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Glyco-Forum section

Letters to the Glyco-Forum

Systematic nomenclature for sialyltransferases

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Sialyltransferases are a family of glycosyltransferases that transfer sialic acid from the donor substrate CMP-sialic acid to acceptor oligosaccharide substrates (Paulson and Colley, 1989). Successful efforts to clone the cDNAs of this family of enzymes have revealed a homologous gene family that is larger than previously recognized. The present nomenclature for distinguishing the various sialyltransferases is inadequate to unambiguously distinguish one enzyme from another, particularly when multiple names often exist in the literature to describe the same enzyme. Accordingly, we propose a systematic nomenclature similar to that used in describing other glycosyltransferase families (e.g., N-acetyl glucosaminyl- and fucosyl-transferases). Some additional features of this nomenclature may be of value in developing a systematic nomenclature for other glycosyltransferase families.

At least 13 distinct sialyltransferase cDNAs have been cloned (Table I) using various approaches. These include cloning of the enzymes using information derived from the peptide sequence of the purified protein. The cloning of the cDNA was also achieved by expression cloning using the antibodies generated against the purified enzymes. However, these strategies have proven laborious for cloning of sialyltransferases due to the low abundance of these enzymes in tissues, thus resulting in difficulty of their purification. Nonetheless, six distinct sialyltransferases have been purified to homogeneity (Sadler *et al.*, 1979; Weinstein *et al.*, 1982; Gu *et al.*, 1990; Melkerson-Watson and Sweeley, 1991; Preuss *et al.*, 1993), and information obtained from three of these has successfully been used to clone their respective cDNAs (Weinstein *et al.*, 1987; Gillespie *et al.*, 1992; Wen *et al.*, 1992).

A polymerase chain reaction (PCR) based method has been highly successful in obtaining multiple additional sialyltransferase cDNAs, even without any prior knowledge of the enzymes cloned. This method did not require any purification of the enzyme. Instead, it has taken advantage of the comparison of the sequences of other cloned sialyltransferases (Weinstein *et al.*, 1987; Gillespie *et al.*, 1992; Wen *et al.*, 1992), which has revealed the presence of two highly conserved motifs, termed as 'L-sialylmotif' and 'S-sialylmotif', in the catalytic domain of these enzymes (Wen *et al.*, 1992; Drickamer, 1993; Livingston and Paulson, 1993; Kurosawa *et al.*, 1994a). These two motifs have been successfully used to clone nine new members of this gene family (Livingstone and Paulson, 1993; Lee *et al.*, 1994; Kitagawa and Paulson, 1994a; Kurosawa *et al.*, 1994a,c; Yoshida *et al.*, 1995a,b; Sjoberg *et al.*, 1996; M.Kono, Y.Yoshida, N.Kojima, and S.Tsuji, unpublished observations) using a PCR homology approach involving degenerate synthetic primers to these conserved elements that might also be expected to be found in other members of the gene family. In fact, all the sialyltransferases cloned to date contain these two conserved motifs, which are recently implicated in binding the donor substrate CMP-NeuAc (Datta and Paulson, 1995, 1996).

The expression-cloning method originally described by Lowe and colleagues for cloning of galactosyl- and fucosyltransferases (Larsen *et al.*, 1989, 1990) has also been successfully used by several groups to clone cDNAs of additional distinct sialyltransferases (Sasaki *et al.*, 1993, 1994; Haraguchi *et al.*, 1994; Nara *et al.*, 1994; Eckhardt *et al.*, 1995; Nakayama *et al.*, 1995, 1996).

As the sialyltransferase family has grown and there has been discovery of two classes of cell adhesion receptors that recognize sialoside ligands, many groups have begun to participate in research related to sialyltransferases and the products they synthesize. At present, there is considerable confusion regarding the naming of sialyltransferases. The IUPAC nomenclature has not kept up, with each group of authors using their own abbreviations, thus giving rise to multiple abbreviated names for the same enzyme and even the same name for different enzymes (see review, Harduin-Lepers *et al.*, 1995). We wish to propose a simplified nomenclature system that is unique for each sialyltransferase gene while providing some information on the specificity of the enzyme. The goal is not to provide a nomenclature that completely defines the functional properties of the enzymes but instead to have a distinct name for the enzyme produced by each unique sialyltransferase gene. To date, unique sialyltransferase genes cloned from the same species typically exhibit <50% homology while the same gene cloned from another species is expected to exhibit >95% homology. Thus, it is expected that sialyltransferase genes will be recognized as being unique by comparison to previously cloned sequences regardless of whether or not the two genes being compared were cloned from the same species. We have also disregarded whether or not the sialyltransferase transfers sialic acid to glycoproteins, glycolipids, or both, since several of these enzymes are being shown to work with both kinds of substrates and would add needless complexity to the nomenclature.

To introduce the system, we take an example of the first cloned sialyltransferase (EC2.4.99.1), which elaborates the Neu5Acα2,6Galβ1,4GlcNAc sequence on glycoprotein (and glycolipid) substrates and has the systematic name by the

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Table I. Systematic nomenclature of the sialyltransferase gene family

Linkage formed	Systematic name	Previous abbreviation(s)	Acceptor(s)[a]	Reference(s)b
Neu5Acα2,6Gal	ST6Gal I	ST6N, SiaT-1	**Gal**β1,4GlcNAc	Weinstein *et al.*, 1987; Grundmann *et al.*, 1990; Bast *et al.*, 1992; Stamenkovic *et al.*, 1990; Hamamoto *et al.*, 1993; Kurosawa *et al.*, 1994b
Neu5Acα2,3Gal	ST3Gal I	ST3O, ST3GalA.1, SiaT-4a	**Gal**β1,3GalNAc	Gillespie *et al.*, 1992, Kitagawa and Paulson, 1994b; Lee *et al*, 1993; Kurosawa *et al.*, 1995
	II	ST3GalA.2, SAT-IV, SiaT-4b	**Gal**β1,3GalNAc	Lee *et al.*, 1994; Kojima *et al.*, 1994
	III	ST3N	**Gal**β1,3(4)GlcNAc	Wen *et al.*, 1992; Kitagawa and Paulson, 1993
	IV	STZ, SAT-3, SiaT-4c	**Gal**β1,3GalNAc/ **Gal**β1,4(3)GlcNAc	Sasaki *et al.*, 1993; Kitagawa and Paulson, 1994a
Neu5Acα2,6GalNAc	ST6GalNAc I		**GalNAc**	Kurosawa *et al.*, 1994a
	II		Galβ1,3**GalNAc**	Kurosawa *et al.*, 1994c, 1996
	III		Neu5Acα2,3Galβ1,3**GalNAc**	Sjoberg *et al.*, 1996
Neu5Acα2,8Neu5Ac	ST8Sia I	SAT-II/SAT-III	**Neu5Ac**α2,3Galβ1,4Glc-Cer [GM3]	Sasaki *et al.*, 1994, Nara *et al.*, 1994; Haraguchi *et al.*, 1994
			Neu5Acα2,8Neu5Ac α2,3Galβ1,4Glc-Cer [GD3]	Nakayama *et al.*, 1996
	II	STX	**(Neu5Ac)**$_n$-N-Glycan	Livingston and Paulson, 1993; Kojima *et al.*, 1995a,b; Scheidegger *et al.*, 1995
	III		**Neu5Ac**α2,3Galβ1,4GlcNAc	Yoshida *et al.*, 1995b
	IV		**(Neu5Ac)**$_n$-N-Glycan	Eckhardt *et al.*, 1995; Yoshida *et al.*, 1995a; Nakayama *et al.*, 1995
	V	SAT-V/SAT-III	**Neu5Ac**α2,3Galβ1,3GalNAcβ1,4 (Neu5Ac α2,3)Galβ1,4Glc-Cer [GD1a]	Kono,M., Yoshida,Y., Kojma,N , and Tsuji,S , unpublished
			Neu5Acα2,3Galβ1,3GalNAcβ1,4(Neu5Acα2,8 Neu5Acα2,3)Galβ1,4Glc-Cer [GT1b]	
			Neu5Acα2,8Neu5Acα2,3Galβ1,4Glc-Cer [GD3]	

[a]The boldface on the acceptor(s) indicates the attachment site for the sialic acid transferred.
[b]References cited are for the initial publications of the cDNA sequence for each sialyltransferase. For some cases the cDNA sequences from several different species are cited.

IUPAC nomenclature CMP-Neu5Ac: Galβ1,4GlcNAc α2,6 sialyltransferase. The proposed abbreviation is: ST6Gal I.

The four elements that make up this system are as follows: ST,x,y,z, where ST denotes sialyltransferase family, x is the carbon on the acceptor sugar to which the sialic acid is transferred (e.g., 6 for Neu5Acα2,6 Gal), y is the acceptor sugar to which sialic acid is transferred (Gal, GalNAc, Neu5Ac, etc.), and z is a roman numeral assigned consecutively to each new distinct gene in the subgroup.

The following rules are recommended for the nomenclature of any new sialyltransferase:

1. This nomenclature system must be applied only to a cloned sialyltransferase for which the cDNA sequence is known and the acceptor specificity has been determined.
2. The subdivisions 'y' and 'z' should be assigned for a new sialyltransferase after the enzyme has been cloned, and expressed to clearly differentiate the activity and specificity from those of previously described enzymes.
3. If the newly cloned sialyltransferase belongs to a particular subfamily, the roman numeral for 'z' should be assigned according to the chronological order the cDNA is published (ST8Sia V, for example).
4. When necessary, the species difference for a particular cloned sialyltransferase may be indicated by a prefaced single letter designating the relevant species, e.g., rST6Gal I and hST6Gal I for the rat and human sialyltransferase respectively.

Co-signers

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Sequence alignment and fold recognition of fucosyltransferases

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Introduction

Fucosyltransferases (Fuc-Ts), like other glycosyltransferases, are type II transmembrane proteins that share a common domain structure (Lowe, 1991; Kleene and Berger, 1993). They have a short NH_2-terminal cytoplasmic tail, a 16–20 amino acid signal anchor domain and an extended stem region followed by a large globular, COOH-terminal, catalytic domain (Paulson and Colley 1989; Joziasse 1992). The catalytic do-