B CELL RECRUITING ONCOLYTIC VIROTHERAPY (B-ROV): A NOVEL APPROACH TO INDUCE TERTIARY LYMPHOID STRUCTURES FOR ENHANCED IMMUNITY TO BREAST CANCER.

Kwame Twumasi-Boateng[1], David R. Kroeger[1], Parv N. Chapani [1,2], Dakota J. Peacock[1,2], Jessica L. Pettigrew[1], Katy Milne[1], and Brad H. Nelson[1,2,3]

[1]Trev and Joyce Deeley Research Centre, British Columbia Cancer Agency, Victoria BC
[2] Department of Biochemistry and Microbiology, University of Victoria, Victoria BC
[3] Department of Medical Genetics, University of British Columbia, Vancouver BC

Rationale: Tertiary lymphoid structures (TLS) are associated with robust antitumor immune responses and favorable prognosis in breast cancer and other malignancies. TLS are highly organized, resemble secondary lymphoid organs and are thought to be sites where antitumor immune responses are initiated and amplified. TLS formation is induced by the CXCL-13, a chemoattractant for B cells. We hypothesized that using a recombinant oncolytic virus (OV) to force CXCL13 expression within tumor tissue would result in the formation of TLS and increased anti-tumour immunity.

Methods: A mCXCL13 transgene was engineered into a tumour-selective strain of VSV (VSV-CXCL13). Mice bearing orthotopic NOP23 mammary tumours were treated with PBS, VSV-CXCL13, or VSV encoding an irrelevant transgene (VSV-GFP). Tumour growth was monitored and lymphocytic infiltrates were assessed by IHC.

Results: T cell and B cell infiltrates were negligible in PBS-treated animals. Both strains of VSV induced robust infiltration of tumours by T cells within 10 days of treatment. As predicted by our hypothesis, VSV-CXCL13-treated tumours showed a >4 fold increase in the number of tumour-infiltrating B cells compared to VSV-GFP treated tumours. This was accompanied by multiple lymphoid aggregates composed primarily of B cells. Median survival was 33 days for PBS-treated animals and 37 days for VSV-GFP-treated animals (n.s.). By contrast, VSV-CXCL13 treatment resulted in a median survival of 56 days ($p = 0.0136$).

Conclusion and future directions: An oncolytic virus encoding CXCL-13 induced B cell infiltrates and aggregates in mammary tumors, and this was associated with improved tumour control. We are currently performing time-course experiments to assess whether VSV-CXCL13-induced lymphoid aggregates ultimately evolve into bona fide TLS. We are also determining whether the recruitment of B cells following VSV-CXCL13 treatment results in the production of tumour-reactive antibodies and more potent anti-tumour T cell responses through enhanced antigen-presentation.