Identification of proteins that can be used in a new MenB vaccine

Final report for The Jessica Bethell Foundation: we are very grateful to The Jessica Bethell Foundation for their support and are pleased to report the study findings now that the project has concluded.

Background

Bexsero is a vaccine which is used routinely in the UK to prevent Meningococcal group B (MenB) disease, and real-world evidence shows the vaccine is providing lasting protection for children, with cases of MenB in young children having reduced by 75% three years after the vaccine programme was introduced.

However, despite its use, MenB continues to cause cases of disease (meningitis and septicaemia), particularly in teenagers and young adults. This is because Bexsero is currently only routinely offered to infants in the UK, and it does not protect against all circulating MenB strains or prevent them from being carried in the back of the nose and throat and being transmitted. Therefore, there is a need to develop new vaccines that can provide broader protection against MenB disease.

Study objectives

The aim of this project was to identify proteins present on the surface of MenB bacteria that in the future, may be able to be used in a new vaccine to provide enhanced protection against MenB disease.

Methods

This project was led by Dr Fadil Bidmos, Advanced Research Fellow and Prof Paul Langford, Professor of Paediatric Infectious Diseases, at Imperial College, who have extensive experience in researching meningitis-causing pathogens as well as developing novel antimicrobial strategies and new vaccines.

The project formally started on the 2nd of May 2023, and was scheduled to run for four months, but in December 2023 MRF approved a short no-cost extension for this project to enable the research team to finalise and validate their results.

In previous research, Dr Bidmos and Prof Langford had identified antibodies from patients that had recovered from meningococcal disease, and it was demonstrated in the laboratory that some of these antibodies were able to effectively kill MenB bacteria. However, due to challenges in traditional identification methods, the team did not know what proteins these 'killing' antibodies were binding to on the surface of the MenB bacteria. Identifying the proteins, known as antigens, is important, as they are potential MenB vaccine candidates.

To address this, in preliminary work, the team employed a technology called phage display. This is a sophisticated method that enables rapid identification of the antigens on the surface of the MenB bacteria that are bound by the antibodies. This approach allowed the target of

one antibody to be identified, and through the research funding provided by the Jessica Bethell Foundation, the team aimed to identify the target antigens of four additional antibodies.

Results

Using the phage display technique, the project successfully identified potential protein targets for two of the antibodies, however the targets did not interact with the antibodies as the team had anticipated. Phage display is however still believed to be a powerful tool, therefore in collaboration with an established professional services company, the research team are working to further optimise the data from the phage display to enable more conclusive results to be obtained.

To complement this research, in a separately funded study, Dr Bidmos and Prof Langford worked with another research group and employed a different approach to examine how antibodies interacted with different meningococcal proteins. One of the antibodies they tested in this study successfully showed a clear target antigen that warrants further research. They found that this antibody also recognises a similar protein in the gonococcus (another bacterium which is a close cousin to the meningococcus), which provided the team with more evidence that it's specific to that target.

Next Steps

The generous support of the Jessica Bethell Foundation has helped find an excellent method to identify proteins that are meningococcal vaccine candidates, an important step in shortening the time to their further evaluation and use in humans. Armed with this valuable technology, the research team are now working to refine the phage display so they can identify the targets of other crucial antibodies they currently have under investigation.

The successful identification of a target antigen in the other research project undertaken by the team also presents an exciting prospect for future vaccine candidate research, and we are delighted to share that Dr Bidmos has secured further funding to continue this important work.

Through this funding, Dr Bidmos will not only continue his research focussed on identification of future MenB vaccine candidates, but innovative research will be kick-started, that aims to develop a combination vaccine that in the future, may provide protection against both meningococcal and pneumococcal disease in a single vaccine. If successful, the overall project has the potential to have a major impact on global health in the development of new MenB vaccines, and potentially vaccines for other important causes of meningitis.