



Canadian
Cancer
Society



Breast Cancer National Research Grant Program

Listed by panel in alphabetical order

Panel I

Davey, Scott

Queen's University

A functional approach to assessing variants of unknown significance in BRCA1 carriers

Mutations in a gene known as BRCA1 can result in a significantly increased risk of developing breast cancer. Genetic testing for BRCA1 mutations has become an option for families experiencing high rates of breast and other cancers, to identify which family members might be most at risk. However, not all mutations cause cancer, and for approximately 15%–20% of the mutations identified, whether they cause cancer or not is unknown. This means that people with these mutations are not currently able to use the information to make informed decisions about their care. Dr Scott Davey will build on previous CBCF funding that resulted in a tool called a BRisk assay, which identifies whether these mutations are harmful (i.e. cause cancer) or not. He has put together a Canada-wide team to support patient enrolment for the study, as well as to inform and support the broad implementation of this tool so that patients have more information to help them with complex decisions regarding their families and their health.

Roseline Godbout

University of Alberta

Targeting p53-mutated triple-negative breast cancer: role of Nuclear Factor IB

Triple-negative breast cancer (TNBC) – so named because it lacks estrogen, progesterone and HER2 receptors – is a particularly difficult to treat type of breast cancer because no targeted therapies currently exist. Researchers have discovered that mutations in a protein called p53 are commonly found in TNBC. Dr Roseline Godbout and her team have discovered what they believe is the cause of tumour cell growth in TNBC with mutated p53 – a protein called Nuclear Factor IB – and plan to further explore its role in this research project. If successful, this research could lead to the development of targeted therapies for TNBCs with p53 mutations.

Gunning, Patrick

University of Toronto

Small molecules targeting aberrant STAT3 activity in breast cancer: killing breast tumour cells and inducing an anti-tumour immune response

This project focuses on a new type of molecule that potently and selectively kills breast cancer cells over normal healthy cells. Specifically, the molecule targets breast cancer cells with high levels of the HER2 protein (HER2+) and those lacking estrogen, progesterone and HER2 receptors (triple-negative). These molecules target a protein called STAT3, which has been shown to play a key role in tumour progression and survival. In the lab, these molecules have shown they can stop tumour growth, while simultaneously triggering the immune system to attack the tumour cells. Dr Patrick Gunning and his team hope this discovery means a potential new therapy for breast tumours with a poor prognosis. In this research, they plan to improve these molecules to the point where they can create a new treatment for aggressive triple-negative and HER2+ breast cancers.

Johnston, Brent

Dalhousie University

Targeting breast cancer via combined natural killer T cell immunotherapy and oncolytic virotherapy

Breast cancer continues to be the most common type of cancer and the second leading cause of cancer deaths in Canadian women. Using the body's own immune system to fight cancer has become a key goal for cancer researchers. Dr Brent Johnston and his team have been examining immune cells called natural killer T (NKT) cells that, when activated by immunotherapy, can control tumour growth and prevent cancer spread (metastasis) in the lab. When combined with other therapies, such as engineered viruses, it is believed that these NKT cells could exert an even greater effect on cancer cells. This research will establish the effectiveness of combining immunotherapy to activate NKT cells with engineered viruses to treat aggressive and metastatic breast cancers.

Khokha, Rama

Princess Margaret Cancer Centre – UHN

Rationalized depletion of mammary progenitors as a program for breast cancer prevention

Researchers believe that breast cancer originates in stem and progenitor cells in the breast – cells that have not yet fully developed and that can divide numerous (and sometimes an infinite number of) times. Dr Rama Khokha has assembled a cross-disciplinary team – including biologists, clinicians, bioinformaticians and those committed to developing new anticancer drugs – to identify new drugs that will deplete breast stem and progenitor cells and prevent cancer formation. From previous CBCF-funded research, they have already identified 2 classes of drugs that they believe will accomplish this objective. Their long-term goal is to identify new therapeutic options to prevent breast cancer and bring them forward for testing in clinical trials. This research could provide women at high risk for breast cancer with an effective prevention alternative to invasive surgery.

Kotsopoulos, Joanne

Women's College Hospital

Delineating a role of RANKL/OPG signalling on breast cancer development

Women with certain BRCA mutations face a high lifetime risk of breast cancer compared to women in the general population. Prevention options are needed for women at high risk, and a better understanding of how breast cancer develops will help to identify new possibilities. Dr Joanne Kotsopoulos and her team have identified a potential marker of risk in women carrying BRCA mutations that will be explored further in this project. They demonstrated that BRCA mutation carriers who developed breast cancer had lower levels of a protein called osteoprotegerin (OPG) in their blood than women who did not develop the disease. They will confirm in this project whether OPG levels accurately predict whether a woman will develop breast cancer or not. If confirmed, this finding can also be used to target treatments for women at higher risk of developing breast cancer.

Lee, Jonathan

University of Ottawa

Control of breast cancer by cooperation between the PI4KIII β lipid kinase and the Rab11a GTPase

Breast cancer development is a complex process that researchers continue to explore. With previous CBCF funding, Dr Jonathan Lee and his team have been focusing on a gene called PI4KIII β , believed to directly promote breast tumour development and spread (metastasis). In this project, they will enhance their understanding of the gene's function and how it contributes to cancer cell growth, develop new models of breast cancer related to PI4KIII β and ultimately work toward identifying a drug that inhibits PI4KIII β function and can be further explored for patient use.

Ross, Colin

University of British Columbia

Pharmacogenomic discovery of predictive cardiotoxicity biomarkers in breast cancer patients receiving anthracycline chemotherapies

One of the most widely used and effective chemotherapies for breast cancer treatment is anthracycline chemotherapy. Anthracycline treatment has contributed greatly to the increased survival from breast cancer over the past several decades, but its use is associated with a potential for severe and occasionally life-threatening damage to the heart. Genetic factors have recently been linked to the risk of experiencing these side effects, and Dr Colin Ross and his team have developed a genomic test for pediatric patients to predict this risk. In this project, they will attempt to develop a similar test for adult breast cancer patients. If successful, this test would allow physicians to more accurately assess the risk of serious side effects due to anthracycline chemotherapy and provide personalized chemotherapeutic options to patients.

Panel II

Cescon, David

Princess Margaret Cancer Centre – UHN

Novel cell-free DNA assays to predict relapse and guide systemic therapy in early breast cancer

Breast cancer that has spread to other parts of the body is responsible for the majority of deaths related to breast cancer. Even when breast cancer is diagnosed early, cancer cells may have escaped the tumour, eventually growing in another part of the body, resulting in metastatic disease. Treatment with chemotherapy and other drugs that travel throughout the body (known as systemic therapies) can successfully eradicate this microscopic disease, but not all women diagnosed with breast cancer are given these treatments – nor do they need to be. Dr David Cescon and his multidisciplinary team of researchers will work to develop a more accurate tool for identifying patients with microscopic disease that has escaped the original tumour, using a technique that involves testing blood samples for tumour DNA shed from cancer cells. If a blood test can be successfully created, it will not only help to identify women most at risk of having their cancer come back, but will also recognize which treatments are most effective for a given patient, ultimately reducing breast cancer mortality.

Lohrisch, Caroline

BC Cancer Agency

LA LEAST. Luminal A, Limited Endocrine Adjuvant Systemic Therapy, a phase II trial of abbreviated hormone therapy for low-risk hormone receptor–positive, HER2-negative early breast cancer

Endocrine therapy, also known as hormone therapy, is a long-standing treatment for estrogen receptor–positive breast cancers. Where 5 years of endocrine therapy was originally thought to be optimal, we now know that 10 years of therapy is better for women whose breast cancer has a high likelihood of coming back. For women with breast cancer who have a very low risk of recurrence, the benefit from taking these drugs is not as pronounced and the harms may in fact outweigh the benefits of long-term use. Dr Caroline Lohrisch and her team intend to study whether 2 years of endocrine therapy is sufficient for women with very low risk breast cancers – those with less than a 5% chance of their cancer recurring. This research will help women to make more informed decisions regarding their treatment. Uniquely, this study will also measure the fear and anxiety of recurrence that accompanies a breast cancer diagnosis, allowing the researchers to better understand the kinds of psychological support required by low-risk breast cancer patients after a diagnosis.

Metcalfe, Kelly

University of Toronto

Breast cancer treatment in women with PALB2 mutations

PALB2 is a gene shown to be associated with breast cancer risk. Testing for mutations in this gene and others is available through genetic testing. There is some early evidence that PALB2-associated breast cancers may be aggressive, and survival may be worse when compared to women without a PALB2

mutation. However, it is unclear how women with PALB2-associated breast cancer should be treated to reduce the chance of recurrence and death. Dr Kelly Metcalfe and her team will build on previous CBCF-funded work to determine the 5-year survival rates and the optimal breast cancer treatment for this group of breast cancer patients. The results from this study could influence both the treatment and survival of women with PALB2 mutations.

Nielsen, Torsten

University of British Columbia

Clinical utility of immune response biomarkers for aggressive breast cancers

Individuals do not react to treatments in the same way. To maximize the benefit and minimize the harm from new immunotherapy drugs being tested in breast cancer patients, it is critical to develop tools that can accurately identify which patients will respond to these drugs and which will not. Dr Torsten Nielsen and his team, who successfully developed the PAM50/Prosigna risk test, plan to evaluate a range of different tests, with the goal of identifying those that best predict which patients will respond favourably to treatments that prime the immune system to fight breast cancer.

Shepherd, Lois

Queen's University

Quantitative standardized estrogen receptor (ER), progesterone receptor (PR) and human epidermal growth factor receptor 2 (HER2) for prognostic and/or predictive index for response to adjuvant aromatase inhibitors exemestane or anastrozole

The decision to give hormone or anti-HER2 therapy to someone with breast cancer is determined by whether their tumour expresses estrogen (ER), progesterone (PR) or HER2 receptors, often regardless of the degree of expression due to inconsistencies in measurement of the receptors. Evidence shows, however, that the risk of relapse for patients with high levels of these receptors is much different than patients with low levels. Dr Lois Shepherd and her team plan to standardize the assessment of these markers and develop new clinical tools that could significantly impact decision-making for and improve the treatment of breast cancer.

Whelan, Timothy

McMaster University

Prospective cohort study evaluating risk of local recurrence following breast conserving surgery alone in low-risk luminal A breast cancer

Radiation to the breast is often given after breast conserving surgery in women diagnosed with early-stage breast cancer to reduce the risk of recurrence. Radiation can have significant short- and long-term side effects. Research has demonstrated that there is a subset of women with breast cancer who may be able to avoid radiation altogether given their very low risk of recurrence. Dr Timothy Whelan and his team will continue their research with low-risk breast cancer patients to identify which characteristics

may be associated with a very low risk of recurrence, allowing some women to avoid unnecessary radiation – and improving quality of life without affecting survival.