Univerzita Karlova
1. lékařská fakulta

Studijní program: Doktorské studijní programy v biomedicíně
Studijní obor: Biochemie a patobiochemie

UNIVERZITA KARLOVA
1. lékařská fakulta

RNDr. Jan Novák

Imunitní odpověď paratenického hostitele na infekci *Toxocara canis*, možné ovlivnění průběhu experimentální autoimunitní encefalomyelitidy

Immune response of the paratenic host to *Toxocara canis* infection, possible influence on the course of experimental autoimmune encephalomyelitis

Abstrakt dizertační práce

Školitel: prof. RNDr. Petr Horák, Ph.D.
Konzultant: prof. RNDr. Libuše Kolářová, CSc.

Praha, 2022

ABSTRACT

The most complex interactions between host and infectious agent are generated during helminth infections, which represent a significant source of serious health problems worldwide. Because many helminths migrate after entering the host, these infections are characterized by the gradual development of a range of clinical symptoms. These are not only due to the damage to various organs but also to the modified host's immune response. The published studies show that, on the one hand, the immune response is stimulated in order to eliminate the parasite, but on the other hand, helminths possess a number of mechanisms that may lead to immune modulation and thus ensure their long-term survival in the host. An indirect consequence of such a situation may then be an amelioration of the symptoms of autoimmune diseases. Therefore, in order to contribute to the elucidation of the course of the immune response of the paratenic host to one of the most common infections caused by *Toxocara canis*, we also studied the effect of infection on experimental autoimmune encephalomyelitis, a model for multiple sclerosis.

Although *T. canis* is a parasite of canids, it often infects a variety of paratenic hosts, including humans. In these hosts, the larvae survive in various tissues at the L3 larval stage, with a large proportion found in the brain. The pathogenesis of infection is the result of mechanical damage to the tissues and the action of excretory-secretory products of larvae. Our experiments in immunocompetent mice have shown that even a small number of larvae leads to a serologically significant response, which, however, is not accompanied by severe pathological changes. However, after subsequent induction of experimental autoimmune encephalomyelitis, we observed that infection with L3 *T. canis* larvae worsened the course of this model disease. Compared to the uninfected control group, we observed higher clinical symptom scores and higher weight loss in these mice. These negative effects were associated with significant increases in serum cytokine levels, probably as a consequence of dysfunctional regulation of the immune system. In the central nervous system, we found an increased percentage of $CD4^+$ cells of non-Treg phenotype, suggesting infiltration of additional $CD4^+$ cell populations, which are probably responsible for the worsening course of experimental autoimmune encephalomyelitis in infected mice.

Larval toxocariasis is one of the most globally important tissue parasitoses. Older data from the Czech Republic indicate that almost one out of every five individuals has encountered the infection. These studies indicate seroprevalence levels of 18.4% (1998) and 19% (2006). In comparison, we found a decrease in this value to 3.6% (2020). We suppose that the reduction in seroprevalence is probably associated with increased public hygiene and increased use of anthelmintics in dogs.

The majority of the existing tests for the detection of *T. canis*-specific antibodies is limited by lower specificity because they are based on excretory-secretory antigens that cross-react with sera from patients infected with other helminths. In this part of the work, our goal was to identify recombinant excretory-secretory antigens for the detection of *T. canis*-specific antibodies. The use of these alternative recombinant antigens illustrated their possible diagnostic potential as well as differences in the reactivity of mice and human sera.