EVALUATION OF THE SELECTIVE PRESSURE OF THE IMMUNE RESPONSE ELICITED AGAINST PSPA (PNEUMOCOCCAL SURFACE PROTEIN A) IN A CO-COLONIZATION MODEL WITH DIFFERENT STRAINS OF *STREPTOCOCCUS PNEUMONIAE*

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Abstract:

Streptococcus pneumoniae is a major cause of morbidity and mortality caused by pneumonia, bacteremia, and meningitis worldwide. The currently available vaccines are based on the response to the capsular polysaccharide and they have some disadvantages, such as high production cost and coverage restricted to the serotypes included in the formulation, besides the appearance of the phenomenon of substitution of prevalent strains. Pneumococcal surface protein A (PspA) is one of the leading candidates for a protein vaccine against pneumococcal diseases. PspA shows variability and the great majority of strains express PspA from family 1 (clades 1 and 2) or family 2 (clades 3, 4 and 5). The purpose of this study is to evaluate the efficacy of the nasal immunization with recombinant PspAs from different clades in a mouse model of co-colonization of the nasopharynx with two strains, one expressing PspA from family 1 and another expressing PspA from family 2. C57BL/6 mice were immunized twice intranasally with recombinant PspAs from clades 1 to 5 (rPspA1, rPspA2, rPspA3, rPspA4 and rPspA5) using the whole-cell pertussis vaccine (wP) as adjuvant. ELISA results showed an increase in anti-rPspA1 and anti-rPspA4 IgG titers in the group immunized with rPspA1, whereas immunization with rPspA4 elicited an increase only in anti-rPspA4 IgG titers. Mice were then challenged with a mixture of the strains 491/00 (serotype 6B, PspA1) and 472/96 (serotype 6B, PspA4, trimethoprim resistant) and bacteria were recovered from nasal washes 5 days after challenge. Only mice immunized with rPspA1 showed statistically significant reduction in colonization with the PspA1 expressing strain when compared to the control group immunized with the adjuvant wP, whereas only animals immunized with rPspA4 showed statistically significant reduction in the PspA4 expressing strain when compared to the control group immunized with the adjuvant wP. These initial data indicate clade-specific protection in this model. Experiments with challenge with strains of different serotypes (6B and 23F) and expressing different PspAs are underway.

Keywords: *Streptococcus pneumoniae*, PspA, vaccine

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