



Cancer immunotherapy: lessons from the parasites to improve fighting against tumors

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The human body is exposed daily to various types of biological threats, such as bacteria and viruses, therefore to protect itself it relies on an arsenal of defenses, the so-called immune system. Components of this system work together to locate microorganisms, foreign cells and other potential threats and eliminates them (1,2). Although the immune system is vital for the fight against various diseases, it is not infallible. Some diseases, such as cancer, can circumvent these defenses (3). But knowledge and technologies have provided ways to strengthen the immune system and guide it to fight cancer; these innovative techniques are known as immunotherapies (4).

Immunotherapy, more specifically in its most recent form, immunomodulation applied to oncology, is a novel treatment, but still under development. Therapy involves modulating, or regulating, the immune system to enhance the body's ability to cope with disease (4-6). Oncology is increasingly moving towards individualized treatment. Recommendations for treatment are based not only on the disease, but also on the specific type of cancer and patient characteristics. In this context, other options for treatment than traditional chemotherapy have emerged, such as target drugs and principally immunotherapy, which can be used alone or in combination (7).

One of the characteristics of cancer that makes it so hard to fight is its ability to fool the immune system. Without identifying them as threats, the immune system allows diseased cells to proliferate, enabling the development of tumors

and, in some cases, their spread throughout the body (3). Therefore, the basis of immunotherapy in the context of cancer treatment is to introduce substances into the patient that generally stimulate the body's natural defenses and/or help identify and respond to cancer cells. Treatment includes the application of different medications either intravenously or subcutaneously. These continuous developments in immunotherapy, or immunomodulation, has created a new branch in oncology, called immuno-oncology, which seeks to teach the body to identify cancer cells as threats or by providing more effective mechanisms to combat them (7).

To reinforce the immune system in its battle against cancer, immunotherapy aims to mark cancer cells to enable the immune system to more easily identify them, or to utilize resources that increase the body's ability to fight. In addition, immunotherapy may be used in combination with the forms of treatment typically employed, such as targeted therapies, chemotherapy and radiotherapy. As they activate the immune system, immunotherapies can generally be considered for use in populations with varying diagnoses, but immunotherapy can also be customized to each person's individual tumor biology. Therefore, the same drug can be used for many different diagnoses and clinical situations (7).

Although several indications have already been approved, immunotherapy is still in the phase of clinical studies to test efficacy, safety and economic viability with the hope to enable its use worldwide. In this scenario, a revolution in cancer therapy emerges, where the target is no longer

the tumor directly, but the body's response to the tumor. Together with immunotherapy, Target Therapy (or Target Drugs) and CAR T-cells are part of the new generation of therapies that are considered ground-breaking in cancer treatment (8). The CAR T-cell has been created with an incredible technology: the patients' own T-lymphocytes. These cells are taken and modified in the laboratory to bind and eliminate tumor cells. For this, the patient's blood is collected and filtered by an apheresis machine to obtain the T cells. After this procedure, in the laboratory, a gene for a special receptor called the "Chimeric antigen receptor" is inserted into the T cells. Millions of CAR T-cells are stimulated to grow in the laboratory and re-inserted into the patient. These T cells will now recognize and eliminate cancer cells. To date, this therapy has been successfully used in the treatment of hematologic tumors, such as acute lymphoblastic leukemia in children, multiple myeloma and non-Hodgkin's lymphoma (8).

Recent evidence indicates that the fight against cancer can also benefit from our understanding of how parasites modulate their hosts' immune systems. Studies have shown that the mucin-type O-glycans derived from the canine tapeworm, *Echinococcus granulosus* have an antitumor effect in a variety of experimental cancer models, possibly through activating a pro-inflammatory Th-1 immune response from host. Additionally, the parasite secretes the Kunitz type protease inhibitor, EgKI-1, a molecule capable of inhibiting the growth and migration of human tumor lines (9,10). These findings may provide advances in cancer immunotherapy, offering new hope for patients with metastatic disease. Elucidating the underlying mechanism of how the Th-1 response induced by mucin-type parasite O-glycans could enable the development and use of alternative potential anticancer drug candidates.

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