

# A better understanding of cancer metabolism for a more efficient immunotherapy

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## Letter to Editor

Cancers are the second leading cause of death after cardiovascular diseases in industrialized countries, so there is an urgent need to deepen the knowledge of the metabolism and the microenvironment of cancer cells. In fact, new efficient therapeutic approaches are emerged in order to produce the energy required for blocking their proliferation, migration and metastasis. Cancer cells and host cells can use different bioenergetic fuels exchanged across plasma membranes via a special gate called Monocarboxylate Transporters (MCTs), passive transporters that ensure a bidirectional exchange depending on the concentration gradient of their substrates. Two MCT isoforms have been extremely studied and mainly expressed in different cancer cells called MCT1 and MCT4 [1]. Since MCTs gate the activity of different bioenergetics fuels, a new strategy for anticancer treatments will be to target them with specific drugs in the form of MCT inhibitors. Pr. Pierre Sonveaux team are still working on the characterization and the development of these anti-cancer strategies [2].

The immune system interferes usually in early tumour growth, but tumour cells have different mechanisms which escape to the immune response providing the formation of cancer [3,4]. Immunotherapy is one of the revolutionary approaches in the medical field which aims to fight certain types of cancer using resources of our own immune system. In addition, the 2018 Nobel Prize in Medicine and physiology was awarded to Pr. James Allison and Pr. Tasuku Honjo for their discoveries in the field of immunotherapy, the new anticancer strategy which is based on the destruction of tumours by stimulating the immune system. Both scientists worked independently on inhibiting cytotoxic T-lymphocyte antigen-4 (CTL-4) and programmed cell death (PD-1) proteins that consequently inhibit T cells from attacking normal cells [5]. However, like any type of treatment, many side effects are associated such as autoimmunity and nonspecific inflammation, which are fortunately less toxic and more tolerable than those due to chemotherapy.

New insights are emerging related to the virotherapy with functionally significant epigenetic modifications such as histone acetylation and/or DNA methylation. Epigenetic discoveries are in continuous progression and became promising novel targets of cancer therapy enhancing drugs already in use in clinic [6,7]. However, these molecules are toxic and nonspecific which urged the development of new molecules such as histone deacetylase inhibitors and HDACi. As an immunotherapy strategy, both were used in combination with a demethylating agent, decitabine for the treatment of malignant pleural mesothelioma [8].

The advantages of this therapeutic approach are already available and have shown good results against certain cancers as melanoma and some types of lung cancer. The improvement of this strategy was attested by the survival of patients that have shown a recovery state. However, the impossible implementation of the immunotherapy in some types of cancer including brain cancer is due essentially to a low number of resident immune cells in the central nervous system. The induction of autoimmune diseases is another aspect that must be taken to account after administration of certain antibodies that could cause death in patients. So, despite the great potential of this approach, it is certain that immunotherapy has its intrinsic limits on considering as a universal treatment of cancer.

Many advances rather demonstrated the benefits of a combination of immunotherapy with other conventional treatments as surgery, chemotherapy and radiotherapy in order to maximize successful treatment employed. So, cancer research is far from having said its last word!

Immunotherapy remains a very expensive treatment because it based on combination of several different antibodies to improve the therapeutic response. Therefore, the high cost of treatment will be restricted from one category of patients. Currently, glycan structure analysis presents an attractive benefit as a better therapeutic alternative than monoclonal antibodies due to their cost-effectiveness, reduced toxicity and side effects and high specificity [9]. The design of antigen delivery nanocarriers from natural lectins plant may influence the C-type lectin receptors (CLR) targeting efficacy. These CLR are primarily present on immune cells and integrating this novel delivery may provide a new generation of immunotherapeutic vaccine design for the treatment of various human cancers.

The cancer is very complex when it reaches a very advanced stage. The best way to respond effectively to this malignancy is to deepen the knowledge of the metabolism of cancer cells. In fact, the identification of the possible targets could lead to more efficient therapies. In addition, the high mortality rates of the cancer may be reduced by the prevention and the adoption of a healthy lifestyle that will prevent cancer from growing and expressing its immense destructive potential.

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