The terminal glycan motif of *Burkholderial pseudomallei* Capsular polysaccharide is unique among the bacterial species. A bioinformatics approach

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ABSTRACT

Burkholderia pseudomallei, a Gram-negative bacillus, is the causative agent of melioidosis, a potentially fatal infection of humans and animals. It causes mortality, particularly in the endemic regions of Southeast Asia and northern Australia. A recent fatal case also in US alerted health officials. Due to the fact that this organism was previously employed as an agent of biological warfare, *B.pseudomallei* and its closely related *B.mallei* are currently listed as select agents by the CDC and are recognized by the NIAID as a category B Priority Pathogens. Incidentally, no effective method of prevention of melioidosis currently exists. Without prolonged treatment with expensive antibiotics, it can be fatal. It is also intrinsically resistant to penicillin and gentamycin. Moreover, there is no vaccine available for immunization against this emerging infectious disease.

All the pathogenic species of Burkholderia express capsular polysaccharide (CPS), which are both a virulent factor and a protective (to the bacteria) antigen. CPSs are of two types: O-PS I and O-PS II. Studies have shown that O-PS I is present in all the strains of this pathogenic species, which consists of 1,3-linked homopolymer of 2-O-acetylated 6-deoxy-beta-D-manno-heptopyranosyl residues. O-PS II, on the other hand, consists of repeating disaccharide units having the structure, -3)-beta-D-glucopyranose-(1-3)-6-deoxy-alpha-L-talopyranose-(1-, in which the 6-deoxy-L-talopyranosyl residues were partially methylated at the O-2 position and which were also variably substituted by O-acetyl groups. Among the pathogenic strains tested for this Burkholderia species, only the strain 824a showed the exception having only O-PS I but not O-PS II. Thus, O-PS I is unique among all the pathogenic strains of Burkholderia species that can be a potential target for antimicrobial glycoconjugate vaccine development. It can also be used as a diagnostic marker for *Burkholderia pseudomallei.* A monoclonal antibody (mAB) developed earlier (Marchetti, et. al., 2015) has been shown to be specific for this structure raising the possibility that this mAB (4C4) can be used as a potential pre- and post-exposure prophylaxis, if this mouse monoclonal antibody was humanized.

In this study, we searched multiple databases of bacterial glycans including GlyTouCan and found this O-PS I as unique to this *Burkholderia pseudomallei* among the bacterial species. We also searched databases of mammalian glycans (Datta and Sukhija, 2021) including GlyGen and could not find the presence of this unique structure in any mammalian glycans. Thus, the use of this mAB (4C4) establishes it as a potential diagnostic reagent for melioidosis.

References:

Datta, AK., Sukhija, N. (2021). Glycobioinformatics in deciphering the Mammalian Glycocode: Recent Advances. In "Glycome: The Hidden Code in Biology", (D. Banerjee, ed.), pp 323-376 (chapter 16), Nova Science Publishers. ISBN 978-1-53619-437-1.

Marchetti, R., Dillon, MJ., Burtnick, MN, et. al. (2015). Burkholderia pseudomallei Capsular Polysaccharide Recognition by a Monoclonal Antibody Reveals Key Details toward a Biodefense Vaccine and Diagnostics against Melioidosis. ACS Chem Biol., 10 (10): 2295-302.