

## (1) Submission ID#1535617

Role of antibodies induced by the Ng GMMA investigational vaccine in the ability to inhibit Opa-CEACAM interaction and adhesion

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## Background

The Opa proteins are a family of 11 heterogeneous phase-variable outer membrane proteins which undergo antigenic variation through inter- and intra-strain recombination between alleles. Opa proteins significantly contribute to the adherence/invasion of epithelial cells and neutrophils through binding to human carcinoembryonic antigen related cell adhesion molecule (CEACAM) receptors 1, 3, 5 and 6. Every gonococcal circulating strain can express a complement of diverse Opa proteins which can drive these host-pathogen interactions. GSK has developed a multivalent investigational vaccine, Ng GMMA, which contains Opa proteins amongst others.

## Aim/Methods

A Luminex-based assay was developed to measure the interaction of diverse gonococcal strains with recombinant CEACAM 1, 3, 5 and 6. The ability of the mouse antisera, after immunization with the Ng GMMA vaccine, to inhibit bacterial interaction/binding to the distinct CEACAM human ligands as well as to inhibit bacterial adhesion conducted using cellular epithelial models including Detroit 562 (for oropharyngeal tissue) and Ect-1 (for ectocervix tissue) cell lines was assessed.

## Results

The full complement of Opa proteins expressed by each gonococcal strain was determined. The binding of gonococcus to the CEACAMs was shown to be Opa-specific and antisera from the Ng GMMA investigational vaccine differentially inhibited the interaction of the representative panel of strains with diverse CEACAM ligands, presumably depending on the alleles of Opa expressed by the diverse strains. Bacterial adhesion inhibition experiments showed that antibodies induced by the- Ng GMMA vaccine are able to inhibit bacterial adhesion both to Ect-1 and Detroit 562 cell lines.

## Conclusions

We have developed innovative assays to determine antibody functional activity around the inhibition of Opa-CEACAM interactions driving host-pathogen behaviors. Initial results demonstrate that mouse antisera from Ng GMMA vaccine elicits responses that can inhibit interaction with CEACAMs and adhesion to urogenital and oropharyngeal epithelial mucosa likely through, but not limited to, anti-Opa antibodies.