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#### TITLE

**IMMUNIZATION OF MALNOURISHED MICE WITH THE RSM29 SCHISTOSOMA MANSONI ANTIGEN IS NOT ABLE TO REDUCE THE AREA OF HEPATIC GRANULOMA**

#### AUTHORS

Murta, J.A.<sup>1</sup>; Maciel, P.S.\*<sup>1</sup>; Gonçalves, R.<sup>2</sup>; Fontes, I.C.<sup>2</sup> Figueiredo, M.M.<sup>1</sup>; Parreiras, P.M.<sup>3</sup>; Silva, F.M.<sup>4</sup>; Antonelli, L.R.V.<sup>1</sup>; Fonseca, C.T.<sup>1</sup>

#### AFFILIATIONS

- <sup>1</sup> Grupo de Biologia e Imunologia de Doenças Infecciosas e Parasitárias do IRR-Fiocruz Minas  
<sup>2</sup> Laboratório de Biologia de Macrófagos e Monócitos da Universidade Federal de Minas Gerais (UFMG)  
<sup>3</sup> Instituto René Rachou (IRR) - Fiocruz Minas  
<sup>4</sup> Laboratório de Imunologia de Doenças Infecciosas na Universidade de São Paulo (USP)

#### ABSTRACT

**Introduction:** Malnutrition and schistosomiasis are important public health problems. The main pathological alteration in schistosomiasis is a granulomatous reaction in the liver. We have previously demonstrated that malnutrition leads to a reduction in hepatic granuloma area. Also, evidence suggest that malnutrition can impact the efficacy of vaccines. Several *S. mansoni* antigens have been studied as vaccine candidates, such as Sm29 protein. Studies have shown that immunization with rSm29 reduced parasite load and hepatic granuloma area. However, no work has evaluated the immune response and liver pathology in a malnourished host immunized with a vaccine antigen against schistosomiasis that induces anti-pathology effect. **Objective:** Evaluate the impact of malnutrition on the efficacy and immune response induced by rSm29 in malnourished mice. **Methods:** Initially, C57BL/6 mice were separated in 2 groups: Eutrophic: standard 14% protein diet and Malnourished 3% protein diet. The nutritional status was assessed by body weight and biochemical parameters measurements. After the establishment of malnutrition, mice were divided into 4 groups: Eutrophic and Malnourished: inoculated with Saline/CpG/ALUM or immunized with rSm29/CpG/ALUM. Animals received 3 doses of immunization at a 15-day interval. Mice were challenged with 100 cercariae 15 days after the last dose. Fifty days later, mice were perfused to assess the number of worms recovered. Liver sections were collected to assess granuloma area. The egg numbers were assessed in the liver and intestine. Serum was obtained 15 days after each immunization dose to evaluate the levels of specific anti-rSm29 IgG. The spleen was collected 50 days after infection to evaluate the immune response. **Results:** Malnourished mice showed a significant decrease in body weight and in biochemical parameters. No changes in the proportions of the lymphoid and myeloid population were observed in immunized mice. Immunization induced an increased production of IL-6, IL-4, IL-10 and IL-17 by spleen cells and specific IgG antibodies, regardless of the diet. However, antibody titers were higher in immunized eutrophic mice than in immunized Malnourished group. Only eutrophic immunized mice showed a reduction in the granuloma area in relation to saline group. Furthermore, saline Malnourished group showed a decrease in the granuloma area, compared to the saline Eutrophic. No significant changes were observed in the number of worms recovered and eggs retained in the liver or intestine between groups. **Conclusion:** We observed an improvement in liver pathology in immunized eutrophic mice. However, vaccination was not able to reduce the granuloma area in malnourished animals to values lower than the diet-induced reduction. Regardless of the diet, immunization induced the production of cytokines and the activation of the humoral immune response. Despite that, we did not observe a reduction in the parasite burden of immunized animals.

#### KEYWORDS

Malnutrition, Schistosomiasis, Vaccine, Sm29 Antigen

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