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Immunization with surface immunogenic protein induces a decrease of vaginal colonization by group B Streptococcus in an experimental mouse model

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IMMUNIZATION WITH SURFACE IMMUNOGENIC PROTEIN INDUCES A DECREASE OF VAGINAL COLONIZATION BY GROUP B STREPTOCOCCUS IN AN EXPERIMENTAL MOUSE MODEL

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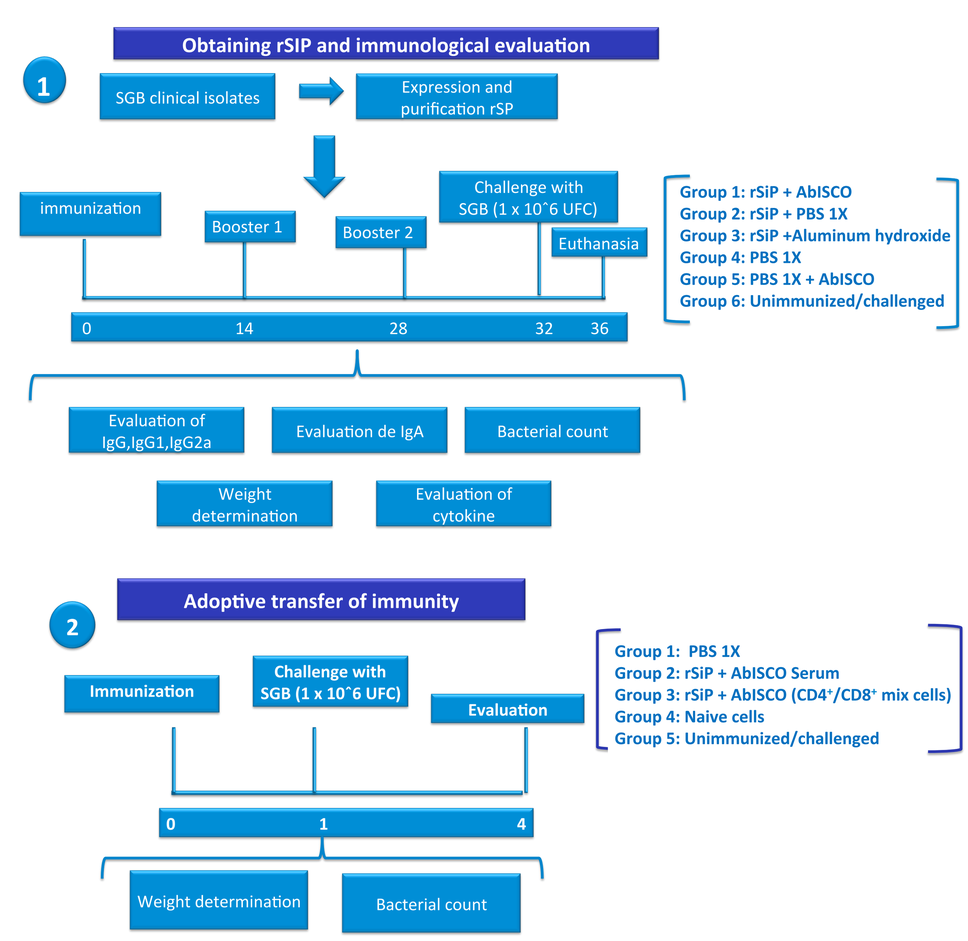
ABSTRACT

The Group B streptococcus (GBS) is the leading cause of neonatal sepsis and meningitis in developed countries and an emerging pathogen in adults. A neonatal infection occurs predominantly during the delivery by either inhalation or ingestion of contaminated secretions of the mother's vagina. Maternal screening by rectovaginal GBS colonization at 35–37 weeks of gestation, with subsequent intra-partum antibiotic prophylaxis (IAP) at the onset of labor, is implemented in some countries to prevent newborn invasive by GBS. Currently, there are not vaccines to prevent the devastating consequences of GBS and a glycoconjugate vaccine is under clinical experimentation (Clinical Trials Phase III).

The Surface Immunological Protein (SIP) of GBS is highly immunogenic and conserved between different serotypes of this bacterium. The SIP had been described to induce antibodies type IgG that induces protective immunity in animal model challenged intraperitoneally with GBS.

Here we describe the immunization with SIP mixed with an AbISCO-100 adjuvant in mice model challenged to GBS vaginal infection. The vaccine has demonstrated to decrease the GBS colonization in infected mouse. The SIP immunization has also increased the circulating IgA, IgG and IgG2a levels against SIP and antigen-specific circulating levels of IFN- γ and IL–2. In conclusion, we have demonstrated that a simple and effective vaccine is able to prevent GBS colonization. To our knowledge, is the first report the SIP-based vaccine reduces the vaginal GBS colonization in an animal model.

METHODS



RESULTS

The rSIP protein was purified and formulated with AbISCO like vaccine prototype. We observed that both experimental groups immunized with rSIP-AbISCO and rSIP alone decreased the GBS vaginal colonization compared with others experimental groups (Figures 1-6). Furthermore, our data suggest that the immune response induced by our vaccine is balanced (cellular/humoral), but with a tendency towards a cellular immune response (Figures 7-8).

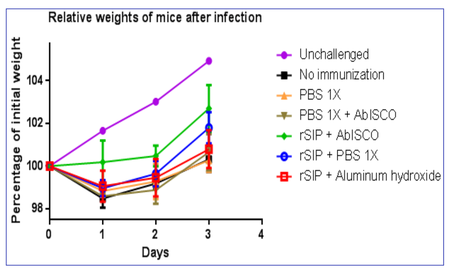


Figure 1. Weights of groups immunized and challenged with SGB. Groups were given an immunization and 2 boosters of 100 µL each of their respective doses. Weights were measured daily from the day of the challenge to the day the animals were sacrificed.

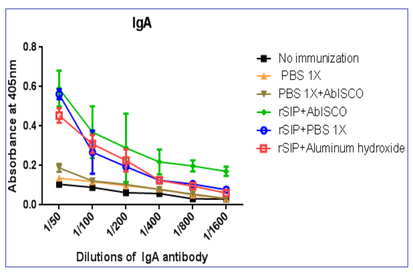


Figure 2. IgA antibody titers of groups immunized and challenged with SGB. ELISA was developed using an anti-mouse IgA antibody conjugated to the enzyme alkaline phosphatase and read in an ELISA reader at 405nm.

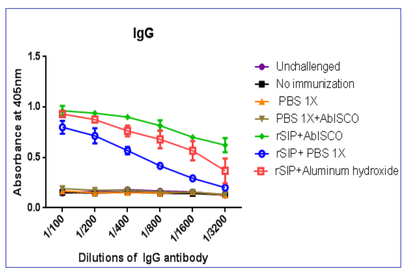


Figure 3. IgG antibody titers of groups immunized and challenged with SGB. ELISA was developed using an anti-mouse IgA antibody conjugated to the enzyme alkaline phosphatase and read in an ELISA reader at 405nm.

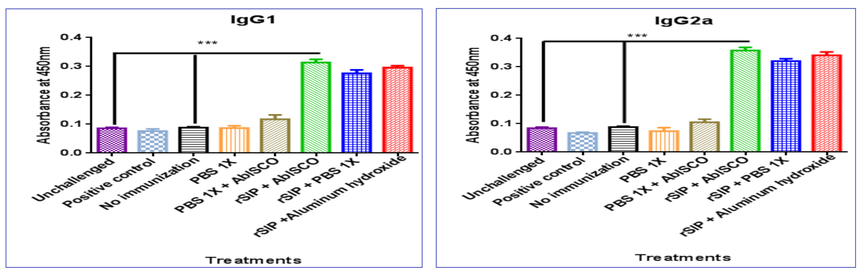


Figure 4. Analysis of IgG1 and IgG2 antibodies of groups immunized and challenged with SGB. ELISA was developed using anti-mouse IgG1 and IgG2 antibodies, respectively, conjugated to the enzyme alkaline phosphatase and read in an ELISA reader at 405nm. The positive control was an antigen of a kit for measuring the subclasses of (PD Pharmingen™). P < 0,05 (*).

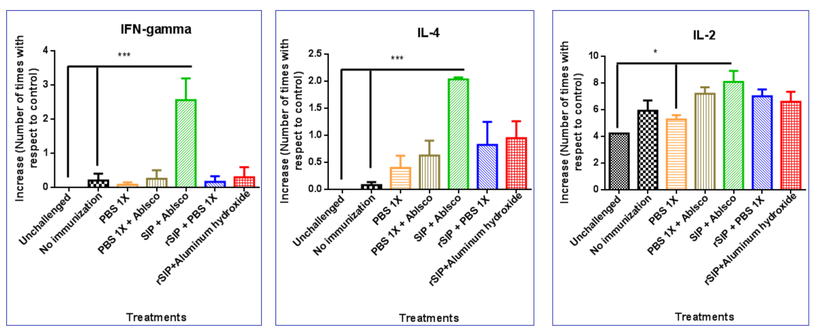


Figure 5. Evaluation of cytokines in groups of mice immunized and challenged with SGB. A: Levels of IFN-y liberated by mice immunized and challenged with SGB. B: Levels of IL-4 liberated by mice immunized and challenged with SGB. C: Levels of IL-2 liberated by mice immunized and challenged with SGB. The control without stimulus was a group without presence of the protein and without SGB challenge. P < 0,05 (*).

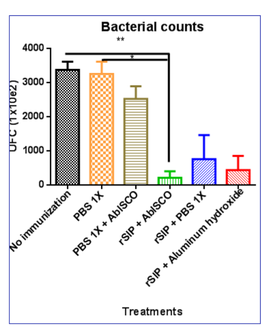


Figure 6. Counts of bacterial colonies seeded in blood agar plates. The samples were vaginal washes of mice submitted to immunization and posterior infection with serotype III SGB. P < 0,05 (*).

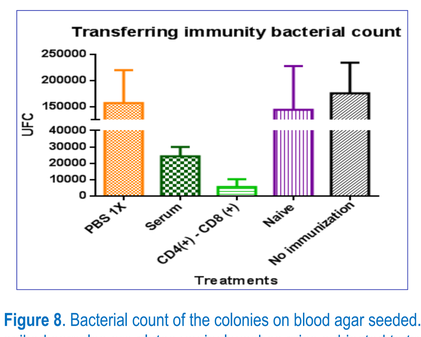


Figure 8. Bacterial count of the colonies on blood agar seeded. In spiked samples are plates vaginal washes mice subjected to transfer immunity and subsequent infection with GBS serotype III. The number of mice per group corresponded to a n = 3.

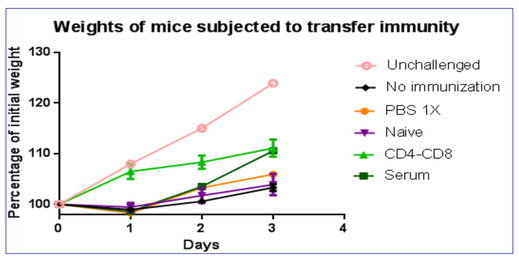


Figure 7. Graph weights of the groups subject to immunity transfer experiment and challenged with GBS. The groups were immunized with 100 µL of each dose as corresponded. The immunization routes were: group 1X PBS and serum was intraperitoneally, while for groups mix-CD4 + CD8 + and CD4 +, CD8 + naive the immunization route was intravenous. Mice were infected with the bacteria 24 hours after immunization and their weights were measured from that day until 72 hours later. The number of mice used per group was n = 3.

CONCLUSIONS

- Our vaccine formulation is able to prevent GBS vaginal colonization in murine model, also we observed balanced Th1/Th2 immune response but with a tendency to cell type response.
- We analyzed passive immunity transfer. Healthy mice were infused with serum or a mixture of CD4/CD8 cells and then challenged with GBS. We observed a low level of GBS vaginal colonization in both experimental groups.
- Our experimental model may be useful by testing new vaccine formulation.

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