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Trichinella spiralis as a Potential Antitumor Agent: An Update

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ABSTRACT

Due to the limited success of therapeutic strategies in treating tumors, a new practical potent approach is needed. This review aimed to investigate previous literature related to tumors and *Trichinella spiralis (T. spiralis*). In recent years, there has been growing interest in utilizing biological, viral, bacterial, yeast, and parasitic agents to cure cancers. According to several studies, some parasites could interferee with the tumors' growth. There has been much discussion about some parasites' applications to cure tumors in animals and humans. In studies, *T. spiralis* was found to have antitumor properties. The active proteins in *T. spiralis*, such as Caveolin-1, Heat shock proteins, and Ribosomal proteins, are thought to inhibit the growth of cancers, such as melanoma, myeloma, sarcoma, leukemia, stomach cancer, colon cancer, breast cancer, and lung cancer. In addition, these proteins are thought to induce apoptosis in specific neoplastic cells. Accordingly, antigens derived from parasites may be helpful in cancer immunotherapy. However, there are still many unanswered questions regarding *Trichinella spiralis'* potential use as a biotherapy agent against cancer. Future studies should focus on the purification of parasite antigens and their use for wider-scale trials in animal models.

Keywords: Antitumor, Apoptosis, Cancer, Immunotherapy, *Trichinella spiralis*

INTRODUCTION

Malignant tumors are one of the most threatening issues concerning people's well-being and are responsible for many human deaths (Carneiro and El-Deiry, 2020). Immunotherapy is a new approach in the field of oncology that confronts cancerous tumors by amplifying natural antitumor defenses (Schirrmacher, 2019; Wu et al., 2020). Detection of tumor antigens indicates that immunotherapy may be beneficial by stimulating the immune system's tumor suppressor mechanisms, and does not have side effects of chemotherapy or surgery (Harrington et al., 2019; O'Donnell et al., 2019). Cancer patients show early treatment improvement with autologous and allogeneic tumor cell vaccines (Pallerla et al., 2021). Many obstacles can hamper clinical success. These obstacles include inadequate antigenic natures, immune tolerance, and active immune evasion mechanisms used by progressing tumors to circumvent the immune system (Martin et al., 2020; Jhunjhunwala et al., 2021). The body's immune system must be stimulated to develop a new cancer treatment (Mulder et al., 2019). Furthermore, the immune system must be ready to attack cancer cells individually (Netea et al., 2020). This specificity will enable the immune system to overcome these obstacles (Bassiony et al., 2020).

The concept of tumor biotherapy has been developed as a clinical strategy for cancer treatment. It aims at suppressing or eradicating tumors using biological agents as therapeutic tools. Examples of these therapies include cytokines, monoclonal antibodies, growth factors, differentiation factors, cancer gene therapy, and antitumor bioactive materials (Kelley and Greten, 2021).

Several parasitic infections have been shown to induce antitumor activity in both laboratory animals and humans (Callejas et al., 2018; Daneshpour et al., 2019; Hu et al., 2019; Berriel et al., 2021). To justify this claim, a documented negative correlation has been established between the prevalence of some parasitic infections and cancer cases (Krementsov, 2009). Some cancer patients infested with certain parasites have reported a much longer lifespan than those who were not (Suresh et al., 2005). However, it is not feasible to activate the anticancer response through parasitic infections due to the morbidity and virulence of parasites. The administration of live vaccines containing non-pathogenic parasites could be an appropriate alternative (Kurup and Thomas, 2020). Acquired and innate immunity, anti-angiogenesis properties, increased cell apoptosis, and common antigen presentation may all contribute to tumor resistance induced by parasites (Albini et al., 2018). Mucins play a critical role in maintaining mucosal homeostasis and are responsible for the differential effector and regulatory responses against many microorganisms, including

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commensals and parasites (Dharmani et al., 2009). It has been found that several parasites share mucin-type O-glycan compounds, which are common antigens between cancer cells and parasites (Tarp and Clausen, 2008; Darani and Yousefi, 2012; Grondin et al., 2020).

In addition, parasites with high amounts of glycosylated antigens like *Echinococcus granulosus* may demonstrate superior anticancer effects against immune tolerance of cancer (Berois et al., 2022).

The active proteins in *T. spiralis*, such as Caveolin-1, Heat shock proteins, and Ribosomal proteins, inhibit cancers, such as melanoma, myeloma, sarcoma, leukemia, stomach cancer, colon cancer, breast cancer, and lung cancer (Kang et al., 2013; Liao et al., 2018). It is not yet known how *T. spiralis* inhibits tumor growth. The intestinal phase of *T. spiralis* is an example of a complex multicellular organism, and its potential to induce a T helper 2 (Th2) immune response is matchless (Ilic et al., 2012). It also secretes lipids, proteins, and metabolites that the immune system recognizes. So, the proliferation, differentiation, and activation of natural killer cells, cytotoxic T cells, and macrophages could be stimulated by *T. spiralis* infection (Zhang et al., 2018; Wang et al., 2020; Sun et al., 2022). Therefore, they would secrete elevated amounts of interleukins, interferons, transfer growth factor, tumor necrosis factor, and colony-stimulating factor (Fabre et al., 2009; Ilic et al., 2011). *In vivo* could activate macrophages to produce oncolytic molecules that kill tumor cells directly (Khan, 2008; Liu et al., 2015). Inhibiting the metastasis and proliferation of neoplastic tumors, Natural Killer (NK) cells serve as the primary defense against tumorigenesis (Pachynski et al., 2012; Smyth et al., 2002). When mice are infected with *T. spiralis* during the early muscle stage, NK cells trigger a cytotoxicity reaction *in vivo* (Patel et al., 2009). Interferon-Gamma (IFN-γ) and Tumour Necrosis Factor alpha (TNF-α) are two of the most potent pro-inflammatory cytokines with a wide range of biological activities (Boshtam et al., 2017; Shapouri-Moghaddam et al., 2018). The IFN-γ and TNF-α can cause tumor cells to necrosis and directly induce apoptosis within them in addition to vascular destruction around neoplasms (Chawla-Sarkar et al., 2003; Cruceriu et al., 2020; van Horssen et al., 2006). Cluster of Differentiation 8+ (CD8+) T cells can be cytotoxic when exposed to Interleukin 10 (IL-10), which has an antitumor function (Gu et al., 2017). Mouse models of tumors with CD8+T cells expressed with IL-10 have been shown to suppress tumor growth by producing higher amounts of IFN-γ (Jarnicki et al., 2006; Ruffell et al., 2014). IL-12 can also kill primary and metastatic tumors via the T helper 1 (T1) reaction and the promoted activation of CD8+T cells (Paijens et al., 2021). Consequently, cellular immune function, mediated by Th1 cells, suppresses malignant cell proliferation and angiogenesis. This review aimed to examine previous literature investigating the relations between *T. spiralis* and tumors.

General features of *Trichinella spiralis*

The *T. spiralis* is a widely distributed food-borne parasite that could trigger antitumor immunity by modulating immune system activity (Liao et al., 2018). *T. spiralis* is an obligate intracellular parasite that causes trichinosis in humans and many animals (Gottstein et al., 2009). Excretory-secretory proteins (ESPs) are complex proteins produced by *T. spiralis* during infestation (Babal et al., 2011). It is believed that polypeptide proteins, as well as ESPs, may inhibit tumor growth during the life cycle of *T. spiralis*, which includes the muscle larva (ML), the newborn larva (NBL), and the adult worm (AD, Romaris et al., 2002). The muscle larva has a more significant effect on enhancing host immunity because it lives longer, compared to the newborn and adult stages (Hewitson et al., 2009). Besides, ML is more accessible to collect than NBL or AD (Figure 1).

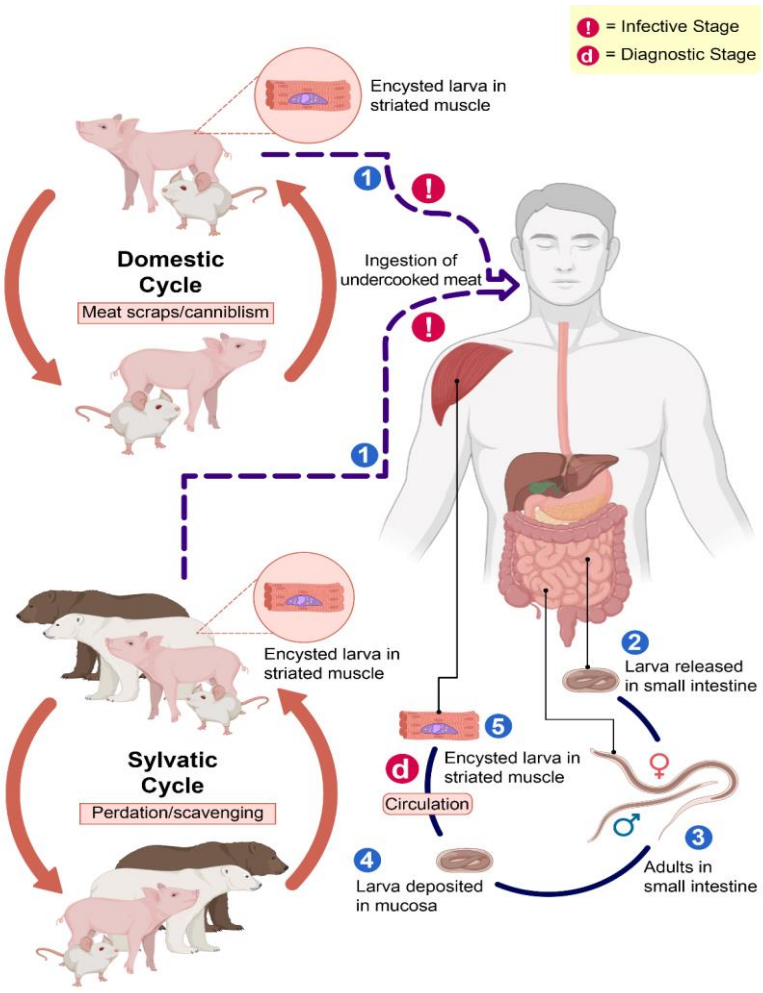

Figure 1. Life cycle of *Trichinella spirali*

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Trichinella spiralis proteins

Translationally controlled tumor protein

Recently some studies demonstrated that Translationally Controlled Tumor Protein (TCTP) has a high conservation level and is an abundant protein across various eukaryotic organisms (Bommer and Thiele, 2004). In tumor reversion, this protein is significantly downregulated (Bommer, 2017). It has been shown that factors, including cell cycle progression, histamine-releasing factors, malignant transformation, antiapoptotic, immunomodulatory functions, and calcium-binding proteins, play a crucial role in cell growth. Translationally controlled tumor protein has been found in *Plasmodium* subspecies and trematodes, and also some parasitic worm species, such as *Trichinella* (Mak et al., 2007; Nagano et al., 2009).

Caveolin-1

The caveolin-1 protein (*cav-1*) is part of the caveolae, which are introversions of the cells' plasma membrane in the form of flasks (Raja et al., 2019; Gokani and Bhatt, 2022). In some cancers, *Cav-1* causes apoptosis and cell cycle arrest at the first stages of tumorigenesis (Volonte and Galbiati, 2020; Arfin et al., 2021). Suppression Subtractive Hybridization (SSH) technique has been used to clone the *cav-1* gene from *T. spiralis* as an adult-specific antigen, which has been demonstrated to be extracted from maturing embryos and oocytes of this parasite (Wu et al., 2021).

Heat shock proteins

In addition to regulating cell growth, survival, and differentiation, heat shock proteins (HSPs) play an active role in the flexibility, intracellular arrangement, and proteolytic turnover of cells (Villesen et al., 2020; Karamanos et al., 2021; Lang et al., 2021). They are considered powerful immunoadjuvants that can lead to more substantial antitumor impacts (Banstola et al., 2020). Heat-inducible proteins, including sHSP, HSP60, HSP70, and histone H3, have been isolated from ES products and somatic extracts of *T. spiralis*, (Sun et al., 2018; Grzelak et al., 2020; Grzelak et al., 2022). Thw HSPs prevent cell death in *T. spiralis* and sustain homeostasis (Bolhassani and Agi, 2019).

Ribosomal proteins

Ribosomal proteins are essential for repairing DNA structure, cell differentiation, and development, generally overexpressed in cancers, such as esophageal, gastric, liver, and colorectal cancer (Mao-De and Jing, 2007; Abraham and Meltzer, 2017; Xie et al., 2018). The use of iRNA therapy within the past 30 years could help researchers treat many types of tumors and tumorigenic viruses with iRNA (Soudyab et al., 2016). There is still an underlying mystery regarding iRNA therapy since other novel cancer immunotherapies have emerged, and the fact that iRNA therapy has not been as practical and valuable as initially believed; therefore, it is unclear how it works (Taghikhani et al., 2020; Di Martino et al., 2021). A recent study of BALB/c mice showed that *Trichinella* iRNA significantly reduced the growth of mouse myeloma tumors (SP2/0). *Trichinella spiralis* also contains two ribosomal proteins, S24 and S24e, involved in DNA repair, cell growth regulation, and cell differentiation and are overexpressed in different types of cancer including gastric, colorectal, esophageal, and liver cancer (Duan et al., 2013).

Tropomyosins

Tropomyosins (Tms) are the core components of microfilaments (or actin filaments), which are the thinnest filaments of the cytoskeleton (Karabinos, 2019). Many eukaryotes contain Tms, which are acidic proteins found in yeasts, worms, flies, crustaceans, frogs, birds, and mammals (Gunning et al., 2008; Choi et al., 2012; Jeong and Park, 2020). A number of studies have demonstrated that Tms suppress both breast and bladder cancer as well as astrocytoma, central nervous system tumors, and colon cancers (Helfman et al., 2008; Humayun-Zakaria et al., 2019). An antitumor response was observed in SP2/0 myeloma cells with *T. spiralis* associated antigen, which could also stimulate cross-protective immunity against the tumor (Gong et al., 2011).

The prevention and treatment effects of *Trichinella spiralis* on cancers

Theantitumorr properties of *T. spiralis* have been demonstrated in numerous studies. It was first described in the 1970s that *T. spiralis* had an antitumor effect (Weatherly, 1970). Nevertheless, only limited progress has been made in this field due to inconsistent research. In this regard, it remains unclear how these inhibitory effects are acted. Furthermore, clinical trials have not provided compelling evidence linking *T. spiralis* to the prevention or treatment of tumors. There is also evidence that *T. spiralis* may trigger or contribute to tumor coinfections which mainly include viral, fungal, and bacterial infections (Hu et al., 2021). *Trichinella spiralis'* antitumor effect is not only attributed to increased innate immune function but may also be due to excretory-secretory (ES), which are complex proteins produced by *T. spiralis* during the infestation may have some antitumor effects indirectly by changing the expression of a tumor gene or directly by affecting antitumor activity including the apoptosis, immunomodulatory and anti-inflammatory effects which suppress the tumor growth (Sofronic-Milosavljevic et al., 2015; Vasilev et al., 2015; Ding et al., 2020b, Figure 2).

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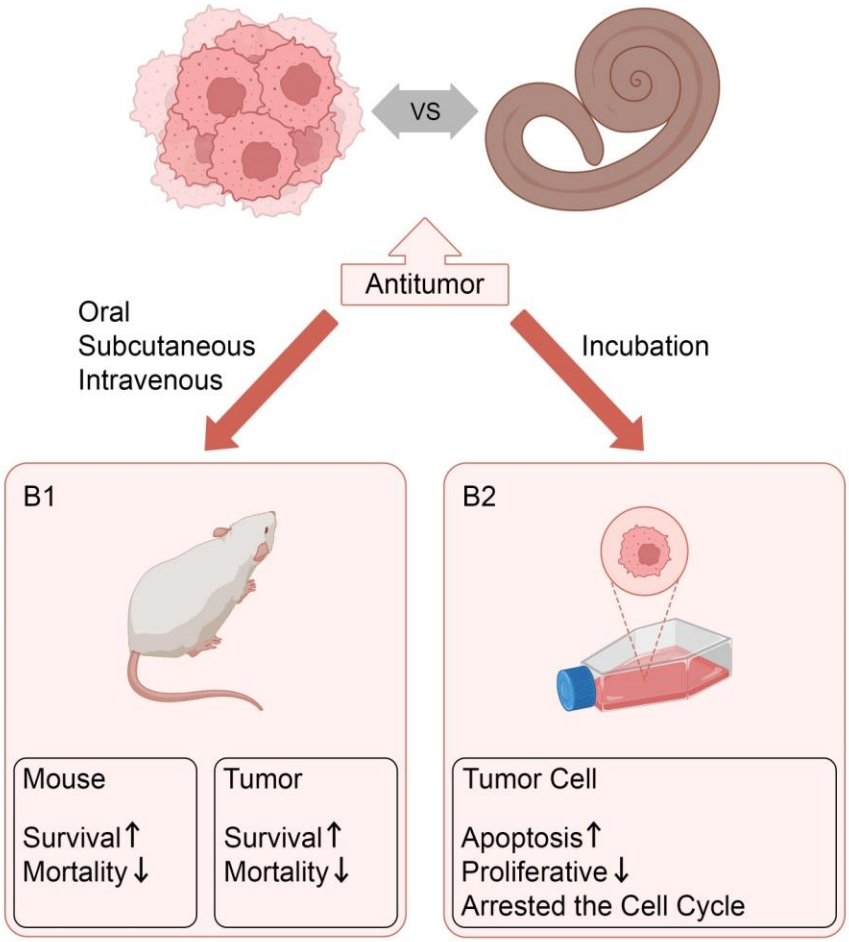

Figure 2. Relations between *T. spiralis* and tumors

Hepatocellular carcinoma

The sixth most prevalent type of cancer is hepatocellular carcinoma (HCC) in humans and animals (Balogh et al., 2016; Heimbach et al., 2018). The prognosis for HCC is driven by the tumor stage, with curative options providing a 5-year survival exceeding 70% for early-stage HCC compared with a median survival of ~1–1.5 years for symptomatic advanced-stage cases treated with systemic therapies (Villanueva, 2019). HCC is an aggressive and highly malignant tumor with a survival rate of less than 5% in 5 years (Grandhi et al., 2016). Available treatment methods have only been effective in some patients. Due to the high mortality rate and high risk of recurrence after treatment, new treatment methods are mandatory (Ringelhan et al., 2018; McGlynn et al., 2021). The regulatory mechanism of *T. spiralis* nurse cell formation is similar to tumor cell apoptosis signal regulation (Elhasawy et al., 2021). *Trichinella spiralis* nurse cell formation is a complex process and involves differentiation and cell cycle arrest of infected muscle cells. In other words, the nurse cell formation apoptotic pathways may be activated by antitumor genes that can suppress cell proliferation or induce apoptosis of the tumor cells (Wang et al., 2009). Although several parasites have been described for their ability to fight tumors, *T. spiralis* has proven particularly effective in cancer immunotherapy (Dabrowska et al., 2008). Many cytokines produced by T. spiralis are capable of inhibiting tumor growth. In addition, skeletal muscle cells are affected by *T. spiralis* infection during nurse cell formation, causing various changes (Dabrowska et al., 2016). As a result of these changes, muscle cells begin to differentiate, and apoptosis occurs, then the infected cells are stopped in the G2/M phase of the cell cycle (Wang et al., 2013). Additionally, *T. spiralis* and its extract inhibit tumor growth and induce apoptosis in tumor cells by stimulating mitochondrial pathways and death receptor pathways and apoptosis-related genes (Ding et al., 2020a; Ding et al., 2021). As part of the immune response to *T. spiralis* infection, the expression of c-Ski protein (a tumor suppressor protein) and genes associated with signaling pathways such as *p53* (apoptosis genes are expressed), *SMAD2*, and *SMAD4* are activated (Zakeri, 2017; Boros et al., 2019). These changes occur simultaneously with the increased activity of apoptosis factors involved in a mitochondrial pathway, such as caspase 9 and Bcl-2 associated protein X (BAX), as well as a death receptors pathway, such as tumor necrosis factor-alpha (TNF-α), caspase 8, and caspase 3 (Wu et al., 2005). *Trichinella spiralis* can induce apoptosis in HCC, because its infection has similar regulatory mechanisms to cancer cell apoptosis signals and it represents a promising approach to overcoming this cancer.

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Lung cancer

Among all malignant cancers worldwide, lung cancer has the highest mortality rate in humans (Bade and Cruz, 2020). Numerous factors, including population aging, smoking, and environmental pollution, have contributed to an increase in the mortality rate due to lung cancer in recent years (Rudin et al., 2021). Unfortunately, lung cancer is mostly identified at late stages, and the survival rate is less than 15% in 5 years. Due to the quick multiplication time in small cell lung cancer (SCLC), lung cancer has a poor prognosis (de Groot et al., 2018; Barta et al., 2019; Schabath and Cote, 2019; Thandra et al., 2021). Chemotherapy is the primary therapeutic option for advanced SCLCs but has significant side effects, including an increased risk of cancer recurrence (Yang et al., 2019; Oronsky et al., 2022). Contrarily, biological therapy is regarded as a secure and effective therapeutic approach. As a result, numerous experimental studies have been carried out to investigate how biological therapy can inhibit the growth of cancers, including those that examine the antineoplastic properties of parasites. According to numerous studies, *T. spiralis has two different types of antineoplastic mechanism*s. First, *T. spiralis* may cause an immunized response in the host by parasitizing tumor antigens of cancer cells. Second, *T. spiralis* may contain substances that directly start the apoptosis of cancer cells (Liao et al., 2018). *T. spiralis* could cause cell apoptosis through mitochondrial apoptosis pathways by first activating caspase-9 and then caspase-3 (Yu et al., 2014). The expression of pro-apoptosis genes like *BAX*, *Cyt-C*, *Apaf-1*, *caspase-9*, and *caspase-3* may be upregulated by ESPs, whereas the expression of anti-apoptosis genes *Bcl-2* and *Livin* may be downregulated (Bruschi et al., 2022). Therefore, it could be concluded that ESPs can activate mitochondria to release high levels of Cyt-C into the cytoplasm (Akl et al., 2014). The polymerization caused by Cytochrome C (Cyt-C) with Apoptotic protease activating factor-1 (Apaf-1) and procaspase-9 may further stimulate caspase-9 and caspase-3, which would then cut substrate proteins in the cell (Martínez-Lostao et al., 2015). The ESPs may also prevent the anti-apoptosis protein Livin from performing its apoptosis regulation functions on the cascade reaction, which would ultimately influence apoptosis in H446 cells, a small cell lung cancer cell line (Luo et al., 2017). As a result, *T. spiralis* Muscle larva (ML) ESPs trigger intrinsic mitochondrial pathways, which in turn cause apoptosis in H446 SCLC cells. In conclusion, it was found that *T. spiralis* ML ESPs may prevent human H446 SCLC cells from proliferating and trigger their apoptosis by activating mitochondrial apoptosis pathways.

Melanoma

The most aggressive type of skin cancer is melanoma in humans and animals (Miller and Mihm Jr, 2006). Because this tumor is largely resistant to conventional chemotherapy, patients with advanced disease have a poor prognosis (Garbe and Leiter, 2009; Schadendorf et al., 2018). Finding new therapeutic strategies for the treatment of melanoma could be a valuable subject for research to find substances that can affect the apoptotic process of the disease (Schadendorf et al., 2015; Domingues et al., 2018; O'Neill and Scoggins, 2019). All three stages of the T. *spiralis* life cycle appear to contain elements that can control malignancy based on a few studies currently available in this field. *Trichinella spiralis* can inhibit the growth of B16 melanoma by the action of ES L1 antigens (a component unique to the chronic phase of this infection, Kang et al., 2013). Studies conducted *in vitro* showed that ES L1 antigens affect B16 melanoma cells that are both anti-survival and pro-apoptotic (Vasilev et al., 2015).

CONCLUSION

Today, the knowledge of *T. spirals'* role in antitumor therapy has greatly improved due to advancements in research on the relationships between the organism and tumors. Antigens derived from parasites may be helpful in cancer immunotherapy in humans and animals. Studies conducted *in vitro* showed that *T. spiralis* antigens affect different cancer cells in hepatocellular carcinoma, lung cancer, and melanoma by activating mitochondrial apoptosis pathways. Cellular immune function, mediated by Th1 cells, suppresses malignant cell proliferation and angiogenesis. Clinical trials have not provided compelling evidence linking *T. spiralis* to the prevention or treatment of tumors. Future studies should focus on the purification of parasite antigens and their use for wider-scale trials in animal models.

DECLARATIONS

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Authors' contribution

Soheil Sadr was the principal author who directed and prepared the review paper. Zahra Yousefsani, Pouria Ahmadi Simab, Ahad Jafari Rahbar Alizadeh, and Narges Lotfalizadeh participated in the preparation of the final version of the manuscript. Hassan Borji participated as a supervisor and assisted in preparing and proofreading of the manuscript. All authors have read and approved the final version of the manuscript for publication in the present journal.

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The ethical considerations including plagiarism, consent to publish, misconduct, fabrication and/or falsification of data, dual publication and/or submission, and redundancy checked by authors.

REFERENCES

Abraham JM and Meltzer SJ (2017). Long noncoding RNAs in the pathogenesis of Barrett's esophagus and esophageal carcinoma. Gastroenterology, 153(1): 27-34. DOI: https://doi.org/10.1053/j.gastro.2017.04.046

Akl H, Vervloessem T, Kiviluoto S, Bittremieux M, Parys JB, De Smedt H, Bultynck G (2014). A dual role for the anti-apoptotic Bcl-2 protein in cancer: mitochondria versus endoplasmic reticulum. Biochimica et biophysica acta (BBA)-molecular cell research, 1843(10): 2240-2252. DOI: https://doi.org/10.1016/j.bbamcr.2014.04.017

Albini A, Bruno A, Noonan DM, and Mortara L (2018). Contribution to tumor angiogenesis from innate immune cells within the tumor microenvironment: implications for immunotherapy. Frontiers in immunology, 9: 527. DOI: https://doi.org/10.3389/fimmu.2018.00527

Arfin S, Jha NK, Jha SK, Kesari KK, Ruokolainen J, Roychoudhury S, Rathi B, and Kumar D (2021). Oxidative stress in cancer cell metabolism. Antioxidants, 10(5): 642. DOI: https://doi.org/10.3390/antiox10050642

Babal P, Milcheva R, Petkova S, Janega P, and Hurnikova Z (2011). Apoptosis as the adaptation mechanism in survival of *Trichinella spiralis* in the host. Parasitology Research, 109(4): 997-1002. DOI: https://doi.org/10.1007/s00436-011-2343-2

Bade BC and Cruz CSD (2020). Lung cancer 2020: epidemiology, etiology, and prevention. Clinics in chest medicine, 41(1): 1-24. DOI: https://doi.org/10.1016/j.ccm.2019.10.001

Balogh J, Victor III D, Asham EH, Burroughs SG, Boktour M, Saharia A, Li X, Ghobrial RM, and Monsour Jr HP (2016). Hepatocellular carcinoma: a review. Journal of hepatocellular carcinoma, 3: 41-53. DOI: https://doi.org/10.2147/JHC.S61146

Banstola A, Jeong JH, and Yook S (2020). Immunoadjuvants for cancer immunotherapy: A review of recent developments. Acta biomaterialia, 114: 16-30. DOI: https://doi.org/10.1016/j.actbio.2020.07.063

Barta JA, Powell CA, and Wisnivesky JP (2019). Global epidemiology of lung cancer. Annals of global health, 85(1): 8. DOI: https://doi.org/10.5334/aogh.2419

Bassiony M, Aluko AV, Radosevich JA (2020). Immunotherapy and cancer. Precision Medicine in Oncology, 5: 133-156. DOI: https://doi.org/10.1002/9 and 781119432487.ch5

Berois N, Pittini A, and Osinaga E (2022). Targeting Tumor Glycans for Cancer Therapy: Successes, Limitations, and Perspectives. Cancers, 14(3): 645. DOI: https://doi.org/10.3390/cancers14030645

Berriel E, Freire T, Chiale C, Rodríguez E, Morón G, Fernández-Graña G, Crispo M, Berois N, and Osinaga E (2021). Human hydatid cyst fluid-induced therapeutic anticancer immune responses via NK1.1+ cell activation in mice. Cancer Immunology, Immunotherapy, 70(12): 3617-3627. DOI: https://doi.org/10.1007/s00262-021-02948-x

Bolhassani A and Agi E (2019). Heat shock proteins in infection. Clinica Chimica Acta, 498: 90-100. DOI: https://doi.org/10.1016/j.cca.2019.08.015

Bommer UA (2017). The translational controlled tumour protein TCTP: biological functions and regulation. TCTP/tpt1-Remodeling Signaling from Stem Cell to Disease, 64: 69-126. DOI: https://doi.org/10.1007/978-3-319-67591-6_4

Bommer UA and Thiele BJ (2004). The translationally controlled tumour protein (TCTP). The international journal of biochemistry & cell biology, 36(3): 379-385. DOI: https://doi.org/10.1016/S1357-2725(03)00213-9

Boros Z, Gherman CM, Lefkaditis M, and Cozma V (2019). The oncogenic and oncostatic action of *Trichinella* spp. in animals. Scientia Parasitologica, 20(1-2): 5-11. DOI: http://www.scientia.zooparaz.net/2019_20_01/05-11-SP-2019-Boros.pdf

Boshtam M, Asgary S, Kouhpayeh S, Shariati L, and Khanahmad H (2017). Aptamers against pro-and anti-inflammatory cytokines: a review. Inflammation, 40(1): 340-349. DOI: https://doi.org/10.1007/s10753-016-0477-1

Bruschi F, Ashour D, and Othman A (2022). Trichinella-induced immunomodulation: Another tale of helminth success. Food and Waterborne Parasitology, 27: e00164. DOI: https://doi.org/10.1016/j.fawpar.2022.e00164

Carneiro BA and El-Deiry WS (2020). Targeting apoptosis in cancer therapy. Nature reviews Clinical oncology, 17(7): 395-417. DOI: https://doi.org/10.1038/s41571-020-0341-y

Chawla-Sarkar M, Lindner DJ, Liu YF, Williams B, Sen GC, Silverman RH, and Borden EC (2003). Apoptosis and interferons: role of interferon-stimulated genes as mediators of apoptosis. Apoptosis, 8(3): 237-249. DOI: https://doi.org/10.1023/A:1023668705040

Choi C, Kim D, Kim S, Jeong S, Song E, and Helfman DM (2012). From skeletal muscle to cancer: insights learned elucidating the function of tropomyosin. Journal of structural biology, 177(1): 63-69. DOI: https://doi.org/10.1016/j.jsb.2011.11.016

Cruceriu D, Baldasici O, Balacescu O, and Berindan-Neagoe I (2020). The dual role of tumor necrosis factor-alpha (TNF-α) in breast cancer: molecular insights and therapeutic approaches. Cellular Oncology, 43(1): 1-18. DOI: https://doi.org/10.1007/s13402-019-00489-1

Dabrowska M, Skoneczny M, Zielinski Z, and Rode W (2016). Wnt signaling in regulation of biological functions of the nurse cell harboring *Trichinella* spp. Parasites & vectors, 9(1): 483. DOI: https://doi.org/10.1186/s13071-016-1770-4

Dabrowska, M, Skoneczny M, Zieliński Z, and Rode W (2008). Nurse cell of *Trichinella* spp. as a model of long-term cell cycle arrest. Cell Cycle, 7(14): 2167-2178. DOI: https://doi.org/10.4161/cc.7.14.6269

Daneshpour S, Kefayat AH, Mofid MR, Rad SR, and Darani HY (2019). Effect of hydatid cyst fluid antigens on induction of apoptosis on breast cancer cells. Advanced Biomedical Research, 8: 27. DOI: https://doi.org/10.4103/abr.abr_220_18

Darani HY and Yousefi M (2012). Parasites and cancers: parasite antigens as possible targets for cancer immunotherapy. Future Oncology, 8(12): 1529-1535. DOI: https://doi.org/10.2217/fon.12.155

de Groot PM, Wu CC, Carter BW, and Munden RF (2018). The epidemiology of lung cancer. Translational lung cancer research, 7(3): 220. DOI: https://doi.org/10.21037/tlcr.2018.05.06

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Dharmani P, Srivastava V, Kissoon-Singh V, and Chadee K (2009). Role of intestinal mucins in innate host defense mechanisms against pathogens. Journal of Innate Immunity, 1(2): 123-35. DOI: https://doi.org/10.1159/000163037

Di Martino MT, Riillo C, Scionti F, Grillone K, Polerà N, Caracciolo D, Arbitrio M, Tagliaferri P, and Tassone P (2021). miRNAs and lncRNAs as novel therapeutic targets to improve cancer immunotherapy. Cancers, 13(7): 1587. DOI: https://doi.org/10.3390/cancers13071587

Ding J, Liu X, Bai X, Wang Y, Li J, Wang C, Li S, Liu M, and Wang X (2020a). *Trichinella spiralis*: inflammation modulator. Journal of helminthology, 94: E193. DOI: https://doi.org/10.1017/S0022149X20000802

Ding J, Liu X, Tang B, Bai X, Wang Y, Li S, Li J, Liu M, and Wang X (2020b). Murine hepatoma treatment with mature dendritic cells stimulated by *Trichinella spiralis* excretory/secretory products. Parasite, 27: 47. DOI: https://doi.org/10.1051/parasite/2020045

Ding J, Liu X, Tang B, Bai X, Wang Y, Li S, Li J, Liu M, and Wang X (2021). *Trichinella spiralis* ESP inhibits tumor cell growth by regulating the immune response and inducing apoptosis. DOI: https://doi.org/10.21203/rs.3.rs-257172/v1

Domingues B, Lopes JM, Soares P, and Pópulo H (2018). Melanoma treatment in review. ImmunoTargets and therapy, 7: 35-49. DOI: https://doi.org/10.2147/ITT.S134842

Duan L, Li J, Cheng B, Lv Q, Gong Pt, Su Lb, Cai Y, and Zhang X (2013). Identification of a novel gene product expressed by *Trichinella spiralis* that binds antiserum to Sp2/0 myeloma cells. Veterinary parasitology, 194(2-4): 183-185. DOI: https://doi.org/10.1016/j.vetpar.2013.01.051

Elhasawy F A, Ashour DS, ElSaka AM, and Ismail HI (2021). The apoptotic effect of *Trichinella spiralis* infection against experimentally induced hepatocellular carcinoma. Asian Pacific Journal of Cancer Prevention: APJCP, 22(3): 935-946. DOI: https://doi.org/10.31557/APJCP.2021.22.3.935

Fabre M, Beiting D, Bliss S, and Appleton J (2009). Immunity to *Trichinella spiralis* muscle infection. Veterinary parasitology, 159(3-4): 245-248. DOI: https://doi.org/10.1016/j.vetpar.2008.10.051

Garbe C and Leiter U (2009). Melanoma epidemiology and trends. Clinics in dermatology, 27(1): 3-9. DOI: https://doi.org/10.1016/j.clindermatol.2008.09.001

Gokani S, Bhatt LK (2022). Caveolin-1: A promising therapeutic target for diverse diseases. Current Molecular Pharmacology, 15(5): 701-715. DOI: https://doi.org/10.2174/1874467214666211130155902

Gong P, Zhang J, Cao L, Nan Z, Li J, Yang J, Fang H, Jiao H, Jiang T, and Su L (2011). Identification and characterization of myeloma-associated antigens in *Trichinella spiralis*. Experimental Parasitology, 127(4): 784-788. DOI: https://doi.org/10.1016/j.exppara.2010.12.001

Gottstein B, Pozio E, and Nöckler K (2009). Epidemiology, diagnosis, treatment, and control of trichinellosis. Clinical microbiology reviews, 22(1): 127-145. DOI: https://doi.org/10.1128/CMR.00026-08

Grandhi MS, Kim AK, Ronnekleiv-Kelly SM, Kamel IR, Ghasebeh MA, and Pawlik TM (2016). Hepatocellular carcinoma: from diagnosis to treatment. Surgical oncology, 25(2): 74-85. DOI: https://doi.org/10.1016/j.suronc.2016.03.002

Grondin JA, Kwon YH, Far P M, Haq S, and Khan WI (2020). Mucins in intestinal mucosal defense and inflammation: learning from clinical and experimental studies. Frontiers in immunology, 11: 2054. DOI: https://doi.org/10.3389/fimmu.2020.02054

Grzelak S, Bień-Kalinowska J, and Stachyra A (2022). *Trichinella britovi* recombinant proteins produced in Pichia pastoris expression system for specific IgG antibody detection in the sera of mice and pigs infected with *Trichinella* spp. Experimental Parasitology, 242: 108386. DOI: https://doi.org/10.1016/j.exppara.2022.108386

Grzelak S, Stachyra A, Stefaniak J, Mrówka K, Moskwa B, and Bień-Kalinowska J (2020). Immunoproteomic analysis of *Trichinella spiralis* and *Trichinella britovi* excretory-secretory muscle larvae proteins recognized by sera from humans infected with Trichinella. PLoS One, 15(11): e0241918. DOI: https://doi.org/10.1371/journal.pone.0241918

Gu T, De Jesus M, Gallagher HC, Burris TP, and Egilmez NK (2017). Oral IL-10 suppresses colon carcinogenesis via elimination of pathogenicCD4+ T-cells and induction of antitumor CD8+ T-cell activity. Oncoimmunology, 6(6): e1319027. DOI: https://doi.org/10.1080/2162402X.2017.1319027

Gunning P, O'neill G, and Hardeman E (2008). Tropomyosin-based regulation of the actin cytoskeleton in time and space. Physiological reviews, 88(1): 1-35. DOI: https://doi.org/10.1152/physrev.00001.2007

Harrington K, Freeman DJ, Kelly B, Harper J, and Soria JC (2019). Optimizing oncolytic virotherapy in cancer treatment. Nature reviews Drug discovery, 18(9): 689-706. DOI: https://doi.org/10.1038/s41573-019-0029-0

Heimbach JK, Kulik LM, Finn RS, Sirlin CB, Abecassis MM, Roberts LR, Zhu AX, Murad MH, and Marrero JA (2018). AASLD guidelines for the treatment of hepatocellular carcinoma. Hepatology, 67(1): 358-380. DOI: https://doi.org/10.1002/hep.29086

Helfman DM, Flynn P, Khan P, Saeed A (2008). Tropomyosin as a regulator of cancer cell transformation. Tropomyosin, Advances in Experimental Medicine and Biology book series, 644: 124-131. DOI: https://doi.org/10.1007/978-0-387-85766-4_10

Hewitson JP, Grainger JR, and Maizels RM (2009). Helminth immunoregulation: the role of parasite secreted proteins in modulating host immunity. Molecular and biochemical parasitology, 167(1): 1-11. DOI: https://doi.org/10.1016/j.molbiopara.2009.04.008

Hu C, Zhu S, Wang J, Lin Y, Ma L, Zhu L, Jiang P, Li Z, and Pan W (2019). Schistosoma japonicum MiRNA-7-5p inhibits the growth and migration of hepatoma cells via cross-species regulation of S-phase kinase-associated protein 2. Frontiers in oncology, 9: 175. DOI: https://doi.org/10.3389/fonc.2019.00175

Hu X, Liu X, Bai X, Yang L, Ding J, Jin X, Li C, Zhang Y, Li Y, and Yang Y (2021). Effects of *Trichinella spiralis* and its excretory/secretory products on autophagy of host muscle cells *in vivo* and *in vitro*. PLoS Neglected Tropical Diseases, 15(2): e0009040. DOI: https://doi.org/10.1371/journal.pntd.0009040

Humayun-Zakaria N, Arnold R, Goel A, Ward D, Savill S, and Bryan RT (2019). Tropomyosins: Potential biomarkers for urothelial bladder cancer. International journal of molecular sciences, 20(5): 1102. DOI: https://doi.org/10.3390/ijms20051102

Ilic N, Gruden-Movsesijan A, and Sofronic-Milosavljevic L (2012). *Trichinella spiralis*: shaping the immune response. Immunologic research, 52(1): 111-119. DOI: https://doi.org/10.1007/s12026-012-8287-5

Ilic N, Worthington JJ, Gruden-Movsesijan A, Travis MA, Sofronic-Milosavljevic L, and Grencis RK (2011). *Trichinella spiralis* antigens prime mixed Th1/Th2 response but do not induce de novo generation of Foxp3+ T cells *in vitro*. Parasite Immunology, 33(10): 572-582. DOI: https://doi.org/10.1111/j.1365-3024.2011.01322.x

Jarnicki AG, Lysaght J, Todryk S, and Mills KH (2006). Suppression of antitumor immunity by IL-10 and TGF-β-producing T cells infiltrating the growing tumor: influence of tumor environment on the induction of CD4+ and CD8+ regulatory T cells. The journal of immunology, 177(2): 896-904. DOI: https://doi.org/10.4049/jimmunol.177.2.896

Jeong KY and Park JW (2020). Insect allergens on the dining table. Current Protein and Peptide Science, 21(2): 159-169. DOI: https://doi.org/10.2174/1389203720666190715091951

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Jhunjhunwala S, Hammer C, and Delamarre L (2021). Antigen presentation in cancer: insights into tumour immunogenicity and immune evasion. Nature Reviews Cancer, 21(5): 298-312. DOI: https://doi.org/10.1038/s41568-021-00339-z

Kang YJ, Jo JO, Cho MK, Yu HS, Leem SH, Song KS, Ock MS, and Cha HJ (2013). *Trichinella spiralis* infection reduces tumor growth and metastasis of B16-F10 melanoma cells. Veterinary parasitology, 196(1-2): 106-113. DOI: https://doi.org/10.1016/j.vetpar.2013.02.021

Karabinos A (2019). Intermediate filament (IF) proteins IFA-1 and IFB-1 represent a basic heteropolymeric IF cytoskeleton of nematodes: A molecular phylogeny of nematode IFs. Gene, 692: 44-53. DOI: https://doi.org/10.1016/j.gene.2018.12.069

Karamanos NK, Theocharis AD, Piperigkou Z, Manou D, Passi A, Skandalis SS, Vynios DH, Orian-Rousseau V, Ricard-Blum S, and Schmelzer CE (2021). A guide to the composition and functions of the extracellular matrix. The FEBS journal, 288(24): 6850-6912. DOI: https://doi.org/10.1111/febs.15776

Kelley RK and Greten TF (2021). Hepatocellular carcinoma—origins and outcomes. New England Journal of Medicine, 385(3): 280-282. DOI: https://doi.org/10.1056/NEJMcibr2106594

Khan W (2008). Physiological changes in the gastrointestinal tract and host protective immunity: learning from the mouse-*Trichinella spiralis* model. Parasitology, 135(6): 671-682. DOI: https://doi.org/10.1017/S0031182008004381

Kim M, Min HJ, Won HY, Park H, Lee JC, Park HW, Chung J, Hwang ES, and Lee K (2009). Dimerization of translationally controlled tumor protein is essential for its cytokine-like activity. PLoS One, 4(7): e6464. DOI: https://doi.org/10.1371/journal.pone.0006464

Krementsov N (2009). Trypanosoma cruzi, cancer and the Cold War. História, Ciências, Saúde-Manguinhos, 16: 75-94. DOI: https://doi.org/10.1590/S0104-59702009000500005

Kurup VM and Thomas J (2020). Edible vaccines: promises and challenges. Molecular biotechnology, 62(2): 79-90. DOI: https://doi.org/10.1007/s12033-019-00222-1

Lang BJ, Guerrero ME, Prince TL, Okusha Y, Bonorino C, and Calderwoo SK (2021). The functions and regulation of heat shock proteins; key orchestrators of proteostasis and the heat shock response. Archives of toxicology, 95(6): 1943-1970. DOI: https://doi.org/10.1007/s00204-021-03070-8

Liao C, Cheng X, Liu M, Wang X, and Boireau P (2018). *Trichinella spiralis* and tumors: cause, coincidence or treatment? Anticancer Agents in Medicinal Chemistry (Formerly Current Medicinal Chemistry-Anti-Cancer Agents). 18(8): 1091-1099. DOI: https://doi.org/10.2174/1871520617666171121115847

Liu P, Cui J, Liu RD, Wang M, Jiang P, Liu LN, Long SR, Li LG, Zhang SB, and Zhang XZ (2015). Protective immunity against *Trichinella spiralis* infection induced by TsNd vaccine in mice. Parasites vectors, 8(185): 1-10. DOI: https://doi.org/10.1186/s13071-015-0791-8

Luo J, Yu L, Xie G, Li D, Su M, Zhao X, and Du L (2017). Study on the mitochondrial apoptosis pathways of small cell lung cancer H446 cells induced by *Trichinella spiralis* muscle larvae ESPs. Parasitology, 144(6): 793-800. DOI: https://doi.org/10.1017/S0031182016002535

Mak C, Poon M, Lun H, Kwok P, and Ko R (2007). Heat-inducible translationally controlled tumor protein of *Trichinella pseudospiralis*: cloning and regulation of gene expression. Parasitology Research, 100(5): 1105-1111. DOI: https://doi.org/10.1007/s00436-006-0373-y

Mao-De L and Jing X (2007). Ribosomal proteins and colorectal cancer. Current genomics, 8(1): 43-49. DOI: https://doi.org/10.2174/138920207780076938

Martin JD, Cabral H, Stylianopoulos T, and Jain RK (2020). Improving cancer immunotherapy using nanomedicines: progress, opportunities and challenges. Nature reviews Clinical oncology, 17(4): 251-266. DOI: https://doi.org/10.1038/s41571-019-0308-z

Martínez-Lostao L, Anel A, and Pardo J (2015). How do cytotoxic lymphocytes kill cancer cells? Clinical cancer research, 21(22): 5047-5056. DOI: https://doi.org/10.1158/1078-0432.CCR-15-0685

McGlynn KA, Petrick JL, and El-Serag HB (2021). Epidemiology of hepatocellular carcinoma. Hepatology, 73: 4-13. DOI: https://doi.org/10.1002/hep.31288

Miller AJ and Mihm Jr MC (2006). Melanoma. New England Journal of Medicine, 355(1), 51-65. DOI: https://doi.org/10.1056/NEJMra052166

Mulder WJM, Ochando J, Joosten LA, Fayad ZA, and Netea MG (2019). Therapeutic targeting of trained immunity. Nature reviews Drug discovery, 18(7): 553-566. DOI: https://doi.org/10.1038/s41573-019-0025-4

Nagano-Ito M and Ichikawa S (2012). Biological effects of Mammalian translationally controlled tumor protein (TCTP) on cell death, proliferation, and tumorigenesis. Biochemistry research international, 2012: 204960. DOI: https://doi.org/10.1155/2012/204960

Nagano I, Wu Z, and Takahashi Y (2009). Functional genes and proteins of *Trichinella* spp. Parasitology Research, 104(2): 197-207. DOI: https://doi.org/10.1007/s00436-008-1248-1

Netea MG, Domínguez-Andrés J, Barreiro LB, Chavakis T, Divangahi M, Fuchs E, Joosten LA, van der Meer JW, Mhlanga MM, and Mulder WJ (2020). Defining trained immunity and its role in health and disease. Nature Reviews Immunology, 20(6): 375-388. DOI: https://doi.org/10.1038/s41577-020-0285-6

O'Neill CH and Scoggins CR (2019). Melanoma. Journal of surgical oncology, 120(5): 873-881. DOI: https://doi.org/10.1002/jso.25604

O'Donnell JS, Teng MW, and Smyth MJ (2019). Cancer immunoediting and resistance to T cell-based immunotherapy. Nature reviews Clinical oncology, 16(3): 151-167. DOI: https://doi.org/10.1038/s41571-018-0142-8

Oronsky B, Abrouk N, Caroen S, Lybeck M, Guo X, Wang X, Yu Z, and Reid T (2022). A 2022 update on extensive stage small-cell lung cancer (SCLC). Journal of Cancer, 13(9): 2945. DOI: https://doi.org/10.7150/jca.75622

Pachynski RK, Zabel BA, Kohrt HE, Tejeda NM, Monnier J, Swanson CD, Holzer AK, Gentles AJ, Sperinde GV, and Edalati A (2012). The chemoattractant chemerin suppresses melanoma by recruiting natural killer cell antitumor defenses. Journal of Experimental Medicine, 209(8): 1427-1435. DOI: https://doi.org/10.1084/jem.20112124

Paijens ST, Vledder A, de Bruyn M, and Nijman HW (2021). Tumor-infiltrating lymphocytes in the immunotherapy era. Cellular & molecular immunology, 18(4): 842-859. DOI: https://doi.org/10.1038/s41423-020-00565-9

Pallerla S, Abdul AuRM, Comeau J, and Jois S (2021). Cancer vaccines, treatment of the future: With emphasis on her2-positive breast cancer. International journal of molecular sciences, 22(2): 779. DOI: https://doi.org/10.3390/ijms22020779

Patel N, Kreider T, Urban Jr JF, and Gause WC (2009). Characterisation of effector mechanisms at the host: parasite interface during the immune response to tissue-dwelling intestinal nematode parasites. International journal for parasitology, 39(1): 13-21. DOI: https://doi.org/10.1016/j.ijpara.2008.08.003

Raja SA, Shah STA, Tariq A, Bibi N, Sughra K, Yousuf A, Khawaja A, Nawaz M, Mehmood A, and Khan MJ (2019). Caveolin-1 and dynamin-2 overexpression is associated with the progression of bladder cancer. Oncology Letters, 18(1): 219-226. DOI: https://doi.org/10.3892/ol.2019.10310

Ringelhan M, Pfister D, O'Connor T, Pikarsky E, and Heikenwalder M (2018). The immunology of hepatocellular carcinoma. Nature immunology, 19(3): 222-232. DOI: https://doi.org/10.1038/s41590-018-0044-z

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Romaris F, North SJ, Gagliardo LF, Butcher BA, Ghosh K, Beiting DP, Panico M, Arasu P, Dell A, and Morris HR (2002). A putative serine protease among the excretory–secretory glycoproteins of L1 *Trichinella spiralis*. Molecular and biochemical parasitology, 122(2): 149-160. DOI: https://doi.org/10.1016/S0166-6851(02)00094-4

Rudin CM, Brambilla E, Faivre-Finn C, and Sage J (2021). Small-cell lung cancer. Nature Reviews Disease Primers, 7(3): 1-20. DOI: https://doi.org/10.1038/s41572-020-00235-0

Ruffell B, Chang-Strachan D, Chan V, Rosenbusch A, Ho CM, Pryer N, Daniel D, Hwang ES, Rugo HS, and Coussens LM (2014). Macrophage IL-10 blocks CD8+ T cell-dependent responses to chemotherapy by suppressing IL-12 expression in intratumoral dendritic cells. Cancer cell, 26(5): 623-637. DOI: https://doi.org/10.1016/j.ccell.2014.09.006

Schabath MB, and Cote ML (2019). Cancer progress and priorities: lung cancer. Cancer epidemiology, biomarkers & prevention, 28(10): 1563-1579. DOI: https://doi.org/10.1158/1055-9965.EPI-19-0221

Schadendorf D, Fisher DE, Garbe C, Gershenwald JE, Grob JJ, Halpern A, Herlyn M, Marchetti MA, McArthur G, and Ribas A (2015). Melanoma. Nature Reviews Disease Primers, 1(15003): 1-20. DOI: https://doi.org/10.1038/nrdp.2015.3

Schadendorf D, van Akkooi AC, Berking C, Griewank KG, Gutzmer R, Hauschild A, Stang A, Roesch A, and Ugurel S (2018). Melanoma. The Lancet, 392(10151): 971-984. DOI: https://doi.org/10.1016/S0140-6736(18)31559-9

Schirrmacher V (2019). From chemotherapy to biological therapy: A review of novel concepts to reduce the side effects of systemic cancer treatment. International journal of oncology, 54(2): 407-419. DOI: https://doi.org/10.3892/ijo.2018.4661

Shapouri-Moghaddam A, Mohammadian S, Vazini H, Taghadosi M, Esmaeili SA, Mardani F, Seifi B, Mohammadi A, Afshari JT, and Sahebkar A (2018). Macrophage plasticity, polarization, and function in health and disease. Journal of cellular physiology, 233(9): 6425-6440. DOI: https://doi.org/10.1002/jcp.26429

Smyth MJ, Hayakawa Y, Takeda K, and Yagita H (2002). New aspects of natural-killer-cell surveillance and therapy of cancer. Nature Reviews Cancer, 2(11): 850-861. DOI: https://doi.org/10.1038/nrc928

Sofronic-Milosavljevic L, Ilic N, Pinelli E, and Gruden-Movsesijan A (2015). Secretory products of *Trichinella spiralis* muscle larvae and immunomodulation: implication for autoimmune diseases, allergies, and malignancies. Journal of Immunology Research, 2015. DOI: https://doi.org/10.1155/2015/523875

Soudyab M, Iranpour M, and Ghafouri-Fard S (2016). The role of long non-coding RNAs in breast cancer. Archives of Iranian medicine, 19(7): 508-517. DOI: http://journalaim.com/PDF/75_july2016_0011.pdf

Sun GG, Song YY, Jiang P, Ren HN, Yan SW, Han Y, Liu RD, Zhang X, Wang ZQ, and Cui J (2018). Characterization of a *Trichinella spiralis* putative serine protease. Study of its potential as sero-diagnostic tool. PLoS Neglected Tropical Diseases, 12(5): e0006485. DOI: https://doi.org/10.1371/journal.pntd.0006485

Sun Q, Huang J, Gu Y, Liu S, and Zhu X (2022). Dynamic changes of macrophage activation in mice infected with *Trichinella spiralis*. International Immunopharmacology, 108: 108716. DOI: https://doi.org/10.1016/j.intimp.2022.108716

Suresh S, Spatz J, Mills JP, Micoulet A, Dao M, Lim C, Beil M, and Seufferlein T (2005). Connections between single-cell biomechanics and human disease states: gastrointestinal cancer and malaria. Acta biomaterialia, 1(1): 15-30. DOI: https://doi.org/10.1016/j.actbio.2004.09.001

Taghikhani A, Farzaneh F, Sharifzad F, Mardpour S, Ebrahimi M, and Hassan ZM (2020). Engineered tumor-derived extracellular vesicles: potentials in cancer immunotherapy. Frontiers in immunology, 11: 221. DOI: https://doi.org/10.3389/fimmu.2020.00221

Tarp MA and Clausen H (2008). Mucin-type O-glycosylation and its potential use in drug and vaccine development. Biochimica et Biophysica Acta (BBA)-General Subjects, 1780(3): 546-563. DOI: https://doi.org/10.1016/j.bbagen.2007.09.010

Thandra KC, Barsouk A, Saginala K, Aluru JS, and Barsouk A (2021). Epidemiology of lung cancer. Contemporary Oncology/Współczesna Onkologia, 25(1): 45-52. DOI: https://doi.org/10.5114/wo.2021.103829

van Horssen R, Ten Hagen TL, and Eggermont AM (2006). TNF-α in cancer treatment: molecular insights, antitumor effects, and clinical utility. The oncologist, 11(4): 397-408. DOI: https://doi.org/10.1634/theoncologist.11-4-397

Vasilev S, Ilic N, Gruden-Movsesijan A, Vasilijic S, Bosic M, and Sofronic-Milosavljevic L (2015). Experimental immunology Necrosis and apoptosis in *Trichinella spiralis*-mediated tumour reduction. Central European Journal of Immunology, 40(1): 42-53. DOI: https://doi.org/10.5114/ceji.2015.50832

Villanueva, A (2019). Hepatocellular carcinoma. N. Engl. J. Med. 380: 1450-1462 DOI: https://doi.org/ 10.1056/NEJMra1713263.

Villesen IF, Daniels SJ, Leeming DJ, Karsdal MA, and Nielsen MJ (2020). The signalling and functional role of the extracellular matrix in the development of liver fibrosis. Alimentary Pharmacology & Therapeutics, 52(1): 85-97. DOI: https://doi.org/10.1111/apt.15773

Volonte D and Galbiati F (2020). Caveolin-1, a master regulator of cellular senescence. Cancer and Metastasis Reviews, 39(2): 397-414. DOI: https://doi.org/10.1007/s10555-020-09875-w

Wang N, Bai X, Tang B, Yang Y, Wang X, Zhu H, Luo X, Yan H, Jia H, and Liu M (2020). Primary characterization of the immune response in pigs infected with *Trichinella spiralis*. Veterinary research, 51(1): 1-14. DOI: https://doi.org/10.1186/s13567-020-0741-0

Wang XL, Fu BQ, Yang SJ, Wu XP, Cui GZ, Liu MF, Zhao Y, Yu Y.L, Liu X.Y, Deng HK et al. (2009). *Trichinella spiralis*-A potentialantitumorr agent. Veterinary Parasitology, 159: 249-52. https://doi.org/10.1016/j.vetpar.2008.10.052

Wang X, Liu M, Sun S, Liu X, Yu L, Wang X, Chu L, Rosenthal B, Shi H, and Boireau P (2013). Anantitumorr protein produced by *Trichinella spiralis* induces apoptosis in human hepatoma H7402 cells. Veterinary Parasitology, 194(2-4): 186-188. DOI: https://doi.org/10.1016/j.vetpar.2013.01.052

Weatherly NF (1970). Increased survival of Swiss mice given sublethal infections of *Trichinella spiralis*. The Journal of Parasitology, 56(4): 748-752. DOI: https://doi.org/10.2307/3277722

Wu SY, Fu T, Jiang YZ, and Shao ZM (2020). Natural killer cells in cancer biology and therapy. Molecular cancer, 19(1): 1-26. DOI: https://doi.org/10.1186/s12943-020-01238-x

Wu Z, Nagano I, Boonmars T, and Takahashi Y (2005). Tumor necrosis factor receptor-mediated apoptosis in *Trichinella spiralis*-infected muscle cells. Parasitology, 131(3): 373-381. DOI: https://doi.org/10.1017/S0031182005007663

Wu Z, Nagano I, Khueangchiangkhwang S, and Maekawa Y (2021). In *Trichinella* and Trichinellosis, Proteomics of Trichinella: 103-183. DOI: https://doi.org/10.1016/B978-0-12-821209-7.00009-3

Xie X, Guo P, Yu H, Wang Y, and Chen G (2018). Ribosomal proteins: insight into molecular roles and functions in hepatocellular carcinoma. Oncogene, 37(3): 277-285. DOI: https://doi.org/10.1038/onc.2017.343

Yang S, Zhang Z, and Wang Q (2019). Emerging therapies for small cell lung cancer. Journal of Hematology & Oncology, 12(1): 47. DOI: https://doi.org/10.1186/s13045-019-0736-3

Yu YR, Deng MJ, Lu WW, Zhang JS, Jia MZ, Huang J, and Qi YF (2014). Endoplasmic reticulum stress-mediated apoptosis is activated in intestines of mice with *Trichinella spiralis* infection. Experimental Parasitology, 145: 1-6. DOI: https://doi.org/10.1016/j.exppara.2014.06.017

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Zakeri A (2017). Helminth-induced apoptosis: a silent strategy for immunosuppression. Parasitology, 144(13): 1663-1676. DOI: https://doi.org/10.1017/S0031182017000841

Zhang J, De Toledo SM, Pandey BN, Guo G, Pain D, Li H, and Azzam EI (2012). Role of the translationally controlled tumor protein in DNA damage sensing and repair. Proceedings of the National Academy of Sciences, 109(16): E926-E933. DOI: https://doi.org/10.1073/pnas.1106300109

Zhang N, Li W, and Fu B (2018). Vaccines against *Trichinella spiralis*: progress, challenges and future prospects. Transboundary and Emerging Diseases, 65(6): 1447-1458. DOI: https://doi.org/10.1111/tbed.12917

To cite this paper: Sadr S, Yousefsani Z, Ahmadi Simab P, Jafari Rahbar Alizadeh A, Lotfalizadeh N, and Borji H (2023). *Trichinella spiralis* as a Potential Antitumor Agent: An Update. *World Vet. J.*, 13 (1): 65-74. DOI: https://dx.doi.org/10.54203/scil.2023.wvj7