


RESEARCH ARTICLE

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Regulatory effects of *Trichinella spiralis* and a serine protease inhibitor on the endoplasmic reticulum stress response of intestinal epithelial cells

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Abstract

The accumulation of unfolded or misfolded proteins in the endoplasmic reticulum can cause an endoplasmic reticulum stress (ERS) response. If ERS continues or cannot be alleviated, it will cause the production of proapoptotic factors and eventually lead to apoptosis. Therefore, this study mainly explored whether *Trichinella spiralis* Kazal-type serine protease inhibitor (TsKaSPI) contributed to the invasion of intestinal epithelial cells during the infectious stage of *T. spiralis* by regulating ERS. First, in the *T. spiralis* infection model, H&E staining was used to analyse the damage to jejunum tissue, a TUNEL assay was used to examine cell apoptosis, and the expression of ERS-related and apoptosis-related molecules was also measured. The results showed that ERS occurred during the intestinal phase of *T. spiralis* infection, while remission began during the cyclic phase. Then, we selected TsKaSPI, one of the important components of *T. spiralis* ES antigens, for in vitro experiments. The results showed that TsKaSPI could induce apoptosis in a porcine small intestinal epithelial cell line (IPEC cells) by activating ERS and promote activation of the NF- κ B signalling pathway. Inhibition experiments confirmed that the occurrence of ERS was accompanied by the activation of NF- κ B, and the two processes regulated each other. Finally, we conducted in vivo experiments and administered TsKaSPI to mice. The results confirmed that TsKaSPI could activate ERS and lead to apoptosis in intestinal epithelial cells. In conclusion, *T. spiralis* infection and TsKaSPI can promote cell apoptosis by activating the ERS response in intestinal epithelial cells and activate the NF- κ B signalling pathway to promote the occurrence and development of inflammation.

Keywords: Endoplasmic reticulum stress response, apoptosis, *Trichinella spiralis*, TsKaSPI

Introduction

Trichinellosis is a serious foodborne zoonotic parasitic disease with a worldwide distribution [1, 2]. Intestinal invasion is an important stage of *Trichinella spiralis* (*T. spiralis*) infection, which determines the occurrence

and development of the disease [3]. *T. spiralis* excretion-secretion (ES) antigens may play key roles in the pathogenic process [4]. Serine protease inhibitor (SPI), which is an important component of ES antigens, can not only regulate enzyme activity to interfere with protein metabolism but also participate in some important physiological and pathological processes, such as complement activation, the inflammatory response and apoptosis [5–7]. Piekarska et al. found that the intestinal stage of *T. spiralis* infection could induce apoptosis in cells in the villous lamina propria [8, 9]. Therefore, we hypothesized

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