IMMUNIZATION OF MICE WITH PspA HYBRIDS INDUCES BROAD PROTECTION FROM FATAL PNEUMOCOCCAL INFECTION, CORRELATING WITH AN INCRESASE IN COMPLEMENT DEPOSITION ON THE BACTERIAL SURFACE

DARRIEUX M[1], Miyaji EN[1], Ferreira DM[1], Ren B[2], Hollingshead SK[2], Briles DE[2] and Leite L.C.C[1]. [1]Instituto Butantan - São Paulo, Brazil. [2]University of Alabama – EUA.

Streptococcus pneumoniae is a major cause of pneumonia, meningitis and sepsis. Among the vaccine candidates against this pathogen is Pneumococcal Surface Protein A (PspA), an exposed protein present in all pneumococcal strains, and protective against sepsis in animal models. PspA interferes with complement deposition on pneumococcal surface, thus protecting the bacteria from phagocytosis by the immune system. Nevertheless, PspA exhibits high structural diversity – there are two major families - and its effectiviness is limited to the same family. This work investigates the potencial of PspA hybrids (containing the N-terminus from families 1 and 2 fused) to be used as an anti-pneumococcal vaccine with broader coverage. Sera from mice immunized with these hybrids led to an enhacement of complement deposition on pneumococcal strains bearing PspAs from both families, as seen by FACS analysis. Furthermore, the immunized mice were protected from fatal infection with diverse pneumococci. These data demonstrate that PspA hybrids are promising candidates in a future PspA based vaccine, and suggest that the mechanism of pneumococcal clearance from blood stream in presence of anti-PspA antibodies involves increased complement deposition and opsonophagocytosis.

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