HIMM2

emop 2021 XIII Belgrade
changing climate
changing parasites

Transcriptome-driven exploration of *Trichobilharzia regenti* (Schistosomatidae) neuroinvasion in mice: mechanisms of the immune response and pathogenicity

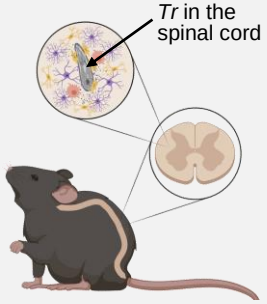
Tomáš Macháček[1], Roman Leontovyč[1], Barbora Šmídová[1], Martin Majer[1], Oldřich Vondráček[1], Iveta Vojtěchová[2,3], Tomáš Petrásek[2,3], Petr Horák[1]

[1]Faculty of Science, Charles University, Prague, Czechia; [2]National Institute of Mental Health, Klecany, Czechia; [3]Lab. of Neurophysiology of Memory, Institute of Physiology of the CAS, Prague, Czechia

INTRODUCTION

Helminth neuroinfections severely impact human health. However, the host-parasite interplay often remains poorly understood, partly due to the unavailability of suitable experimental models.

Here, we explored mechanisms of the host immune response and neuropathogenicity in mice infected with the neurotropic schistosome *Trichobilharzia regenti* (*Tr*). After percutaneous infection, *Tr* migrates *via* nerves towards the spinal cord where it dies.



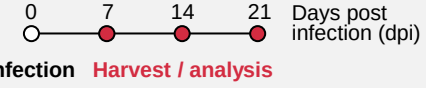
EXPERIMENTAL WORKFLOW

Infection of mice with 2000 *Tr* cercariae

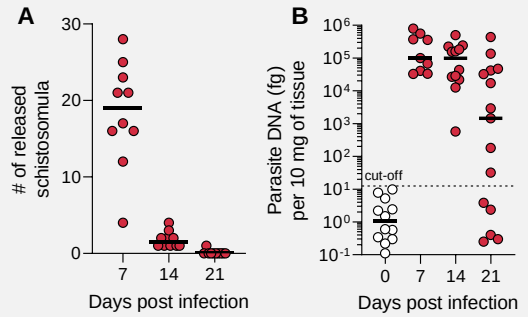
Assessment of parasite burden in the spinal cord
- a) Dissection, parasite DNA content (qRT-PCR)

Behavioral testing of the mice
- a) Coordination, endurance/strength

In-depth exploration of the infected spinal cord
- a) Histopathological examination
- b) Flow cytometry immunophenotyping
- c) Transcriptomic analysis (identification of differentially expressed genes)

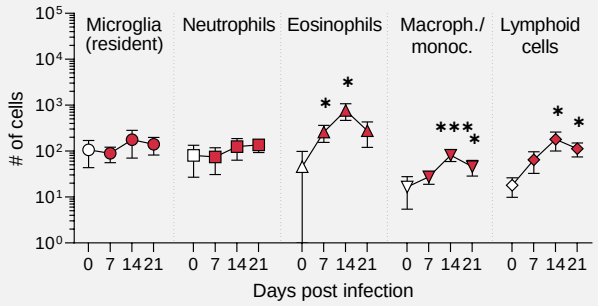


1 *Tr* schistosomula burden peaked 7 dpi, but *Tr* DNA persisted up to 21 dpi



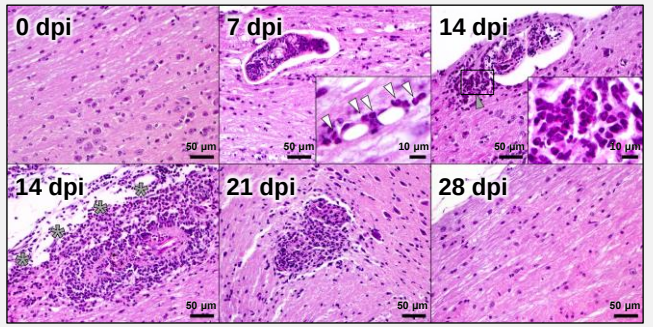
A: Number of *Tr* schistosomula released from the spinal cord of infected mice. **B:** Amount of *Tr* DNA isolated from the spinal cords (10 mg). Quantification performed by qRT-PCR.

2 Eosinophils were the most numerous cells infiltrating the *Tr*-infected spinal cord



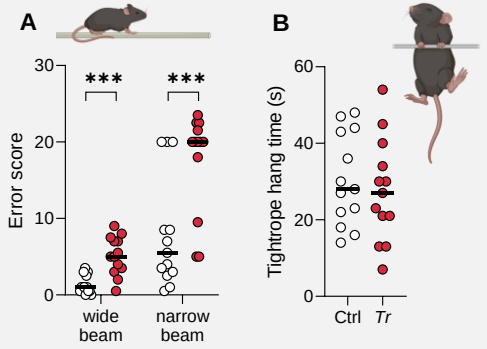
Dynamics of major immune populations in the spinal cord during *Tr* infection. Total amount of cells is shown as revealed by flow cytometry. Asterisks denote sigificant difference compared to uninfected (0 dpi) mice.

3 Eosinophil-rich infiltrates entrapped and likely eliminated *Tr* schistosomula in the spinal cord



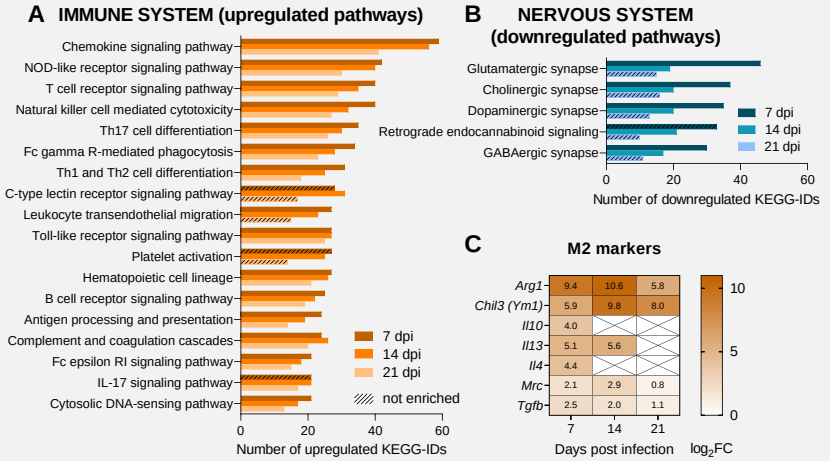
0 dpi: Control. **7 dpi:** Intact schistosomula and eosinophil extravasation (◹). **14 dpi:** Eosinophil-rich rocket-tail infiltration (◺) and inflammatory lesion incl. leptomeningeal spaces (✻). **21 dpi:** Fading lesion. **28 dpi:** Recovered tissue.

4 Motor function deficits affected the lower body of *Tr*-infected mice 7 dpi



A: Infected mice made more errors when traversing a wide or narrow beam. **B:** In the bar holding task, depending predominantly on forelimb strength, the performance was unaltered in infected mice, suggesting that the motor functions of lower body were only affected.

5 Infected spinal cords displayed upregulation of immune pathways, disruption of neurophysiological functions and increased expression of M2 markers (~ alternatively activated microglia/macrophages)



Transcriptomic analysis of infected spinal cords. **A:** Upregulation of immune system pathways. **B:** Downregulation of pathways related to neurophysiological functions. **C:** Increased expression of M2 markers associated with alternatively activated microglia/macrophages.

CONCLUSIONS

Invasion of the mouse spinal cord by *Tr* is associated with:

- eosinophilic inflammation, which likely eliminates migrating schistosomula,
- downregulation of neurophysiological functions and motor disorders,
- upregulation of M2 markers, which presumably prevent tissue damage.

Funding: Czech Science Foundation (18-11140S), ERDF and Ministry of Education, Youth and Sports, CZ (CZ.02.1.01/0.0/0.0/16_019/0000759), Charles University Grant Agency (1374119) and institutional funding (PROGRES Q43, UNCE/SCI/012-204072/2018, SVV 260432/2018). Some images we created by BioRender.

tricho_tom

tomas.machacek@natur.cuni.cz