July 2014 (INNOV14-2) Competition Awarded Innovation Grants

Listed by panel in alphabetical order

I1a Biomarkers and Genomics

Chi, Kim
BC Cancer Agency (Vancouver)
Genomic profiling of circulating tumour DNA (ctDNA) as a predictive biomarker for patients with castration resistant prostate cancer (CRPC)

Despite recent advances in treatments for castration-resistant prostate cancer, the disease remains incurable. Dr Chi is studying circulating tumour DNA (ctDNA), which can be found in the blood of people with cancer, to identify biomarkers that could predict patient response to therapy. He will analyze genetic changes in the ctDNA from men with advanced prostate cancer before and after treatment with 2 therapies targeting the androgen receptors, including changes to the androgen receptor gene. Because this research will identify the different effects of drugs on different patients, it could help develop a blood test that would identify what treatments are the best options for an individual patient.

Dumeaux, Vanessa
McGill University
Interactions between the tumour-microenvironment and the systemic response of breast cancer patients

The effects of cancer not only depend on the inherent tumour, but also on the body's response to the tumour. Dr Dumeaux is studying how the body responds to the presence of a cancer and how this response influences the course of the disease. She will study the genes and processes that help a breast tumour interact with the patient's circulating blood cells, and importantly, how these genes and processes might differ depending on the type of breast cancer and the patient's prognosis. This study will improve the understanding of tumour progression and prediction of a patient's prognosis.

Foulkes, William
Lady Davis Institute (affil. McGill)
Towards a biological understanding of small cell carcinoma of the ovary, hypercalcemic type

Small cell carcinoma of the ovary, hypercalcemic type (SCCOHT) is a rare and often fatal type of ovarian cancer mainly affecting girls and young women. Previous research has found that almost all cases of SCCOHT are caused by mutations in a gene called SMARCA4, which usually helps other genes work normally but is unable to do its job correctly when mutated. In this study, Dr Foulkes aims to identify and better understand how genes are poorly controlled by SMARCA4 in these tumours. This research could lead to the discovery of new targets for treatment of this and related cancers.

Guidos, Cynthia
Hospital for Sick Children
Single cell biomarkers for pathway-targeted leukemia therapies

New drugs are being developed against B-cell acute lymphoblastic leukemia (B-ALL) that target the signaling pathways through which cancer cells receive instructions to grow. However, it is mostly unknown which signaling pathways are relevant in a particular patient's leukemia, making it difficult to choose which drug to use. Using a large collection of B-ALL specimens, Dr Guidos is developing a new method to identify biomarkers for various activated signaling pathways in each patient's leukemia cells. Then she will determine if these biomarkers can predict leukemia sensitivity to the drugs. This method has the potential to improve outcomes for B-ALL patients by helping physicians choose the right drugs to treat each patient's leukemia.

Lewis, John
University of Alberta
miRNA-based biofluid diagnostics to predict prostate cancer metastasis

Current biomarker-based tests for prostate cancer, such as the PSA test, do not adequately predict whether the cancer will metastasize (spread), and spreading is responsible for most prostate cancer deaths. This means that treatment decisions must be made without this important knowledge about the aggressiveness of the cancer. Small molecules called microRNAs (miRNAs) are believed to help regulate cancer cell signaling pathways that tell cancer cells to spread. Dr Lewis and his team will be looking for miRNAs in the blood that can be used as biomarkers for predicting the risk of prostate cancer metastasis. They will use a chicken embryo cancer metastasis model to screen for miRNAs that promote prostate cancer metastasis, and will then test patients to see if these biomarkers are valid. The goal is to find miRNA biomarkers that could ultimately be used to predict how a patient's cancer may progress, and therefore, inform better treatment decisions on how aggressively to treat.

Li, Yingfu
McMaster University
Development of a noninvasive method for early colorectal cancer detection

Colonoscopy is the gold standard for colorectal cancer (CRC) screening; however, it is highly invasive and can lead to complications. Dr Li is working on developing a less invasive and more cost-effective CRC screening test to detect CRC in stool samples. This test would use DNAzymes, fluorescent DNA molecules that "light up" when cancer biomarkers are detected. Dr Li will isolate and select a panel of DNAzymes for the detection of CRC-specific biomarkers. He will then determine whether they can accurately detect CRC using patient stool samples. This research could lead to a simpler population-based CRC screening test, and ultimately, to more cancers detected earlier and more lives saved.

Tabori, Uri
Hospital for Sick Children
Utilization of THOR hypermethylation for stratification and noninvasive detection of cancer

Cancer cells have a limitless ability to divide, and this requires the help of an enzyme called telomerase. A specific part of telomerase, called THOR (TERT hypermethylated oncological region), undergoes a change called methylation, only found in cancer. Using blood and urine samples, Dr Tabori will delve deeper into this process to learn how THOR methylation can be used as a signature to diagnose and predict cancer progression and recurrence for individual patients. This research could lead to tests used to monitor cancer, so that the physician can develop a personalized treatment plan.

Tsao, Ming-Sound
Ontario Cancer Institute/PMCC - UHN
Oncogenic drivers in KRAS wild type pancreatic ductal adenocarcinoma

Pancreatic cancer has one of the poorest survival rates of all cancers. The main driver of pancreatic cancer has been believed to be in the mutation of a gene called KRAS, for which there is currently no effective treatment. However, it was recently discovered that up to a quarter of these cancers do not have this mutation. To date there have been limited studies on the genetic differences between KRAS-normal and KRAS-mutated pancreatic cancer. With a large collection of mouse models that contain human pancreatic cancers, Dr Tsao proposes to identify key genetic mutations in KRAS-normal cancers to learn more about this disease. This research could lead to important knowledge about how to treat the 20-25% of pancreatic cancer patients who do not have the KRAS mutation.

I1b Gene Regulation

Borden, Katherine
University of Montreal
The eukaryotic translation initiation factor eIF4E regulates a new level of mRNA metabolism

One of the processes involved in the onset of cancer is the uncontrolled production of proteins. The production of proteins is essential for the survival of normal cells, but when working abnormally, proteins may be produced that help cancer cells grow and spread. Building on exciting new discoveries by her lab, Dr Borden will use cutting-edge technologies to study newly identified mechanisms that lead to the abnormal production of proteins.

Bremner, Rod
Mount Sinai Hospital
Influence of cell death on cancer initiation

Cancer must be treated aggressively because cancer cells have special abilities that normal cells do not – such as the ability to avoid death. Although anticancer treatments may be designed to defy this ability, Dr Bremner's research has shown that there may be a signal sent by dying cells that actually promotes cancer in neighbouring cells, thus causing new tumours to grow even after a successful treatment. By studying an eye cancer called retinoblastoma, Dr Bremner will determine exactly what these signals are and how they cause cancer. This research has the potential to improve the effectiveness of treatments against many cancers.

Davie, James
University of Manitoba
Nuclear RNA and PRDX1

Molecules called RNA, which exist in every cell, carry out many important functions in both normal and cancer cells, such as interpreting information in genes and even dictating which genes get activated. However, scientists are still uncertain about the role played by some types of RNA. Dr Davie is studying a type of RNA called nuclear RNA and how it interacts with a protein, PRDX1, that is mutated in triple-negative breast cancer, a form of the disease that defies treatment and has poor outcomes for patients. His research could reveal a mechanism that sheds new light on how to treat this deadly form of breast cancer.

Fish, Jason
The Toronto Hospital (General Division) - UHN
Control of tumour growth by circulating anti-inflammatory microRNAs

The risk of cancer is linked to many conditions and diseases – including obesity, diabetes and old age – through a common feature: inflammation. Although this link is known, there is still a poor understanding of how inflammation contributes to cancer. Dr Fish is studying small particles called exosomes that travel in our blood and carry microRNA molecules that reduce inflammation. In cancer, the amount of microRNAs in the blood is changed. In this research study, Dr Fish will test whether the reduced amount of anti-inflammatory microRNAs in aging, obesity and diabetes promotes cancer and whether increasing these microRNAs will minimize inflammation and cancer growth. This research could add new understanding about how cancer grows and how its linkages to other health conditions can be leveraged to reduce risk.

Gibbings, Derrick
University of Ottawa
Autophagy degrades circular RNAs to control microRNAs and invasion of breast cancer cells

Many important discoveries that advance our knowledge of cancer are at the molecular level: microscopic processes that are essential to the onset, or spread, of cancer. Dr Gibbings will be studying 2 types of molecules – microRNA and a recently discovered type called circular RNA – that appear to be involved in the metastasis, or spread, of cancer cells. His research will attempt to uncover whether these molecules are degraded by autophagy (a process of recycling cell components) in breast cancer cells and how this contributes to cancer spreading. Once cancer metastasizes, a patient's chances of survival dramatically decrease, so this research has the potential to help scientists discover ways to prevent the potentially fatal spread of cancer.

Kim, Philip
University of Toronto
Discovery and validation of novel cancer drug targets using large peptide lentiviral libraries

A major challenge in developing new cancer treatments is that there are so many proteins in the body that could play a role in cancer and so many drugs that might have an effect on each of these proteins. Testing each combination could take a tremendous amount of time. Imagine the numbers on a bingo card: there are over 500 septillion possible combinations of letters and numbers, but only some combinations will be the correct match to win. Fortunately, Dr Kim has developed a new strategy to find the winning combinations that could fight the growth of cancer. He will do this by developing a large library of molecules called peptides, which he will use to both discover potential targets and identify promising peptide drugs against them. This research has the potential to identify many new cancer treatments that will require further development and validation.

Lupien, Mathieu
Ontario Cancer Institute/PMCC - UHN
Identifying the changes to the chromatin landscape imposed by genetic predispositions in breast cancer

Often, scientists discover that something – a process, a gene, an interaction between cells – is important to cancer growth long before they are able to pin down exactly why it's important. The genetic variations associated with breast cancer are a good example: there are over 80 of these variations linked to increased breast cancer risk, but we still have a limited understanding of what these variations actually do. Building on methods used in his lab, Dr Lupien will study over 30 variations that are linked to higher risk of breast cancer to determine what modifications they make on other genes to encourage the development of cancer. While this knowledge alone is important for discovering new ways to treat breast cancer, the method Dr Lupien is refining could also help other scientists learn more about the genetics of other cancers.

Masson, Jean-Yves
Laval University
APRIN: A novel regulator of DNA repair and tumour suppression in breast and ovarian cancer

Only 10%–15% of breast and ovarian cancers are related to mutations in genes called BRCA1 and BRCA2. When these genes are operating normally, their function is to help repair damaged DNA and thus avoid cancer. Dr Masson's lab has discovered that another gene, called APRIN, works with BRCA2 and others to help repair damaged DNA. In this project, they will study how APRIN interacts with other genes to prevent tumours from growing. Their findings could identify a new target in APRIN for the design of treatments for breast and ovarian cancer.

Pelletier, Jerry
McGill University
Functional analysis of cancer genomes using a Cas9-based engineering platform

Genetic instability leads to mutations in genes, which in turn can lead to cancer. A tumour's genetic profile may reveal both mutations that are necessary for the tumour's development and progression, and mutations whose purposes – if any – are not clear. To build a better understanding of the purpose of these mystery mutations, Dr Pelletier is developing a new system using a technology that can create different mutations in both cells and a mouse model to see what function they perform in cancer. This information could identify important mutations, leading to new drugs to control them. Although this project is focused on Burkitt's lymphoma, there is the potential for extension to other cancers.

Sidhu, Sachdev
University of Toronto
Engineered ubiquitin variants for selective modulation of p53 activity

Much of the work that cells do in our body is helped by proteins: molecules that perform important tasks and deliver instructions to cells on how to behave. One of these proteins, p53, is known to protect cells against growing out of control and becoming cancerous. Another protein, ubiquitin, is known to attach itself to p53 in normal cells to help keep the level of p53 balanced so it can do its job. Too much ubiquitin attachment, however, interferes with p53's protective function. Dr Sidhu is developing protein drugs in the lab that can target ubiquitins attached to p53 proteins and detach them, so that p53 is free to continue its protective function. This research will

lead to a better understanding of p53 biology in cancer cells and could pave the way to new treatment options that are more effective with fewer side effects.

Triggs-Raine, Barbara
University of Manitoba
Evaluation of hyaluronidase 2 as a target for cancer prevention

Occasionally, scientists can draw lessons about how cancer operates in humans by observing how it operates in other beings in nature. Recently it was reported that the naked mole rat, which has a lifespan of 30 years and does not get cancer, may be protected by its large amount of hyaluronan in the microenvironment around its cells. Hyaluronan is a large chain of sugar molecules that works with other molecules to tell cells how to behave. Dr Triggs-Raine is studying how this molecule confers cancer resistance in mice, which has the potential to impact cancer prevention strategies.

I2 Imaging and Technology Development

Arnaout, Angel
Ottawa Hospital Research Institute
The specimen margin assessment technique (SMART) Trial : A novel 3D method of identifying the most accurate method of specimen orientation in breast cancer surgery

The principal reason for breast cancer to return after surgery is that the whole cancer was not removed. Currently, there are no overarching guidelines to advise surgical centres on a recommended margin of breast tissue to remove around tumours to reduce as much as possible the risk of a recurrence and need for further surgery. Dr Arnaout has developed a novel 3-D method to help identify the best technique for determining margins. This method will be tested using artificial tumours inserted into real breast tissue donated by women having routine surgeries to remove tissue from their breasts (breast reduction or preventive mastectomy). This research will identify, out of the 2 commonly used techniques, which one is a more accurate assessment for tumour removal. Dr Arnaout's work may have a significant impact on surgical practice in Canada and potentially worldwide, and reduce the risk of breast cancer recurrence.

Hirasawa, Ken
Memorial University of Newfoundland
Exploiting modulation of PpIX accumulation by Ras/MEK: an innovative approach towards photodynamic therapy

Photodynamic therapy, or PDT, is a cancer treatment that uses a substance called protoporphyrin IX (PpIX) to make cancer cells more sensitive to light. This has 2 effects: the cells become more fluorescent so they can be detected, and when a special red light is used on them, they can be destroyed. Unfortunately, this therapy is currently only effective on small collections of cells, not large or aggressive tumours. Dr Hirasawa will combine PDT with a type of molecule that is known to slow the growth of cancer and – they have discovered – makes cells carry larger amounts of PpIX. This combination could lead to a new therapy to help destroy tumours more efficiently.

Martel, Anne
Sunnybrook Research Institute
Quantitative assessment of tumour burden in breast cancer

The more scientists learn about the many different types of cancers, the more it is possible to deliver personalized treatments to different patients and increase their chances for a good outcome. For this reason, when cancer is diagnosed, specialists collect information about the tumour size and type before a treatment is chosen. Dr Martel's research is aimed at improving this process by developing a computer software that can automatically assess the severity of a patient's breast cancer from a digital image of the tumour. This computerized method will help cancer doctors more quickly and accurately make treatment decisions based on the tumour's characteristics.

Mes-Masson, Anne-Marie
Centre de recherche du CHUM - Pav. Notre-Dame (affil U de Montreal)
Microfluidic based empirical testing versus predictive biomarkers to stratify cancer care in ovarian cancer patients

There are many types of chemotherapy drugs available, but as they can work selectively on different cancers and different patients, doctors often have a difficult task in determining which treatment to assign. Current technology to test tumour samples for their specific response to a drug require tissue from samples that are in small supply, limiting the ability of scientists to perform these tests – until now. Dr Mes-Masson, working in the field of microfluidics, is developing a technology capable of testing a drug's effectiveness on just a tiny piece of a tumour. By combining this analysis with the identification of biomarkers – molecular signs of cancer that can tell us about the effectiveness of a treatment – her research could lead to more precise ways to prescribe treatments and monitor their progress.

Yasufuku, Kazuhiro
The Toronto Hospital (General Division) - UHN
Image-guided localization platform for minimally invasive lung surgery

Lung cancer is still the leading cause of cancer-related death in Canada. A standard treatment for lung cancer involves surgical removal of the diseased parts of the lung. This is a challenging task, as it can be very difficult to locate all cancerous areas ahead of time to make sure the surgery is complete and accurate. Dr Yasufuku will test a new cutting edge technology in animal models to dramatically improve these surgeries. He will take advantage of a flaw in cancers: that their blood vessels are so new that nanoparticles injected into the bloodstream can easily pass through the flimsy vessel walls into the tumour. These tiny particles will be loaded with fluorescent dye to accurately show their location in real time with a special CT scan, so that surgeons will know exactly where to operate. With this technique, surgeries to remove lung cancer could be more successful, leading to more positive outcomes for patients with this deadly disease.

I3 Immunology, Signalling and Stem Cells

Côté, Jean-François
IRCM - Institut de Recherches Cliniques de Montréal (affil. U de Montreal)
Investigating the roles of a subset of oncogene-induced Interferon Type I genes in HER2 breast cancer metastasis

Proteins play important roles in the function of cells, and while some proteins help cells remain healthy, others – when mutated – promote the development of cancer. Dr Côté is studying a group of proteins whose role in cancer was unclear before now; he has found that 2 categories of proteins, called RTP4 and ISGylation, are linked with poor survival of HER2+ breast cancer patients. His research will explore whether RTP4 and ISGylation contribute to breast cancer progression and metastasis (spread). As metastasis is the main cause of death related to breast cancer, his research could lead to ways to prevent metastasis and improve survival.

Craig, Andrew
Queen's University
Targeting receptors that drive cancer metastasis using synthetic antibodies

The leading cause of cancer-related deaths is metastasis. Dr Craig will engineer new synthetic antibodies that target the drivers of metastasis, specifically the cell-changing process EMT (epithelial-to-mesenchymal transition) and MMPs (matrix metalloproteinases), both of which give the cell the power to invade other tissues. He will test these new antibodies in cancer cell lines and mouse models for their ability to minimize metastatic properties and tumour spread. This research could provide the foundation to develop new treatments that prevent the spread of tumour cells in humans, leading to improved patient survival.

Dick, Frederick
Western University
Disrupting cell cycle arrest to kill dormant metastases

Cancer cells have the ability to remain dormant – that is, they can stop their growth as a strategy to resist chemotherapy – and then start growing again after treatment is stopped. This is what happens when cancer recurs. Dr Dick will study how dormant cancer cells use a protein complex called DREAM to stop growing. This research will help determine if dormant cancer cells, normally resistant to treatment, can be forced into an active state by disrupting DREAM so they can be killed while unprepared. This research may lead to an understanding of how cancer cells control their growth, offering new ways of preventing relapse in advanced stage cancer.

Eaves, Connie
BC Cancer Agency (Vancouver)
Development of a new system to analyze the initial process of human breast cancer development

Breast cancer usually starts with normal cells and progresses in stages into full-blown breast cancer. Dr Eaves will study aggressive tumours that begin as normal human breast cells and map out how these cells genetically change/mutate and behave along the way. She will introduce specific mutant genes into different types of normal human breast cells and then study the early changes the cells undergo as they become cancerous. This research will help explain the relationship between the original cell and the breast cancer cell it transforms into and may help in future work to identify new targets for treatments and early detection.

Hui, Chi-chung
Hospital for Sick Children
Roles of Spop and Spopl in medulloblastoma

Medulloblastoma (MB) is the most common malignant childhood brain tumour and is a leading cause of death in pediatric cancer patients. Dr Hui will study the function of 2 molecules, Spop and Spopl, that are involved in the formation and growth of MB. He will develop a new mouse model to allow him to study these molecules at great detail. This research will not only build a better understanding of Spop and Spopl but will also provide a new mouse model that can then be used by other scientists in the discovery of and research on new treatments for MB.

Ilangumaran, Subburaj
Universite de Sherbrooke
Enhancing tumour immunogenicity using NOD-like receptor family CARD domain containing protein 5 (NLRC5)

Our immune systems are on guard against the development of cancer and launch attacks to help protect us. Unfortunately, cancer cells have evolved many strategies to counter these attacks, such as making themselves appear invisible to the lymphocyte “soldiers” of the immune system. Recent findings have implicated a protein, NLRC5, in preventing this evasion strategy. Dr Ilangumaran, working in the field of immunotherapy, intends to improve the understanding of how NLRC5 enhances an immune attack against cancer cells. Results from this study may impact the development of cancer immunotherapies by harnessing the value of NLRC5.

Jiang, Xiaoyan
BC Cancer Agency (Vancouver)
A novel treatment approach to overcome TKI resistance in CML

Chronic myeloid leukemia (CML) is a form of blood cancer that often becomes resistant to drugs, leading to relapses for patients. Research has shown that this is caused by blood cancer stem cells which are difficult to kill. Dr Jiang and her team have focused on understanding the genetic changes in cancer stem cells that cause drug resistance and have recently identified a potential drug target in the cancer-causing gene called ILK. This research will explore the possibility of combination treatments with novel drugs targeting ILK and another mutated gene, in order to overcome drug resistance. If her research highlights a new way to eliminate blood cancer stem cells, her findings could help form the basis of clinical studies to improve the treatment of CML.

Minden, Mark
Ontario Cancer Institute/PMCC - UHN
Identification of alternatives to steroid therapy in lymphoid malignancies

Acute lymphoblastic leukemia (ALL) is highly treatable, but unfortunately there are side effects associated with treatment - in particular the use of steroids, which can affect mood, weight, memory, and even lead to diabetes and bone problems. Dr Minden and his team will be studying how steroids work to kill leukemia cells through altering cancerous genes, with the goal of finding a more focused treatment which can accomplish the same thing without the harmful side effects. Their research could lead to the development of safer yet effective treatments for people with ALL.

Mossman, Karen
McMaster University
Combining oncolytic HSV with ICD-inducing chemotherapeutics in a spontaneous breast tumour model

Breast cancer is a great success story of cancer research, with growing survival rates year by year. However, there is still little that can be done for a patient if their breast cancer metastasizes (spreads). Dr Mossman is developing a novel treatment that combines two components to enhance the immune system's ability to fight cancer: oncolytic viruses that are designed to kill cancer cells only while leaving healthy cells alone; and clinically approved chemotherapy drugs that trigger the immune system to attack cancer. If effective, this combination strategy could work to control tumour growth and prevent metastasis not only in breast cancer but in other forms of cancer as well.

Santos, Manuela
Centre hospitalier de l'Université de Montréal
Colon cancer and inflammation: the interplay of iron, microbiota and host at the mucosal interface

People with diseases involving inflammation of the bowel, such as inflammatory bowel disease (IBD), bear a higher risk than the general population for developing colon cancer. While all healthy people have bacteria in their digestive system, people with these diseases have imbalances in their gut bacteria, which causes inflammation and can lead to cancer. Iron is an important food source for bacteria, and different types of gut bacteria grow in response to different types of iron supplements. Dr Santos is studying how different iron supplements affect the gut bacteria balance, and in turn, the onset of colon cancer. These findings will help identify safe iron supplements for high-risk individuals.

Siegel, Peter
McGill University
Control of focal adhesion dynamics in metastatic breast cancer

Breast cancer has one of the highest survival rates of cancer, but when it metastasizes, or spreads, the result is often fatal. Cancer cells are assisted in their ability to spread by focal adhesions: structures that assemble inside of cells and act like a motor. Dr Siegel is studying how a protein called LPP, which is abnormal in cancer cells, is associated with focal adhesions to help them migrate more easily. His research may lead to a better understanding of how breast cancer spreads, and in turn, how to prevent its spread, which so often leads to death.

Turcotte, Simon
Centre hospitalier de l'Université de Montréal
Harnessing the mutation-reactive T-cell response against metastatic colorectal cancer

Many scientists are searching for ways to more effectively harness our immune systems against cancer. Dr Turcotte will be investigating, in patients with colorectal cancer that has spread to the liver, the potential to identify T-cells that recognize cancer mutations. The identification and use of mutation-specific T-cells from patients could improve the development of immunotherapies customized to the cancer of each individual patient.

I4 Novel Therapeutics

Bedard, Philippe
Ontario Cancer Institute/PMCC - UHN
Molecular basket trial in multiple malignancies with common target pathway aberrancies (MOBILITY-002)

Although research has led to significant improvements in the survival rate for cancer in general, some cancers remain very difficult to treat. Often this is because these cancers contain mutations in their genes, which make them resistant to drugs. In this project, Dr Bedard will provide patients who have advanced pancreatic or colorectal cancer that is resisting treatment with a new drug combination that may help fight their cancer. He will take blood and tumour samples before, during and after treatment to see whether the drug has made any changes in the genes and proteins over time, and compare responders and non-responders. These findings will better our understanding of treatment resistance so that therapies can be better tailored to individuals to improve outcomes.

Frappier, Lori
University of Toronto
Epigenetic-based therapeutic approaches for Epstein-Barr Virus-induced cancers

Epstein-Barr virus (EBV) is an infection that almost all people carry. Since it causes cells to rapidly reproduce, it can also lead to many types of cancer. Dr Frappier's research will test several chemicals to identify which ones can stop or kill EBV-infected cells by targeting EBV, so that promising candidates can be developed into drugs to treat or prevent cancers caused by EBV.

Hoang, Trang
University of Montreal
Towards a targeted and mechanism-based therapy in T-cell leukemia

Acute lymphoblastic leukemia (ALL) is the most common childhood cancer. There is a high survival rate for children treated for ALL, but they suffer severe side effects. In comparison, at least half of adolescents and adults with ALL will die from the disease. Dr Hoang is studying genetic mutations in the stem cells that give rise to leukemia and contribute to relapse. In this research study, she will screen a panel of drugs that successfully target these stem cells and destroy them.

Jan, Eric
University of British Columbia
Effective delivery and translation of therapeutic mRNA in hypoxic tumours

Cancers are caused by genetic alterations, or mutations, which throw a wrench in the production of normal proteins, the workers that perform so many important functions for normal cells. One way to combat this is gene therapy, which delivers an anti-cancer gene to tumours in order to produce normal anti-cancer proteins. A new safer form of gene therapy using messenger RNA (mRNA), the template for protein production, is promising, but unfortunately scientists have found that there are problems getting it to the tumours so it can do its work. Dr Jan and his team will address this by improving the mRNA "cargo", and developing a strong transport system to deliver this cargo to cells, called a lipid nanoparticle (LNP). The testing of this approach in a prostate cancer mouse model, if successful, could lead to a new way to effectively deliver gene therapy directly to tumours.

Nepveu, Alain
McGill University
Exploiting DNA repair properties of cancer cells

One of the processes that helps both normal and cancer cells survive is DNA repair. Cancer cells are more sensitive to DNA damage because they multiply so rapidly. Radiotherapy, which causes DNA damage, is therefore a favoured cancer treatment. Some cancer cells, however, seem to be able to cope with the repairs better than others. Working with a recently discovered type of gene involved in DNA repair, Dr Nepveu will study the mechanism that helps cancers resist radiotherapy. The knowledge his team produces could help researchers develop new drugs to make cancers more vulnerable to radiotherapy.

Roberge, Michel
University of British Columbia
Chemical suppressors of nonsense mutations in cancer

Genes contain information that, when "read," serves as an instruction manual to build the proteins necessary to help cells work normally. When genes are mutated, the result is similar to an instruction manual that is missing pages or switches language halfway through. If a protein is built on incorrect instructions, it will not work properly and can allow cancer to grow. Dr Roberge is studying the ability of chemicals to prevent a specific type of mutation that is known to cut off a gene partway through its instructions. In this research, he will test several chemicals. By identifying chemicals that are best able to prevent genes from being cut off and restore function, his research could pave the way for new treatments to prevent cancer.

Roux, Philippe
University of Montreal
Role of CK1 in tumour growth and resistance

When cancer becomes resistant to treatment, there is very little that can be done for the patient. Dr Roux and his team have discovered a protein involved in colorectal cancer that may play a role in drug resistance. In this research they will test new drugs that block this protein in combination with current drugs to see whether this strategy can overcome drug resistance. Dr Roux will also attempt to determine whether successful treatment can be predicted by the amount of this protein present. If this drug strategy makes cancer more receptive to treatment in their pre-clinical model, Dr Roux's findings could lead to treatments to extend disease-free survival for many colorectal cancer patients.

Shoichet, Molly
University of Toronto
Cancer drug delivery via self-aggregation into colloidal nano-particles

An important advance in cancer treatment in recent decades has been the development of vehicles that deliver drugs directly to cancer cells, minimizing the toxic effects of drugs on the normal cells nearby. A persistent challenge, however, is that more vehicle than drug is often delivered to the cancer, limiting the treatment's impact. Dr Shoichet's research capitalizes on her recent discovery that many cancer drugs naturally form, without help, into a type of particle called a colloid. These colloids are like small capsules capable of travelling through the bloodstream without the help of a carrier. Dr Shoichet will determine whether these colloids prefer to enter tumour cells, while sparing normal cells. In addition, the outside of these colloids will be decorated with antibodies against cancer-specific markers, to further help them find and kill cancer cells. If successful, their research will create a targeting therapy that does not require a carrier, leading to more effective treatments for patients with fewer side effects.

Steinberg, Gregory
McMaster University
Defining the roles of systemic and direct tumour effects of biguanides to optimize treatment

Metformin, a drug used to treat type 2 diabetes, has recently been found to have anticancer properties. However, the exact effect it has on cancer cells is still poorly understood. Scientists believe that metformin either reduces the fuel supply for cancer by lowering blood sugar and insulin or it directly interrupts the vital communications that tell cancer cells to grow. Dr Steinberg proposes to clarify this by determining how metformin actually works against cancer using a mouse model of colon cancer. By identifying the nature of metformin's anticancer activity, this research could suggest ways to identify the most likely candidates to be successfully treated with metformin, with its effects that are known to be significant and long-lasting.

Wang, Yuzhuo
BC Cancer Agency (Vancouver)
Identification of lead compounds of cytotoxic MTAP substrates for treatment of MTAP-deficient cancers

Many advanced cancers are missing a protein, called MTAP, that is needed for important chemical processes in cells to work normally. At present, there are no drugs available to reverse this effect, which contributes to poor outcomes for patients. Dr Wang has identified this deficiency in advanced prostate cancer and is using an innovative computer-based method and mouse model to test for chemicals that are toxic to cancer cells missing MTAP. This research could lead to the development of drugs that may give hope to people with advanced cancers.

Wouters, Bradly
Ontario Cancer Institute/PMCC - UHN
Targeting lactate and pyruvate transport in tumours

Cancers are "clever", in that they are able to adapt to their environment and find ways to grow faster and fuel themselves more efficiently. Cancer cells speed up their own activity by consuming great amounts glucose (sugar). As they consume glucose they produce a waste product called lactate, which is cleared away by two key helper proteins so that cancer cells continue eating. Dr Wouters is developing novel therapeutic antibodies known as biologics, which are treatments that will block these helpers so that the lactate continues to build, preventing cancer cells from eating and growing. This project will also develop a novel imaging technology which will help monitor the effectiveness of this treatment. Because this process is common to most fast-growing cancers, this research could lead to new treatments across a range of cancer types.

I5 Prevention and Cancer Outcomes

Barrera, Maru
Hospital for Sick Children
Improving quality of life in children with cancer through psychosocial screening and improved communication in health care providers

A diagnosis of pediatric cancer and its aggressive treatment can have a devastating effect on children and their families. There are tools in use for healthcare workers to assess how these children and families are coping, yet it is not clear whether workers and families find these tools valuable. Dr Barrera will interview doctors, nurses, social workers, and families with a child newly diagnosed with cancer to determine how useful they find tools like these. This research could identify gaps in supporting these families, and ways to improve the existing support systems available to ease the cancer treatment process.

Bottorff, Joan
University of British Columbia (Okanagan)
Dads in Gear: An innovative men-centred approach to smoking cessation

It has been well-known for decades that smoking is a key lifestyle factor contributing to cancers and other diseases, yet it is such an addictive habit that once taken up, it is incredibly difficult to quit. Dr Bottorff has designed a smoking cessation program targeted at new fathers called Dads In Gear which focuses on helping these men quit smoking, live healthier lives, and gain confidence in fathering. In this project she and her team will test whether the program is acceptable and practical in 6 communities and use feedback to refine it, so it can be delivered in more communities. This project will not only help new fathers reduce their risk of cancer and other diseases, but model healthy behaviours for their children.

Caperchione, Cristina
University of British Columbia
If THEY build it, will THEY act? Novel approaches to increasing physical activity among breast cancer survivors

Research has shown that physical activity has significant health benefits for survivors of breast cancer, and yet this group tends to report low levels of activity. To encourage breast cancer survivors to become more active, Dr Caperchione will take an innovative community-based approach by offering small grants to local groups of female breast cancer survivors in Okanagan, BC, to help them implement their own physical activity program suited to their needs. This type of approach has been found to be more effective at achieving uptake in the targeted

community as it is designed by those who will participate. These programs could increase activity and improve health outcomes in this survivor population.

McEwen, Sara
Sunnybrook Research Institute
Development and pilot evaluation of a rehabilitation consult for survivors of head and neck cancer

Survivors of head and neck cancer (HNC) can have rehabilitation needs different from those of other cancer survivors, such as problems with swallowing, speech, sensation and cognitive function. Dr McEwen proposes a pilot study of an intervention that incorporates a rehabilitation consultant into aftercare for HNC patients, to better identify the patients' special needs and assign a customized personalized rehabilitation plan to aid their recovery and improve their quality of life. She will design this intervention after consultation with patients and their doctors and others involved in their care. The intervention has the potential to be used more broadly with different cancers.