ANTI-TUMOR NANOVACCINES MAY HOLD THE KEY FOR IMPROVING CANCER IMMUNOTHERAPIES

Researchers from the University of Lisbon and the Tel Aviv University developed anti-tumor vaccines that may hold the key to improve the clinical outcomes of cancer therapies and be extremely relevant to design new cancer treatment strategies in the near future.

In a study just published in *Nature Nanotechnology* (*DOI: 10.1038/s41565-019-0512-0*), led by Prof. Helena F. Florindo, from the Faculty of Pharmacy, University of Lisbon, and Prof. Ronit Satchi-Fainaro, from the Sackler Faculty of Medicine, Tel Aviv University, describe that the combination of their novel biodegradable anti-tumor vaccines with therapies available in the clinic, leads to remarkable tumor inhibition and prolonged survival in preclinical models of this disease.

This research was performed by Dr. João Conniot, from the University of Lisbon, and Dr. Anna Scomparin, from the Tel Aviv University, and describes the design and development of biodegradable nanoparticles, optimized for the delivery of combinations of multiple bioactive molecules with complementary mechanisms of action, such as tumor markers and immune adjuvants, to antigen-presenting cells of the immune system. “Once these cells, mainly dendritic cells, interact with our nanoparticles, they become activated and can trigger an anti-tumor specific immune response, by interacting with T cells. We demonstrated that the presence of the simple sugar mannose on the surface of our nanovaccine was essential to achieve the extensive tumor infiltration of T cells capable of recognizing those malignant cells that expressed the specific tumor markers and thereby inducing their destruction. This nanovaccine does not target directly the tumor cells, but rather uses our own immune system to achieve the selective destruction of cancer cells. This is important for cancer patients who suffer from severe side effects caused by anticancer agents in normal tissues and organs, due to the lack of tumor selectivity. These not only limit patient quality of life, but also often prevent treatment continuation” explains Prof. Florindo.

Although there are already cancer therapeutic vaccines in the market, actually they are cell-based therapies that involve laborious procedures with isolation and culture of autologous cells from patients, often inducing adverse effects. This may lead to variable yield and quality of the treatment, depending on the condition of the patients and the stage of the disease. According to Prof. Florindo, “Our biodegradable

nanovaccines may constitute a potential off-the-shelf product as alternative to the cell-based vaccines. It is therefore a product to be administered to patients, acting by direct modulation of the patient immune system".

In this study, researchers also reported that the increased infiltration of immune suppressor cells within tumors, namely myeloid-derived suppressor cells, may be responsible for limiting the outcomes of cancer immunotherapies. "When these cells were inhibited, the full potential of our strategy was unveiled." explains Prof. Florindo.

"Currently, we are assessing the efficacy of our nanovaccines in several cancer models, such as breast, colorectal, and pancreatic." Prof. Florindo says. "Cancer is a very complex and multifactorial disease. The most aggressive forms do require the combination of different therapeutic strategies as an effort to increase the life expectancy of these patients. We believe that vaccination will play an important role in cancer therapies in the future, particularly in modulating the patients' own immune system. This will also improve the outcomes and safety of treatments already in the clinic, that heavily limits the lives of patients affected by such aggressive diseases" she concludes.

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