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The target of a patient-derived fully-human monoclonal antibody is a novel cross-protective antigen

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Background

Currently-available protein-based vaccines, when deployed, have successfully limited the burden of invasive meningococcal disease due to MenB strains. Reductions in case incidence have been observed in the 4CMenB vaccine-eligible cohort in the UK; however, changing epidemiology of ciruclating MenB strains is affecting long-term vaccine efficacy and mandates non-cessation of vaccine discovery efforts.

Aim/Methods

In our lab, we employed a strategy that involved the cloning of fully-human monoclonal antibodies (hmAbs) from convalescing IMD patients for the discovery of novel cross-protective antigens.

Results

We have previously reported the successful cloning of 18 anti-meningococcal hmAbs from 5 paediatric patients. These hmAbs exhibited broad cross-reactivity, binding to a surface-exposed epitope on 22 out of a 23 MenB strain panel. Accruing data from whole-cell ELISAs show that these hmAbs target epitopes specific for pathogenic Neisseria only - no discernible reactivity with commensal Neisseria was observed. At least 5 of these hmAbs have confirmed serum bactericidal activity (SBA), including against strains non-susceptible to 4CMenB human immune sera. In addition, data from antibody-mediated complement deposition assays suggest an opsonophagocytic property of some of these bactericidal hmAbs via the recruitment of complement factor C3b to the meningococcal surface. Unequivocal determination of the identities of the antigens/epitopes cognate to these hmAbs has been attempted with a variety of approaches. With classical immunoproteomics (IP), for example, non-specific interactions between non-hmAb targets and the Protein G-coated particles used for immobilisation of hmAbs in pulldown assays is a significant limitation. Using a multiproteome protein array developed in collaboration with Antigen Discovery Inc., the identity of the ~35 kDA target of one of these functional hmAbs, P02-1A1, was discovered. Here, the description of P02-1A1 cognate antigen, a membrane protein not previously considered for vaccine candidacy, will be presented. At the time of submitting this abstract, the identity of the target cannot be revealed because of ongoing intellectual property right (IPR) discussions.

Conclusions

Thus, we have shown the applicability of the Reverse Vaccinology 2.0 platform to meningococcal vaccine antigen discovery. Crucially, the RV 2.0 platform is capable of revealing entirely novel vaccine candidates, which have been missed by conventional or other high-throughput screening protocols.