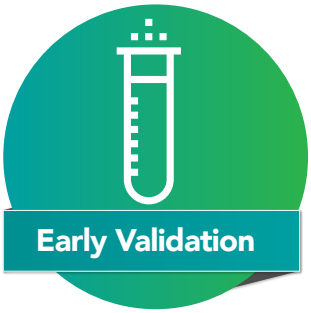
PROJECT TITLE

Identifying an MLH1 small molecule inhibitor for combination with immune checkpoint inhibitors



PRINCIPAL INVESTIGATOR

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PROJECT SUMMARY

Prostate cancer (PCa) is the most common cancer to affect Canadian men. One in seven men will be Recently, a new class of cancer drugs called immunotherapies have entered the oncology field. These drugs are different from chemotherapy in that they do not directly kill cancer cells but help the immune system better attack tumours. The main advantage of immunotherapy is the ability of these drugs to confer long-term remission to patients with advanced cancers. However, most cancers, including pediatric cancers, do not respond to these treatments.

We aim to develop a new drug that will make most types of cancers responsive to immunotherapy, including neuroblastoma, the most common cancer in babies, and breast cancer, the most common cancer in women. Currently, immunotherapy does not work in neuroblastoma because the tumour can stay hidden from the immune system and not recognized by the immune cells that immunotherapy aims to help. Immunotherapy does not work that well in breast cancer either. We believe it is possible to make neuroblastoma and breast cancer tumours responsive to immunotherapy with a new drug that makes these cancers visible to the immune system. Like all other cells, cancer cells have mechanisms to protect their DNA from unwanted changes. In our preliminary studies, we have shown that disabling a specific protein called MLH1, that is key in a DNA repair pathway known as mismatch repair, can make neuroblastoma tumour cells visible to the immune system and consequently responsive to immunotherapy. Here we will further establish MLH1 and its binding partner PMS2 as proper targets for a drug discovery campaign by doing experiments in mouse and human cell lines. We will also develop screening assays to enable our team to find small molecules that will inhibit MLH1. This will allow us to take the initial steps to developing a new cancer drug that can be combined with immunotherapy to treat neuroblastoma and breast cancer. Developing this new drug will potentially open a new line of treatment not only for those cancers but also for most solid tumours that currently do not respond to immunotherapy.