Editorial Commentary



# Immunotherapy approaches to beat tumors

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To understand the role, as well as the successes and prospects, of cancer immunotherapy, we must first take a glance at how the immune response works and behaves in the attack of tumor cells. Our immune system has the crucial function of fighting infectious agents and is at the ready to use this arsenal to prevent the emergence and expansion of cancer cells (1). At the same time, it has some counter-regulatory mechanisms to avoid an exaggerated reaction, which could be detrimental to the body itself. It is from this somewhat dynamic, yet generally balanced immune battlefield, that cancer takes advantage to gain ground. Tumor cells are able to escape the immune system in two ways: by hiding from our defenses or directly inhibiting the action of immune cells against tumor cells (1,2).

External intervention to aid our defenses in the fight against cancer is not exactly new. For decades, research groups around the world have been testing various immune intervention strategies (3). One immunotherapy approach that has yielded positive results is known as adoptive transfer. This involves activating immune cells taken from the patient in a laboratory setting and re-introducing them into the same patient to ensure a more effective cellular response against the cancer cells (4). Another method that modifies defense cells to our advantage is the use of CAR-T Cells. The main difference here is that immune cells are taken from the blood of the patient and genetically engineered in the laboratory to gain shock capability against cancer. Once injected into the patient, they unleash an attack against the tumor cells. There have been successful cases against some types of leukemia and lymphoma using this approach (5).

Other classical strategies in the fight against cancer involve the treatment with cytokines to regulate or stimulate an immune response. Cytokines are signaling proteins produced by white blood cells that enable communication between cells during an immune response (6). Therapy-based vaccinations are also part of immunotherapy, but they are quite different from those used for disease prevention. They are usually produced from the patient's own tumor cells or from substances collected from tumor cells, such as tumor-associated antigens, in order to treat established cancers by strengthening the body's natural defenses against the disease (7). Some vaccines have been tested for cancer prevention but the results have not yet proved satisfactory. However, one field that has demonstrated effectiveness is vaccination against cancer-related biological agents, particularly the human papilloma virus (HPV), associated with cancer of the cervix, anal canal and oropharynx (8).

A second line of immunotherapy tactics is based on drugs called checkpoint inhibitors. Cancer takes advantage by using natural mechanisms of turning off immunity to their advantage. Therefore this new generation of immunotherapeutic drugs relies on antibodies that inhibit these containment mechanisms, blocking molecules that act as a brake on our defense units in T lymphocyte-dependent cellular responses. This new way of treating the disease is the result of research that earned the 2018 Nobel Prize in Medicine. Immunologists, James Allison from the US, and Tasuku Honjo from Japan, discovered some of the molecules that, once annulled, allow the body to direct its forces against the tumor (9). Although initial studies with these drugs were performed with patients who did not respond well to other therapeutic options, we now know that immunotherapy can already be considered a the first choice, rather than a last resort, in some contexts. There have been significant advances in the fields of lung cancer and melanoma, the most aggressive skin tumor (10).

The use of this option depends on assessment by the oncologist, who will look at the type, stage of the tumor

and the patient's condition, and evaluate tests that help discriminate genetic characteristics of both the patient and the tumor. For example, we know that cancer cases that respond well to immunotherapy are those with a large number of mutations (11). Clinical research indicates the great advantages when the choice to use immunotherapy has been well assessed for the individual. The arrival of immunotherapy based on monoclonal antibodies has brought important new hopes for cancer patients. Antibodies are produced in the laboratory to bind to a specific target in tumor cells and can elicit an immune response that destroys cancer cells as well as marking them, making them easier for the immune system to find and identify (12). Current research now aims to combine immunotherapies with each other as well as with chemotherapies or targeting agents.

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## References

1. Dirnhofer S, Zippelius A. Cancer immunology, inflammation, and tolerance: an introduction. Virchows Arch 2019;474:405-6.
2. d'Onofrio A. Multifaceted kinetics of immuno-evasion from tumor dormancy. Adv Exp Med Biol 2013;734:111-43.
3. Zhao Z, Zheng L, Chen W, et al. Delivery strategies of cancer immunotherapy: recent advances and future perspectives. J Hematol Oncol 2019;12:126.
4. Ishikawa T, Okayama T, Sakamoto N, et al. Phase I clinical trial of adoptive transfer of expanded natural killer cells in combination with IgG1 antibody in patients with gastric or colorectal cancer. Int J Cancer 2018;142:2599-609.
5. Agarwal S, Weidner T, Thalheimer FB, et al. In vivo generated human CAR T cells eradicate tumor cells. Oncoimmunology 2019;8:e1671761.
6. Guimarães PPG, Gaglione S, Sewastianik T, et al. Nanoparticles for Immune Cytokine TRAIL-Based Cancer Therapy. ACS Nano 2018;12:912-31.
7. Westdorp H, Creemers JHA, van Oort IM, et al. Blood-derived dendritic cell vaccinations induce immune responses that correlate with clinical outcome in patients with chemo-naive castration-resistant prostate cancer. J Immuther Cancer 2019;7:302.
8. Hawes SE. HPV Vaccination: Increase Uptake Now to Reduce Cancer. Am J Public Health 2018;108:23-4.
9. Huang PW, Chang JW. Immune checkpoint inhibitors win the 2018 Nobel Prize. Biomed J 2019;42:299-306.
10. Formenti SC, Rudqvist NP, Golden E, et al. Radiotherapy induces responses of lung cancer to CTLA-4 blockade. Nat Med 2018;24:1845-51.
11. Nielsen JS, Sedgwick CG, Shahid A, et al. Toward Personalized Lymphoma Immunotherapy: Identification of Common Driver Mutations Recognized by Patient CD8+ T Cells. Clin Cancer Res 2016;22:2226-36.
12. Parakh S, King D, Gan HK, et al. Current Development of Monoclonal Antibodies in Cancer Therapy. Recent Results Cancer Res 2020;214:1-70.

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