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Development of non-clinical serological assays to evaluate immunogenicity of Neisseria gonorrhoeae vaccine candidate

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Background
Gonorrhea is a sexually transmitted infection caused by Neisseria gonorrhoeae (Ng) that requires urgent and sustainable action due to the emergence of antimicrobial resistant strains. GSK has developed a vaccine against gonococcus currently in a Phase I/II study, named Ng-GMMA, based on genetically detoxified outer membrane vesicles (GMMA) and produced from the FA1090 Ng strain. A crucial step for the identification of the best vaccine candidate was the setup of non-clinical immunological assays that could predict vaccine protection. Although correlates of protection against gonococcal infection have not been defined, there was evidence that complement-mediated killing may predict vaccine efficacy against the disease. While literature suggests the potential value of bactericidal antibodies for the prevention of Ng infection, controversial evidences about the contribution of the opsonophagocytosis to bacterial killing are reported.

Aim/Methods
The aim of this work was to develop non-clinical immunological assays to identify the best gonococcus vaccine candidate to be moved in clinical trial based on its capability to induce highly functional antibodies against different Ng strains. First of all, Luminex-based immunoassays were developed to estimate the humoral response to the homologous Ng-GMMA strain (FA1090). Efforts in research were then focused on the development of Serum Bactericidal Activity assays in presence of human complement (hSBA) to test the functionality of vaccine induced antibodies against the FA1090 homologous strain and the cross-protection against heterologous strains. The opsonophagocytic mechanism in presence of antibodies and complement was also explored.

Results
A high-throughput hSBA assay based on agar-overlay read out was developed on the Ng-GMMA vaccine homologous and heterologous strains selected ad hoc to represent the global variability of gonococcal outer membrane antigens. The method, optimized for mouse, rabbit and rat sera, was applied to select the Ng-GMMA vaccine candidate and to support the toxicology study. Moreover, a robust Luminex-based immunoassays was developed to quantify IgG/IgA in serum and vaginal washes of mice receiving the Ng-GMMA vaccine. Finally, further functional immune mechanisms of antibodies against Ng are currently under investigation, such as opsonophagocytosis.

Conclusions

Immunological and functional assays were developed to support the preclinical selection of a Ng-GMMA vaccine candidate to be tested in clinical studies.