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Review of the Ph.D. thesis by Mgr. Barbora Šmídová: The role of myeloid cells in mice infected with the neuropathogenic schistosome Trichobilharzia regent

The aim of this thesis is to examine the myeloid cell response during the infection of the central nervous system (CNS) of mice by the neuropathogenic schistosome T. regentis. The author presents a comprehensive analysis of the immune response to this parasite, emphasizing the role of eosinophil extracellular traps and the M2 response in general. Additionally, the thesis offers insight into the reaction to parasites during the onset of an inflammatory autoimmune reaction, a topic of significant interest. The results thus provide novel findings regarding the various aspects of neuro-immune crosstalk in the response to helminth infection.

The introduction presents an extensive and well-written literature review. It covers general information about schistosomes and the reaction of the immune system after infection with neuropathogenic helminths. Additionally, it provides a comprehensive description of multiple sclerosis and its mouse experimental model, including information relevant to the studied topic of the possibility that helminth-induced immunomodulation may serve as a treatment for EAE.

The study's objectives are clearly defined and have been successfully achieved. The results are discussed in detail in the context of current knowledge in the field and are presented in a comprehensive manner in the final chapter.

The proposed thesis is based on two published articles (Macháček et al. 2022, PLoS Pathog. IF(2022)= 6.7; and Šmídová et al 2024, Parasitology IF(2023)=2.1). Additionally, there is one manuscript in which Barbora Šmídová is the first author. This provides a solid foundation for the thesis. The contribution of Barbora Šmídová to each individual article is explicitly delineated.

I would like to address the author the following questions:

1) In the thesis, the author examines and summarizes the existing knowledge about the "classical" immune populations. Nevertheless, some minor populations have been identified as significant contributors to diverse immune responses. Is it known whether mast cells, which are situated within the nervous system, contribute to the immune response against helminths? Furthermore, what is the role of ILC2s in this context?

2) I have several queries regarding the use of helminth therapy in autoimmune diseases.
   - Are there specific contraindications for helminth therapy?
   - Which patients are most likely to benefit from helminth therapy?
   - Should live helminths be used, or are helminth-derived products sufficient?

3) In light of the results summarized in Šmídová et al. (2024), would you propose any modifications to the experimental design? If an unlimited budget were available, which experiments would you undertake to further investigate the potential treatment of MS/EAE with helminths or their products?

In conclusion, I wish to express my appreciation for the quality of the submitted thesis. During her doctoral studies, Barbora Šmídová demonstrated proficiency in a range of experimental approaches. The results of the research and the quality of the submitted papers demonstrate that the candidate is a mature scientist capable of independent research and, thus, meets the criteria set by the Parasitology Board of Doctoral Studies for the award of the PhD degree.

Prague, September 5, 2024

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