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MenB-4C vaccination elicited IgG antibodies recognize meningococcal and cross react with gonococcal lipooligosaccharides (LOS)

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Background

Antigens in the outer membrane vesicles (OMVs) of the Neisseria meningitidis (Nm) group B-directed vaccine MenB-4C (Bexsero) may protect against infections with N. gonorrhoeae (Ng). The immunologic basis for this protection remains unclear. The lipooligosaccharide (LOS) of vaccine strain NZ98/254 is a mixture of L1 and L3 structures with an inner core 3-PEA-HepII modification. Previous work has shown that the OMV-based vaccines generate serum antibodies to OMV proteins and LOS .

Aim/Methods

The aim of this study was to characterize the human serum IgG antibodies against Nm and Ng LOSs elicited by MenB-4C. Ten paired sera obtained pre- and post-immunization (one month after a third vaccine dose, Vaccine 2015;33(29):3322-30) were used in Western blots to probe Nm and Ng whole cell lysates after

removal of proteins by protease K. Three post MenB-4C sera were then used to probe the structurally defined meningococcal LOS immunotypes (L1-L12) and LOSs of Nm and Ng strains and mutants.

Results

Post (but not pre-immune) MenB-4C sera recognized both Nm and Ng LOS species, accounting for ~5-9% of total IgG response to gonococcal OMV antigens. Nm and Ng LOSs were broadly recognized by post-immunization IgG antibodies but with individual variability in structural specificity. Terminal sialyation of the α-chains had minimal impact on recognition. A maltose (Glc-Glc; L5, L10 and L11), instead of lactose (Gal-Glc), linkage to HepI significantly diminished or eliminated reactivity. Deep truncation of LOS, specifically the rfaK mutant without glycosylation of α-, β- or γ-chains, was not recognized by any post vaccine sera. The 3-PEA-HepII could be part of the conformational epitope; serum 7v5 IgG antibodies predominantly recognized the L1 (Gal-Gal-Glc-HepI) α-chain with a 3-PEA-HepII β-chain. Replacing with a 3-Glc at HepII blocked antibody recognition. Serum 19v5 recognized inner core LOSs with truncated α-chain structures (Gal-Glc-HepI, L8) and the 3-Glc-HepII also interferes with antibody binding. LOS antibodies in serum 17v5 recognized an intact α-chain, either L3 lactoneotetraose (LNT) or L1, and contributed to serum bactericidal activity against gonococci.

Conclusions

MenB-4C vaccination elicited serum IgG antibodies to conformational epitopes involving HepI and HepII glycosylated LOS structures shared between Nm and Ng that may be a bactericidal target.