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# *Trichinella Spiralis* Impact on Mesenchymal Stem Cells: Immunohistochemical Study by Image Analyzer in Murine Model

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ABSTRACT

This study aims to elucidate whether *Trichinella spiralis* infection or its crude antigen administration can stimulate recruitment of $CD105^{+ve}/CD45^{-ve}$ cells that could represent MSCs in intestine and skeletal muscle of experimental BALB/c albino mice compared to healthy control mice. Studied mice were divided into: 20 healthy control, 20 with orally induced *T. spiralis* infection, 20 received adult worm crude antigen orally and 20 received larval crude antigen intramuscular. According to specific timing schedule, mice were sacrificed and tissue sections were examined for CD105 and CD45 immunohistochemical expression using image J image analyzing software, to compare different study groups. *T. spiralis* infection induced a significant increase in density of $CD105^{+ve}/CD45^{-ve}$ cells that could represent MSCs in both intestinal and muscle sections, similarly the intramuscular injected larval crude antigen caused more infiltration of such cells in muscles compared to muscle sections from healthy control mice. However, no significant difference was noticed in intestinal sections after oral adult crude antigen administration compared to healthy control mice. So, injected *T. spiralis* crude antigen might be a successful stimulant to MSCs attraction and recruitment in tissues nearby injection site. This could be beneficial for cell regeneration and tissue repair in case of presence of a disease induced damage.

## 1. Introduction

Mesenchymal stem cells (MSCs) are non-hematopoietic stromal cells that have the ability to differentiate into mesenchymal tissues like; bone, cartilage, muscle, ligament, tendon, nerve and adipose tissues. They normally contribute in regeneration in such tissues during physiological aging process or on exposure to external insult. In spite of being ready to continuously replace lost cells after inflicted damage through life time, MSCs have only limited numbers (Osakada et al., 2010). They have also been proved to induce immunomodulatory effects through suppression of T-cell proliferation and cytokine production (Svobodova et al., 2012).

Recently, stem cells have showed many therapeutic uses for a variety of diseases. These new therapies depend on using either the regenerative potentiality or the immunomodulatory effects of MSCs (Najar et al., 2016). MSCs have been successfully isolated from various tissues as bone marrow, muscle, fat, brain, heart, skin and Wharton's jelly of umbilical cord (In't Anker et al., 2004; Malgieri et al., 2010). Medications using stem cells may give many promises for tenacious immune-mediated diseases that still lack a definite therapy up till now (Griffin et al., 2013).

Many parasites, especially nematodes, are famous for their ability to manipulate their host's physiology. Some parasites can even alter the morphological architecture of the surrounding tissue in order to establish a new environment to guarantee the parasites' survival in its host as long as it can. *T. spiralis* is a nematodal worm that gives a typical example for that. The infection starts in the intestine of the host where many larvae will be given birth and then pass into the circulation to settle in the skeletal muscles. Larvae build their own home in the infected myocytes in the form of a capsule composed of a collagenous wall for parasite protection and cellular components that has been named “nurse cell” as it helps in parasite metabolism. Both components of larvae home are of host, not parasite, origin (Wu et al., 2008).

How does *Trichinella* alter host cells and construct such unique place for living in host muscles, what are the tools it uses, and does it induce MSCs proliferation in this process is still not definitely known in spite of extensive studies and still triggers many discovering potentialities. In intestinal phase of *Trichinella* infection, an increase in Paneth, goblet, intermediate and enteroendocrine cell numbers occurs in the small intestinal mucosa with associated alterations in villous and crypt morphology for the sake of worm expulsion. This cascade has been recently proved to occur through the regulating function of intestinal

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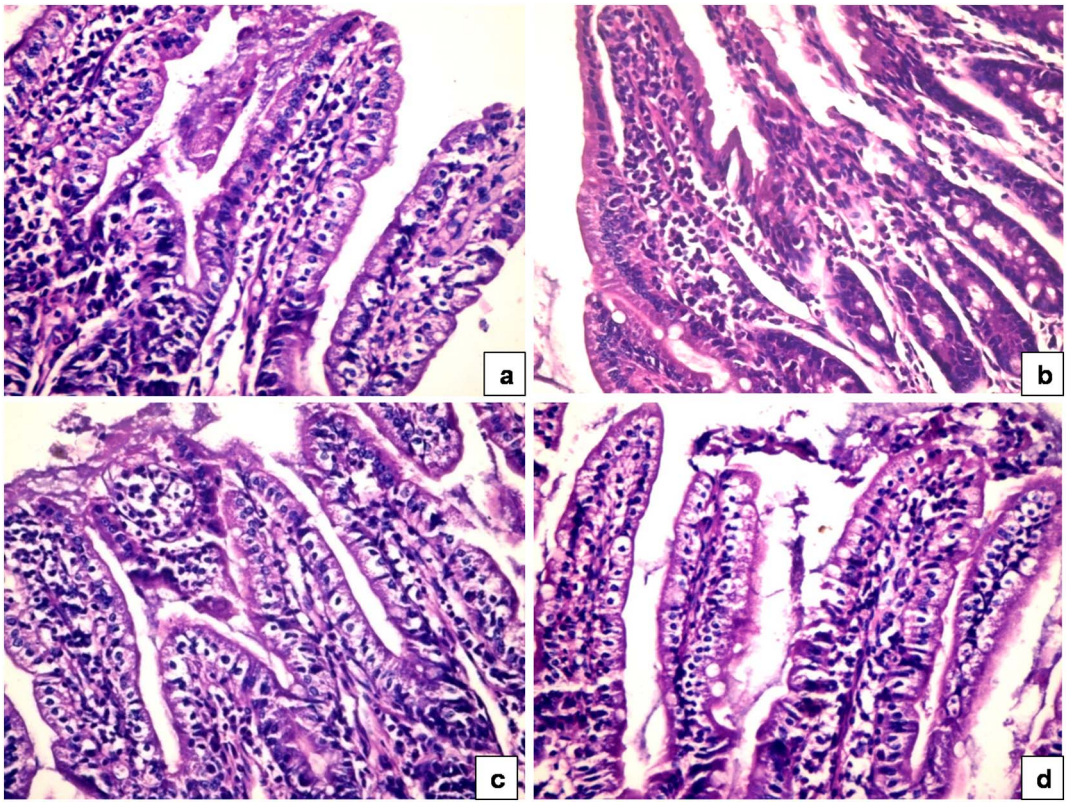


**Fig. 1.** Histopathological intestinal features showing dense mucosal infiltration of mononuclear cells and eosinophils appearing in the core of intestinal villi in *T. spiralis*, infected (a), crude adult antigen vaccinated (b) groups. The infiltrate is of less density in larval antigen injected (c), control (d) groups [H & E X400].

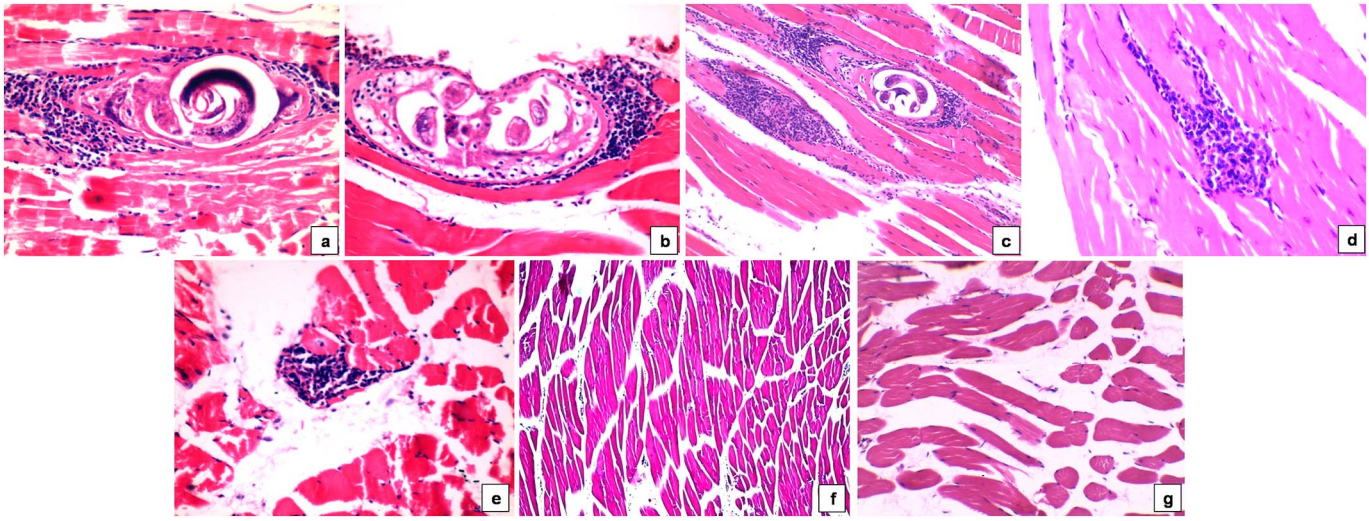


**Fig. 2.** Thigh muscle sections from different studied groups. *T. spiralis*, infected group showing basophilic transformation of muscle cells, coiled *T. spiralis*, larvae surrounded with an eosinophilic well-formed capsule giving the nurse cell structures (a, b), intense cellular infiltrate surrounding the nurse cells and scattered within the muscle sheath (c); larval crude antigen injected subgroup shows similar cellular infiltrate (d), in buffer only injected control infiltrate was much less (e), and was absent in adult crude antigen vaccinated subgroup (f) & healthy control (g) [H & E X400 (a, b, d, e, g) & X200 (c, f)].

epithelial stem cells (Fre et al., 2005).

MSCs can be identified by the expression of many molecules including CD105, CD73 and CD90. They lack expression of CD45, CD34, CD14 or CD11b, CD79α or CD19 and HLA-DR surface molecules (Dominici et al., 2006). The properties of MSCs make these cells potentially ideal candidates for tissue engineering as reported by Chamberlain et al. (2007).

The aim of this work was to elucidate if *T. spiralis* infection and/or its prepared adult and larval antigens cause increase in number of $CD105^{+ve}/CD45^{-ve}$ cells that could represent MSCs at site of lesion in intestine and skeletal muscle compared to healthy control. This work was done as a preliminary study in an attempt to evaluate if we can benefit from such parasitic effect on MSCs as a cellular therapy in the repair of various kinds of tissue damage such as degenerative and immune mediated diseases like autoimmune osteoarthritis in experimental animal model of further upcoming studies?