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Title: Using intratumoral myeloid dendritic cells to reinvigorate the cancer immunity cycle

Cancer immunotherapy aims to restore the response of our immune system to eradicate tumors. The development of immune checkpoint inhibitors has boosted the field, but it is clear that these drugs only work in a proportion of patients. Therefore we focus on combining immune checkpoint inhibition with myeloid dendritic cell (myDC) vaccination to enhance the stimulation of a tumor-specific T cell response. Trafficking of myDCs into tumors is often defective and by reconstituting these myDCs by intratumoral injection we postulate to reinvigorate the cancer immunity cycle. By combining intratumoral myDC vaccination with administration of oncolytic viruses (T-VEC) or intratumoral immune checkpoint antibodies (inducing tumor cell death via ADCC), we aim to provide an elegant source of autologous tumor antigens.

In our first phase I clinical trials, we used non-manipulated CD1c (BDCA-1)$^+$ myDCs isolated from the blood of cancer patients for intratumoral administration in immune checkpoint refractory patients. The treatment was well tolerated with mainly low-grade adverse events and provided encouraging first indications towards its anti-tumor activity.

In this project, we aim to extensively analyze the phenotypic and functional characteristics of myDC isolated from cancer patients and explore their interaction with oncolytic viruses and immune checkpoint antibodies. Upon therapeutic administration of myDCs to patients, we will evaluate their localization in tumors using RNAScope and explore any changes to the immune infiltration in the tumors by multiplex immunohistochemistry using longitudinal on-treatment biopsies. Finally, since we use a tumor antigen agnostic approach, we aim to unravel which T cells mediate tumor cell eradication and which antigens they recognize. In a preclinical setting, we aim to optimize the composition of our myDC vaccine and completely unravel its biological function.

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