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Alteration in Toll-like Receptors Activation During Trichinella spiralis Infection

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Editorial

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Trichinella spiralis [*T. spiralis*] is a widespread zoonotic helminth. It can be considered as the most successful parasite in its two intracellular habitats; the intestine and skeletal muscles. All the stages in the life cycle of *T. spiralis* can occur in a single host; the adult, newborn larvae and encysted muscle larvae [1].

The chronic nature of *T. spiralis* infection in the muscles indicates that this parasite could subvert the host immune system through different mechanisms including induction of regulatory T and B cells and alternatively activated macrophages and production of anti-inflammatory cytokines e.g. interleukin [IL]- 10 and transforming growth factor [TGF]- β [2]. One more important mechanism is by interfering with both the expression and function of toll- like receptors [TLRs] [3].

T. spiralis can modulate the immune system producing T helper [Th]1/Th2 immune response with predominant cell type Th2 response with induction of T-regulatory [Treg] cells. This immunomodulation is beneficial for both the human host and the parasite; it could protect helminthes from being eradicated and, at the same time, protect the host from excessive pro-inflammatory responses that may lead to organ damage [4].

In the past few years, new insights have been gained about the role of TLRs in health and disease. TLRs are expressed by many immune and non-immune cells such as dendritic cells, macrophages, neutrophils, lymphocytes and endothelial cells. This differential pattern of expression is one mechanism to ensure a more diverse response to different types of pathogens [3]. TLRs play essential roles in innate immune responses by recognizing various pathogen-derived components. TLRs signaling pathways triggered various transcription factors e.g. nuclear factor [NF]-κB and activating protein [AP]-1, which are responsible for inflammatory responses [5].

TLRs play an important role in the immune responses against helminth infections, because excretory- secretory [ES] proteins and glycoproteins from helminthic parasites have been demonstrated to activate immune cells via an immune re¬sponse related to TLRs [6, 7]. *T. spiralis* in particular releases abundant glycoproteins throughout its life which act as TLR ligand [8]. Different stages of *T. spiralis* had different impacts on the expression of TLRs and related signaling molecules that may influence cytokine response of host [9]. However, few studies report the variation of TLR gene expression and their related signal pathway during *T. spiralis* infection.

Myeloid differentiation factor 88 [MyD88] is a signaling adaptor molecule that propagates the response to most TLRs initiating cascade that ultimately leads to the activation of pro-inflammatory genes by the transcription factor NF-κB [9, 10] reported that the expression of MyD88 is upregulated during the intestinal and muscle phases of *T. spiralis* infection.

T. spiralis can activate and negatively regulate TLRs and interfere with the expression of several genes related to TLR-mediated signal transduction pathways to adjust the immune system to its advantage. At intestinal stage of *T. spiralis* infection, the mRNA expression of TLR1, TLR2, TLR3, and TLR4 and TLR9 is up regulated and TLR5 and TLR6 are transiently down regulated.

Once the newborn larvae appear, all TLR expression is inhibited, except for TLR2 and only transient up regulation of TLR5 and TLR6 at the encapsulated phase [9,11].

The modulated TLR expression in the small intestine and muscle tissue during *T. spiralis* infection might be closely associated with Treg cell-mediated immune responses and increased cytokine gene expression; IL-10 and TGF-β.[11] TLR2 and TLR4 have been regarded as the main sensors for *T. spiralis* infection. An in vitro study showed that *T. spiralis* ES products suppress dendritic cell maturation by TLR4 [6]. TLR2 and TLR4 are influential by limiting rather than promoting the intestinal immunity; therefore their deficiency accelerated expulsion of the adult worms [12].

In conclusion, *T. spiralis* infection can modulate the immune response by regulating the expression of TLRs and their signaling pathways to protect itself from excessive inflammatory responses while maintaining defense against persistent pathogens. Therefore, targeting the central mediators in the inflammatory cascades; TLRs will modulate pathway activation at an earlier point and reduce disease severity. However, further understanding of TLRs and their ligands can lead to novel therapeutic and prophylactic strategies for parasitic infections [13, 14].

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