# ABSTRACT

Helminth neuroinfections represent a serious health issue, but the mechanisms of the host immune response often remain neglected despite the fact they might contribute to pathogenesis. This is partly due to the unavailability of clinical samples and the lack of suitable laboratory models. Herein, I focused on the characterization of several aspects of the immune response of mice infected with the neuropathogenic avian schistosome *Trichobilharzia regenti*.

After the percutaneous infection of mice (accidental hosts), most *T. regenti* schistosomula are entrapped and eliminated in the skin, but the parasite antigens initiating the protective immune reaction are not known. Our *in vitro* experiments revealed that *T. regenti* cathepsin B2, a cysteine peptidase used for the skin penetration, activates bone marrow-derived dendritic cells much stronger than the parasite homogenate, suggesting its role in initiating the mixed type1/2 host immune response. However, some schistosomula manage to escape from the skin and continue their migration to the spinal cord. Here they crawl preferentially within the white matter which we demonstrated by the robust 3D imaging techniques, ultramicroscopy and micro-CT. The invasion of the spinal cord is accompanied by striking hypertrophy of astrocytes and microglia. We showed that living schistosomula induce production of interleukin 6 in astrocyte cultures, but their homogenate or active isoforms of *T. regenti* cysteine peptidases trigger even stronger reaction, including the increased secretion of tumor necrosis factor α and nitric oxide by astrocytes and/or microglia. It seems that these glial cells actively participate in maintaining the neuroinflammation initiated by the infection. Finally, we examined the role of nitric oxide in the host immune response. Our data show that nitric oxide is produced early in the skin phase of the infection, but it does not directly kill the schistosomula. It rather continuously debilitates the parasite by disrupting its proteolytic machinery.

Taken together, the thesis markedly extends the knowledge of the host-parasite immune interactions between the neuropathogenic schistosomes and their accidental mammalian hosts. These novel data set a good starting point for further research on *T. regenti* neuropathogenicity and the impacts of helminth-caused neuroinflammation on the host. Such findings will be valuable not only in the field of parasitic neuroinfections but might also be appreciated in the research of (autoimmune) neurodegenerative diseases.



Key words: avian schistosomes, *Trichobilharzia regenti*, immune response, skin, spinal cord, astrocytes, microglia, nitric oxide, cysteine peptidases, 3D imaging.