Research project summary

Development of Viral Sensitizing Antibody Drug Conjugate and Oncolytic virus Combination Regimens for the Treatment of Breast Cancer

- Principal Investigator: Jean-Simon Diallo
- Co-Investigators: Rozanne Arulanandam, Fanny Tzelepis
- Partner Organization: Center for Drug Research and Development (CDRD)
- Awarded $776,475 from the Canadian Institutes of Health Research (CIHR) in January 2018

Oncolytic viruses are safe viruses engineered to specifically infect and kill cancer cells, and can also stimulate the immune system to recognize tumors. Although they have the potential to treat a broad range of malignancies, the inconsistency of treatment response remains a major challenge and poor infection of tumors is a recognized issue. We have pioneered the development of small molecules that we termed "viral sensitizers" that are able to sensitize tumors to viral infection and potentiate the activity of oncolytic viruses. However, for these molecules to act at maximum efficacy, they currently need to be injected directly into the tumor, which is often not possible. To overcome this issue, we propose to exploit a technology that allows for targeting chemotherapeutics to tumors by piggy-backing on tumor-targeting antibodies. This strategy has notably led to Kadcyla®, an approved chemotherapy-conjugated version of Trastuzumab® (Herceptin®) that targets the tumor protein HER2 expressed in a subset of breast cancers. Coincidentally, we have discovered that the type of chemotherapeutic conjugated to Kadcyla has viral sensitizing properties and we have gathered data in cell lines and in immune-deficient mice carrying human breast tumors that combining an oncolytic virus with Kadcyla leads to improved cancer control. This particular approach could be rapidly tested in humans, but before this, we must gather more data in mice with HER2-expressing breast cancer that have immunological characteristics that more closely resemble what we would observe in a human. Furthermore, we will attempt to modify this strategy to deliver our most promising viral sensitizing molecules, and to bypass the need for tumors to express HER2 in order to be effective. To maximize the likelihood of success and eventual impact on cancer outcomes, we have partnered with antibody-drug conjugation experts at the Centre for Drug Research and Development.

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