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A novel virus-like particle vaccine platform elicits robust IgG responses against selected meningococcal antigens in vivo

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Background

Background: bacterial meningitis remains a significant threat to public health in several countries worldwide. There have been several attempts to develop a comprehensive vaccine using bacterial outer membrane proteins.

Aim/Methods

Aim: we report the use of a novel virus-like particle (VLP) assembly platform, which has the potential to elicit strong antibody responses against multiple antigens simultaneously. Here we have adapted the Hepatitis B core antigen (HBc), which is widely used as a scaffold for heterologous antigen presentation, to bind to any antigen fused to an antibody Fc domain (termed ‘AbBind’). Fusion to Fc stabilises conformational epitopes in the antigens, and the modified scaffold allows the attachment of multiple antigens in any desired combination. The primary aim of this project was to investigate whether the AbBind VLP platform was able to induce a robust immune response against a selection of broadly cross-protective antigens from Neisseria meningitidis. Methods: the assembly platform was tested using variants 1 and 3 of factor H binding protein (fHbp), and the adhesin A (NadA). Each antigen was fused to mouse IgG2a Fc fragment, expressed in human embryonic kidney 293 (HEK) cells and purified to homogeneity. Bio-Layer Interferometry assay confirmed the binding of the engineered VLP core particle to the antigen-Fc-fusions. VLP:antigen-Fc complexes were inoculated into female Balb/c mice using doses which ensured equimolar amounts of antigen in each group: this equated to total protein administered between 3 and 8 µg per dose.

Results

Results: mice vaccinated with VLP:antigen-Fc complexes produced robust titers of IgG antibodies against the component antigens at doses as low as 0.053 nmol antigen. Antibodies against antigen-Fc fusion produced in HEK293 cells cross-reacted against the same antigen expressed and isolated from E. coli. Encouragingly, mice immunised with a combination of the VLP scaffold and fHbpV1 and fHbpV3 elicited antibodies against both variants. The mice tolerated the putative vaccine well, with no signs of reactogenicity following inoculation.

Conclusions

Conclusions: we conclude that the engineered AbBind VLP provides a safe and versatile platform that can boost IgG antibody levels and improve strain coverage.