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Analysis of human monoclonal antibodies from 4CMenB vaccinees reveals PorB epitopes inducing cross-strain protection

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Background
Several reports have described a moderate cross-protection of OMV-based vaccines across meningococcal strains of diverse PorA-serotypes, despite PorA being considered as the immunodominant antigen. More recently observational case-controlled studies have reported effectiveness of 4CMenB on gonococcal infection. In a recent study we isolated human monoclonal antibodies (HumAbs) from plasmablasts derived from 3 subjects after vaccination with 4CMenB and revealed these HumAbs to target a number of OMV components, with a large number of PorB specific HumAbs being identified.

Aim/Methods
To elucidate the potential cross-protective nature of the PorB HumAbs we characterized their ability to bind diverse meningococcal and gonococcal strains using a protein array with OMV prepared from the strains panel, as well as their bactericidal activity on 18 OMV-indicator meningococcal strains and a test gonococcal strain. Western Blot, flow cytometry and electron microscopy methods were performed to investigate in detail the binding behavior of the PorB HumAbs on the bacterial surface of diverse meningococcal strains. The HumAb sequences were used to generate 3D models and computationally predict paratope structures for docking experiments against the trimeric crystal structure of meningococcal PorB. Furthermore, docking of the HumAb structures on PorB alleles from susceptible strains was completed to gain insights in silico into the cross-functional epitopes that may be involved.

Results
Binding studies using diverse techniques on the 20 PorB HumAbs grouped these into distinct classes by means of their behaviour on diverse strains and phase-variable susceptible nature of the binding. The accessibility of different PorB epitopes on diverse meningococcal strains was largely strain-dependent. Docking experiments with representatives of the classes predicted in silico the best pose of each model paratope structure on the model structure of the PorB immunogen. Three diverse epitopes on PorB could be predicted from these computational studies leading to the killing of diverse strains. Structural mass spectrometry will be employed to confirm the epitopes.

Conclusions
Collectively, through the application of multiple approaches, we are characterizing the human antibody response to the PorB immunogen, deconvoluting its antigenic nature and predicting functional epitopes contributing to the protection induced by the OMV-component of the 4CMenB vaccine.