies of cellular differentiation, screening bioactive agents, or profiling the molecular signature as well as the functional properties of cells from controls vs patients. There will be an emphasis on appropriate validation of iPS cells and their derivatives, evaluating the hetero/homogeneity of any cell populations to be screened and use of cellular assays relevant to normal development, organ function and disease. Contact: Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AG-106 Developing molecular signatures for heart, vascular, lung, and blood diseases by profiling reprogrammed induced pluripotent stem cells derived from affected individuals of defined genotype.** Large-scale profiling of RNA, proteins, and metabolites derived from normal and disease tissues has been instrumental in identifying the molecular etiologies of numerous disorders, but the applicability of this approach has been limited by the availability of relevant biological materials. Cell-based models of disease generated from stem cell technologies could be readily profiled with available high-throughput methods. Contact: Dr. Ronald Kohanski, 301-496-6402, Kohanskir@mail.nih.gov **14-AR-101* Delineate Factors That Control The Differentiation Of Pluripotent Stem Cells In The Skin And Musculoskeletal System Into Different Lineages**. Define the cells' phenotypes as they differentiate along these pathways. Develop a common vocabulary for stem cell differentiation. NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **14-AR-102 Discovery Technologies for Multipotent and Induced Pluripotent Stem Cells from Human Skin and Musculoskeletal Tissues.** Manipulation of stem cells offers exciting opportunities to understand disease and indentify new effective therapies. Identify and characterize multipotent stem cell populations in adult tissues of the skin and musculoskeletal system and develop methods for isolation of these cells. Develop more efficient methods to generate induced pluripotent stem cells from skin cells without the risk of future malignancy due to integration of viral vectors. Delineate factors that control the differentiation of these multipotent and induced pluripotent stem cells into different lineages. Define the cells' phenotypes as they differentiate along these pathways. Develop a common vocabulary for stem cell differentiation. NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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	14-CA-101 Tumor Stem Cells. The role of cancer stem cells remains a controversial and poorly understood area of biology. Some of the pending questions include: the existence and characteristics of tumor stem cells in different tissue types; the relationship between stem cells, tumor cells and dormant cells; role of the microenvironment in the development and harboring of stem cells; the effect of cancer stem cells on treatment. Contact: Dr. Allan Mufson, 301-496-7815, mufsonr@mail.nih.gov **14-CA-102 Understanding the Heterogeneity of Cancer and its Environment.** Cancer is not a disease of a single cell but multiple cells interacting in a timely way to develop and progress through the cancer continuum. These cells make up the greater cancer micro-environment and can include transformed cells, tumor stem cells, differentiating cells and associated stromal cells. Efforts are needed to identify and characterize this cellular milieu so that we can better understand the biology. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **14-CA-103 Cancer\ Stem Medicine.** Development of new technologies to identify and understand intracellular and intercellular communication, algorithms and processes of cancer stem cells (CSCs). This will enable the biomedical community to understand whether CSCs are responsible for the development and spread of cancer and why the disease is resistant to many conventional treatments and able to reestablish itself after therapy. Contact: Dr. Henry Rodriguez, 301-496-1550, rodriguezh@mail.nih.gov **14-CA-104 Resource Development for Stem Cells Research.** There is increasing evidence that cancers may originate in tissue stem or progenitor cells through dysregulation of the normally tightly regulated process of self renewal (1). Further genetic and epigenetic alterations in these cells generate tumors that are driven by a cellular sub-component that retains stem cell properties. These tumor initiating or “cancer stem cells” have been identified in an increasing number of human cancers. This suggests that tissue stem cells or their products might serve as valuable biomarkers for early cancer detection. Furthermore, if cancers originate in these cells then these biomarkers may also prove useful in chemoprevention studies. The identification of cancer stem cells in multiple tumor types has facilitated an initial characterization of molecular pathways which regulate these cells. Interestingly, a number of developmental pathways appear to play a common role in the regulation of both normal and malignant stem cells in multiple organs. Contact: Dr. Sudhir Srivastava, 301-435-1594, srivasts@mail.nih.gov **14-CA-105 Stem Cells for Chemopreventive Interventions.** Cancer stem cells that display tumor-initiating properties have recently been identified in several distinct types of malignancies, holding promise for more effective targeted therapeutic strategies for the most difficult and aggressive cancers. Translational science and genomic studies are needed to validate this hypothesis, as well as to develop a comprehensive understanding of the molecular differences that constitute cancer stem cells. Focus of research in the area will include targeting cancer stem cells to develop effective chemopreventive interventions. Premalignant lesions such as ductal carcinoma in situ of the breast, villous adenomas of the colon and atypical nevi are lesions that are thought to be generated and maintained by progenitor stem cells. Identification of the progenitor stem cells in premalignant lesions and characterization of targetable pathways for elimination of progenitor stem cells in premalignant lesions constitute a challenge area with great potential for cancer prevention. Contacts: Dr. Asad Umar, 301-594-7671, Asad.Umar@nih.gov; Dr. Karen Johnson, 301-402-3666, johnsonn@mail.nih.gov

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	14-DA-101 Generating human neurons with iPS to screen and develop bioactive agents for the treatment of nicotine addiction. Studies are encouraged that use iPS cells for the induction of dopaminergic neurons and other cortical neurons, for the screening and development of bioactive agents for the treatment of nicotine addiction. iPS cells will be generated from addicts and individuals who have been exposed to drugs of abuse but have not become addicted, for biological responses that are genome and genetic specific. In addition, other tissues such as liver, heart, kidney and lung will also be generated to screen for drug toxicity. Contact: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov **14-DA-102 Generating germline-competent ES cells for rodent strains.** The generation of germline-competent ES cells ES cells from many rat and mouse inbred strains has been problematic. This has made the generation of targeted mutations in different genetic background difficult and has prevented the creation of better animal model of disease. Furthermore, ES cell panels, with their broad differentiation potential, are powerful tools for performing complex genetic experiments in vitro. Thus, the development of germline-competent ES cells using iPS or other technologies for different rodent strains is requested. Contact: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov **14-DA-103 Developing iPS cells for addiction and co-morbid mental disorders**. NIDA seeks applications that characterize the physiological response of neurons and glia derived from induced pluripotent stem cells from individuals with addiction and co-morbid mental disorders (autism, schizophrenia, mood disorders). Contacts: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov and Dr. Geraline C. Lin, 301-435-1305 glin@nida.nih.gov **14-DA-104 Exploratory studies of induced pluripotent stem (iPS) cells from healthy individuals and patients with mental/nervous system disorders.** NIDA seeks to support studies that generate and characterize neurons and glia derived from iPSCs from individuals addicted to drugs and controls. Research topics can include maximizing derivation efficiency, maintenance, or reproducibility, studies of cellular differentiation, screening bioactive agents, or profiling the molecular signature as well as the functional properties of cells from controls vs patients. There will be an emphasis on appropriate validation of iPS cells and their derivatives, evaluating the hetero/homogeneity of any cell populations to be screened and use of cellular assays relevant to normal development, organ function and disease. Contacts: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov and Dr. Geraline C. Lin, 301-435-1305, glin@nida.nih.gov **14-DA-105 Induced pluripotent stem cells: Cellular and humanized mouse models of disease.** Studies are encouraged that use iPS cells for the induction of dopaminergic neurons and other cortical neurons, for the screening and development of bioactive agents for the treatment of nicotine addiction. iPS cells will be generated from addicts and individuals who have been exposed to drugs of abuse but have not become addicted, for biological responses that are genome and genetic specific. In addition, other tissues such as liver, heart, kidney and lung will also be generated for functional genomics and for drug toxicity screens. Contacts: Dr. Jonathan D. Pollock, 301-435-1309, jpollock@mail.nih.gov and Dr. Geraline C. Lin, 301-435-1305, glin@nida.nih.gov **14-DA-106 Induced-Pluripotent Stem Cells (iPS) and Cellular Reprogramming Technology in Drug Abuse and Addiction.** Induced pluripotent stem (iPS) cells and cellular reprogramming technology will be used to define the pathophysiology of drug abuse and addiction, including drug-induced neurotoxicity. The knowledge gained will be

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	utilized to repair/restore functions, develop treatment drugs, screen drug toxicity, replace defected cells (where damages are beyond repair/restoration), and make disease diagnosis. Contact: Dr. Geraline C. Lin, 301-435-1305, glin@nida.nih.gov **14-DE-101* Precise Reprogramming of Cells from Oral and Craniofacial Tissues.** Recent advances in reprogramming of somatic cells into induced pluripotent stem cells (iPS) cells constitute an important breakthrough, but the utility of iPS cells for future cell-based therapies is limited by the scarcity of efficient differentiation protocols to guide developmentally primitive iPS cells through a long progression of developmental stages toward fully-differentiated functional somatic cells. Goal: Development of novel approaches for partial reprogramming of somatic cells of the oral and craniofacial complex (e.g. periodontal ligament cells, pulp cells, oral mucosal cells, salivary acinar cells, fibrocartilaginous cells of the temporomandibular joint) for cell-based therapies to heal and restore these tissues following disease or trauma. Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov **14-DE-102 Characterizing the Normal and Pathological Oral Mucosal Stem Cell Niche.** Despite efforts in oral cancer research, the molecular and cellular events leading to the initiation and early progression of oral cancer remain elusive. Notably, the structure and function of the normal oral mucosal stem cell niche that support the regenerative capacity of oral mucosa have not been characterized and the mechanisms of malignant transformation of normal mucosal cells are unknown. Goal: Elucidation of the interactions between the stem cell niche, the stromal microenvironment and the immune system that induce and support oral cancer progression and control regeneration of normal mucosa. Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov **14-DE-103 Enhancing Human Embryonic Stem (ES) Cell Culture Systems.** Cell differentiation and tissue morphogenesis during normal development is guided by the highly orchestrated temporal, spatial and combinatorial action of multiple of ligands, signaling pathways, transcription factors, and extracellular matrices. In light of this tremendous complexity, the existing human ES cell *in vitro* culture systems lack appropriate sophistication thus necessitating the need for strategies to better mimic normal developmental processes. Recent progress in the fields of bioengineering, nanotechnology, biomaterials and bioimaging offer a wealth of tools that can lend tight control of the multiple parameters needed to improve the existing human ES culture systems. **Goal**: Integration of engineering disciplines with developmental biology and with ES cell technology for deriving a new generation of human ES cell culture protocols that will facilitate the application of ES cell-based therapies for the treatment of a multitude of human tissue degenerative diseases and trauma, including those of oral and craniofacial complex. Contact: Dr. Nadya Lumelsky, 301-594-7703, Nadya.Lumelsky@nih.gov **14-DK-101* Induced pluripotent stem cells--cellular and humanized mouse models of disease.** Somatic cells, such as fibroblasts, from patients with diseases can be used to create cell lines, tissues and, perhaps, organ systems, through induced Pluripotent Stem Cell (iPSC) technology. Such models could be used to elucidate underlying pathology of disease or screen for agents that could be used therapeutically. Combining this approach with mouse strains able to accept multiple human tissues without rejection could provide the microenvironmental milieu to support the tissue's physiological function within the context of the whole organism, enabling greater understanding of disease pathogenesis and providing a platform for preclinical testing of drug candidates. Contact**:** Dr. Dan Wright, 301-594-7717, wrightdan@mail.nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov; NIAMS Contact: Dr. Joan McGowan, 301-

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	594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **14-DK-102 Discovery of methods to program stem or progenitor cells.** These methods would allow manipulation of stem or progenitor cells in a predictable manner to differentiate into cells/tissues of NIDDK relevance; such as, hematopoietic cells, bladder, liver, intestine, pancreas, kidney, prostate, etc. Studies may rely upon model organisms with a goal of application to humans. Contact**:** Dr. Sheryl Sato, 301-594-8811, smsato@mail.nih.gov. **14-DK-103 Generation of stem cells from patients with NIDDK-relevant genetic diseases.** Stem cells from patients (either derived directly or reprogrammed into induced pluripotent stem cells (iPS)/progenitor cells) can be used to explore disease processes as they develop from stem, progenitor or iPS cells. This model cell system can then be used from patients to test therapeutics. Contact**:** Dr. Dan Wright, 301-594-7717, wrightdan@mail.nih.gov. **14-DK-104 In vitro differentiation of human Embryonic Stem Cells (ES)/ Induced Pluripotent Stem Cells (iPS) to NIDDK relevant cells/tissues.** Strategies could be developed to direct the differentiation of pluripotent stem cells toward a desired cell fate. The identification of small molecules/growth factors that could carry out this process efficiently would enable the generation of novel cellular replacement therapies for NIDDK relevant diseases. Contact: Dr. Sheryl Sato, 301-594-8811, smsato@mail.nih.gov. **14-EB-101 Synthetic Delivery Systems for Generating Pluripotent Stem Cells.** Induced Pluripotent Stem Cells (iPSCs) are rapidly becoming an important new source of cells for regenerative medicine. Recent publications indicate that the expression of a small number of endogenous pluripotent factors for a short period of time, can reprogram differentiated cells back to a pluripotent state. The method so far has required the use of viral vectors and thus has limited therapeutic potential due to the increased potential for tumor formation. Therefore, it is necessary to develop new delivery methods for the transient expression of the relevant reprogramming genes, without permanent integration into the genome. Applications focused on the development of synthetic delivery systems for the safe, effective and efficient targeting and delivery of genes to produce iPSCs is encouraged. Contact: Dr. Rosemarie Hunziker, 301-451-1609, hunzikerr@mail.nih.gov **14-EB-102 Imaging Stem Cell Migration and Differentiation**. Stem cells, which have the ability to differentiate into a diverse range of specialized cell types, have the potential to dramatically change the treatment of human disease. Imaging will play an important role in monitoring stem cell therapy. NIH invites applications that will allow imaging of stem cell migration and differentiation *in vivo* using novel molecular imaging approaches. Contact: Dr. Guoying Liu; 301 594-5220; liug@mail.nih.gov. **14-ES-101 Effects of exposures to pluripotent cells growth, development and function.** Tissues that have the potential to differentiate into a variety of cell types during maturation may be especially sensitive to the effects of environmental exposures. Support for research that determines the effects of environmentally relevant exposures on differentiation, proliferation, function and survival of multi-potent cells in targeted tissues during a range of windows of susceptibility would increase our understanding of the cellular targets for insult and how the cells respond during different life stages could provide value insight into both prevention and treatment strategies for a variety of diseases. Contact: Dr. Les Reinlib, 919-541-4998, Reinlib@niehs.nih.gov

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	14-ES-102 Use of stem cells for predictive toxicology. A recently released National Academy of Sciences committee report entitled "Toxicity Testing in the Twenty-first Century: A Vision and a Strategy" concluded that a transformative paradigm shift is needed to: (1) provide broad coverage of chemicals, chemical mixtures, outcomes, and life stages, (2) reduce the cost and time of testing, (3)use fewer animals and cause minimal suffering in the animals used, and (4) develop a more robust scientific basis for assessing health effects of environmental agents. Human stem cells or cell lines have the potential to revolutionize toxicity evaluation and risk assessment, reducing the necessity for disease development. Studies are being sought that capitalize on the unique properties of human stem cells to develop high through-put predictive toxicology screens for environmental toxicants. Contact: Dr. William Suk, 919-541-0797, suk@niehs.nih.gov **14-EY-101* Development of stem cell treatment for degenerative diseases of the eye.** The restorative properties of stem cells hold the promise in the treatment of degenerative eye diseases such as macular degeneration, diabetic retinopathy, retinitis pigmentosa and glaucoma, and diseases of the ocular surfaces. There is a need for the identification of biomarkers that can define stem cells and the end-stage cells, as well as reproducible protocols for the generation and purification of viable terminally differentiated cells. Contact: Dr. Grace Shen, 301-451-2020, sheng@mail.nih.gov **14-GM-101 High-efficiency genetic reprogramming of adult cells**. Development of methods to 1) genetically reprogram, at high efficiency, differentiated human cells from adult tissues into cells that indefinitely self-renew and have the full potential of embryonic stem cells to differentiate into any cell type of the human body, and 2) define temporally the molecular steps that accompany this reprogramming. Contact: Dr. Marion Zatz, 301-594-0943, zatzm@nigms.nih.gov **14-HD-101 Stem Cell Research for Down, Rett and Fragile X Syndromes and Other Neurodevelopmental Disorders.** With the successful creation of neurons derived from induced pluripotent stem cells (iPSCs) from individuals with spinal muscular atrophy, researchers are poised to refine and adapt this technology to other neurodevelopmental disorders. Targeted efforts are needed to produce redifferentiated neurons from iPSCs derived from skin fibroblasts of individuals with conditions that share phenotypic characteristics but have different genetic origins, such as Down syndrome, Rett syndrome, and Fragile X syndrome, or that have well-defined genetic origins, such as Williams syndrome or other chromosomal aneusomies. Such research holds the potential to better understand neurodevelopmental disorders at the cellular and molecular level by developing and characterizing iPSCs from individuals with specific genetic conditions or partial duplications or deletions of defined chromosomal regions. Contact: Dr. Mary Lou Oster-Granite, 301-435-6866, granitem@mail.nih.gov. **14-HD-102 Identifying Reprogramming Factors for Oocytes**. Studies aimed at using gene expression arrays to identify oocyte cytoplasmic factors responsible for the reprogramming ability of oocytes offer significant scientific opportunities. Oocyte cytoplasmic factors may be helpful in designing new approaches to the reprogramming of somatic cells into induced pluripotent stem cells (iPSCs) and to help understand the pluripotential properties of embryonic stem cells (ESCS). Research is needed to identify key reprogramming factors and the comparative expression profiling between oocyte cytoplasm, iPSCs and ESCs. Contact: Dr. Richard Tasca, 301-435-6973, rt34g@nih.gov **14-HL-101* Develop molecular signatures for heart, vascular, lung, and blood diseases by profiling reprogrammed induced pluripotent stem cells derived from**

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	affected individuals of defined genotype. Large-scale profiling of RNA, proteins, and metabolites derived from normal and disease tissues has been instrumental in identifying the molecular etiologies of numerous disorders, but the applicability of this approach has been limited by the availability of relevant biological materials. Cell-based models of disease generated from stem cell technologies could be readily profiled with available high-throughput methods. Such studies could be undertaken on small numbers of control and affected individuals or on a larger population that would more broadly sample human genetic variation and thereby allow statistical associations to be established among genotypes, clinical traits, and molecular signatures that may elucidate causal mechanisms underlying complex diseases. Contact: Dr. Alan Michelson, 301-594-5353, michelsonam@nhlbi.nih.gov **14-HL-102 Bio-models and scaffolds for blood cell production and tissue regeneration**. Stem cells have the potential to serve as a virtually unlimited source of all blood cell lineages for use in transfusion medicine, other cellular therapies, and tissue regeneration. Generation of blood cells of the required lineages and in the required numbers, and tissue regeneration uses spatial cues and tissue topography not reproduced in simple cell culture systems. Advances in stem cell technology and blood cell signaling networks have led us to the point that new bio-models and scaffolds can be developed to regenerate tissues and increase blood cell production to levels needed for clinical applications. Contact: Dr. John Thomas, 301-435-0065, thomasj@nhlbi.nih.gov **14-MH-101* Developing iPS cells for mental disorders.** Create human induced pluripotent stem (iPS) cells from individuals with and without mental disorders and conduct exploratory studies. Goals might include maximizing derivation efficiency/reproducibility, modeling trajectories of cellular differentiation, or profiling differences in the molecular signature of cells. Contact: Dr. David M. Panchision, 301-443-5288, panchisiond@mail.nih.gov **14-NS-101* Reverse engineering human neurological disease.** It is now conceivable to reverse-engineer human neurological disease by generating and characterizing iPSCs from human control and patient populations. The relatively easy access of source tissue provides a means of elucidating patient-specific cell dysfunction or response to candidate therapeutics. Research topics can include maximizing derivation efficiency, maintenance, or reproducibility, studies of cellular differentiation, screening bioactive agents, or profiling the molecular signature as well as the functional properties of cells from controls vs. patients. There will be an emphasis on appropriate validation of iPS cells and their derivatives, evaluating the hetero/homogeneity of any cell populations to be screened and use of cellular assays relevant to normal development, organ function and disease. Contact: Dr. David Owens, 301-496-1447, do47h@nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov

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(15) Translational Science	**15-AA-101* Determining If and How Adolescent Behaviors Affect Connections in the Developing Brain.** The brain develops throughout adolescence and into early adulthood, and there is accumulating evidence that behaviors exhibited during this period can influence lifetime health and well-being. Research is needed to address the critical question – do these behaviors actually rewire the developing brain thereby creating vulnerability for a number of persistent health problems including mental health disorders, eating disorders and addiction? Contact: Dr. Antonio Noronha, 301-443-7722, anoronha@mail.nih.gov; ORWH Contact: Dr. Indira Jevaji, 301-402-1770, jevajiip@od.nih.gov **15-AA-102 Neurosteroids in alcohol intoxication, dependence, withdrawal and relapse.** Neurosteroids are important neuroactive substrates that have been demonstrated to be involved in several neurophysiological and disease processes, and alcohol has been shown to significantly increase neurosteroid levels in the brain. Accumulating evidence indicates that neurosteroids interact with neuroendocrine and multiple neurotransmission systems, and may play a crucial role in the pathophysiology of alcohol intoxication, dependence, withdrawal and relapse. Studies are needed to understand the effects and mechanisms of action of acute and chronic alcohol exposures on the homeostasis of neurosteroids and their interactions with the networks of neuroendocrine, neurotransmission and neural signal transduction systems. This research is key to elucidating the molecular and cellular targets of ethanol, exploring the therapeutic potentials of agents acting on the neurosteroid system, and increasing our understanding of the results of animal and clinical studies. Contact: Dr. Qi-Ying Liu, 301 443-2678, liuqiy@mail.nih.gov **15-AA-103 Therapeutics and Therapeutic Screens for Fetal Alcohol Spectrum Disorders.** In utero exposure to ethanol can have a wide range of possible adverse developmental consequences, commonly referred to as Fetal Alcohol Spectrum Disorders (FASD). FASD may cause lifelong debilitating cognitive, behavioral, and emotional impairments. Damage to the developing brain can occur at any stage of pregnancy, even before the woman is aware that she is pregnant. Efforts to encourage women to abstain from alcohol during pregnancy have not been completely successful; therefore, alternative approaches to prevention/amelioration are sought. Among the possibilities are prenatal and postnatal treatments with drugs, nutritional supplements, or gene therapies intended to block or reverse the harmful effects of alcohol. Even if targets are identified, there are no high-throughput screens for identifying successful treatments of FASD. This initiative would provide funding to develop approaches that consider developmental neurobiology in pediatric drug development, and use models that are relevant to the developing brain that test safety and efficacy. The development of high-throughput screens or standardized model systems could identify new targets which have a significant impact on treatment of FASD and other neurodevelopmental disorders. Contact: Dr. Tom Greenwell, 301-443-1192, greenwellt@mail.nih.gov **15-AA-104 PTSD and Alcohol Dependence.** Epidemiological evidence indicates that a percentage of individuals exposed to trauma will go on to develop alcohol abuse and dependence. Of immediate concern are the numbers of military personnel who experience post traumatic stress disorder and alcohol abuse. Recent observations indicate that prazosin, an alpha 1 adrenergic receptor antagonist, has been effective in reducing alcohol consumption. Medications to reverse trauma associated alcohol abuse could have an immediate impact on military veterans but also on civilian victims of trauma. This initiative would support testing of promising molecular targets such as adrenergic receptors, CRF receptors, etc. for effectiveness in animal models. In addition the identification of new

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	targets by examining the neurocircuits involved in fear response is encouraged. Contact person: Dr. Lindsey Grandison, 301-443-0606, lgrandis@mail.nih.gov **15-AA-105 Discovering New Medication Targets for Alcohol Dependence.** To advance development of medications that reduce alcohol drinking and sustain abstinence in alcohol dependent patients, this initiative will support projects evaluating novel pharmacological targets in animal models of alcohol dependence. Several targets have shown promise clinically and in preclinical studies, yet many additional targets (e.g., chemokines, stress and pain pathways) remain to be explored. Expanding the base of promising targets will stimulate testing and discovery of novel pharmacotherapies for alcohol dependence in the future. Contact: Dr. Mark Egli, 301-594-6382**,** megli@mail.nih.gov **15-AA-106 Functional Roles of Neuroimmune Factors in Mediating Binge Drinking.** Neuroimmune factors have significant impacts on both normal brain functions and a variety of neurological and behavioral disorders. Emerging data suggest that the physiological functions of neuroimmune factors, such as cytokines and chemokines, are not restricted to mediating neuroinflammatory responses. This paradigm shift offers a new framework for understanding the roles of neuroimmune factors in mediating alcohol drinking. Although a limited number of studies suggest that neuroimmune factors, particularly chemokines, mediate alcohol drinking behavior, it is essentially unknown how chemokines exert their effects. This initiative encourages research on the roles of chemokines in mediating alcohol drinking behavior. Such research is expected to improve our understanding of the mechanisms of excessive drinking. Contact: Dr. Changhai Cui, 301-443-1678, Changhai@mail.nih.gov **15-AA-107 Refinements of Procedures for Diffusion Tensor Imaging in Rodent Models of Alcohol Dependence.** Diffusion tensor imaging (DTI) has been used in human studies to visualize the direction of white matter tracts in the brain and to provide measurements related to the microstructural integrity of the fiber tracts in health and disease. Many of the technological advances in neuroimaging in humans have only recently been applied to small animal models such as mice and rats. Differences in head size and shape have been one of the issues that have impeded imaging in animals at an acceptable spatial resolution. A number of small animal models have been developed for the study of alcohol dependence and the application of neuroimaging techniques can be of great value in understanding the effects of alcohol in the brain. This initiative will support further development of procedures for DTI in small animals. Contact: Dr. John Matochik, 301-451-7319, jmatochi@mail.nih.gov **15-AA-108 Molecular Mechanisms of Alcohol Dose Effects.** It is well known that, in contrast to heavy alcohol drinking, moderate alcohol consumption can benefit human cognitive functions. Although there is extensive research on the damaging effects of alcohol on the brain, very little is known about neuronal mechanisms underlying the beneficial effects of moderate alcohol consumption. Recent studies have shown that low concentrations of ethanol produce distinct effects on brain functions compared to high concentrations of ethanol. That is, low concentrations of ethanol modulate neurotransmitter receptors and signaling pathways differently compared to high concentrations of ethanol. Thus, depending on concentration, ethanol may exert differential effects on molecular targets in the brain. Further studies are sought on this topic to advance our understanding of the molecular and cellular mechanisms underlying beneficial versus deleterious effects of alcohol. Contact: Dr. Changhai Cui, 301-443-1678, Changhai@mail.nih.gov

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	15-AG-101 Nose-Brain Barrier. Research to manipulate or to design novel vehicles for overcoming the nose-brain-barrier to deliver CNS therapies for age-related neurodegenerative diseases. Contact: Dr. Steven Snyder, 301-496-9350, snyderd@mail.nih.gov **15-AG-102 New models and measures in pre-clinical chronic pain research**. Existing animal models of temporomandibular or orofacial pain conditions inadequately reflect the pathology or the phenotypes of the human state. Development of new animal models to study the transition from acute to chronic pain in temporomandibular joint disorders or other orofacial pain disorders, coupled with the development of new functional and behavioral assays of acute and chronic pain would be a powerful means to enhance our understanding of the biological mechanisms underlying the development of these chronic pain conditions and the responses of patients to therapeutic interventions. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **15-AG-103 Protein misfolding in degenerative diseases of the eye.** A number of ocular genetic diseases occur due to misfolding/aggregation of proteins, for example the visual pigment protein, rhodopsin in retinitis pigmentosa, crystallins in age-related cataracts, and myocillin in glaucoma. Identifying therapeutic pharmacological agents/drugs that prevent the misfolding/aggregation of proteins could provide new tools for treating these diseases. Contact: Dr. Wen Chen, 301-496-9350, ChenW@mail.nih.gov **15-AG-104 Manipulating the blood-brain-barrier to deliver CNS therapies for mental/nervous system disorders.** Develop potentially useful means of CNS drug targeting and delivery systems. A variety of neuro-scientific discoveries have led to promising therapeutic strategies for treatment of severe neurological disorders. However, it remains a major hurdle to deliver potentially exciting agents such as RNA therapies, genes, critical enzymes, antibodies, other molecular entities, or cell therapies past the blood brain barrier. Contact: Dr. Steven Snyder, 301-496-9350, snyderd@mail.nih.gov **15-AG-105 NIH partners in research program: Pathways for translational research.** Develop strategies for dissemination of interventions with demonstrated effectiveness for translation into clinical practice by teams of academic and community research partners. This initiative will provide the knowledge to more rapidly move scientific findings into communities to improve health. Contact: Dr. Chhanda Dutta, 301-435-3048, duttac@nia.nih.gov **15-AG-106 Identification of bioactive macronutrients in the diet that impact metabolic state.** Recent studies suggest that specific types of macronutrients in the diet, such as resistant starch or branched chain amino acids, may have selective effects on nutrient absorption, insulin sensitivity, and lipid metabolism. Elucidation of the metabolic impact of specific dietary components may well result in improved efficacy of lifestyle approaches to reduce obesity and metabolic diseases. This solicitation encourages pilot studies to identify specific bioactive components in the diet and study their mechanisms of action. Contact: Dr. Chhanda Dutta, 301-435-3048, duttac@nia.nih.gov **15-AI-101* Explore the earliest events in HIV infection and use this information to develop new interventions for preventing and treating HIV infection.** Despite recent progress in HIV research, important questions remain: what molecular interactions regulate HIV expression and replication, why the host immune response cannot control the infection, and how reservoirs of infection persist in the body despite highly active antiretroviral treatment. Basic scientific information about how the virus attacks the body

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	and how the body defends itself, especially in the earliest stages of infection, will identify new viral targets for the development of new prevention approaches and therapeutics. Contact: Dr. Sandra Bridges, 301-496-8198, sbridges@niaid.nih.gov **15-AI-102* Develop diagnostics and drugs for multiple or extensively drug-resistant tuberculosis (MDR/XDR TB).** To prevent the further emergence and spread of MDR/XDR TB, there is an urgent need to develop and test reliable technologies to rapidly diagnose TB and to identify drug resistance. There is a similarly urgent need to define the most effective use of existing TB therapies and other antibiotics for treating drug-resistant TB and to develop new drugs, particularly for MDR/XDR TB. Contact: Dr. Christine Sizemore, 301-435-2857, csizemore@mail.nih.gov **15-AI-103* Develop drugs for neglected tropical diseases, with a special emphasis on malaria.** The emergence of drug-resistant parasites has contributed to the spread of malaria in areas and populations where malaria had previously been controlled. A continuous pipeline of new and effective anti-malarial drugs is essential to achieve and sustain progress in disease control. Market forces have been inadequate to support development or deployment of interventions for malaria and other neglected tropical diseases. Therefore, there is an urgent need to support research leading to the development of novel and more effective interventions. Contact: Dr. John Rogers, 301-402-8304, jrogers@mail.nih.gov **15-AI-104 Define the reservoirs of latent HIV infection.** Studies are needed to define the reservoirs of latent HIV *in vivo*, and establish robust cellular models that accurately mimic the properties of the reservoir. Additional studies are needed to demonstrate the feasibility of using these cellular models *in vitro* to define ways of selectively targeting and eliminating reservoirs of infection. Contact: Dr. Sandra Bridges, 301-496-8198, sbridges@niaid.nih.gov **15-AI-105 Discover and develop new antiviral agents for use in pre-and post-exposure prophylaxis to prevent HIV infection**. Contact: Dr. Fulvia Veronese, 301-402-4148, veronesf@niaid.nih.gov **15-AI-106 Translational research focused on high priority pathogens and basic research focused on resistance mechanisms.** High priority pathogens include influenza (e.g. impact of co-infection), tuberculosis (e.g. role of clades and animal host transmission in clinical disease), and malaria (e.g. diagnosis and impact of multiple strain infections). Basic research on resistance mechanisms may include viral resistance. Contacts: Dr. Christine Sizemore, 301-435-2857, csizemore@mail.nih.gov; Dr. John Rogers, 301-402-8304, jrogers@mail.nih.gov **15-AR-101 Interrelationships Between The Immune Response And Regulatory And Structural Components Of Synovium, Cartilage, Bone And Muscle In Health And Disease.** The objective is to promote multi and interdisciplinary research teams and projects that will effectively and swiftly integrate the study of immune mechanisms in the investigation of pathogenesis of chronic musculoskeletal, skin and muscle diseases. Recent work indicates that bone and possibly skeletal muscle and the immune system share some of a complex network of cytokines and molecular mediators that regulate function and homeostasis. Better understanding in normal and pathological situations of interactions between the immune system and bone, muscle, skin and joint tissue will lay the groundwork for future therapies for diseases within the NIAMS mission. Contact: Dr.

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	Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **15-AR-102 Link Genomics, Proteomics, Bioinformatics, And Systems Biology To Clinically Relevant Outcomes in Autoimmune Diseases.** The objective is to develop new, cost effective and accurate tools that will be used to predict, prevent and monitor autoimmune diseases. Define assays that are effective at monitoring disease activity and that predict the development of specific complications. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov **15-AR-103 Joint Structures, Alignment, and Gait.** The development of appropriate therapies and biomarkers for arthritis requires a clear understanding of the risk factors and structural components that are associated with well-phenotyped disease. The goal is to develop collaborative research teams that include bioengineers, kinesiologists, rheumatologists, orthopaedic surgeons, physiatrists and imagers to improve our understanding of the interactions between joint structures, alignment, and gait. Such collaborations could lead to the development of multidisciplinary and multi-systems approaches to treatment and prevention of disease. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **15-AR-104 Bone and the Nervous System.** Nerves thread throughout bones, carrying chemical and electrical messages to and from the brain. Evidence has begun to accumulate suggesting that the nervous system can have significant influence on the balance between bone formation and bone resorption. Understanding this communication between bone and nervous system could lead to new therapies to prevent or reverse bone loss. It could also reveal previously unrecognized side effects of drugs already in wide use for the treatment of high blood pressure, seizures, and depression. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **15-AR-105 Bone And Adipose Tissue**. Recent advances have shown that bone metabolism is closely linked to regulation of energy metabolism, and is sensitive to signals originating in adipose tissue, the digestive system, and the central nervous system. The unanticipated consequences of certain drugs may occur because their targets often have functional roles in several different tissues, and signals can arise in one tissue and act in another. For example, some drugs that are widely used to control diabetes may have deleterious effects on bone. Targeting specific molecules and biochemical pathways that mediate the interactions between bone and adipose tissue will be critical to develop therapies that improve both bone health and energy metabolism. Contact: Dr. Joan McGowan, 301-594-5055, NIAMShelp-NIHChallengeGrants@mail.nih.gov **15-AR-106 Transdermal Drug Delivery.** Transdermal delivery of drugs for local and systemic therapy have several advantages over oral and IV administration and hypodermic injection, including improved bioavailability, prolonged release, increased patient compliance, cost, and the avoidance of needles.. There is a need to improve our understanding of the skin barrier function and identify molecules and processes that could be targeted to affect skin permeability. Transdermal delivery could be extended to hydrophilic small molecules and macromolecules such as peptides, monoclonal antibodies, siRNAs and nanoparticles. In addition, vaccines delivered to skin may generate a stronger immune response through the targeting of epidermal Langerhans' cells and dermal dendritic cells. Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov

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	15-CA-101* **The Role of Cellular Architecture in Normal and Tumor Cell Biology.** The size and shape of a cell, as well as the placement of organelles and the arrangement of chromosomes within the nucleus are highly regulated and ordered. Changes in cell shape or rigidity of the microenvironment affect the patterns of gene expression and cell growth. These findings indicate that extracellular mechanical forces can alter a cell's behavior. Recent studies have demonstrated that genes are differentially positioned within the nucleus when they are silent or expressed. Furthermore, the genome is organized into chromosomal domains whose composition changes in different cell types and in cancer. These studies indicate that cellular architecture plays a critical role in regulating cell phenotype. Further studies are needed to define the relationship between cellular architecture and cell function, in both normal and tumor cells. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **15-CA-102*** **Understanding mechanisms of hormone refractory cancers for therapeutic targeting.** Steroid receptors continue to play a major role in controlling the growth of hormone-refractory cancers and appear to accomplish this by: the activation of steroid receptors by alternate ligands; local production of steroid hormone; stabilization of steroid receptors and mutations that render steroid receptors hypersensitive to very low levels of the ligands. In addition, recent findings demonstrate that in patients treated with herceptin, ER levels and ER-mediated signaling is enhanced, while in patients treated with antiestrogens, Her 2-mediated signaling is enhanced. Furthermore, at least 25% of the genes modulated in these cancers are via non-genomic signaling. A comprehensive understanding of the molecular underpinnings of steroid receptor dependence of hormone-refractory tumors as well elucidating the subtleties of these regulatory pathways and their crosstalk will support personalized, predictive and preemptive medicine in human breast and prostate cancer. Contacts: Dr. Judy Mietz, 301-496-9326, mietzj@mail.nih.gov; Dr. Dinah Singer, 301-496-8636, singerd@mail.nih.gov **15-CA-103** **Thyroid Cancer Cell Line Project.** Thyroid cancer is poorly understood and managed. One of the challenges is model experimental systems. The community needs a set of well defined human thyroid cell lines reflecting the different thyroid diseases and disease states. Contact: Dr. Rihab Yassin, 301-496-7028, yassinr@mail.nih.gov **15-CA-104** **Use of novel mouse genetic resources to elucidate determinants of drug toxicities.** A major limitation of human clinical trials is occurrence of toxicities not anticipated from preclinical studies; one example is cardio-toxicity associated with non-steroidal anti-inflammatory drugs. No preclinical studies at present accurately model the important conditions of clinical trials (e.g., metabolic status, genetic heterogeneity). The NCI [and probably NIDA, NIEHS, and NIAAA] invites projects that exploit new mouse genetic resources to disclose the genetic loci, subtle interactions among them, and interactions with environmental effectors (e.g., diet, activity level, stress) that underlie development of toxicities to common therapeutic and preventive agents. Contact: Dr. Cheryl Marks, 301-594-8778, marksc@mail.nih.gov **15-CA-105** **The Biology of Cancer in Adolescents and Young Adults.** A Progress Review Group, involving the NCI, the Lance Armstrong Foundation and the LIVESTRONG Young Adult Alliance, identified the need to determine if unique biological and molecular differences underlie adolescent and young adult cancer with respect to prognosis and therapeutic outcome and differentiate it from the disease in younger or older patients. Studies are encouraged using existing tissue samples to investigate whether definitive biological and genetic differences exist in cancers in the 15-39 year age group and whether any such differences could account for the different disease outcomes

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	experienced by this group. Appropriate topics of investigation could include epigenetic differences, developmental influences or microenvironment changes. Contact: Dr. Don Blair, 301-496-9740, blaird@mail.nih.gov **15-CA-106 Understanding the Molecular Basis of Cancer Cachexia.** Cachexia is a major problem in cancer patients and a clear understanding of the molecular mechanisms by which this occurs would be of substantial benefit. Cachexia is a pathological state where loss of muscle or muscle and fat and occurs and contributes to significant morbidity and mortality. The most prominent clinical feature of cachexia is weight loss, but it is distinct from starvation and age-related muscle loss. Inflammation and anorexia are frequent characteristics, but they are non-obligatory criteria for the diagnosis of cachexia. Much work is needed to reveal the underlying triggers for cachexia and the metabolic pathways that are disrupted. Development of animals for cachexia would greatly enhance our ability to investigate this process which complicates effective treatment of cancer. Contact: Dr. Barbara Spalholz, 301-496-7028, spalholb@mail.nih.gov **15-CA-107 Multi-scale Modeling: from Molecules to Populations.** At a molecular level cancer can develop from the aberrant expression of critical cancer genes. One of the challenges in modeling cancer is how these mechanistic alterations can be reflected across scales and dimensions. What is the effect of these changes in a cellular or tissue environment? And moving up the scale how can these changes be monitored or study at the patient or population level? Contact: Dr. Jennifer Couch, 301-435-5226, couchj@mail.nih.gov **15-CA-108 Application of Novel Biological Model Systems to Cancer.** The use of Drosophila, Zebrafish, and embryonic microenvironments for the study of cancer progression and for testing paradigms in cancer. Contact: Dr. Judy Mietz, 301-496-9326, mietzj@mail.nih.gov **15-CA-109 Role of lymphangiogenesis in tumor invasion and metastasis.** While the research in the area of tumor cell dissemination via tumor angiogenesis have become a fertile area of basic research resulting in the development of novel therapeutics such as Avastin, our knowledge in understanding the role of lymphatics and lymphangiogenesis in lymph node metastasis is extremely sketchy. Investigations that result in generation of novel lymphangiogenic models as well as deciphering novel signaling pathways of lymphangiogenesis and the role of lymphatics in distant or nodal metastasis is encouraged. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **15-CA-110 Application of the Microbiome to Cancer Understanding.** As the inventory of biological agents in humans becomes realized it will be important to determine the role of these potential agents have in the development and progression of cancer. Contact: Dr. Kevin Howcroft, 301-496-7815, howcrofk@mail.nih.gov **15-CA-111 Infectious Disease and Inflammation in Cancer.** A number of infectious agents have been directly implicated in cancer development. Research is needed to not only examine other potential biological agents but also how these agents can interact with the host to develop an environment of transformation. Contact: Dr. Kevin Howcroft, 301-496-7815, howcrofk@mail.nih.gov **15-CA-112 Cancer Cell Energy Metabolism and Cancer Causation.** Nutrients such as glucose and amino acids are key signals of the signaling network that regulates the survival, growth, and proliferation of mammalian cells. Through a mechanism generally

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	known as “nutrient sensing”, nutrients activate various signal transduction pathways that turn on or off cellular machineries to adapt accordingly. Defects in these signal transduction pathways often uncouples nutrient uptake and proper cellular response, which leads to physiological conditions including obesity that are cancer contributing factors. The objectives of this initiative are to identify metabolic networks distinct to cancer cells; to define the major regulatory nodes for cancer cell energy metabolism; to identify critical steps in adaptation of cancer cells to nutrient deprivation, for example hypoxia; to define differences in metabolic pathways among cell and tissue types; to begin to understand the relationship between the incidence of cancer and the energy networks disregulated in diabetes and obesity. Contact: Dr. Barbara Spalholz, 301-496-7028, spalholb@mail.nih.gov **15-CA-113 Chromosome Structure in Cancer Biology.** DNA is packaged in the nuclease in a sophisticated way in order to control its transcription. New tools and imaging approaches are needed to characterize and understand these processes in the developing cancer. Contact: Dr. Judy Mietz, 301-496-9326, mietzj@mail.nih.gov **15-CA-114 Telomere dysfunction in the development and progression of cancer.** Cancer cells have lost their ability to manage the telomeric ends of their chromosomes leading to the inappropriate addition of telomere repeats by the maintenance enzyme telomerase and to genomic instability resulting from altered telomere structures. Understanding the mechanisms by which telomere dysfunction arises and contributes to the formation and progression of cancer can lead to the development of novel therapeutic treatments for cancer. Contact: Dr. Dick Pelroy, 301-496-9326, pelroyd@mail.nih.gov **15-CA-115 Cancer as a systemic disease.** In addition to the local changes in the tumor microenvironment, several studies suggest that tumor cells induce systemic changes in the host that may promote tumor growth and accelerate metastatic dissemination. Understanding the molecular mechanisms of these pathways will provide novel prevention and therapeutic strategies. Key areas of priorities include: Genotype specific differences in angiogenesis, tumorigenesis susceptibility and risk of metastatic spread. Mechanisms to understand mobilization of bone marrow derived or mesenchymal stem cells by tumors. Mechanisms and clinical relevance of early cancer dissemination and tumor dormancy. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **15-CA-116 The role of bone marrow derived cells (BMDCs) in tumor initiation, progression and metastasis.** Recent evidence suggests that the bone marrow derived or mesenchymal cells can contribute to early tumorigenesis or promote or enhance organ specific metastasis. However the exact mechanism by which this is accomplished is poorly understood. Investigators are encouraged to address critical issues in understanding the role of BMDCs in promoting tumor growth in the primary site as well as promoting metastasis in distant organs such as brain, lung, liver and bone. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **15-CA-117 Tumor dormancy.** Many investigators have demonstrated that tumor cells from the primary organs can disseminate to distant sites early in cancer development and lie dormant for long periods of time before they can be activated to form distant metastases. However, there is a paucity of information as to nature of these dormant cells as well as mechanisms of their activation. There are several key issues in tumor dormancy, an increased understanding of which will help investigators design novel ways to block activation of dormant tumor cells or induce dormancy in active tumor cells. Our major areas of interests are to (1) delineate mechanisms of tumor dormancy in the bone marrow and other organs, and identify critical pathways of activation of dormant tumor

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	cells; (2) identify novel pathways to induce dormancy in aggressive tumor cells and delineate mechanisms of dormant tumor cell activation in the brain microenvironment resulting in brain metastasis. Contact: Dr. Suresh Mohla, 301-435-1878, mohlas@mail.nih.gov **15-CA-118 Biology of carcinoid cancers and related neuroendocrine tumors (NETs).** Carcinoids and NETs are a heterogeneous group of tumors located largely in the gastrointestinal system but also in other tissues including pancreas and lung. Carcinoid tumors originate in hormone-producing cells and can produce an excess of a variety of hormones such as serotonin, bradykinin, histamine, and prostaglandins, resulting in a diverse set of symptoms called "carcinoid syndrome". However research in this area is highly understudied. Areas of high research priorities include: Molecular insights for a better understanding of cellular and molecular biology of neuroendocrine cells and mechanisms of tumorigenesis; identification of molecular markers and improve imaging modalities for early diagnosis, novel markers for identification of high-risk patients and improve understanding of the natural history of this disease; validation of neuroendocrine tumor models and cell lines to probe molecular mechanism of tumor promotion and progression. Contact: Dr. Betsy Snyderwine, 301-435-1878, snyderwe@mail.nih.gov **15-CA-119 Clinical Translation of Nanoparticle-Based Therapies.** Multi-functional nanotechnology-based platforms carry a promise for the development of localized therapies with improved efficacy and reduced side effects. These platforms will produce novel, highly effective treatments which can be stratified to individuals and specific populations, in line with growing importance of personalized medicine approaches. Furthermore, they would enable delivery of highly potent drugs, which currently cannot be used in practice due to unavailability of adequate delivery vehicles. These very promising, nanotechnology-based approaches are now subject of intense research and development with few candidate drugs already approved by FDA and several more in the advanced stage of pre-clinical development in university laboratories and start-up companies. In order to advance these technologies further and allow for their introduction to the clinical use, subsequent IND-enabling studies need to be carried out. Majority of these efforts are carried out by small companies – spin-offs from the universities. The small companies offer now only path to commercializing these technologies, especially concerning current crisis of pharmaceutical industry. Contact: Dr. Piotr Grodzinski, 301-496-1550, grodzinp@mail.nih.gov **15-CA-120 Mapping of Cancer (Disease) Metabolome.** Unlike genome and proteome, there are less than 2,600 metabolites (restricted to only those that are synthesized by the body) and have not been characterized and developed for disease detection. This Trans-NIH effort could lead to the development of diagnostic signatures. Contact: Dr. Sudhir Srivastava, 301-435-1594, srivasts@mail.nih.gov **15-CA-121 Novel Agents for Early Phase ER-negative Breast Cancer Prevention Trials.** Prevention of ER+ breast cancer has been demonstrated in large scale prevention trials (BCPT and STAR) showing a 70% reduction in ER+ tumors without an appreciable change in incidence of ER-negative breast cancer. A major challenge in breast cancer prevention is to identify a prevention intervention that will reduce incidence of ER-negative breast cancer. Preclinical studies have identified a potential role for PARP inhibitors, lapatinib, bexarotene, curcumin and DFMO in preventing ER-negative breast cancer. Recent results suggest that prevention agent effectiveness may be enhanced by co-targeting with DFMO. The Division of Cancer Prevention already has clinical trials agreements for the development of four of these agents: lapatinib, bexarotene, curcumin,

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	and DFMO. Investigators with patient populations at specific risk for ER-negative breast cancer (e.g. BRCA1 mutation carriers) are encouraged to apply for an award to conduct an early phase ER-negative breast cancer prevention trial. Contact: Dr. Karen Johnson, 301-402-3666, johnsonn@mail.nih.gov **15-CA-122 Minority Institution/Cancer Center Partnerships in Translational Research.** Minority-Serving Institutions (MSIs) and NCI-designated Cancer Centers (CCs) have established a history in creating stable, comprehensive, equal, and long-term Partnerships in the areas of basic cancer research, training, career development, outreach, and education. The MI/CCP Translational Research Programs will capitalize on the current partnership program by linking the basic cancer research collaborative outcomes between the MSIs and CCs and translating it into clinical applications that potentially may derived into new targeted therapies that specifically address cancers that affect disproportionately underserved racial and ethnic minority populations and among the socioeconomically disadvantaged. This initiative will potentially create new job opportunities for newly trained scientists, clinicians, allied health personnel, community liaisons, and community cancer educators. Contact: Dr. Nelson Aguila, 301-435-9050, aguilah@mail.nih.gov **15-CA-123 Synthetic lethal database for DNA replication and DNA damage response of human cancer cells.** Human cancers appear to be highly vulnerable to attack on DNA repair/damage signaling pathways that are related to their DNA replication. But frequently two or more repair/signaling pathways requires for DNA replication must be ablated at the same time to induce cell killing. However such combinations (i.e., synthetic lethals) are generally not obvious a priori but require systematic screening to determine potentially killing interactions. Fortunately, DNA damage/repair networks are highly conserved from yeast to humans and putative synthetic lethals can often be identified in more primitive systems and then validated in mammalian systems (e.g., mouse) and human cells. What is lacking is a systematic screen of the lower eukaryotes (yeast, worms, Drosophila, etc) to identify candidate synthetic lethal combinations that can be tested for lethality in human cancer cells. The techniques for high throughput screening that would required exist (e.g., systematic siRNA knowdowns) but would require a comprehensive discovery based program for implementation. A two-year, large-scale effort would lay the foundations for a database of putative synthetic lethal combinations for DNA damage/signaling related to DNA replication and the basis for follow-up validation studies of a more basic research nature and ultimately for translation to cancer therapy. Contact: Dr. Dick Pelroy, 301-496-9326, pelroyd@mail.nih.gov **15-DA-101* Novel Approaches to Improve Immunogenicity of Vaccines Against Small Molecules.** Innovative approaches to enhance the immunogenicity of small molecules (e.g., toxins, carcinogens, influenza epitopes, drugs of abuse) could lead to revolutionary advances in our ability to preempt, minimize the impact, or help reverse the course of preventable diseases. These approaches may leverage a variety of research strategies, including nanoparticle technology, hapten-tagging of virus-like particles, synthetic adjuvant systems, and novel immunomodulators and delivery systems. Contact: Dr. Nora Chang, 301-443-5280 or 301-443-8099, nchiang@nih.gov **15-DA-102 NIH partners in research program: Pathways for translational research.** Develop strategies for dissemination of interventions with demonstrated effectiveness for translation into clinical practice by teams of academic and community research partners. The National Drug Abuse Treatment Clinical Trials Network (CTN) fosters collaborative relationships between academic investigators and front-line community-based substance abuse treatment providers. This well-established network

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	provides a fertile platform for quick-turnaround projects that can advance knowledge on rapidly moving scientific findings into communities to improve health. Contact: Dr. Harold Perl, 301-443-9982, hperl@nida.nih.gov **15-DA-103 Development and Testing of Clinical Practice Algorithms to Improve Quality and Outcomes of Substance Abuse Treatment.** In recent years, many efficacious substance abuse treatment interventions, both pharmacotherapeutic and behavioral, have been developed and validated, and subsequently adopted into clinical practice. However, treatment providers still face a lack of evidence to guide decisions on choosing treatment approaches for individual patients, combining or sequencing interventions, particularly for patients with co-occurring substance use and other mental health disorders, and identifying optimal "rescue" treatments when an initial intervention fails. Research on these questions is needed to facilitate the development of clinical practice algorithms that can guide providers' decision-making and ultimately improve the quality and outcomes of substance abuse treatment. Contact: Dr. Petra Jacobs, 301-451-6338, pjacobs@nida.nih.gov **15-DA-104 Intervention Providers, Settings, and Pragmatic Constraints.** Successful implementation of empirically supported preventive programs and treatments is dependent on multiple factors, but some of which are related to the characteristics of the intervention work force, the nature of the intervention settings, and the practical limitations working against optimal intervention utilization. Well documented national information is not available nor are more local characterizations. This program would determine the characteristics of the treatment work force and prevention providers, characterize the settings and organizations providing interventions, and identify major impediments to program adoption and implementation. Examples of implementation barriers might include competing demands in school settings, inadequate specialized treatment facilities in some areas, etc. Approaches to overcoming the successful adoption of effective evidence based interventions would be determined as part of the expected scope of this program. Contact: Dr. Lori J. Ducharme, 301-443-2279, Lori.Ducharme@nih.gov **15-DA-105 Manipulating the blood-brain barrier to deliver CNS therapies for mental/nervous system disorders.** Substance abuse has been shown to impact the neurological, behavioral, and neurocognitive consequences of HIV infection. A variety of strategies, including use of antiretroviral, anti-inflammatory, and/or neuroprotective therapeutics, have been proposed as potential treatments for neuroAIDS, but delivery of potentially effective agents across the blood-brain barrier remains a hurdle. This initiative is aimed at developing potentially useful CNS drug targeting and delivery systems that will be effective in the context of substance abuse. Contact: Dr. Diane Lawrence, 301-443-1470, lawrencedi@nida.nih.gov **15-DA-106 Exploring the earliest events in HIV infection and use this information to develop new interventions for preventing and treating HIV infection.** Substance abuse is a major cofactor in HIV/AIDS. Early events in HIV infection are important for establishing the rate of progression to AIDS and possibly the development of neurologic and neurocognitive impairment. There is a need to understand how substance abuse affects the earliest stages of HIV infection and pathogenesis in order to identify new targets for interventions. Dr. Diane Lawrence, 301-443-1470, lawrencedi@nida.nih.gov **15-DA-107 The identification, validation, and exploitation of new molecular targets for the treatment of drug addiction disorders**. Projects may utilize techniques ranging from gene knockout technologies, behavioral evaluations, assay development, and

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	targeted library synthesis and screening that could lead to the development of medications for drug addiction treatment. The focus may be on the identification of new molecular targets, and/or the discovery of small molecule selective ligands for previously identified targets, such as muscarinic M5 antagonists, neuropeptide Y antagonists, and neurotensin agonists. Contact: Dr. Jane B. Acri, 301-443-8489, jacri@nih.gov **15-DA-108 Developing approaches for presenting relevant genomic information in an understandable way, in the context of a patient's electronic health record.** As data becomes available on drug abuse and addiction genetics, these data must eventually be integrated into electronic health records in ways that help clinicians and patients to understand the significance of the data. There is a need to provide an avenue for alerting clinicians and patients when new knowledge from basic and clinical research arises to the level of potential clinical impact; and enable linking to effective decision support and treatment implementation. **Contact:** Dr. Joni Rutter, 301-435-0298, jrutter@nida.nih.gov **15-DA-109 Effects of environmental exposures on phenotypic outcomes using non-human models.** Environmental effects mediated thru the central nervous system (especially via the HPA axis) can affect drug abuse behavior and the development of addiction. These exposures may include prenatal drug effects, physical and social stressors, and epigenetic or neurobiological consequences of early adverse experiences. How these exposures change nervous system structure and function to influence drug abuse behavior and the development of addiction is of interest. Contact: Dr. Minda Lynch, 301-435-1322, mlynch1@nida.nih.gov **15-DA-110 Determining if and how adolescent behaviors affect connections in the developing brain.** Research is needed to understand how drug abuse during adolescence affects stem cell and progenitor cell induction, myelination, programmed cell death, guidance of glial and neuronal migration, and regulation of dendritic and axonal outgrowth, navigation, target selection, and synapse formation in the nervous system. Contact: Dr. Da-Yu Wu, 301-435-4649, wudy@nida.nih.gov **15-DA-111 Manipulating the blood-brain barrier to deliver CNS therapies for mental/nervous system disorders.** Methods to deliver peptide/peptidomimetic drugs to CNS, develop drugs that pass blood brain barrier but do not pass through the placental barrier, use of nanotechnology based methodologies for CNS delivery, methods to deliver drugs only through placental barrier but do not cross the BBB, innovative in-vitro models to predict BBB and placental barrier. Contact: Dr. Rao S. Rapaka, 301-435-1304, Rr82u@nih.gov **15-DA-112 New models and measures in pre-clinical chronic pain research.** Existing animal models of pain conditions inadequately reflect the pathology or the phenotypes of the human state. New animal models to study the transition from acute to chronic pain are needed. These could include new functional and behavioral assays of acute and chronic pain. Further, it is important to characterize the impact of analgesics of various classes in these pain models. Of special interest is identifying when drugs without abuse potential (e.g. NSAIDS) are of comparable or better efficacy in attenuating or stopping the transition to chronic pain. Contact: Dr. David Thomas, 301-435-1313, dthomas1@nida.nih.gov **15-DE-101* Molecular Profiling and Developing Mouse Models for Salivary Gland Tumor Research.** The biggest challenge in salivary gland tumor research is the lack of molecular phenotypic characterization of a heterogeneous class of tumors, and the lack of

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	appropriate mouse models for charting the molecular pathogenesis of and testing therapeutic agents for the tumors. **Goal**: Initiation of systematic and comprehensive profiling of the genomics, proteomics, epigenomics, metabolomics and glycomics of salivary gland tumors. Informed by this information, develop xenograft models, MMTV-associated transgene models, and transgenic and knock-out gene-disruption models for preclinical testing in mice. Contact: Dr. Yasaman Shirazi, 301-594-4812, Yasaman.Shirazi@nih.gov **15-DE-102* New Models and Measures in Pre-clinical Chronic Pain Research.** Existing animal models of temporomandibular or orofacial pain conditions inadequately reflect the pathology or the phenotypes of the human state. **Goal**: Development of new animal models to study the transition from acute to chronic pain in temporomandibular joint disorders or other orofacial pain disorders. Coupled with the development of new functional and behavioral assays of acute and chronic pain, these animals models would be a powerful means to enhance our understanding of the biological mechanisms underlying the development of these chronic pain conditions and the responses of patients to therapeutic interventions. Contact: Dr. John Kusiak, 301-594-7984, John.Kusiak@nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; ORWH Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **15-DE-103 Translational Application of Gene Silencing Strategies to Oral and Craniofacial Disorders.** The application of oligonucleotide-based methods for modifying gene expression has emerged as a powerful research tool that has vast potential for understanding disease processes and for the development of new therapeutics. These methods have become widely used based on the ease of designing and testing oligonucleotides for any host gene or pathogen whose nucleic acid sequence is known. **Goal**: Development of translational research by harnessing oligonucleotide-based approaches such as RNA interference (RNAi) to modify the expression of genes associated with oral, dental, and craniofacial diseases and disorders, coupled with technological innovations to improve the efficiency of delivery, specificity, processing or stability of the oligonucleotide-based strategy. Contact: Dr. Yasaman Shirazi, 301-594-4812, Yasaman.Shirazi@nih.gov **15-DE-104 Functional Restoration of Salivary Glands.** Saliva is essential for maintaining oral homeostasis; reduction in salivary function causes serious oral disease. Severe reductions in salivary function occur in patients with Sjögren's syndrome, an autoimmune exocrinopathy that primarily affects women, and individuals who have had external beam radiation for treatment of head and neck cancers. Despite a volume of knowledge in the biology and pathophysiology of salivary glands, few breakthroughs have been made to restore salivary gland function; artificial saliva is not a long-term solution. **Goal**: Development of cell-, protein/peptide-, small molecule-, and gene-based approaches to stimulate fluid secretion by increasing the activities of channels and transport proteins, or repairing defective acinar and ductal cells in secretory units; development of dynamic tools to reliably examine salivary function. Contact: Dr. Lillian Shum, 301-594-0618, Lillian.Shum@nih.gov **15-DE-105 Pathophysiology of Bisphosphonate-associated Osteonecrosis of the Jaw (ONJ).** Published reports on bisphosphonate-associated ONJ have overwhelmingly focused on the epidemiology, presentation and conservative treatment options of this morbid oral condition, whereas the underlying pathophysiology remains unexplored. **Goal**: Elucidation of the underlying pathophysiology and clinical resolution of

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	bisphosphonate-associated osteonecrosis of the jaw, including how bisphosphonates may interfere with bone healing and repair at the genetic, molecular, cellular and tissue levels, and the identification of risk factors, onset, progression and management of this condition in patients. Contact: Dr. Lillian Shum, 301-594-0618, Lillian.Shum@nih.gov **15-DE-106 Developing Oral Topical Formulations for Enhancing Oral Mucosal Defenses and Controlling Oral Infections and Lesions.** Ulcerative oral lesions such as necrotizing ulcerative periodontitis, acute necrotizing ulcerative gingivitis, and aphthous ulcers are a major cause of morbidity in patients with a variety of disease conditions. Oral topical formulations of compounds with combined microbicidal, analgesic and anti-inflammatory activities are not currently available to eradicate oral pathogens, inhibit the spread of infections, and alleviate discomfort and inflammation. **Goal**: Development of new oral topical medication formulations to enhance oral mucosal defenses, eradicate oral pathogens, control oral infections and lesions, and alleviate discomfort and inflammation. Contact: Dr. Isaac Rodriguez-Chavez, 301-594-7985, Isaac@nidcr.nih.gov **15-DE-107 Metagenomics of the Oral Microbiome in Health and Disease**. Studies have shown that the microbial composition of the oral cavity is highly diverse, and that this composition is dynamically altered during the onset, progression and treatment of oral diseases, such as with dental caries or oral infections in immunocompromised patients with HIV/AIDS, stem cell transplantation, and cancer. Goal: Application of metagenomic approaches to characterize the oral microbiomes that are associated with oral diseases and to compare with the core dataset associated with health that is being generated by the Human Microbiome Project, including but not limited to conditions such as dental caries, periodontal diseases, oral manifestation of immunosuppression, and oral complications of cancer therapies. Contact: Dr. R. Dwayne Lunsford, 301-594-2421, lunsfordr@nidcr.nih.gov **15-DE-108 Oral Health in HIV/AIDS Patients with Central Nervous System Manifestations.** A spectrum of neurologic disorders associated with HIV/AIDS infections, including dementia and pain derived from neuropathies and inflammation, affect between 30% and 70% of infected individuals, even for those on antiretroviral therapy. These comorbid conditions adversely affect oral health status and adherence to therapies in HIV/AIDS patients; however, the scope of the problem and risk factors for these neurologic disorders have not been identified. **Goal**: Determination of: 1) the incidence and prevalence of central nervous system manifestations, generation of pain from neuropathies and inflammation, and oral health status in HIV/AIDS patients in demographically and genetically diverse cohorts; and 2) genetic susceptibility to central nervous system manifestations with oral complications among HIV/AIDS patients. Contact: Dr. Isaac Rodriguez-Chavez, 301-594-7985, Isaac@nidcr.nih.gov **15-DE-109 Novel Immunotherapies to Treat HIV/AIDS-related Oral Manifestations and AIDS Malignancies.** While HIV/AIDS-related oral manifestations and AIDS malignancies can be managed, there are few novel immunotherapies in the pipeline that can be developed into effective treatment. Goal: Development of novel immunotherapies for modulation of the immune response against HIV-associated oral pathogens and AIDS malignancies through the use of cytokines, chemokines, adjuvants (e.g., neo-adjuvants, nano-adjuvants, and mucosal adjuvants), antibodies and other molecules of the immune system alone or in combination with other treatment modalities. Contact: Dr. Isaac Rodriguez-Chavez, 301-594-7985, Isaac@nidcr.nih.gov

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	15-DK-101* Identification of bioactive macronutrients in the diet that impact metabolic state. Recent studies suggest that specific types of macronutrients in the diet, such as resistant starch or branched chain amino acids, may have selective effects on nutrient absorption, insulin sensitivity, and lipid metabolism. Elucidation of the metabolic impact of specific dietary components may well result in improved efficacy of lifestyle approaches to reduce obesity and metabolic diseases. Pilot studies are encouraged to identify specific bioactive components in the diet and study their mechanisms of action**.** Contact: Dr. Sue Yanovski, 301-594-8882, yanovskis@mail.nih.gov. **15-DK-102 Develop improved animal models of NIDDK diseases.** Many NIDDK diseases lack appropriate experimental models that mimic human disease. Examples: Development of relevant models in mammalian or model organisms (for example, zebrafish); Introduction of human or human orthologous mutations; cross-species comparisons to elucidate underlying molecular and related metabolic functions; and Development of parallel strains for complementation/mutational analysis. These models would greatly facilitate opportunities for identifying targets for intervention and new therapeutic strategies. Contact: Dr. Kristin Abraham, 301-496-2422, abrahamk@mail.nih.gov. **15-DK-103 Translate discovery of new molecules and pathways in pathogenesis of NIDDK diseases into potential therapies, diagnostics, or research tools.** Examples include: Improve pharmacokinetics, toxicity, or bioavailability of potential leads identified by high throughput screens; Develop assays to screen novel targets with small molecules; and validate novel molecules as therapeutic targets for disease. Contact**:** Dr. Myrlene Staten, 301-402-7886, statenm@mail.nih.gov. **15-DK-104 Develop probiotic systems for delivery of drugs or micronutrients or degradation of deleterious compounds.** Examples: modify gut bacteria to deliver small molecule drugs, vitamins such as vitamin D, or metabolize harmful compounds such as environmental toxins or trans fats to prevent or treat NIDDK diseases. Contact**:** Dr. Robert Karp, 301-451-8875, karpr@mail.nih.gov. **15-DK-105 Comparing prostate morphology and symptom profiles.** The relationships between prostate structure and disease course for treated and untreated benign prostatic hyperplasia (BPH) remain to be fully determined. An assessment of histopathological changes in the prostate relative to changes in evolving symptom profiles for clincial BPH (i.e., BPH with accompanying lower urinary tract symptoms (LUTS)) is needed to inform on disease etiology; aid in the clinical prediction of progression; and may facilitate development of preventative or therapeutic strategies. Contact: Dr. Chris Mullins, 301-451-4902, mullinsc@mail.nih.gov **15-DK-106 Translating basic hematology concepts.** Recent fundamental discoveries have improved our understanding of nonmalignant hematologic processes including heme regulation during erythropoiesis, ribosomal dysfunction in hematologic diseases, iron overload, and the role of erythropoietin receptor in non-hematopoietic cells. Efforts to develop translational tools including improved animal models, biomarkers, and imaging methods will improve our ability to prevent and treat nonmalignant hematologic diseases. Contact: Dr. Terry Bishop, 301-594-7726, bishopt@mail.nih.gov **15-DK-107 Infectious etiologies for urologic chronic pain conditions.** Chronic urologic pelvic pain syndromes Interstitial Cystitis/Painful Bladder Syndrome (IC/PBS) and Chronic Prostatitis/Chronic Pelvic Pain Syndrome (CP/CPPS) have been hypothesized to

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	have an infectious etiology. However, the potential contribution of non-traditional pathogens or changes in the normal flora to these conditions has not been sufficiently addressed. Efforts using new and novel methods are needed to assess the microbiological profile of patients. Resulting insights would have an immediate impact on developing anti-viral or anti-bacterial treatment strategies. Contact**:** Dr. Chris Mullins, 301-451-4902, mullinsc@mail.nih.gov **15-DK-108 Gene expression in GU tract development and GU disease.** Catalog expression of genes and proteins during GU tract development in humans, focusing on pathological tissues derived from patients with GU congenital malformations and GU diseases. Contact**:** Dr. Deborah Hoshizaki, 301-594-7712, hoshizakid@mail.nih.gov. **15-DK-109 Lymphatics research in the digestive system**. Research to identify changes to lymphatics in the digestive system under conditions of inflammation and disease, develop animal models that recapitulate these changes, and develop methods to mitigate these changes in order to alleviate lymphatics-related disease symptoms and progression. Examples of possible lymphatics-associated changes include altered fluid transport and edema, altered nutrient absorption and transport, and altered hormone transport. Contact**:** Dr. Jill Carrington, 301-402-0671, carringj@mail.nih.gov **15-DK-110 Organ smooth muscle function in disease**. Research to understand smooth muscle dysfunction in the digestive and urinary systems. Examples include: isolation and characterization of stem or progenitor cells that contribute to smooth muscle growth after damage or to treat short bowel syndrome; research on the impact of altered smooth muscle physiology on motility disorders and sphincter dysfunction; research on the contribution of smooth muscle to inflammatory conditions; research to understand the interactions of smooth muscle with associated nerve or interstitial cells of Cajal. Contact**:** Dr. Jill Carrington, 301-402-0671, carringj@mail.nih.gov **15-DK-111 The role of gastrointestinal surgical procedures in amelioration of type 2 diabetes.** Resolution or amelioration of Type 2 diabetes after bariatric surgery has been observed both before and after substantial weight loss. Understanding this saluatory effect in animals will help define optimal surgical approaches and identify new targets for therapy and prevention of diabetes. Mechanistic studies of the differential effects of various gastrointestinal surgical procedures may define how altered gut function and physiology impact glucose homeostasis. Contact**:** Dr. Myrlene Staten, 301-402-7886, statenm@mail.nih.gov. **15-EB-101 Towards the Virtual Patient.** Disease prediction, now more than ever, can benefit from the wealth of knowledge of gained from decades of basic biomedical research. Computational models provide the critical tools to integrate this knowledge with a systems approach to diseases. Disease prediction will require the integration of existing physiome models and multiscale models from multiple biological systems. In addition, standardized shared datasets will need to be created to achieve model validation. Contact: Dr. Grace Peng, 301-451-4778, pengg@mail.nih.gov **15-ES-101* Effects of environmental exposures on phenotypic outcomes using non-human models.** The complex etiology of many chronic diseases is difficult to explain. If most diseases arise from an interaction between genetic factors and environmental exposures, experiments that challenge animal models, such as rodents and alternate species, which mimic human disease phenotypes with stressors from the physical and social environment, can provide new information to help elucidate etiology.

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	Non-human models now exist for many diseases and critical phenotypes and can be strategically exploited to understand the basic mechanisms of action in key organ systems. The results from these experiments can lead to enhanced mechanistic understanding of the underlying biology and opportunities for prevention and/or intervention. Contact: Dr. Cindy Lawler, 919-316-4671, lawler@niehs.nih.gov **15-ES-102 The developmental basis of human disease.** Developmental exposures to a variety of environmental chemicals can lead to disease later in life. There are significant data from animal models which support this paradigm developmental in various reproductive and neurodegenerative diseases. However, there is a paucity of data for obesity/metabolic syndrome, immune system disregulation (leading to increased susceptibility to infections), cardiovascular diseases and altered behavior despite efforts to stimulate these research areas. It is critical to conduct research to define the parameters (timing and dose) by which environmental chemical exposures can alter the susceptibility and incidence of these diseases. Contact: Dr. Jerry Heindel, 919-541-0781, heindelj@niehs.nih.gov **15-TW-101 Models to predict health effects of climate change**. Quantitative and predictive models of effects of climate change on disease burden and health outcomes are needed. Approaches may include statistical, spatial or other modeling methods to quantify the current impacts of climate on a diversity of communicable or non-communicable diseases, or project impacts of different climate and socio-economic scenarios on health. For example, new and innovative approaches to develop projections of changes in disease burden in specific regions or populations will facilitate public health planning. Existing databases on population and environmental variables, such as air quality and climatologic episodes should be used to test the utility of these models where possible. Contact: Dr. Joshua Rosenthal, 301-496-1653, joshua_rosenthal@nih.gov; NIEHS Contact: Dr. Caroline Dilworth, 919-541-7727, dilworthch@niehs.nih.gov **15-EY-101* Protein misfolding in degenerative diseases of the eye.** A number of ocular genetic diseases occur due to misfolding/aggregation of proteins, for example the visual pigment protein, rhodopsin in retinitis pigmentosa, crystallins in age-related cataracts, and myocillin in glaucoma. Identifying therapeutic pharmacological agents/drugs, that prevent the misfolding/aggregation of proteins could provide new tools for treating these diseases. Contact: Dr. Neeraj Agarwal, 301-451-2020, agarwalnee@mail.nih.gov **15-EY-102 Determining the structure of membrane proteins involved in phototransduction and the visual cycle to develop therapeutic agents and to understand the mechanisms of action.** The paucity of knowledge of the small conformation changes of proteins involved in phototransduction and retinoid cycle during their activation cycles and formation of transient complexes is a limiting factor in the development of new therapeutic agents. Pharmacologically, the most important membrane proteins are those involved in signal transduction including G protein coupled receptors (GPCRs) of which rhodopsin is the prototypical type. As many as 40% of currently marketed drugs interact with GPCRs yet these target only about 50 GPCRs out of more than 800 encoded in the human genome and are not sufficiently selective for one particular receptor subtype resulting in possible adverse effects, drug interactions, and less than optimal dosing. Contact: Dr. Andrew Mariani, 301-451-2020, mariania@mail.nih.gov **15-HD-101* Developing New Antimicrobials from Oligosaccharides**. Oligosaccharides are the third most prevalent component of human breast milk and have

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	been shown to have antimicrobial properties against organisms including Campylobacter jejuni and caliciviruses. Research is needed to determine how oligosaccharides prevent infections and to stimulate the development of synthetic oligosaccharides that can be used to treat such conditions as necrotizing enterocolitis, newborn sepsis, or other infections in children or adults that may have become resistant to existing antibiotics. Contact: Dr. Gilman Grave, 301-496-5593, gg37v@nih.gov **15-HD-102*** **Pelvic Pain**. New animal models and epidemiologic studies are urgently needed to increase understanding of the mechanisms underlying the development of chronic pelvic pain conditions in women, including but not limited to uterine fibroids, vulvodynia, and endometriosis. Research is needed specifically to identify and measure the biological, clinical, and behavioral factors involved in determining the responses of patients to therapeutic interventions for chronic pelvic pain conditions. Contact: Dr. Estella Parrott, 301-435-6971, parrotte@mail.nih.gov; ORWH Contact: Dr. Lisa Begg, 301-402-1770, BeggL@od.nih.gov **15-HD-103** **Understanding Drug-Induced Fetal Effects**. There is a lack of a mechanistic approach to studying drug-induced fetal effects, including the impact of medications on fetal malformations. A large percentage of pregnancies are unintended, and, since women take a large number and range of medications, research is needed to understand the fetal effects of medications. Within a two-year timeframe, mechanistic animal models could be developed to enable new drugs to be developed that would avoid the potential of causing malformations. Contact: Dr. Anne Zajicek, 301-435-6865, zajiceka@mail.nih.gov **15-HD-104** **Multi-drug Combination Therapy for TBI and Stroke Treatment.** The potential to capture the earliest recovery window, via early neuroprotection, is a major priority for treatment of traumatic brain injury (TBI) and stroke. Key first steps (addressed via partnership with industry and academia), will be to develop preclinical data on multiple drug combination interventions as a precursor to clinical research in humans; to provide pilot data to assess the safety and benefit of combination pharmacotherapies; and to determine optimal dosing and schedules for drug combinations. These data will provide the basis to launch clinical trials in humans using these optimal combinations. Contact: Dr. Beth Ansel, 301-496-5289, ba25e@nih.gov **15-HD-105** **Models to predict health effects of climate change.** Quantitative estimates and predictive models of effects of climate change on disease burden and health outcomes are needed. Approaches may include statistical, spatial or other modeling methods to quantify the current impacts of climate on a diversity of communicable or non-communicable diseases, or project impacts of different climate and socio-economic scenarios on health. For example, new and innovative approaches to develop projections of changes in disease burden in specific regions or populations will facilitate public health planning. Existing databases on population and environmental variables, such as air quality, and climatologic episodes should be used to test the utility of these models where possible. Contact: Dr. Rebecca L. Clark, 301-296-1175, rclark@mail.nih.gov **15-HD-106** **Environmental and Child Health: Exposure to Cooking Emissions:** Home cook stove emissions in low resource settings, including the developing world, are a major risk for pneumonia (the leading cause of death in children under the age of 5 --more than malaria, measles, and HIV combined). These emissions produce black carbon, the second leading green house emission in the world, but unlike CO_2, they have a short half-life in the atmosphere, so interventions to reduce cooking emissions would have prompt

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	environmental benefits. Research is needed to assess the impact of inexpensive, more efficient cooking stoves on environmental pollution, carbon particulate exposure, low birth weight, and infections such as sepsis and pneumonia. Immediate research results in this area could underscore the need for expanded U.S. production of this environmentally-friendly export technology. Contact: Dr. Linda L. Wright, 301-402-0830, wrightl@mail.nih.gov **15-HL-101 Develop improved biocompatible surfaces for implantable blood-contacting medical devices.** Implantable blood-contacting medical devices such as stents, prosthetic heart valves, vascular grafts, and circulatory support devices, are widely employed therapies that have benefited many people. They are also, however, often a site for thrombosis, inflammation, and infection. Improved biocompatible surfaces for such devices could reduce thrombosis, inflammation, and infection and thereby significantly reduce patient morbidity and mortality. Contact: Dr. Martha Lundberg, 301-435-0513, lundbergm@nhlbi.nih.gov **15-HL-102 Develop new therapeutic strategies for heart, lung, and blood diseases based on microRNA technology**. MicroRNAs (miRNA) are involved in regulating gene expression at the post-transcriptional level. About 500 human miRNAs have been discovered. Initial evidence suggests that they play significant roles in endothelial cell migration, proliferation, vascular and airway inflammation and fibrosis and remodeling, and in the airway response to cigarette smoking, all of which are key mechanisms in atherosclerosis and thrombosis and chronic lung disease. Research is needed to improve our understanding of the miRNA network and its function related to heart, lung and blood diseases and to develop new targets and therapeutic strategies including gene therapy based on MiRNA technology to treat them. Contact: Dr. Pothur Srinivas, 301-435-0550, ps241g@nih.gov **15-HL-103 Establish the infrastructure to obtain, in a standardized manner, diseased and healthy human cardiac tissue obtained at surgery for immediate electromechanical studies to further the fundamental understanding of cardiac rhythm and contractility**. Most deaths among patients with CAD are due to ventricular fibrillation and other tachyarrhythmias. Contemporary approaches to prevent sudden cardiac arrest and subsequent deaths SCA/D continue to be limited. Although implantable cardioverter defibrillators (ICDs) in primary prevention of SCA/D are life-saving, as currently applied they are also inefficient and costly. Traditional antiarrhythmic drugs have not reduced mortality and in some cases, are proarrhythmic. Failed pharmacotherapy may be due to the gathering of preclinical data from inappropriate animal models, and to the clinical dissociation between prevention of premature ventricular depolarizations and SCA/D. Fundamental electromechanical studies of living human cardiac tissues will fill the gaps left by animal studies and lead to optimal diagnosis, treatment, and prevention of potentially fatal arrhythmias. Contact: Dr. Dennis Przywara, 301-435-0506, przywarad@nhlbi.nih.gov **15-HL-104 Characterize the role and effects of the respiratory and/or intestinal microbiota on the presence and clinical phenotype of lung disease.** The development and progression of lung diseases are strongly influenced by the behavior of immunological defense mechanisms in the airways, and a major contributor to individual immune phenotypes is the microorganisms that establish themselves in a person immediately after birth and subsequently throughout life. Very little is known about the respiratory tract microbiome or the relationship of lung disease to microbes in the respiratory tract or in other parts of the body, particularly the gut. Investigations of the relationships between

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	individual microbiomes and lung diseases will not only provide important insights into the causes and mechanisms of lung diseases such as asthma, COPD, and pulmonary fibrosis but also offer great potential for rapid translation of research results into improved approaches for lung disease prevention and treatment. Contact: Dr. Hannah Peavy, 301-435-0222, peavyh@nhllbi.nih.gov **15-HL-105 Employ metabolomic approaches to Improve diagnose, stage, and select therapies for lung diseases.** Because of the great cellular diversity and environmental exposure of the lung, pulmonary diseases are often highly complex, involving many molecular pathways, varied clinical manifestations, and multiple therapeutic targets. Single chemical, laboratory, or physiological measures are often inadequate for properly characterizing the presence, severity, and phenotype of lung disease. Metabolomic analyses are of particular interest for lung diseases because they may capture the behavior of the pulmonary system as a whole. Metabolomic analyses of exhaled breath, sputum, blood, and/or urine offer great promise for characterization of patients with complex pulmonary conditions; and exploratory studies of metabolomic profiles in lung diseases will likely yield discoveries that are of great importance for early diagnosis, clinical phenotyping, and therapeutic stratification of lung diseases. Contact: Dr. Weiniu Gan, 301-435-0202, ganw2@nhlbi.nih.gov **15-LM-101* Presenting genome information in electronic health records**. Develop approaches for presenting relevant genomic information in an understandable way, in the context of a patient's electronic health record**.** As genomic data becomes available for more individuals, these data must be integrated into electronic health records in ways that: help clinicians and patients to understand the significance of the data; provide an avenue for alerting clinicians and patients when new knowledge from GWAS, etc. rises to the level of potential clinical impact; and enable linking to effective decision support. Contact: Dr. Jane Ye, 301-594-4882, yej@mail.nih.gov **15-LM-102 Computational hypothesis generation for biology and medicine**. Employing two or more sources, use advanced computational approaches to generate a new and meaningful hypothesis in biomedical science, capable of being tested by bench or clinical research. One source must be full-text published biomedical literature; the other source should be either (1) a database storing primary data from basic biomedical research or (2) data drawn from the electronic health records used for routine clinical care or from the data accumulated for a clinical research project. The user interface of an integrated hypothesis generation system should support easy use by the intended users (i.e., by biomedical researchers or clinicians). Mining techniques should involve minimal human intervention. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **15-LM-103 In silico hypothesis testing for biology and medicine**. Employing two or more sources, use advanced computational approaches to test rigorously *in silico* a new and meaningful scientific hypothesis in biomedicine, one which otherwise would require laboratory or clinical verification. One source must be full-text published biomedical literature; the other source should be either (1) a database storing primary data from basic biomedical research or (2) data drawn from the electronic health records used for routine clinical care or the from the data accumulated for a clinical research project. The approach should involve minimal human intervention. Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov **15-MH-101 Effect of psychotropic medications on neurodevelopment and behavior in animal models.** Examine the effects of commonly prescribed psychotropic

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	medications on neurodevelopment and behavior in juvenile and adolescent animals across significant developmental transitions. Studies would collect information about the safety of these medications and how they may alter developmental trajectories in fundamental affective, cognitive, and behavioral systems. Contact: Dr. David M. Panchision, 301-443-5288, panchisiond@mail.nih.gov **15-MH-102 Gene x environment x development (GxExD) studies of brain function and mental disorders.** Conduct exploratory studies in model systems to examine gene x environment x development (GxExD) phenomena relevant to understanding brain function and mental disorders. Profile regional changes in gene expression in the brain for at least three defined developmental timepoints and in response to relevant prenatal and/or postnatal manipulations. Contact: Dr. Andrea Beckel-Mitchener, 301-443-3825, amitchen@mail.nih.gov **15-MH-103 Mapping the neural connectivity of a mouse model.** Use high-throughput implementations of existing methods at the light microscopic-level to demonstrate systematically and comprehensively the neural connectivity of the 8-week-old, C57Bl/6J mouse to create a connectional database for comparison with the existing gene expression data for this age and strain available through the Allen Brain Atlas. Contact: Dr. Michael F. Huerta, 301-443-1815, Mhuert1@mail.nih.gov **15-MH-104 Mouse models containing human genes implicated in mental disorders.** Create novel mouse models containing human genes or genetic elements that have been implicated in mental disorders in order to study how these human alleles alter brain function and behavioral outcomes. Contact: Andrea Beckel-Mitchener, 301-443-3825, amitchen@mail.nih.gov **15-MH-105 Strategies to support uptake of interventions within clinical and community settings.** Develop and pilot comprehensive implementation strategies to support the broader uptake of interventions within clinical and community settings. Contact: David Chambers, 301-443-3747, dchamber@mail.nih.gov **15-MH-106 Mental health programs designed for college students with mental illness.** Examine the effectiveness of mental health programs designed for college students with mental illness. Projects might include developing measures of program effectiveness or developing a collaborative research network with common data management systems. Contact: Dr. Denise M. Juliano-Bult, 301-443-3364, djuliano@mail.nih.gov **15-MH-107 Targets for drug discovery for mental disorders.** Identify and validate novel targets for drug discovery for mental disorders, including screening to identify lead compounds for further therapeutic development. Contact: Dr. Jamie Driscoll, 301-443-5288, Jdrisco1@mail.nih.gov **15-MH-108 Screening approaches to identify pharmacologic treatments for mental disorders.** Develop and validate innovative *in vivo* screening approaches aimed at identifying new lead pharmacologic agents for treatment of mental disorders that have improved efficacy and decreased risk. Contact: Lois Winsky, 301-443-5288, lwinsky@mail.nih.gov **15-MH-109 Prefrontal cortex regulation of higher brain function and complex behaviors.** Examine mechanisms by which the developing and mature prefrontal cortex

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	interacts with other cortical and subcortical systems in the regulation of higher brain functions and complex behaviors. The focus should be on supporting innovative approaches to the manipulation of neural circuits. Contact: Kevin J. Quinn, 301-443-1576, kquinn@mail.nih.gov **15-MH-110 Understanding the mechanism of action of deep brain stimulation.** Conduct basic and clinical research on the mechanism of action of deep brain stimulation. Studies should be relevant to its use in the treatment of mental disorders. This initiative will also establish a registry of clinical data, electrode targeting, and device settings which will be available for analysis and meta-analysis. Contact: Dr. Steven J. Zalcman, 301-443-1692, szalcman@mail.nih.gov **15-NR-101* NIH Partners in Research Program: Pathways for Translational Research.** This two year initiative will develop strategies for dissemination of interventions with demonstrated effectiveness for translation into clinical practice by teams of academic and community research partners. This initiative will provide the knowledge to more rapidly move scientific findings into communities to improve health. Contact: Dr. David Banks, 301-496-9558, Banksdh@mail.nih.gov **15-NS-101* Manipulating the blood-brain-barrier to deliver CNS therapies for Mental/Nervous System Disorders.** Neuroscience discoveries have led to promising therapeutic strategies for treatment of severe neurological disorders. However, the blood brain barrier presents a major hurdle to delivering potentially exciting agents such as RNA therapies, genes, critical enzymes, antibodies, other molecular entities, or cell therapies. The challenge is to develop potentially useful means of CNS drug targeting and delivery systems. Contact: Dr. Tom Jacobs, 301-496-1431, tj12g@nih.gov; NIAAA Contact: Dr. Samir Zakhari, 301-443-0799, szakhari@mail.nih.gov **15-NS-102 Translation of Gene Silencing Therapeutics.** Technologies for gene silencing (antisense RNA, morpholino RNA, RNAi, miRNA, site-directed excision/repair, etc) have been rapidly developed and refined in cell culture and rodent models of disease. RNAi strategies now utilize viral vectors to deliver and continually express the gene silencing construct. In some cases this can be accomplished in a regulated and/or allele-specific manner. To realize the potential of these technologies, however, experiments in non-human primates or appropriate large animal models, are necessary to determine the feasibility of this therapeutic approach for the treatment of chronic neurological/mental health diseases with either focal or diffuse pathologies. Contact: Dr. Margaret Sutherland, 301-496-5680, sutherlandm@mail.nih.gov **15-NS-103 Demonstration of "proof-of-concept" for a new therapeutic approach in a neurological disease.** Entry into the NINDS translational research program requires evidence that a new therapeutic approach is efficacious in an animal or cell model of a neurological disease. The NINDS seeks grants to conduct research that establishes proof-of-concept sufficient to initiate a preclinical therapeutic development effort. Contact: Dr. Jill Heemskerk, 301-496-1779, jh440o@nih.gov **15-NS-104 Early-stage therapy development**. Recent genetic/molecular discoveries in basic and disease research offer new opportunities for treatment of neurological disorders. This Challenge would support the transition of basic/disease research findings into the pipeline for pre-clinical development of therapeutics. This could include the identification and validation of new treatment targets and the development of cell-based assays or animal models for translational research. Contact: Dr. Laura

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	Mamounas; 301-496-5745, lm92t@nih.gov **15-NS-105 Translational-2 research pilots.** Translational-2 (T-2, or dissemination) research identifies and measures barriers to translating clinical trial findings into widespread practice, and develops and tests models and strategies to overcome those barriers, in order to reduce the burden of neurological disease. Despite the success of past neurological and neurosurgical trials and the potential impact of trial outcomes on public health, the actual utilization of many of these findings has been low. Studies of the barriers and strategies to overcome these barriers in clinical neuroscience are encouraged, as both will aid in the refinement of future clinical trials – such that barriers are taken into account when trials are designed – and in the development of clinical practice guidelines by nonfederal organizations. Both outcomes will enhance the impact of neurological/neurosurgical trials and will ensure that maximal health output is gleaned from these often costly public investments. Contact: Dr. Deborah Hirtz, 301-496-5821, dh83f@nih.gov. **15-NS-106 Identifying mechanisms that underlie nervous system development and function.** Despite a wealth of emerging data, determining the organizing principles that guide the development and function of the nervous system remains a challenge. Mechanistic studies that elucidate these principles at the molecular, cellular, and systems level are encouraged, as well as analyses of how normal mechanisms are perturbed in neurological and neurobehavioral disease. Contact: Dr. Robert Riddle, 301-496-5745, rr260c@nih.gov **15-OD(ORDR)-101* Pilot projects for prevention, early detection and treatment of rare diseases.** Design research projects to provide preliminary results to demonstrate feasibility of novel approaches to rare diseases. Potential approaches to research in rare diseases could include but will not be limited to: identification of molecular targets for rare diseases; development of models (vertebrate, invertebrate, computational); development of micro arrays and tissue micro arrays which are applicable to screening or detection of rare diseases; development of tools for drug discovery (e.g. development of assays for screening compounds); and clinical trials. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov **15-OD(ORDR)-102* Collaborative translational research platform for rare diseases.** Create a collaborative platform by disease area to allow researchers to create virtual project teams, update status reports, collaboratively score targets and nominate molecules for screening. Having these data in a centralized, common system should reduce redundancy and potentially identify non-obvious associations of research across the rare disease spectrum. Contact: Dr. Rashmi Gopal-Srivastava, 301-402-4336, gopalr@mail.nih.gov **15-OD-101 Mouse and Metabolic profiling of MLPCN Probes.** Metabolic profiling of probes identified through the Molecular Libraries program (https://mli.nih.gov/mli/mlp-probes/). Probes produced by the Molecular Libraries Probe Production Centers Network have the potential to be important research tools. Often, however, a barrier standing in the way of utilization of the probe is the need for optimization and/or characterization to enhance its effects on physiology and pathophysiology. The challenge is to optimize the probes to achieve adequate bioavailability for use in animal models of disease to allow phenotypic profiling to assess the efficacy of the probe against an important target. The results of the work would increase the utility of the probes for identifying underlying mechanisms of disease, new potential therapeutic targets, and changes in gene

Broad Challenge Area	Specific Challenge Topic
	expression in affected tissues. Contact: Dr. Ron Margolis (NIDDK), 301-594-8819, margolisr@mail.nih.gov and Dr. Dan Zaharevitz (NCI), 301-435-9172, ZaharevD@mail.nih.gov. **15-OD-102 Analysis of PubChem data sets.** The Molecular Libraries Probe Production Centers Network (MLPCN) implements high throughput screens for a number of biological targets and develops probe compounds from the results. The emphasis is on finding useful probes for a wide variety of targets rather than on an in depth investigation of each target or the interactions between them. The NIH will support projects based on MLPCN data available through Pub Chem (http://pubchem.ncbi.nlm.nih.gov) that combine informatics, chemical synthesis and non-high-throughput biological testing to enable the scientific community to take full advantage of the ML resources. Contact: Dr. Ajay (NHGRI), 301-594-7108, ajaydr@mail.nih.gov. **15-RR-101* Applied translational technology development.** This program will support two-year applied translational projects to move advanced technologies from the prototype stage into the clinic. Novel, cost-effective tools for clinical care or clinical research will be modified, hardened, and tested. Interdisciplinary teams of technology developers, basic researchers and clinicians will address scientific and engineering problems associated with clinical applications of new technologies. Contact: Dr. Douglas Sheeley, 301-594-9762, sheeleyd@mail.nih.gov; NIDA Contact: Dr. Kris Bough, 301-443-9800, boughk@mail.nih.gov **15-RR-102 Develop a nationwide electronic Material Transfer Agreement (MTA) Database System**. Develop a nationwide electronic MTA system that will facilitate the rapid exchange of research materials. Such a web-based workflow management database system would be available as a national resource that would facilitate the rapid location of research materials and allow for near instantaneous MTA turn around time. The system should strive to appear as a peer-to-peer material location and transfer system to researchers, simultaneously providing institutional technology transfer offices with efficiency and management of materials, as well as, automation of MTA negotiation and processing. In addition, the system will provide broad metrics related to materials, their funding sources, and the granting agency. Contact: Dr. Lili Portilla, 301-451-1467, Lilip@nih.gov **15-TW-101* Models to predict health effects of climate change**. Quantitative and predictive models of effects of climate change on disease burden and health outcomes are needed. Approaches may include statistical, spatial or other modeling methods to quantify the current impacts of climate on a diversity of communicable or non-communicable diseases, or project impacts of different climate and socio-economic scenarios on health. For example, new and innovative approaches to develop projections of changes in disease burden in specific regions or populations will facilitate public health planning. Existing databases on population and environmental variables, such as air quality and climatologic episodes should be used to test the utility of these models where possible. Contact: Dr. Joshua Rosenthal, 301-496-1653, joshua_rosenthal@nih.gov; NIAMS Contact: Dr. Susana Serrate-Sztein, 301-594-5032, NIAMShelp-NIHChallengeGrants@mail.nih.gov; NHLBI Contact: Dr. Lawrence Fine, 301-435-0305, finel@nhlbi.nih.gov; NLM Contact: Dr. Valerie Florance, 301-594-4882, florancev@mail.nih.gov