September 2018 (IMP-19) Competition Awarded Impact Grants

Listed in alphabetical order

Bell, John
Ottawa Hospital Research Institute

Engineering of virally based multiplex immunotherapeutics

Cancer-killing, or oncolytic, viruses hold great promise in treating different types of cancer. Dr John Bell is a world leader in the field of oncolytic viruses. With a previous grant from the Canadian Cancer Society, he and his team developed viruses that could selectively attack cancer cells without harming healthy cells. They also discovered that the viruses turned on the immune system, prompting it to recognize cancer cells as foreign objects that need to be contained. In this new project, Dr Bell and his team will create what they call "immunotherapy battleships" – new virus-based therapies that are loaded with multiple immune-stimulating molecules. The goal of these therapies is to awaken a patient's own immune system and teach it to recognize and attack the patient's tumour. If successful, these treatments will not only eliminate the tumour, but also help keep the cancer from coming back.

Hawkins, Cynthia
The Hospital for Sick Children

Investigating the role of oncohistones in cancer development

Brain tumours are the leading cause of cancer-related death in children. The deadliest type of brain tumour is DIPG, a highly aggressive and difficult to treat cancer that starts in the brainstem at the base of the brain. Dr Cynthia Hawkins and her team of clinician-scientists built one of the largest DIPG tissue banks in the world. Using this incredible resource and building on the success of a previous CCS Impact Grant, they discovered that roughly 80% of DIPG tumours have a specific genetic mutation in histone proteins, which play a crucial role in turning genes on and off. Their discovery was cited by the World Health Organization in their updated classification of pediatric brain tumours. The researchers will now develop a new diagnostic test to detect this specific histone mutation in the cerebrospinal fluid, which will spare children from risky brain surgery. They will also create animal models to help them understand how this histone change contributes to tumour initiation and growth and to uncover and test new drug targets for this deadly disease.

Khokha, Rama
Princess Margaret Cancer Centre - UHN

Hormone signalling in mammary cells informs breast cancer risk & treatment

While we know that exposure to progesterone, a hormone produced by the ovary, is a risk factor for breast cancer, we know little about how the hormone contributes to breast cancer development. With a previous Impact grant from the Canadian Cancer Society, Dr Rama Khokha and her team discovered that progesterone causes stem cells in the breast to multiply, which could lead to the early start of breast cancer. Now, the researchers will embark on an in-depth study of how progesterone contributes to breast cancer development. They will examine breast stem cells from healthy women and those at high risk of breast cancer to look for unique molecular features that can predict risk. Their work will allow them to identify and test new drugs that can block the progesterone-driven onset of breast cancer in women with genetic mutations that put them at the highest risk of getting the disease.

Ohashi, Pamela
Princess Margaret Cancer Centre - UHN

Exploring immune inhibitory mechanisms in the breast tumour microenvironment

Immunotherapy is arguably the most promising new cancer treatment in recent years. While immunotherapy drugs have shown tremendous success against some cancers, they are much less effective in others. Dr Pamela Ohashi and her team will try to understand why breast cancer responds poorly to immunotherapy by looking at the different kinds of immune cells in breast tumours. They will test whether the immune cells found in breast tumours can block the activity of immunotherapy drugs and whether there are specific genetic changes that are associated with the presence of these inhibitory immune cells. The goal of this project is to uncover the ways in which breast tumours resist immunotherapy treatment so that new combination therapies can be developed to boost treatment response for this promising class of drugs.

Rennie, Paul
University of British Columbia

Development of anti-estrogens with a novel mechanism of action for treatment of hormone resistant breast cancer

Hormone therapy is often given to patients with breast cancer to prevent the disease from spreading or coming back. In many cases, the treatments are effective at first but gradually lose their power as the tumour evolves to become hormone resistant. Dr Paul Rennie is leading a team of researchers from different scientific fields to develop and test a new class of drugs that can effectively treat hormone resistant breast cancer. They will use advanced computer tools to design drugs that target a specific part of breast cancer cells separate from the areas targeted by hormone therapy. The researchers will also study how these new drugs interact with tumour cells so that they can design better second-generation drugs. Their research addresses the great need for therapies that can overcome hormone resistance for patients with this disease.

Therrien, Marc
Université de Montréal

Novel strategies for therapeutic targeting of RAF kinases

A number of cancers, including colorectal, lung and skin cancers, are driven by a protein called RAF, which makes it an important target for cancer drug development. Dr Marc Therrien has been studying RAF proteins for a long time. His research found that RAF proteins must pair up in order to become active and that this pairing is also what causes some RAF-inhibiting drugs to fail. Current drugs that target RAF in skin cancer show promise but, in some cases, they also cause the proteins to pair up and become active, leading to cancer growth. Building on his in-depth knowledge of how RAF proteins work, Dr Therrien and his team developed new drugs that can block RAF without causing the proteins to inadvertently pair up and promote cancer cell growth. Now, the researchers will study whether these new drugs can be combined with existing therapies and immunotherapy drugs to effectively attack RAF-driven tumours.

Une protéine appelée RAF est à l'origine de plusieurs cancers, dont les cancers colorectal, du poumon et de la peau, et est donc une cible de choix pour la mise au point de médicaments anticancéreux. Le Dr Marc Therrien étudie les protéines RAF depuis longtemps. Ses recherches ont révélé que les protéines RAF doivent former des paires pour devenir actives, et que ce jumelage cause également l'échec de certains médicaments inhibiteurs des RAF. Les médicaments ciblant les RAF qui sont actuellement utilisés contre le cancer de la peau semblent prometteurs mais, parfois, entraînent aussi un jumelage et une activation des protéines et permettent à la maladie d'évoluer. Forts de leur connaissance approfondie du mode d'action des protéines RAF, le Dr Therrien et son équipe ont développé de nouveaux médicaments capables de bloquer les RAF sans provoquer de jumelage malencontreux des protéines et

favoriser la croissance des cellules cancéreuses. Les chercheurs vont maintenant évaluer s'il est possible de combiner ces nouveaux médicaments aux traitements et aux médicaments d'immunothérapie existants pour attaquer efficacement les tumeurs dépendantes des RAF.

Whelan, Timothy
McMaster University

Randomized trial of hypofractionated regional radiotherapy for breast cancer

Many women with breast cancer will undergo radiation after surgery to help prevent the cancer from coming back. The current standard of care involves daily radiation treatment over a 5-week period, but studies suggest that a higher dose of radiation given over a shorter period of time could be just as effective. However, we do not know if a higher daily dose of radiation will lead to more swelling in the arm and hand, which would negatively impact a patient's quality of life. To answer this question, Dr Timothy Whelan and his team will be leading a clinical trial to test if using a higher dose over a 3-week period is as safe and effective as the current 5-week treatment. This trial has the potential to change the current standard of care for women who need radiation after breast cancer surgery. A shorter treatment period would reduce the number of required hospital visits for patients, increase health system savings and allow more people to be treated with the available resources.