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TRICHINELLA SPIRALIS MUST INHIBIT THE IMMUNE SYSTEM TO SURVIVE

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ABSTRACT

Trichinella spiralis is a parasitic nematode that infects various mammals, including humans. This tissue-dwelling parasite plays its pathological role by affecting the immune system and causes the disease trichinellosis. T. spiralis generates a variety of proteins that protect it from the host's immune system and it releases inhibitory proteins such as proteases, antioxidant enzymes, and immunomodulatory molecules. T. spiralis modulates T-cell and macrophage responses, reducing the immunological response launched against it by the organism. By producing proteases, the parasite inhibits the infiltration of immune cells that would help fight the infection. These anti-immune effects help T. spiralis survive. In addition, this parasite helps the response shift from Th1 to Th2, an effect that is less effective in eliminating infections. Recently, it has been reported that antigens secreted by T. spiralis can interact with immune cells by binding to the toll-like receptor (TLR), reducing the inflammatory response. It can be concluded that T. spiralis affects the immune system to survive and carry out its pathological action, but it can also produce immunity-stimulating antigens, an effect that could be useful to fight certain autoimmune diseases that are currently incurable.

KEYWORDS: *Trichinella spiralis, helminth, parasite, nematode, immunity*

INTRODUCTION

Helminths are pathological parasites that act on the host's immune system by activating and modulating it. Trichinella spiralis is a parasitic nematode that infects various mammals, including humans, and causes trichinellosis (or trichinosis) when organisms consume raw meat containing its larvae.

T. spiralis includes many species such as T. native, T. nelsoni, T. britovi, T. murrelli, and the new species, T. chanchalensis (1), and is present in many low income and industrialized countries. Some species of T. spiralis, such as T. pseudospiralis, T. papuae, and T. zimbabwensis are not encapsulated (2). The biological cycle is immediate; eggs are released into the external environment and the larva develops. When the climatic conditions are mild, the parasite remains infectious for 5-8 years (3). To establish and maintain infection, it must evade and manipulate the host immune system (4).

T. spiralis is very effective at evading the immune system. Trichinellosis, the infection caused by this parasite, is a disease where there is immune stimulation due to antigen molecules of the parasite. The molecular mechanisms by which T. spiralis achieves this are diverse and sophisticated, involving both evasion and active suppression of immune responses.

The parasite can induce both pro-inflammatory and anti-inflammatory cytokines, which can have varying effects on the immune system (5,6). The acute phase of infection is associated with a strong pro-inflammatory Th1 response (7),

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while the chronic phase often involves a shift toward an anti-inflammatory Th2 response, characterized by the production of cytokines like IL-4, IL-10, and TGF-β (8).

It has been reported that T. spiralis might have a protective effect against certain autoimmune diseases (9). However, the relationship between T. spiralis and autoimmunity is complex and has multifaceted aspects.

DISCUSSION

T. Spiralis modulates host immune responses in different ways. The parasite secretes a variety of proteins that help it avoid detection and destruction by the host immune system (10). These proteins can interfere with antigen presentation and reduce the host's ability to mount an effective immune response (11). Furthermore, the parasite can directly suppress immune cell function. For example, T. spiralis can modulate the activity of T cells and macrophages to reduce their ability to attack the parasite (12,13).

When activated, T. spiralis releases excretory and secretory products such as protease inhibitors, antioxidant enzymes, immunomodulatory molecules, and other enzymes. Protease inhibitors are molecules that can inhibit host proteases, which are part of the host's immune defense mechanisms (14). By inhibiting these enzymes, T. spiralis can prevent tissue damage and immune cell infiltration that would otherwise help clear the infection (7).

The parasite also produces antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, which neutralize reactive oxygen species (ROS) produced by immune cells (15). This helps the parasite survive the oxidative burst that is part of the host's immune response.

T. spiralis can secrete immunomodulatory molecules that mimic host cytokines or interfere with cytokine signaling (12). This can skew the immune response towards a Th2 type response, which is less effective at clearing helminth infections compared to a Th1 type response (16). Excretory and secretory antigens are specific proteins secreted by T. spiralis that can directly interact with immune cells to alter their function. For example, some excretory/secretory antigens can bind to toll-like receptors (TLRs) on immune cells, altering their signaling pathways and reducing inflammatory responses (12,17).

T. spiralis infection can lead to the induction of regulatory T cells (Tregs), expanding these immune cells that suppress other immune responses. This helps create an environment that is more permissive for the parasite's survival. T. spiralis can also modify host tissues and affect cells they are in contact with (18). T. spiralis larvae form cysts within host muscle tissues, creating a physical barrier that protects them from immune cells (19). The cyst wall is also immunologically inert, meaning it does not provoke a strong immune response.

T. spiralis also modulates gene expression, affecting microRNAs (miRNAs) (20). This helminth can release miRNAs that are taken up by host cells, leading to changes in the host gene expression profile (21). This can downregulate genes involved in the immune response and create a more favorable environment for the parasite (21,22).

Specific molecules and pathways are affected by T. Spiralis. The T. spiralis serine protease TsSerp is involved in degrading host proteins and modulating immune responses by interfering with cytokine production and immune cell signaling pathways (24). T. spiralis excretory/secretory (Ts-ES) antigens include a variety of proteins and glycoproteins that interact with host immune cells (12). They can modulate dendritic cell function, inhibit T cell proliferation, and alter cytokine production (18, 23).

T. spiralis can induce the production of vascular endothelial growth factor (VEGF), which helps in creating a favorable environment for the larvae in the host muscle by promoting angiogenesis and tissue repair processes that may help in cyst formation and maintenance (25).

The antigenic molecules expressed by this parasite can activate innate immunity with consequent stimulation of adaptive immunity. The antigens act on antigen presenting cells (APCs) such as macrophages and dendritic cells which downregulate adaptive immune cells, such as Tregs and regulatory B cells, activating a sort of immunosuppression (18). This immunosuppression is induced by inhibitory cytokines such as IL-10, IL-17, and TGF-β, and this reaction is exerted by T. spiralis to avoid the immune response and allow its survival (12,26). This mechanism could be useful for suppressing the overstimulated immune system in chronic inflammatory diseases such as autoimmune diseases, transplant rejection, and allergic diseases such as asthma (27-29).

T. spiralis larvae can invade the intestine and activate epithelial cells with the secretion of cytokines IL-25 and IL-33 (also called alarmin). These cytokines activate type 2 innate lymphoid cells (ILC2), which in turn produce IL-5 and IL-13 cytokines that act on the precursors of epithelial cells to increase the production of immunosuppressive cytokines (30).

The type 2 immune response induced by the antigenic molecules causes the stimulation of IgE, IgG1, and IgG4 antibodies and anti-inflammatory cytokines including IL-4, IL-13, and IL-33 (31,32). These cytokines facilitate the proliferation of basophils, eosinophils, and macrophages, increasing allergic phenomena and mucus secretion, which are elements of the parasitic immune defense (16).

By implementing these strategies, T. spiralis escapes the host's immune system and survives. The infection causes an increase in eosinophilic granulocytes, which is a hallmark characteristic of parasitic infections that protects the parasite (33). Proteins derived from T. spiralis larvae are phagocytosed by macrophages, altering their ability to present antigen and activate T cells, a reaction which is mediated by STAT4 (6). The negative regulation of STAT4 and the cytokine IL-12 causes an inhibition of interferon-gamma (IFN-γ) that allows the T. spiralis to evade the immune response (34).

CONCLUSIONS

Understanding the biology and the mechanisms by which T. spiralis evades the immune response and affects host tissue is crucial for developing strategies to combat the infection and for designing new therapeutic approaches that can overcome the parasite's immune evasion tactics. In addition, immune system activation by helminths is currently being studied for its application in the treatment of diverse pathologies, including autoimmune diseases, that have a poor response to treatment.

Conflict of interest

The authors declare that they have no conflict of interest.

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