PROJECT TITLE

Validation and assay optimization for a novel breast cancer target

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PROJECT SUMMARY

Breast cancer is the second most commonly occurring cancer in Canadian woman, and the second leading cause of cancer-related deaths after lung cancer. If diagnosed early before tumour cells have spread to distant sites, most patients survive after treatment. However, if the tumour has spread to distant sites including include the lungs, liver, bones, or brain, survival rates are considerably lower, and treatment primarily focuses on disease management and improving quality of life. As a result, there is an urgent unmet need to develop new treatments that would help to reduce the spread of breast cancer cells as well as reducing tumour growth.

Metastatic breast cancer may be treated with combinations of surgery, radiation therapy, immunotherapy, hormonal therapy and chemotherapy. More recently, several key drivers of breast cancer have been identified, and they may be targeted with specific forms of therapy tailored to the individual patient. However, no drugs currently used in the clinic was designed to both reduce the growth of breast cancer patients and to target the processes that enable the spread of metastatic cells.

An internal structure in cells akin to a skeleton, known as the cytoskeleton, undergoes dramatic rearrangements to enable individual tumour cells to break away from the original tumour, to move through tissues, enter blood or lymphatic vessels, and establish new growths at different sites. Our question is whether blocking a specific protein has been shown to be a major regulator of cytoskeleton organization and dynamic rearrangements would be an effective way to reduce the metastatic spread of breast cancers.

By expressing and purifying the protein under study from bacteria, we have established a set of procedures to determine how active the protein is when combined with drug-like compounds. The structure of this protein was used to choose compounds from a virtual library that might block its function. A subset of candidate compounds was made and tested, and one compound did indeed block the activity of the protein. By varying the structure and composition of the hit compound, we continue to learn which parts can be changed to increase its effectiveness. In parallel, we are conducting experiments on breast cancer cells grown in the laboratory to determine how the ways in which the protein under study contributes to breast cancer cell growth and spread.

Ultimately, the goal of the study is to enable the development of novel drugs that act by blocking both the growth and spread of metastatic breast cancers. During the process of developing such a drug, it is also anticipated that a substantial body of knowledge will be acquired regarding metastatic breast cancer, which will also enable additional future drug discovery efforts on this and other drug targets.