EXPERT OPINION:

The Use Of Oncolytic Viruses To Trigger Immune Response

There is a push in the immuno-oncology community to develop effective new therapeutic strategies with maximum patient benefit. One of these approaches is the use of oncolytic viruses, which have previously been viewed as tools for directly killing cancer cells but which are now seen to have potential triggering an immune response in the body against cancer. We sat down with Sonia Feau, Associate Director of Immunology at Oncorus, to learn more about her company's oncolytic viral platform and why they believe it will have such an impact on cancer treatment.

SONIA FEAU

Associate Director of Immunology, Oncorus

Sonia Feau, PhD is the Associate Director of Immunology at Oncorus and leads the Immunology group responsible for designing, optimizing and evaluating new immune enhancer payloads to be expressed by Oncorus' oncolytic viruses. Dr. Feau has 20 years of immuno-oncology experience. Prior to Oncorus, Dr. Feau worked at Merck & Co. and Merrimack Pharmaceuticals, where she proposed and evaluated several new immuno-oncology targets. Dr. Feau 's experience in Immunology spans both innate and adaptive immune responses. She received her post-doctoral training at the La Jolla Institute for Immunology in San Diego, CA with Professor Stephen Schoenberger where she studied CD8 T cell memory formation after bacterial and viral infections. Sonia received her Ph.D. in Immunology and Biotechnology from the University of Milano-Bicocca, Italy and University Toulouse III, France studying dendritic cells biology.

Your company's platform is focussed on oncolytic viruses. Why do you think this approach could be so transformative for immuno-oncology?

Oncolytic viruses induce tumour cell killing. This killing releases tumour antigens (Ag) as well as DAMPS (damage-associated molecular patterns) and PAMPs (pathogen-associated molecular patterns) which activate the antigen presenting cells (APCs). The activated APCs then migrate to the draining lymph-nodes to present the tumour Ag to the T cells. The specific T cells are activated and circulate to the tumour to kill the cancer cells. In OV therapy the tumour Ag do not need to be known a priori. OV-mediated lysis elicits many tumor antigens. The immune system selects out the most potent antigenic targets. Since the response is likely to many different antigens, it may be more robust and prevent tumor escape/ recurrence. Moreover, those viruses can be armed with payloads that can enhance those immune responses which make them very potent to revert the immune suppression in the tumour microenvironment (TME). Clinical data (albeit uncontrolled) suggest a strong benefit, with roughly a doubling of response rate in melanoma patients by combining the first generation OVs (i.e., T-VEC (oHSV) and, CAVATAK (CVA21)) with both PD-1 and CTLA4 checkpoint inhibitors

What are the main challenges of developing oncolytic viruses?

The main challenges in the oncolytic virus field is to solve the trade-off of safety vs. efficacy. Attenuation of viral replication to prevent replication in healthy tissues is often done by deleting genes that are also important for virus replication in tumor cells and resistance to host anti-viral responses. We believe at Oncorus that we may have solved this problem by designing novel microRNA- based switches to allow unencumbered replication only in tumor cells. The second challenge is the ability to generate systemic immune responses.

Our first candidate is injected intratumorally and elicits strong systemic response in preclinical models of cancer. We are also developing a novel synthetic virus platform that allows for repeat intravenous administration of oncolytic viruses.

What are your main priorities across the next year?

Our main priority at Oncorus is to drive the successful clinical evaluation of ONCR-177, our first clinical candidate. Our second priority is to push toward an IND for our first, armed synthetic viral immuno-therapy programs.

What are the most important technologies impacting immuno-oncology currently?

The combination of RNASeq, IHC multiplexing, Cytometry, Imagery have allowed a better understanding the complexity of the tumor microenvironment (TME) and what are the signals that can predict a better response to Immuno-therapies.

Outside of oncolytic approaches, what therapeutic modalities do you think have the most potential in immuno-oncology currently?

mRNA delivery is a very interesting approach to promote the expression of immune stimulatory genes by tumor cells or stromal immune cells. A key challenge remains the specific delivery to the desired cell type and sparing normal tissues such as liver. Progress have been made in delivering mRNA to APCs to elicit specific T cell responses.

Antibodies modalities, such as bispecific or probody, are also a developing area, in so far that they allow a stronger and targeted immune modulation at tumor sites. They can be engineered structurally to create a variety of formats for modulating half-live, biodistribution and pharmacodynamic activity and be targeted to multiple targets potentially reducing toxicity.

What are the advantages of developing combination therapies in immuno-oncology?

Cancer is a very complex disease that involves a complex interplay of multiple cell types: cancer cells, stroma and Immune cells, this is the reason why the one-target one-drug concept has only had great success in monogenic disease such as CML. For most cancers, combination therapy is a requirement, a concept that brings us back to the field of oncolytic viruses, and particularly ONCR-177, that can both elicit direct killing of tumor cells and express in tumors a potent combination of immune payloads that may otherwise not be achievable with the usual systemic route of administration.

Find out more about Sonia and her involvement with the Immuno-Oncology Congress HERE