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Letter to the Editor

IMMUNITY AND CANCER: IS THE VACCINATION READY FOR USE?

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INTRODUCTION

Cancer is a global disease and a leading cause of death worldwide, second only to cardiovascular disease in Western countries (1). Tumor cells replicate irregularly and form metastasis which tend to invade surrounding and distant tissues. In recent years, there has been a continuous evolution in the field of immunotherapy against tumors. This is also due to new diagnostic techniques and investigations such as positron emission tomography (PET), computed tomography, and magnetic resonance imaging (MRI). Immunotherapy is a therapeutic route often used by researchers that utilizes molecular investigations both for the diagnosis and treatment of tumors.

Immunotherapy makes use of the knowledge of natural killer cells (NK), CD3, CD8, and of the study of Chimeric Antigen Receptor (CAR) T cells, a type of immune cell (now the focus of many laboratories) which utilizes a patient's T lymphocytes which are then genetically modified in a laboratory to allow them bind to cancer cells, attacking the cancer (2). For example, it has been seen that some types of oncolytic viruses destroy tumor cells without killing healthy tissue cells, inducing anti-tumor immune responses with a promising therapeutic strategy (3). The anti-cancer vaccination is making its way in small steps and is based on the use of target antigens, even if these appear very weak and of low immunogenicity. This makes it difficult to induce clinical responses and address the problem of therapeutic tumor vaccination.

Researchers are working to develop therapeutic vaccines against cancer. The use of vaccine vectors, both biological and synthetic, can improve the responses of the immune system regarding T cells, as well as B-lymphocytes and antigen-presenting cells (APC) such as macrophages and dendritic cells (4). These therapeutic strategies act on the mechanisms used by tumor cells to evade and inhibit the immune system. To date, several types of vaccines against tumors have been developed, such as antibodies that attack tumor cells, proteins, peptides, RNA, DNA, and antigens, however these are still under investigation (5). In the wake of the mRNA vaccine used against COVID-19, vaccines of this type have also been used as a new method against tumors (6). These vaccines are based on the inoculation of mRNA which encodes the production of specific tumor antigens by the host with triggering of the immune response (7). By isolating tumor mRNA, this therapy can be adapted to each type of cancer. But before these vaccines can be employed in the clinic, many challenges must be overcome, such as identifying the route of administration, mRNA efficacy, specificity, and side effects. Vaccine immunotherapy against tumors has proved to be encouraging, promising, and safe, but phase III results are still needed for the application of these vaccines in clinical oncology.

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DISCUSSION

Lethal brain tumors have poor immune responses and are difficult to treat as they produce substances that escape the immune system (8,9). Targeting tumor antigens could reduce the development of the tumor and decrease immunosuppression. Microglia and infiltrating cells such as monocytes and lymphocytes can fuel tumor cell replication by producing pro-inflammatory and immunosuppressive cytokines (10). Targeting the tissue that provides nourishment and support of a malignant tumor, such as vascularized connective tissue and infiltrated immune cells, could be of therapeutic help. However, this stromal system, on one hand, constitutes a defense reaction of the organism to fight cancer; while on the other, it allows the tumor to develop by supplying it with the elements necessary for growth (11). Non-immune cells also contribute to the immunosuppressive environment by producing different compounds. The development of therapeutic vaccines against cancer are engaging many researchers around the world. Although cancer cells evade and suppress the immune system, it is hoped that in the future cancer vaccinations can create effective and side-effect-free anti-tumor immunity.

To date, many types of cancer vaccines have been tested which target a specific type of antigen, but so far none have been completely satisfactory (12). For example, astrocytes are cells that produce factors that feed the growth of tumor cells and favor metastasis, while neurons favor the proliferation of tumor cells by generating molecules such as neuroligin-3, a protein encoded by the NLGN3 gene that can act as a specific ligand of junction site for beta-neurexins and may be involved in central nervous system (CNS) synapses.

In recent decades, cancer therapies have had a significant improvement, also in terms of survival (13). However, despite new treatments, this effect does not apply to brain tumor therapies, which statistically, do not improve survival rates. Neoantigens are specific to the tumor and are generated by expressed gene mutations of the tumor cells (14). Therefore, personalized neoantigen vaccines can be created for therapy against certain types of tumors (15). Neoantigens can generate immune responses causing tumor rejection. In addition, neoantigenic (multi-epitope) vaccination is used for some cancers, including glioblastoma which usually has a relatively low number of mutations. This type of vaccination can stimulate neoantigen-specific CD4+ and CD8+ T lymphocytes, positively modifying the immune system of patients with glioblastoma (16). This method marks a new, encouraging step towards the immunotherapy of brain tumors.

CONCLUSIONS

In conclusion, the progress in the field of tumor immunotherapy and in vaccines against tumor antigens, is a promising new frontier in the battle against cancer. However, the results obtained thus far are not satisfactory and therefore more studies are needed to improve outcomes for this important disease which afflicts the worldwide population.

Conflict of interest

The author declares that they have no conflict of interest.

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