

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

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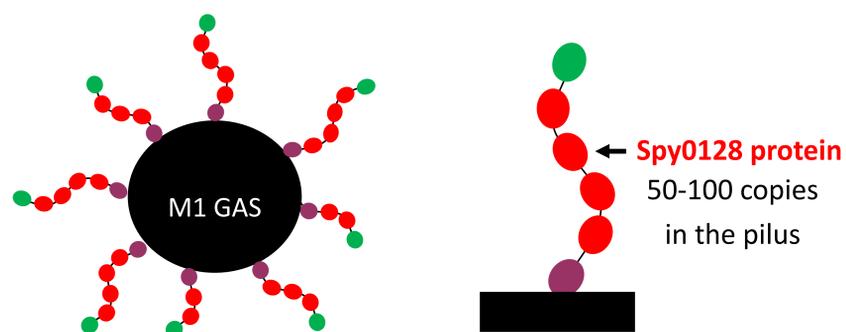


Why do we need a Group A Streptococcus (GAS) vaccine?

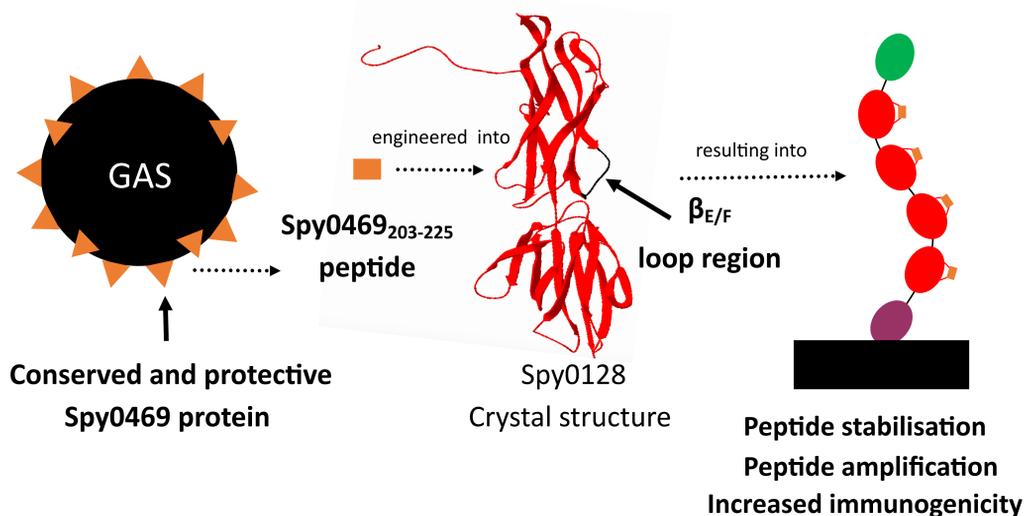
- GAS causes a major global disease burden.
 - > 633,000 new invasive GAS diseases cases and 163,000 deaths each year
 - 350,000 deaths globally due to acute rheumatic fever each year
- There is no currently licensed vaccine against GAS.

The PilVax strategy used to develop a GAS vaccine

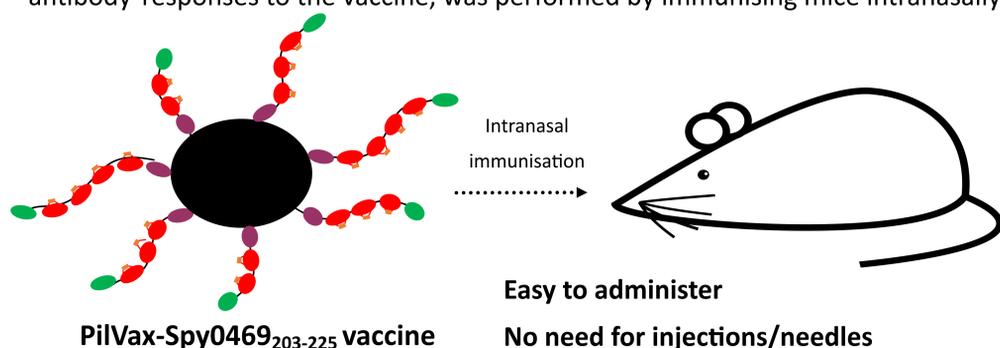
1. M1 GAS expresses the **highly stable pilus** on the cell surface. It consists of repeated copies of the Spy0128 protein.



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



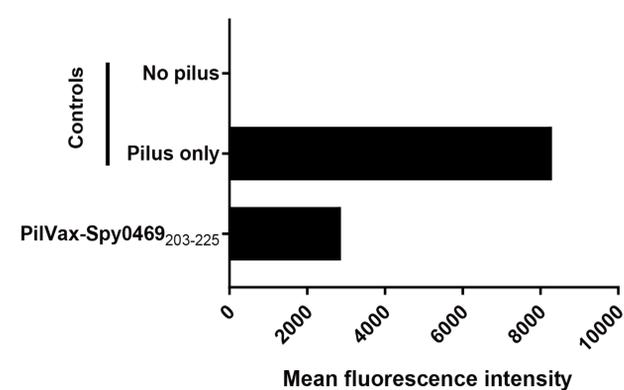
3. The food-grade bacterium *Lactococcus lactis* is used as a **safe and cheap** vaccine delivery vehicle via the mucosal route. A pilot study to investigate the antibody responses to the vaccine, was performed by immunising mice intranasally.



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*



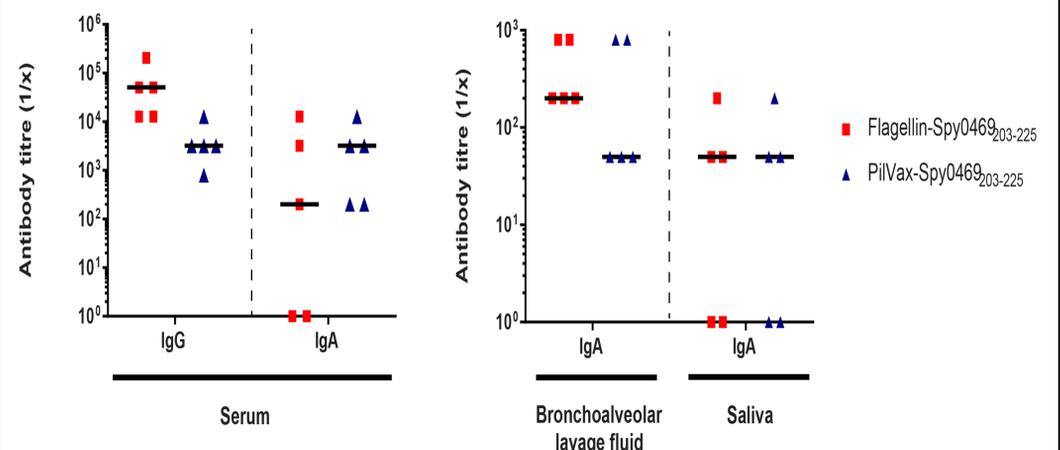
Western blot analysis of *L. lactis* cell wall extracts



Cell wall extracts were probed with anti-Spy0128 rabbit polyclonal antibodies.

- 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.