

## ABSTRACT

Sand flies (order Diptera) are vectors of *Leishmania* parasites (Trypanosomatida), which are inoculated into the host skin together with the vector saliva. Sand fly saliva plays the important role in the *Leishmania* transmission; in naive host it suppresses the host immune response assisting *Leishmania* to establish the infection, while in repeatedly bitten host it elicits a protective immune response.

The submitted thesis focuses on the effect of sand fly saliva on macrophages, the key cells in the infection control. In the first part of the thesis we established a laboratory model *L. major* – *P. papatasi* – Balb/c to describe the protective effect of saliva immunization on *Leishmania* infection development. Immunized mice were protected against *Leishmania* infection which was reflected in the ear lesion size, parasite load in the ear dermis and draining lymph nodes but also in cytokine production. On the contrary, produced lower amount of nitric oxide, while arginase activity was comparable with nonimmunized group. The IgG antibodies against saliva served as a marker of exposure to sandflies while IgG antibodies against *Leishmania* antigens served as a marker of infection severity.

The experiments were aimed on the possibility of cross-protectivity in Balb/c mice against *L. major* between closely related species *P. papatasi* and *P. duboscqi*. The cross protection was confirmed in a group of immunized mice by significantly smaller ear lesion size and reduced parasite load in the draining lymph node as compared to the control group. However, the production of cytokines and nitric oxide remain comparable between the groups.

The second part of this thesis was focused on the effect of sand fly saliva, *Leishmania* or both factors on the macrophages from mice sensitive (Balb/c) or resistant (C57BL/6) to *Leishmania* infection. Our results indicate that salivary gland homogenate downregulates nitric oxide production. The strong inhibitory effect occurred with promastigotes or promastigotes with 1/4 salivary gland. Conversely, inhibitory effect was neutralized when macrophages were incubated with promastigotes and 1/2 salivary. Since the macrophages were activated via classical pathway (with a combination of IFN- $\gamma$  and LPS) the production of urea as a marker of alternative activation was mostly comparable to controls.

**Key words:** *Phlebotomus*, *Lutzomyia*, saliva, *Leishmania*, macrophages, cytokines, nitric oxide, arginase