Using the PilVax strategy to develop a vaccine against Group A Streptococcus

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Why do we need a Group A Streptococcus (GAS) vaccine?

- GAS causes a major global disease burden.
  > 633,000 new invasive GAS diseases cases and 163,000 deaths each year
  > 350,000 deaths globally due to acute rheumatic fever each year
- There is no currently licensed vaccine against GAS.

The PilVax strategy used to develop a GAS vaccine

1. M1 GAS expresses the highly stable pilus on the cell surface.
   It consists of repeated copies of the Spy0128 protein.

2. The M1 GAS pilus is used as a peptide antigen carrier.
   A GAS peptide antigen was incorporated into the βE/F loop region of the Spy0128 protein by genetic engineering.

3. The food-grade bacterium Lactococcus lactis is used as a safe and cheap vaccine delivery vehicle via the mucosal route. A pilot study to investigate the antibody responses to the vaccine, was performed by immunising mice intranasally.

Results

1. The PilVax-Spy0469203-225 vaccine expressed the recombinant M1 GAS pilus on the surface of L. lactis.

   Flow cytometry to determine Spy0128 protein expression on the recombinant L. lactis

   Western blot analysis of L. lactis cell wall extracts

   - Flow cytometry and Western blot results show that incorporation of the Spy0469203-225 peptide moderately reduced the pilus expression and assembly.

2. The PilVax-Spy0469203-225 vaccine is immunogenic.

   - ELISA results show that the PilVax-Spy0469203-225 vaccine induces specific IgG and IgA antibodies against the Spy0469203-225 peptide.
   - The positive control, the Spy0469203-225 peptide fused to flagellin (Flagellin-Spy0469203-225) induces higher serum IgG, but lower IgA antibody titre than the PilVax-Spy0469203-225 vaccine.
   - The PilVax-Spy0469203-225 vaccine induces similar saliva IgA, but lower bronchoalveolar lavage fluid IgA antibody titre than the Flagellin-Spy0469203-225 vaccine.

Conclusion and future directions

- The PilVax-Spy0469203-225 vaccine is immunogenic and can produce specific serum IgG and IgA antibodies against the Spy0469203-225 peptide.
- In vivo protection studies will provide further evidence for antibody functionality.