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Dynamic pilin glycosylation patterns during Neisseria meningitidis serogroup A meningitis outbreaks in the African meningitis belt

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Background

In sub-Saharan Africa's meningitis belt, cyclic meningococcal epidemics often occur alongside clonal waves of Neisseria meningitidis carriage and invasive disease. Meningococcal isolates were collected during meningococcal outbreaks from 1998 to 2011 in Ghana and Burkina Faso as part of longitudinal colonization and disease studies, specifically from closely related hypervirulent A:ST-5, A:ST-7, and A:ST-2859 clones. A comparative whole-genome sequencing study of 100 of these isolates showed the pilin glycosylation (pgl) locus as a hotspot for recombination. The frequent lateral gene transfer of pgl genes in N. meningitidis results in variations in the glycosylation patterns of pilin and other cell surface glycoproteins. Importantly, pili glycosylation of N. meningitidis is crucial in binding to the platelet activating factor receptor on human bronchial epithelial cells for colonization and understanding the role of pilin glycosylation in N. meningitidis colonization and disease in the meningitis belt can provide critical insights into the pathogenesis of

meningococcal epidemics.

Aim/Methods

This study aims to analyse the resulting glycan structures from various pgl alleles and their variable expression resulting from both recombination and phase variation of the pgl genes.

Results

The results of the study revealed that all the serogroup A meningococcal isolates analysed contained pglA, pglE, and pglI glycotransferase genes with high numbers of phase variable repeats. The basal O-linked sugar of the glycans expressed by these isolates is obscured by various additional mono- or di-saccharide structures whose expression varies greatly due to the phase variable expression of these pgl genes. Additionally, two isolates with pgl loci that have undergone recombination showed a different unknown basal glycosylation structure.

Conclusions

Pilin glycosylation is an essential component of the cell surface of N. meningitidis. The glycan structures decorate key surface proteins, including the pilin protein that plays a critical role in bacterial adherence to host cells. Our findings indicate that variations in N. meningitidis protein glycosylation may be crucial for bacterial adaptation to evade herd immunity in semi-immune populations. Investigating pilin glycosylation in N. meningitidis can shed light on the mechanisms by which this pathogen evades the host immune response, and may help identify potential targets for novel therapies and vaccines.