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TITLE

DEVELOPMENT OF A VACCINE CANDIDATE AGAINST SCHISTOSOMA MANSONI: PRODUCTION, IMMUNOGENICITY ASSESSMENT AND VACCINE PROTECTION ASSAY IN RHESUS MACAQUES

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ABSTRACT

Schistosomiasis is a disease caused by blood flukes from the Schistosoma genus that affects more than 200 million people worldwide. The treatment indicated today is the use of praziquantel, which cannot prevent reinfection. One way to prevent the disease would be a prophylactic vaccine. Over the last decades, several vaccine candidates have been tested, but no vaccine against schistosomiasis is available today. Our group aims at developing a new vaccine candidate by unraveling the mechanisms behind the self-cure of rhesus macaques from a Schistosoma mansoni infection. Previously, we identified S. mansoni peptide epitopes recognized by rhesus macaques' antibodies using phage-display and peptide microarray assays. In the present work our objective is to evaluate the possible immunogenicity and protection generated in rhesus macaques against a S. mansoni infection using as an immunogen a chimeric protein comprised of thirteen previously identified peptide epitopes. The chimeric protein was produced together with a Rhizavidin motif as an adjuvant in its C-terminal portion. Twelve female rhesus macaques were immunized with three doses of the chimeric protein-rhizavidin, each dose spaced four weeks apart. Biotinylated Outer Membrane Vesicles from Neisseria lactamica and alum were used as adjuvants. At week 12 post-first-immunization (pfi), all macaques were challenged with 700 S. mansoni cercariae and the course of the infection was followed until week 36 pfi. We collected blood and feces samples at week 0 (before), and at weeks 2, 4, 6, 8, 10, 12, 13, 16, 18, 20, 22, 24 and 28 pfi to evaluate (i) the rhesus macaques'immune response, (ii) parasite development by Circulating Anodic Antigen (CAA) measurements, and (iii) eggs per gram of feces (EPG) using the Percoll gradient technique. The same samples will be collected at week 36 pfi, when the macaques will be euthanized and perfused. As a control group for comparison, we will use the data already collected from twelve female rhesus macaques non-immunized and infected from our previous work, which were submitted to the same experimental procedures that are being performed in this project. The results show that the average EPG decreased by half at the peak of infection establishment (week 10 post-infection) compared with the peak EPG of non-immunized macaques. We analyzed the antibody profile against the chimeric protein by ELISA and we were able to detect a considerable immunogenic capacity of the construct after each of the three doses. In conclusion, there is preliminary evidence that a mild protection against S. mansoni infection was induced in the rhesus macaques immunized with the vaccine candidate. Parasite CAA will be quantified at all time points to be used as the metric to determine possible protection induced by the immunization. Peptide microarray assays will be performed to identify and map within the chimeric protein the main targets of the antibodies responses elicited after immunization.

KEYWORDS

Schistosomiasis; Vaccine Candidate; Protection Assay; Chimeric Protein; Rhesus Macaques

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