

BACKGROUND

Results of Genome Canada-CIHR 2012 Large-Scale Applied Research Project Competition in Genomics and Personalized Health

Genome Canada and the Canadian Institutes of Health Research (CIHR), in partnership with the Cancer Stem Cell Consortium, are pleased to announce the 17 successful projects resulting from the 2012 Large-Scale Applied Research Competition in Genomics and Personalized Health.

QUEBEC

Personalized medicine in the treatment of epilepsy

Project leader: Patrick Cossette

Project co-leaders: Berge Minassian, Jacques Michaud

Centre hospitalier universitaires de l'Université de Montréal

Every time someone with epilepsy has a seizure there is a risk of brain damage. This is particularly true for children. Unfortunately, today's anti-epileptic drugs simply don't work on about one third of patients.

The team led by Drs. Patrick Cossette, Berge Minassian and Jacques Michaud will identify genes that are associated with epilepsy and that are predictive of the response to various anti-epileptic drugs. This will result in earlier and more effective care and potentially prevent cognitive decline in children.

Biomarkers for pediatric glioblastoma through genomics and epigenomics

Project leader: Nada Jabado

Project co-leaders: Jacek Majewski, Tomi Pastinen

McGill University Health Centre

A type of incurable brain cancer called high-grade astrocytomas (HGA) is taking the lives of children and young adults. Genome Canada and CIHR-funded researchers have identified mutations in a particular gene in a significant fraction of children and young adults with this brain tumor. These mutations partly explain why this cancer remains unresponsive to treatments.

Now, the team led by Drs. Nada Jabado, Jacek Majewski and Tomi Pastinen will develop new tools that will help healthcare providers identify these mutations in brain tumors, allowing children to receive the best treatment strategy. Using next-generation genomic technologies, they are looking for potential targets for drug treatment.

Personalized cancer immunotherapy

Project leader: Claude Perreault

Project co-leader: Denis-Claude Roy

Hôpital Maisonneuve-Rosemont

About half of patients with a hematologic cancer develop resistance to chemotherapy. For these patients, the usual treatment is to transplant bone marrow cells from a healthy donor. This is known as immunotherapy because immune cells from the donor target tumor cells in the recipient. Unfortunately, there are two problems with this treatment: the effectiveness of the transplanted cells varies widely; and there is the chance of rejection by the patient. In some cases, the donor cells actually attack the patient—something known as “graft versus host disease” (GVHD).

Drs. Claude Perreault, Denis-Claude Roy and team are developing a genetic test that will predict GVHD, leading to safer use of bone marrow transplants. This will also improve immunotherapy by targeting the right immune cells to the right tumor cells, leading to more effective treatment.

IBD Genomic Medicine Consortium (iGenoMed): translating genetic discoveries into a personalized approach to treating Inflammatory Bowel Diseases

Project leader: John Rioux

Project co-leader: Alain Bitton

Montreal Heart Institute

With over 230,000 cases, Canada has among the highest frequency of people in the world with inflammatory bowel diseases (IBD), including Crohn’s and Ulcerative Colitis. While there are a several drugs available on the market to treat IBDs, currently physicians are unable to predict which drug would be most effective for a given patient.

Drs. John Rioux, Alain Bitton and team will develop tests allowing doctors to match the right drug with the right patient. This will prevent patients from receiving ineffective (and often expensive) medication and improve the quality of patient life. In addition, once the project is fully implemented, it will save the health care system more than \$10 million annually by avoiding costly hospitalizations and surgeries.

While the research will focus on two specific drugs, the project is in fact creating a system that will become an even greater asset for a large number of new drugs, which are expected to reach the Canadian market in coming years.

PEGASUS: Personalized Genomics for prenatal Aneuploidy Screening Using maternal blood

Project leader: François Rousseau

Project co-leader: Sylvie Langlois

Université Laval

Every year in Canada, about 10,000 pregnant women undergo amniocentesis to screen for genetic abnormalities such as Down syndrome. This procedure represents a non-negligible risk and tragically, 70 healthy fetuses are lost due to complications from the procedure. Recently, however, scientists have discovered that fetal DNA present in the mother's blood can be used to test for genetic abnormalities, and this through a simple blood test.

Drs. François Rousseau, Sylvie Langlois and team will compare different genomic technologies for their effectiveness to successfully detect genetic abnormalities using the mother's blood. The goal of the study is to implement the most suitable technology into the Canadian health care system to eventually offer, in the context of standard clinical care, non-invasive prenatal screening to all Canadian women.

Innovative chemogenomic tools to improve outcome in acute myeloid leukemia

Project leader: Guy Sauvageau

Project co-leader: Josée Hébert

Institute for Research in Immunology and Cancer

Acute myeloid leukemia is a particularly lethal type of cancer among young people, with most dying within two years of being diagnosed. At the moment, analyzing cancer cell chromosomes is the best way to determine the prognosis for patients. Unfortunately, about 45 per cent of those tested show no anomalies, leaving doctors with little information to go on. Recent developments in DNA sequencing, however, allow for a more complete analysis of these tumors.

Drs. Guy Sauvageau, Josée Hébert and team will use personalized DNA from patients to determine how they should be treated, based on the specific genetic makeup of their tumors. This will lead to better diagnosis and improved outcomes for patients. They are also developing new models for tracking cancer cells that are left behind after a patient is treated. These cancer stem cells can multiply over time and lead to a relapse. This research could lead to new ways of preventing such relapses by providing new insights into the biology of this disease.

Personalized risk stratification for prevention and early detection of breast cancer

Project leader: Jacques Simard

Project co-leader: Bartha-Maria Knoppers

Université Laval

Currently, mammography is used to screen for breast cancer in women over 50 years of age. While screening younger women could have significant benefits in terms of early detection and intervention, it is simply not economical. What's needed is a way of identifying those who are most at risk, based on a wide variety of factors.

The team led by Drs. Jacques Simard and Bartha-Maria Knoppers are developing just such a screening program so that women with a high risk of breast cancer will be identified—and tested—sooner. Younger women who are currently missed by age-based screening will have their cancer caught at an earlier stage, leading to better treatment, improved prognosis and lower costs for the healthcare system.

Personalized medicine strategies for molecular diagnostics and targeted therapeutics of cardiovascular diseases

Project Leader: Jean-Claude Tardif

Project Co-Leader: Marie-Pierre Dubé

Montreal Heart Institute

Cardiovascular disease is the leading cause of death and hospitalization in the world. In Canada 80,000 people died in 2010 of cardiovascular disease, which accounts for 35 per cent of all deaths in the country. Currently, 1.3 million Canadians suffer from cardiovascular disease, causing a serious economic burden. The cost is estimated to \$22.2 billion per year, which constitutes the highest direct healthcare costs.

The team led by Drs. Jean-Claude Tardif and Marie-Pierre Dubé are applying their expertise in how genes influence drug efficacy and toxicity to provide guidance to health professionals in the selection and dosing of a specific drug. This will improve patient care, reduce harmful side effects and lower health care costs by reducing the use of ineffective drugs and unnecessary spending by healthcare payers.

ONTARIO

Enhanced CARE for RARE genetic diseases in Canada

Project leader: Kym Boycott

Project co-leader: Alex MacKenzie

Children's Hospital of Eastern Ontario and University of Ottawa

Gene mutations cause not only well-recognized rare diseases such as muscular dystrophy and cystic fibrosis, but also thousands of other rare disorders. While individually rare, these disorders are collectively common, affecting one to three percent of the population. It is estimated that as many as half of Canadians with rare disorders are undiagnosed. Drs. Kym Boycott, Alex MacKenzie and team will use powerful new gene sequencing technologies to identify the genes implicated in many of these rare diseases.

Besides providing important new understanding into human disease, this project will yield other benefits, including: avoiding invasive procedures, stopping ineffective treatments, developing earlier and better diagnoses, devising more appropriate treatment, and predicting the chances that one of these rare diseases could be passed on to offspring.

Once the disease-causing genes have been identified, researchers will test drugs that are currently on the market to identify those that might be effective against these rare diseases.

Autism spectrum disorders: genomes to outcomes

Project leaders: Stephen Scherer

Project co-leader: Peter Szatmari

The Hospital for Sick Children

Genome Canada and CIHR-funded research has already led to some exciting breakthroughs in our understanding of autism spectrum disorder, a complex condition that affects normal brain

The logo for Canada, featuring the word "Canada" in a serif font with a small Canadian flag above the letter "a".

development, social relationships, communication and behaviour. Among these breakthroughs is the identification of specific DNA anomalies associated with the illness. Now, Drs. Stephen Scherer, Peter Szatmari and team are going to the next level, aiming to identify the remaining genetic risk factors.

This ground-breaking work will mark Canada's contribution to an ambitious international initiative that aims to sequence and analyze the genomes of 10,000 people with autism spectrum disorder. With a more complete understanding of the genetic elements of autism, doctors will be able to make earlier diagnoses, provide better, more personalized care to patients and reduce the enormous cost autism imposes on our health care system.

Early detection of patients at high risk of esophageal adenocarcinoma

Project leader: Lincoln Stein

Project co-leader: Tony Godfrey

Ontario Institute for Cancer Research

Chronic heartburn can damage the lining of the esophagus, leading to a condition known as "Barrett's esophagus". Patients with Barrett's esophagus have a much higher chance of developing cancer of the esophagus.

Until recently, the only way to diagnose Barrett's esophagus was through endoscopy—an uncomfortable and time-consuming procedure. However, a swallowable sponge under development in the United Kingdom allows for quick and painless diagnosis of Barrett's esophagus in a doctor's office. The team led by Drs. Lincoln Stein and Tony Godfrey aim to supplement this test with genomic technologies, allowing doctors to follow patients over time to identify and treat those progressing to cancer. Early detection, treatment and even prevention of these cancers could save the healthcare system over \$300 million a year.

The microbiota at the intestinal mucosa-immune interface: A gateway for personalized health

Project leader: Alain Stintzi

Project co-leader: David Mack

Children's Hospital of Eastern Ontario and University of Ottawa

Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are incurable debilitating lifelong diseases that can affect children. Early detection is critical to avoiding complications and improving their quality of life. At the moment, however, there is no single test to determine the presence or type of IBD and the tests that exist are very uncomfortable for children.

Drs. Alain Stintzi, David Mack and team are developing a simple, non-invasive approach to detecting IBD that will also be more cost effective. Using cutting-edge technology, the scientists will examine intestinal bacteria to develop better ways of identifying IBD and determining its severity. This work could also lead to new treatment, enhancing the quality of life for children everywhere.

ALBERTA

PACE-‘Omics: Personalized, Accessible, Cost-Effective applications of ‘Omics technologies

Project leader: Christopher McCabe

Project co-leader: Tania Bubela

University of Alberta

Personalized medicine should allow doctors to tailor treatment to patients' biological characteristics. This should mean better treatments with fewer adverse reactions to drugs and other therapies, which could make for a much more efficient and cost-effective healthcare system. However, current processes for developing and licensing medical technologies are a threat to the realisation of this potential.

The project led by Drs. Christopher McCabe and Tania Bubela will give policymakers and investors the tools they need to make the right investment decisions on technology development, regulatory pathways, cost-effectiveness and benefit to the Canadian health system. The project will develop approaches to properly reflect the views and values of Canadians in making decisions for introducing personalized medicine into cash-strapped healthcare systems. Bringing together experts in health economics, health policy, regulation, commerce, law and ethics, they will provide practical decision-making tools and completed analyses that will lead to informed policy-making. At the same time, by helping to establish the “ground rules” for the development of personalized medicine, the project will make Canada a less risky and more attractive base for developers, thereby supporting economic development in the Canadian life sciences industries.

BRITISH COLUMBIA

Personalized treatment of lymphoid cancer: British Columbia as model province

Project leader: Joseph Connors

Project co-leaders: Marco Marra, Randy Gascoyne

BC Cancer Agency

Thanks to new research, scientists can now decode the genetic instructions in both normal and malignant cells. Armed with this information, doctors will soon be able to select the best cancer treatment for each individual. Lymphoid cancers are special because even when they have spread widely in the body they can still be cured. Recent research has shown that genomic sequencing can recognize special lymphoid cancers that are often not cured today but which could be treated more effectively using personally designed treatments.

Drs. Joseph Connors, Marco Marra and Randy Gascoyne’s research team will apply genetic sequencing to lymphoid cancers—the fourth most common type of cancer. This research could increase the cure rate of several lymphoid cancers by 20 per cent—this means more than forty lives saved annually in BC and upwards of \$2.5 million savings to the healthcare system in that province alone, and immeasurable dollars recovered from the ripple-effect of disease impacts such as lost work days and family suffering. This research will use BC as a pilot project to show how to use genomic analysis to cost-effectively cure more cancer patients in a way that can readily be duplicated elsewhere around the world.

Canada

Viral and human genetic predictors of response to HIV therapies

Project Leader: Richard Harrigan

Project Co-Leader: Julio Montaner

BC Centre for Excellence in HIV/AIDS, St. Paul's Hospital

The HIV drug “cocktail” has transformed AIDS from a fatal disease to a manageable condition. Unfortunately, HIV can become resistant to these drugs, leading to the development of full-blown AIDS in the patient and increasing the chances of further transmission of the virus.

Drs. Richard Harrigan and Julio Montaner's research team will develop a test for drug resistance personalized to an individual's DNA and the DNA of the virus. Lifetime drug costs for HIV are between \$250,000 and \$500,000 but there are numerous multipliers of the economic impact of an HIV infection. Nations with high HIV-infection rates see the significance of those impacts on GDP to a point of unsustainability.

The project is also developing real-time surveillance systems for monitoring drug resistance to provide an early warning of geographic or population “hotspots” where resistance rates are highest and the risk of transmission greatest. Mathematical modeling suggests that implementing this pilot project in Vancouver's Downtown East Side and Prince George could avert as many as 173 HIV infections in the first five years, which represents approximately \$65 million in avoided lifetime HIV treatment costs.

Reducing stroke burden with hospital-ready biomarker test for rapid TIA triage

Project leader: Andrew Penn

Project co-leaders: Christoph Borchers, Shelagh Coutts

Victoria General Hospital

Every year, 50,000 Canadians have a stroke, making it the leading cause of disability in the country. However, an equal number of people suffer what are called transient ischemic attacks, or TIAs, which, while less serious, can lead to strokes. The problem is that many conditions, including migraines, can present as TIAs, leading to expensive neuroimaging testing. What's needed is a quick, inexpensive test that would differentiate TIAs from other conditions.

The team led by Drs. Andrew Penn, Christoph Borchers and Shelagh Coutts are developing just such a test, which will provide results within an hour or so, for a fraction of the cost of imaging. With the results of this test, doctors will know whether to keep patients for further care or send them home. This will reduce unneeded imaging risks and costs as well as prevent TIAs from progressing to a full stroke. Averting just 4,000 strokes would save \$210 million per year in direct health care costs. The Heart and Stroke Foundation of Canada will work to ensure that physicians, allied healthcare providers, the public and other stakeholders are aware of the outcomes and clinical impacts of this project.

Clinical implementation and outcomes evaluation of blood-based biomarkers for COPD management

Project leader: Don Sin

Project co-leader: Raymond Ng

St. Paul's Hospital, University of British Columbia, PROOF Centre for Excellence

Canada

Chronic Obstructive Pulmonary Disease (COPD) damages the airways inside of our lungs, making it difficult to breathe. Patients suffer “lung attacks”, characterized by coughing, breathlessness and a dramatic increase in sputum. If caught early enough—or better yet, prevented—these lung attacks can be effectively treated with medication. Unfortunately, many of the symptoms of lung attacks can resemble pneumonia, heart attacks or even the flu. Lung attacks reduce patient quality of life and cost the Canadian health care system nearly \$4 billion dollars each year in direct and indirect costs.

Drs. Don Sin, Raymond Ng and team will develop new blood tests that will identify patients at high risk for lung attacks as well as differentiate these attacks from other conditions. This means lung attacks can be prevented or treated earlier than was previously possible. Ultimately, patients who need preventative drugs will receive them, resulting in fewer attacks, as well as reduced hospitalization and emergency visits. At the same time, patients at low risk of an attack will be able to avoid unnecessary drugs and their potential side effects.