March 2018 (i2I-18) Competition Awarded Innovation to Impact Grants

Listed by panel in alphabetical order

I1a Biomarkers and Genomics

Brooks-Wilson, Angela
BC Cancer Agency (Vancouver)

Genetic buffering in cancer

The risk of many diseases such as cancer and Alzheimer's disease increases as you age. Some people, known as Super-Seniors, are lucky enough to live to an old age without these developing diseases even if they have genetic risk factors that increases their odds of getting cancer. Dr Angela Brooks-Wilson and her team are leading a study looking for small changes in the DNA of these Super-Seniors. Their goal is to identify variations that protect against known genetic risk factors. By understanding how that protection is conferred, their research will provide valuable insights into how we can design better prevention strategies that mimic these protective DNA variations.

Karsan, Aly
BC Cancer Agency (Vancouver)

Mechanisms of resistance to 5-Azacytidine

Myelodysplastic syndromes (MDS) are a group of diseases in which the bone marrow doesn't make enough healthy mature blood cells. In 1 out of 3 people with the disease, MDS will progress to acute myeloid leukemia. There are few treatments available for MDS. The main therapy is a drug called 5-azacytidine. This drug only works in half of all patients and even in those patients, the drug eventually stops working. Dr Aly Karsan and his team are trying to understand why. The researchers are turning to the stem cells that give rise to cancer cells to gain an understanding of why some patients respond to 5-azacytidine while others don't. By understanding the reasons behind 5-azacytidine resistance, the researchers hope to develop a test to help predict which patients will respond to the drug. This will spare some patients from the toxic side effects of a drug that will not work for them.

I1b Gene Regulation and Cell Biology

Gingras, Anne-Claude
Mount Sinai Hospital

Endocytic organelles as sites of cellular growth control

Human cells are always asking the question, to grow or not to grow? The decision is largely made by special machines in the cell called lysosomes, which act like little stomachs by eating, digesting and recycling nutrients. Unlike healthy cells, which rely directly on the food we eat, cancer cells mostly depend on recycled nutrients scavenged from their surroundings. Using sophisticated technologies developed with a previous CCS grant, Dr Anne-Claude Gingras and her team are learning how cancer cells can turn these recycled materials into fuel for growth. By understanding this key process, which is at the heart of cancer development, they hope to identify new and innovative ways to treat the disease.

Kislinger, Thomas
Princess Margaret Cancer Centre - UHN

Molecular analyses of the protocadherin fat 2: a novel therapeutic target in head and neck cancers

Roughly 60% of cancer drugs target proteins found on the surface of cancer cells. With funding from CCS, Dr Thomas Kislinger and his team conducted a large, comprehensive study of surface proteins found on different cancer cells. This work led them to discover a new surface protein called FAT2 that is common in head and neck cancers, the fifth most common cancer worldwide. The researchers are now trying to understand the role of FAT2 in head and neck cancer development. They are also partnering with Canada's national Centre for Drug Research and Development to develop drugs that can target FAT2 and become new therapies for this common cancer.

Pratt, Christine
University of Ottawa

Role of the DNA damage response in promotion of BRCA2 breast cancer

Women who have a mutation in the BRCA2 gene have a 60-80% risk of developing breast cancer in their lifetime. This is because BRCA2 is important for repairing DNA and without it, cells are unable to fix the mistakes that arise in DNA every time a cell grows and divides into two. Dr Christine Pratt and her team found that cells missing BRCA2 also make signals that allow them to continue to grow and replicate despite the mistakes accumulating in their DNA. The researchers are trying to understand how these signals drive abnormal cell growth and whether blocking these signals can stop the uncontrollable cell growth seen in cancer. Their work will also shed light on whether these signals can be used to predict breast cancer risk in women who do not have mutations in the BRCA2 gene.

Stirling, Peter
BC Cancer Agency (Vancouver)

Exploiting R-loop associated genome instability in high grade serous ovarian cancer

Mutations in DNA drive cancer formation and progression. Dr Peter Stirling and his team are working to uncover where mutations come from in a common and deadly type of ovarian cancer called high grade serous ovarian cancer (HGSOC). The researchers found that when DNA is copied in growing cancer cells, they are likely to form a shape called an R-loop. Healthy cells have tools to prevent R-loop formation which, in turn, protects DNA from getting damaged and allows the cell to survive. Cancer cells, on the other hand, typically lack these tools, making them especially vulnerable to DNA damages caused by R-loops. Dr Stirling and his team are studying how R-loops contribute to the development of HGSOC. They will also look for ways to deliberately form R-loops in cancer cells with the hopes that the DNA damages caused by these R-loops will cause the cancer cells to die.

I2 Imaging and Technology Development

Duzenli, Cheryl
BC Cancer Agency (Vancouver)

Reducing toxicity in whole breast adjuvant radiotherapy using a novel breast positioning device

Women having radiation therapy for breast cancer often experience severe skin reactions in their skin folds when the breast is not supported during therapy. Up to 40% of patients undergoing radiation therapy experience painful and worrisome skin reactions, which impacts their quality of life and discourages them from continuing this potentially life saving therapy. Without good breast support, the heart and lung may also receive more radiation than they need to, increasing the risk of secondary cancers. Dr Cheryl Duzenli and her team have created a new breast positioning device that reduces skin folds and improves breast positioning during radiation without interfering with the treatment. They will now conduct a randomized clinical trial to determine whether the new positioning device is more effective at preventing skin reactions than currently used positioning techniques. If successful, this device could improve the quality of life and long-term health of breast cancer survivors.

Hirasawa, Kensuke (Ken)
Memorial University

Improving photodynamic diagnosis and therapy by targeting the MEK-ABCB1 axis

Protoporphyrin IX (PpIX) is a glow-in-the-dark molecule that can build up only in cancer cells. Its brightness is used to distinguish cancer from healthy tissue during surgical removal of tumours. Cancer cells with high levels of PpIX can also be killed with light, making it a valuable tool to destroy any remaining cancer cells after surgery. With a previous Innovation Grant from CCS, Dr Ken Hirasawa and his team discovered that some drugs can cause cancer cells to accumulate even more PpIX. Now, the researchers are testing if these drugs can enhance the effectiveness of PpIX used to detect and treat cancers. To do this, they will first develop a drug delivery system that uses microscopic particles called nanoparticles. The drugs they are using have already shown to be safe and effective in clinical trials for other cancers. If the researchers are successful, their combination strategy could directly improve the success of cancer surgeries.

Martel, Anne
Sunnybrook Research Institute

Quantitative assessment of tumour burden in breast cancer

Women with locally advanced breast cancer may be treated with chemotherapy before surgery in order to shrink the tumour first. How the tumour responds to this therapy is determined by pathologists who examine the breast tissue removed during the surgery. By looking for cancer cells in the breast tissue and estimating the size of any remaining tumours, the pathologist can estimate how likely it is that the cancer will come back. However, this is a time-consuming process that can give different results depending on the pathologist. Dr Anne Martel and her team are developing automated tools to carry out these measurements by training a computer program to search for cancer cells and measure the tumour size. Their program can also tell if a cancer is invasive or not. The researchers can then combine all of the information from the computer program to create a score that can help predict whether a cancer will return. A fully automated program like this will help ensure that healthcare decisions can be made faster and more accurately, improving the patient experience and outcomes.

Schaffer, Paul
University of British Columbia

Pursuit of a clinical application for direct, aqueous, F-18 photo-fluorination of amino acids and peptides

Many cancer imaging techniques rely on radioactive molecules called tracers that allow doctors to see tumours noninvasively and make a diagnosis. The development of newer, more targeted tracers has been slow because radioactive fluorine, the most widely available radioactive molecule, is exceptionally hard to work with. Fluorine's chemistry makes it very difficult to incorporate into new tracers. With a previous Innovation Grant from CCS, Dr Paul Schaffer and his team have developed an innovative way to add fluorine to a wide range of cancer-targeting molecules. Building on this success, the researchers will use this new technology to create better tracers for breast and prostate cancer. These tools will allow doctors to detect cancer earlier, diagnose it faster and more accurately, and monitor the disease better.

I3 Immunology, Signalling and Stem Cells

Nelson, Brad
BC Cancer Agency (Victoria)

The interface of malignant and immunologic clonal dynamics in high grade serous ovarian cancer: towards actionable immunotherapy strategies

Not all the cells in a tumour are identical. Most cancers are complex mixtures of tumour "cells" with distinct biological features. Dr Brad Nelson and his team previously discovered that patients whose immune systems react strongly against their tumours have higher survival rates but the strength of the immune response can vary widely even within the same patient. Most patients have at least one tumor site that is protected from the immune system by physical barriers that block the entry of immune cells. The researchers are now investigating how these barriers are made and what drugs might be used to disrupt them. The results will help us design more effective immunotherapies for cancer.

Reedijk, Michael
Princess Margaret Cancer Centre - UHN

Targeting USP9x to inhibit Notch in triple-negative breast cancer

A tumour is made up of not only cancer cells, but also many normal, healthy cells. Dr Michael Reedijk and his team are studying how the cancer cells trick the normal cells in the tumour to help the cancer grow and spread. They discovered that the tumour environment, which is low in nutrients and oxygen, turns on a protein called Notch. Notch plays a key role in allowing cancer cells to not just survive in these difficult conditions, but to thrive and spread. The researchers also discovered that in order for Notch to work, it requires another helper protein. They will now test drugs that blocks the helper protein to see if they can prevent Notch from working, therefore blocking tumour growth.

Siegel, Peter
McGill University

Deciphering mechanisms that control focal adhesion dynamics and invadopodia formation in metastatic breast cancer

Metastatic breast cancer is a lethal form of the disease that has spread from the breast to other places in the body. A key feature of metastatic breast cancer cells is their ability to move through andinvade tissues. Dr Peter Siegel and his team are studying the mechanics of how breast cancer cells move by using innovative and sophisticated techniques to study the cells as they move in real time. These include powerful microscopes that will allow them to see the cells move from one tissue to another. By understanding how cancer cells move, the researchers hope to pinpoint important structures and proteins that could be targeted by drugs aimed at preventing cancer spread.

Zuniga-Pflucker, Juan Carlos
Sunnybrook Research Institute

A simple and effective approach to generate T cells for immune-regeneration

T cells are critical for a working immune system but are often damaged by cancer treatments like radiation and chemotherapy. Without enough healthy T cells, patients are at risk of infections and cancer relapse. Dr Juan Carlos Zúñiga-Pflücker and his team are developing an innovative method to create T cells in the lab using stem cells found in the blood. They have figured out a way to turn these stem cells into functioning T cells and are now trying to scale up their system so that enough cells can be made for clinical use. Giving these lab-made T cells to patients after their cancer treatment could help restore their immunity and reduce the risk of complications. Building on this work, Dr Zúñiga-Pflücker and his team are also designing and producing specialized T cells that recognize and kill cancer cells as a form of immunotherapy.

I5 Prevention and Quality of Life

Ringash, Jolie
Princess Margaret Cancer Centre - UHN

Efficacy of the rehabilitation planning consult for survivors of head and neck cancer: a phase II randomized controlled trial

Survivors of head and neck cancer often live with several disabilities as a result of their disease and its treatments. Compared to survivors of other cancers, they have higher levels of unmet rehabilitation needs and more limited access to specialized rehabilitation services. To address these needs, Dr Jolie Ringash and her team developed a unique rehab consultation program that teaches survivors to use self-management and problem-solving strategies to meet their goals. In an early study, the researchers found that survivors of head and neck cancer who took part in the program had better quality of life and were more confident about finding the rehab services they need. They will now test the program in a larger clinical trial to compare its effectiveness against the current services offered. By reducing barriers to rehab access, the consultation program can improve the long-term health and quality of life in survivors of head and neck cancer.