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Characterisation of a patient-derived fully-human monoclonal anti-gonococcal antibody

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Background

The isolation of multi-drug resistant Ng accompanied by exponential increases in the number of gonorrhoea cases worldwide and the absence of novel antibiotics provide the impetus for research into alternative treatment options and/or prevention of disease via vaccination. A powerful and sequential approach involving the cloning of human monoclonal antibodies (hmAbs) from convalescing patients, termed Reverse Vaccinology 2.0, exploits the adaptive immune response by using functional antibodies cloned from patient plasmablasts (or memory B cells of healthy human subjects) as a route to identifying antigens that can compose effective vaccines. With the meningococcus, we have cloned bactericidal hmAbs cognate to antigens that are absent from currently-licensed Nm vaccines. With the pneumococcus, we have also cloned functional (in vitro and in vivo) hmAbs whose cognate epitopes are present in 21 out of 23 serotypes of current global significance.

Aim/Methods

We aimed, in this proof-of-principle study, to clone functional anti-gonococcal hmAbs from convalescing patients as a route to identifying vaccine candidate antigens and/or alternative immunotherapeutics.

Results

First, we identified 2 patients (blood sampled on day of presentation at clinic, and at 7 and 14 days afterwards i.e. day 0, 7 and 14 respectively) that presented with plasma that possessed serum bactericidal activity against multiple Ng strains. Interestingly, for one of these patients, plasma SBA was detected at the day-7 timepoint only and not the day 0 nor day 14 timepoints. From a small subset of memory B cells isolated from these patients, one antibody (Ng42k) was cloned. Ng42k bound to a cognate epitope on 100% of Ng strains assessed (n=11), including FA1090 and MS11-B12, in whole cell immunoassays. Ng42k was also reactive with a surface epitope on 68% of a meningococcal strain panel (n=40) but not pneumococcal strain D39 nor E. coli HST08; measured fluorescence intensities with meningococcal strains was significantly lower than with gonococci. The functional properties of Ng42k (bactericidal and/or opsonophagocytic) as well as the identity of its cognate epitope are currently being assessed.

Conclusions

Thus, we have shown the utility of RV 2.0 in the potential identification of therapeutic anti-gonococcal antibodies and vaccine candidate antigens.