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Regulatory effects of a novel cysteine protease inhibitor in *Baylisascaris schroederi* migratory larvae on mice immune cells

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Abstract

Background: The giant panda (*Ailuropoda melanoleuca*) is a well-known, rare and endangered species. *Baylisascaris schroederi* is a pathogenic ascarid. Infection with *B. schroederi* may cause death in giant pandas. At present, the immune evasion mechanism of *B. schroederi* is little known. Cysteine protease inhibitors (CPI) play important roles in the regulation of host immune responses against certain nematodes. In this study, we focused on the analysis of the regulation of *B. schroederi* migratory larvae CPI (rBsCPI-1) on mice immune cells.

Methods: First, the pattern recognition receptors on the surface of peripheral blood mononuclear cells (PBMCs) and the signal pathways that transduce extracellular signals into the nucleus activated by rBsCPI-1 were identified. Then, the regulatory effects of rBsCPI-1 on PBMCs physiological activities were detected. Finally, the effects of rBsCPI-1 on TLR signaling pathway activation and NF-κB phosphorylation in mice immunized with recombinant protein were analysed.

Results: The results suggested that rBsCPI-1 secreted by *B. schroederi* migratory larvae is mainly recognized by TLR2 and TLR4 on PBMCs. Extracellular signals are transduced into the nucleus through the MAPK and NF-κB signaling pathways, enhancing the phagocytosis, migration, and apoptosis of PBMCs; meanwhile, rBsCPI-1 induces high expression of NO. Thus, rBsCPI-1 plays a role in immune regulation. In addition, the high expression of negative regulatory factors also ensured that TLR activation is maintained at the optimal level.

Conclusions: rBsCPI-1 can transduce regulatory signals into immune cells by activating the TLR2/4-NF-κB/MAPK signaling pathway, having a certain regulatory effect on the physiological activities. Meanwhile, rBsCPI-1 can maintain the immune response in a balance by limiting the over-activation of the TLRs signaling pathway and thus contributes to *B. schroederi* immune evasion.

Keywords: *Baylisascaris schroederi*, Cysteine protease inhibitor, PBMC, TLRs signal pathway, Immune evasion mechanism

Background

The giant panda (*Ailuropoda melanoleuca*), a well-known, rare and endangered species, is a powerful symbol of species conservation. Owing to their highly simplistic bamboo diet, various serious infectious diseases threaten the species [1]. Among them, parasitic infection seems to be one of the crucial factors bringing its population on the verge of extinction [2, 3]. As the obligate host of *Baylisascaris schroederi* (*B. schroederi*), giant pandas in various nature reserves and artificial breeding centers in China are commonly found to be infected with *B. schroederi* [4]. Although previous studies have experimentally investigated *B. schroederi* biology,

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