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Development of Pneumococcal surface protein antigen (PspA) based Pneumococcal vaccine showing enhanced protective immunity when conjugated to Vi capsular polysaccharide from *Salmonella typhi*

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Background & Aim: Data from Phase-I clinical trials showed that protein based pneumococcal vaccines induced poor immune responses. To address this problem the protein needs to be presented in a way that will induce a stronger antibody response that is more likely to protect humans. Our aim was to develop a more immunogenic vaccine by conjugating α-helical region of PspA family 1 and 2, a protein common to all *Streptococcus pneumoniae* to Vi capsular polysaccharide from *Salmonella typhi*. The candidate vaccine provides better protection against lethal intravenous challenge with broad range of *S. pneumoniae* strains.

Method: A high yielding, scalable method for fermentation and purification of Vi polysaccharide and of PspA family 1 and family 2 proteins have been optimized. Conjugation processes developed have more than 60-80% recoveries of both PspA and Vi polysaccharide and amongst a series of conjugates the most immunogenic conjugate was selected for protection studies against a range of *S. pneumoniae* strains. We tested the feasibility of formulating a bivalent vaccine containing Vi-PspA conjugates with PspA from both families 1 and 2 and tested its ability to induce cross-protection against strains with different PspAs. Spleen cell culture of immunized mice was checked for induction of both Th1/Th2 cytokines.

Results: A series of Vi-PspA conjugates are prepared and tested in mice. Both Anti-Vi and Anti-PspA family 1 and family 2 responses are significantly boosted upon conjugation (P<0.05). A high level of protection of vaccinated mice was observed when challenged with a Pneumococcal strain expressing a clade that was present in the vaccine (monovalent or bivalent vaccine). Induction of a combination of Th1/Th2 cytokines was observed upon conjugation of protein with 'Vi' polysaccharide.

Conclusion: The bivalent conjugate vaccine consisting of PspA from families 1 and 2 bound to 'Vi' polysaccharide has the potential to protect against typhoid fever and infection caused by a broad range of *S. pneumoniae* stains. The vaccine has the added advantage that an adjuvant is not required to mount a robust protective response. It is anticipated that this vaccine can be produced at low cost and thus be made available to the world's poorest communities at an affordable price.

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