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Neisseria lactamica and protection against meningococcal colonisation

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Background

Unlike the potent glycoconjugate vaccines, subcapsular antigen-based vaccines targeting serogroup B N. meningitidis (Nmen) strains do not protect against pharyngeal colonisation and are therefore unlikely to induce herd immunity. For optimal public health control of serogroup B disease, alternative strategies will be required. Natural, and experimentally induced colonisation with Neisseria lactamica (Nlac) provides broad spectrum protection against Nmen colonisation. Nlac formulated as an intranasally-administered Live Bacterial Product (LBP) could feasibly be utilised to limit Nmen carriage. Here, we demonstrate that: (1) the protective effect of Nlac on Nmen may be due to induction of cross-reactive adaptive immunity, (2) anti-Nmen adaptive immunity

generated following Nlac colonisation can be enhanced through genetic modification of Nlac.

Aim/Methods

We conducted two controlled human infection experiments using either wild type (WT) or genetically-modified Nlac (GM-Nlac) expressing the meningococcal vaccine antigen, NadA.

Results

Colonisation with WT Nlac induced anti-Nlac- and anti-Nmen-specific IgG, plasma cells (BPLAS) and memory B cells (BMEM). B cell dynamics suggested that Nlac colonisation recalled pre-existing Nmen-cross-reactive IgG BMEM. Nlac colonisation density correlated inversely with the magnitude of anti-Nlac immunoglobulin titres and BPLAS responses, suggesting a role for these responses in bioburden control. Colonisation with GM-Nlac was safe and generated anti-NadA IgG, BPLAS, and BMEM. In contrast to WT Nlac, GM-Nlac induced serum bactericidal antibodies against serogroup B strain 5/99.

Conclusions

Nasal inoculation with both WT Nlac and GM-Nlac is safe and protects against Nmen colonisation. Current evidence suggests this effect is driven by generation of cross-reactive adaptive immunity. The observation that GM-Nlac induced anti-NadA adaptive immune responses, including generation of SBA titres, justifies further studies to assess the impact of GM-Nlac on protection against Nmen colonisation and disease. To that end, we will discuss current progress in the development of GM-Nlac expressing multiple Nmen antigens (including NadA and fHBP) suitable for use in controlled human infection, experimental medicine and as a potential LBP.