GenomeCanada

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BACKGROUNDER

2015 Disruptive Innovation in Genomics Competition
Results for Phase 1

In June 2015, Genome Canada launched the Disruptive Innovation in Genomics (DIG) Competition. The major objective of the competition is to support the development of **disruptive innovation** in the field of genomics, which is defined as *a new genomics-based technology or the application of an existing technology from another field, applied to the field of genomics, that is truly transformative in that it has the potential to either displace an existing technology, disrupt an existing market or create a new market. A disruptive innovation offers the capability to do things not previously possible and is not an incremental improvement of an existing technology.*

To maximize the benefits for the genomics community, the DIG program is being delivered in two phases:

Phase 1 supports activities to prove the feasibility of an "idea" – does this technology work and what can it do? This phase supports ideas for potential disruptive innovations from either individuals with a need (i.e. users of genomics), technology developers or others with great ideas.

Phase 2 supports the development of a prototype (e.g. process, product and/or method) to advance the "idea". Two rounds of Phase 2 funding are available (the second Round open only to eligible Phase 1 projects.)

Twenty projects have been selected for funding under Phase 1 with an investment of approximately $5 million from Genome Canada. No co-funding sources were required for these projects. (The first round of Phase 2 projects are listed in a separate backgrounder.)

BRITISH COLUMBIA

A chemo-affinity toolkit for methylation proteomics

Project Lead: Fraser Hof, University of Victoria
Administrative Lead Genome Centre: Genome British Columbia
Total Funding: $238,800

Human cells contain tens of thousands of proteins, most of them controlled by modifications that can be as small as a single carbon atom ("methyl group") added in subtly different ways. Researchers and clinical testing centres worldwide lack a global, reliable and universally accepted method for doing methyl analysis. The market for methyl-targeted research and diagnostics is growing rapidly and ripe for disruption. Dr. Fraser Hof and his team at the University of Victoria will adapt a family of binding chemicals that can bind methylated proteins. With this proof-of-concept work, the team will transform methylation research, lead to new medicines and diagnostics, and drive sales, new jobs, and new science in dozens of research labs and thousands of diagnostics centres.

Reimagining genome browsing for the era of single cell genomics

Project Leader: Sohrab Shah, University of British Columbia
Co-Leader: Cydney B. Nielsen, University of British Columbia
Lead Genome Centre: Genome British Columbia
Total Funding: $250,000

Genetic diversity within cancer tumours contributes to drug resistance, spread and disease progression. While researchers can sequence the individual cells, there are no tools to effectively visualize the millions of genomes that exist in a single tumour. Dr. Sohrab Shah of the University of British Columbia is introducing highly scalable search-engine technology called Elasticsearch to the field of single-cell genomics. This technology will have immediate impact in the international cancer research community and, ultimately, lead to better understanding how the genomes of individual tumour cells influence their response to treatments, revealing mechanisms of resistance and new therapeutic targets.

GNOmics: Graphs 'N' Omics

Project Leader: Wyeth Wasserman, University of British Columbia
Administrative Lead Genome Centre: Genome British Columbia
Total Funding: $250,000

Sequencing individual human genomes can lower healthcare costs and improve outcomes by permitting highly personalized treatment and preventive medicine. Individual human genomes need to be analyzed in the context of a reference genome, however, which serves the same purpose as a picture of a completed jigsaw puzzle – it accelerates the placement of pieces. Dr. Wyeth Wasserman of the University of British Columbia will implement a novel graph model, the GNOmics (Graphs 'N' Omics) Genome Model (GGM), which will provide a robust new

computational framework for the analysis of genetic variation that includes a unified reference database of publically available genetic data. The GGM incorporates significantly more information when representing genomic data, potentially allowing for improved accuracy without compromising speed or dramatically increasing the strain on computational resources.

ONTARIO

AbSyn Technology for Identification of Synergistic Cancer Therapeutics

Project Leader: Charles Boone, University of Toronto
Co-Leader: Jason Moffat, University of Toronto
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $249,389

Genome sequencing has revolutionized our understanding of the genetic changes that lead to cancer. Unfortunately, treatment still remains in the relative Dark Ages, with decades-old treatments that can be highly toxic and that don't consider the subtle genetic differences among each patient's disease. Dr. Charles Boone and his team at the University of Toronto are developing AbSyn, a new technology that will identify combination therapies tailored to individual cancers. AbSyn stands for the development of antibodies (Ab), whose promise for treating cancer has been hugely under-realized, and synergistic (Syn) therapies for cancer based on these antibodies. AbSyn will change the way we prioritize and discover new cancer drugs, building a new bridge between the gap of biological understanding and the commercial drug discovery process.

RNA-seq in patient derived ex-vivo models: genetic diagnostics beyond whole exomes

Project Leader: James Dowling, The Hospital for Sick Children
Co-Leader: Michael Brudno, The Hospital for Sick Children
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

There are more than 6,000 rare diseases caused by mutations in a single gene; together they affect more than 500,000 Canadian children. Exactly what gene is causing a disease is unknown in more than half the cases. RNAseq may provide a strategy for discovering novel genetic mutations that cause rare diseases – but can't be used without obtaining the specific tissues in which the disease is present. Drs. James Dowling and Michael Brudno, of The Hospital for Sick Children will use *ex vivo* disease models created at Sick Kids in place of tissue biopsies to perform RNAseq for gene mutation discovery. By combining recent advances in cell biology, genomics and bioinformatics, the lab will develop a new diagnostic methodology, fundamentally transforming the clinical diagnostics process.

Massively parallel single molecule protein sequencing in situ

Project Leader: Andrew Emili, University of Toronto
Administrative Lead Genome Centre: Ontario Genomics
Total funding: $250,000

Proteins in cells are responsible for virtually every biological process. When they don't work properly, the result can be human diseases such as cancer, Alzheimer's, diabetes and heart disease. Dr. Andrew Emili of the University of Toronto will develop a revolutionary new sub-microscopic imaging technology that will allow researchers to identify and quantify each and every one of the many millions of different protein molecules present in human cells and tissues at an unprecedented level of detail. The proprietary chemical probes and tool "kits" he and his team develop will be applicable to a wide diversity of biomedical specimens, displacing existing technologies and ultimately changing the study of human cell biology and medicine.

RapidAIM: a high-throughput assay of individual microbiome

Project Leader: Daniel Figeys, University of Ottawa
Co-Leader: Alain Stintzi, University of Ottawa
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

The more than 1,000 different species of bacteria that colonize our gastrointestinal tract are collectively known as our microbiome. Dr. Daniel Figeys and Dr. Alain Stintzi of the University of Ottawa are developing RapidAIM to gain information on how drugs affect the microbiome and vice versa. The team will also develop a computational program that will combine and analyze these results, to better predict drug efficacy and clinical outcomes. RapidAIM could allow rapid screening of candidate or current drugs for potential adverse microbiome effects. The economic benefits will come in the form of a commercializable assay and computational platform for the screening of human microbiomes.

Development of advanced genetic toolbox for *Sinorhizobium meliloti* to enable genome scale engineering

Project Leader: Turlough Finan, McMaster University
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

Genetic engineering seeks to improve agricultural outcomes by enhancing traits such as disease resistance, drought tolerance or superior levels of production. Conducting this engineering, however, requires a host where genes can be implanted and researchers perform genetic manipulations – a process known as synthetic biology. Drs. Turlough Finan, Bogumil Karas and Trevor Charles are developing a bacterial surrogate host system (*Sinorhizobium meliloti*) that allows replication and engineering of large DNA fragments before reintroducing them back to the original organism. In addition to its general application for genome engineering, the *S.*

meliloti surrogate host-system technology can be used in short-term technology developments, including the generation of large DNA libraries for bioprospecting.

Cell biosensors for rapid screening of insect attractants

Project Lead: Peter J. Krell, University of Guelph
Co-Leader: Daniel Doucet, Natural Resources Canada
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $233,901

Forestry and agriculture together contribute close to eight per cent of GDP in Canada, but insect pests pose a continual threat. Functional genomics has long promised to bring new solutions to recurrent and new pest problems. Dr. Peter J. Krell of the University of Guelph, in collaboration with Drs. Daniel Doucet and Jeremy Allison (NRCan), is creating highly sensitive surveillance and mitigation systems targeting insects, using a family of insect genes known as odorant receptors (ORs). This innovation should not only disrupt the discipline of functional genomics, but also the field of insect pest management, making surveillance and mitigation more feasible and faster, while helping preserve Canada's position as a leading exporter of forest and agricultural products.

Economical high throughput de novo whole genome assembly

Project Leader: Stephen Scherer, The Hospital for Sick Children, Toronto
Co-Leader: Si Lok, The Hospital for Sick Children
Lead Genome Centre: Ontario Genomics
Total Funding: $241,467

"De novo" sequencing, or constructing an individual's genome from his or her own data alone (as opposed to comparing it to a reference genome), is a formidable task, akin to assembling a jigsaw puzzle comprising hundreds of millions of small blank pieces. Drs. Si Lok, Stephen Scherer, and their colleagues from The Hospital for Sick Children are developing a new "mate-pair" technology that would overcome the financial and logistical barriers to de novo sequencing by linking sequences to one or more other reads in precisely known orientations and distances. Mate-pair technology would create a high-resolution backbone to enable de novo sequencing to be carried out in a single simple step. This new adaptation of mate-pair sequencing is a disruptive technology that could supersede all current methods of de novo sequencing, thereby representing a leap forward in many areas of research and, ultimately, in healthcare.

Development of SIMPL, a novel protein-protein interaction assay based on split intein for biomedical research

Project Leader: Igor Stagljar, University of Toronto
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

Proteins control every function of every cell in our body. Proteins, however, never act alone; rather, they interact with many other proteins in what are called protein-protein interactions (PPIs). Gain or loss of PPIs can be the driving force behind disease development. Dr. Igor Stagljar of the University of Toronto is leading a team to develop and implement a novel disruptive genomics technology that can detect and monitor PPIs in human cells. This technology can be used to identify novel proteins as components of many essential cellular processes, leading to greater understanding of the role of specific proteins in our cells. Furthermore, the technology also has the potential to identify drugs that disrupt a defined set of PPIs when the PPIs cause disease.

Solid-State Nanopore-based Quantification of Low-Abundance Biomarkers

Project Leader: Vincent Tabard-Cossa, University of Ottawa
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

Many illnesses, such as cancer or cardiovascular disease, leave physical evidence in our bodies, called biomarkers. Spotting these biomarkers early would make it possible to begin treatment with personalized, targeted therapy, or even prevent disease entirely. Solid-state nanopore-based devices can do this, but are too expensive for widespread use. Dr. Tabard-Cossa's laboratory has pioneered a technique to fabricate nanopore devices more rapidly and at substantially lower cost than present-day technology. They are integrating the devices into a disposable cartridge within compact platforms offering comprehensive sample-in, answer-out capability. The lab is positioned to develop a point-of-care prototype that can be used in the lab and the clinic, resulting in significant economic and health benefits for Canada.

Functional Genomics in Human Cells for Drivers of Lethal Metastatic Human Cancers

Project Leader: Michael Taylor, Hospital for Sick Children
Co-Leader: Rama Khokha, Princess Margaret Cancer Centre
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

Often in cancer it's the spread of the cancer to other areas of the body, a process called metastasis, that kills. This is particularly the case with two highly lethal types of cancer, medulloblastoma (MB), the most common malignant brain tumour in children, and pancreatic adenocarcinoma, the fourth leading cause of cancer deaths in Canadians. Recent results from the lab of Dr. Michael Taylor of The Hospital for Sick Children have shown that the biology of the metastases is extremely different from the primary tumour, making it unlikely that treatments developed to treat the primary tumour will work on the metastases. Dr. Taylor has teamed with Dr. Rama Khokha (Princess Margaret Cancer Centre) to develop and deploy unique tools to discover the drivers of metastasis, helping to improve survival rates of Canadians with these deadly human cancers.

Development of a digital microfluidic platform to identify and target single cells from a heterogeneous cell population for lyses in an ultra-low volume

Project Leader: Aaron Wheeler, University of Toronto
Co-Leader: Elena Kolomietz, Mount Sinai Hospital
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $250,000

Genetic abnormalities are a leading cause of death among Canadian newborns and infants. Less invasive, less expensive prenatal diagnostic techniques that are able to provide relevant information at earlier stages of pregnancy are needed. Scientists and physicians at Toronto's Mount Sinai Hospital have developed a method to collect and isolate fetal cells non-invasively, using a technique similar to a PAP smear. Now Dr. Aaron Wheeler's research group at the University of Toronto is developing techniques to isolate and analyze these cells for prenatal diagnosis of genetic abnormalities. If successful, these techniques could transform the way prenatal diagnosis is delivered, resulting in higher coverage of the population, reduced patient anxiety, increased medical options for at-risk pregnancies and significant reductions in healthcare costs.

SANGRE-seq (systematic analysis of blood gene regulation by sequencing) – bringing RNA-seq to clinical diagnostics

Project Leader: Michael Wilson, The Hospital for Sick Children
Co-Leader: Adam Shlien, The Hospital for Sick Children
Administrative Lead Genome Centre: Ontario Genomics
Total Funding: $249,934

Diagnostic tests based on blood samples are mainstays of the healthcare system. Adding RNA sequencing (RNA-seq) can extract more information from blood samples, including a snapshot of all the genes active in a patient's blood cells. Such a snapshot can tell us about the current condition of the patient's immune system, whether there are cancer cells in the blood and/or whether blood cells are fighting an infection. Drs. Michael Wilson and Adam Shlien of The Hospital for Sick Children are developing an RNA-based clinical test called SANGRE (systematic analysis of blood gene regulation in blood) that will provide unprecedented power to use RNA expression as a routine and affordable test that can better diagnose disease, disrupting clinical practice and improving the health of Canadians.

QUÉBEC

Laser-assisted single-cell genomics

Project Leader: Santiago Costantino, Hôpital Maisonneuve-Rosemont
Co-Leader: Claudia L. Kleinman, McGill University
Administrative Lead Genome Centre: Génome Québec
Total Funding: $250,000

Single-cell genomics is a powerful new generation of technologies promising to transform our understanding of diseases where unique cells play a major role. Single-cell analyses allow researchers to understand cell-to-cell variation and to study the specific cells responsible for disease progression. However, a versatile, efficient and non-invasive technology to identify and capture these cells is lacking. Santiago Costantino, PhD, of Hôpital Maisonneuve-Rosemont is developing a method that enables instant, specific tagging of living cells with a laser, using the same instrument used for imaging. The approach is simple and low cost. The team will demonstrate its potential with a study designed to, for the first time, identify micro-environmental signals produced by liver cells that promote breast cancer metastasis.

Single exosome multi-omic analysis

Project Leader: David Juncker, McGill University
Administrative Lead Genome Centre: Génome Québec
Total Funding: $ 249,999

Exosomes (EX) are nanometer-sized, fluid-filled vesicles ("bubbles") that are secreted in large amounts by cancer cells and can be retrieved from blood. EXs contain molecules characteristic of their parental cells and could be used to identify different types of cancer cells simply by collecting a few droplets of blood. David Juncker, PhD, and his lab at McGill University have made key advances in nanotechnology that they will leverage to develop a novel single-EX analysis tool that could disrupt and transform cancer management by providing a sensitive means for disease diagnosis and monitoring. The successful outcome of the proposed research would add EX monitoring as a powerful tool to the arsenal used to track cancer and guide therapy.

The RNA zipcode discovery pipeline: emerging tools for targeting therapeutic molecules at subcellular resolution

Project Leader: Éric Lécuyer, Institut de recherches cliniques de Montréal (IRCM)
Co-Leader 1: Mathieu Blanchette, McGill University
Co-Leader 2: Jérôme Waldispühl, McGill University
Administrative Lead Genome Centre: Génome Québec
Total Funding: $250,000

Every human develops from just one cell. But that one cell differentiates into trillions of cells, each of which has its own role to play. For each cell to carry out its assigned task, it has to organize its inner components at precise locations. When this organization doesn't work, it can predispose us to diseases such as neuromuscular disorders or cancer. Just as the post office uses postal codes to direct mail, there are signature "zipcodes" that do the same with cell components. Éric Lécuyer, PhD, and his team are identifying the "zipcodes" in different types of RNA molecules. With this knowledge, RNA molecules can be used to manipulate cellular behaviour and develop novel treatments for diseases that involve defects in cellular organization, including genetic disorders for which no treatments are currently available.

Plasmonic PCR: Rapid Diagnostics through Plasmonics

Project Leader: Mark Trifiro, Jewish General Hospital
Co-Leader: Andrew G. Kirk, McGill University
Administrative Lead Genome Centre: Génome Québec
Total Funding: $ 249,976

The outbreak of an infection in a hospital or agricultural/forest community can lead to severe consequences for the people and organizations affected. Dr. Mark Trifiro of Montreal's Jewish General Hospital has developed a light and nanotechnology-driven PCR technology platform called Plasmonic that provides near-instant point-of-care infectious agent recognition by DNA diagnostics. This information will allow informed decisions over how to treat and contain infection, reducing the human and economic costs of these infections.

A cell microfactory platform for *in vivo* biosynthesis and delivery of genetically encoded natural products and synthetic antibodies

Project Leader: Michael Tyers, Université de Montréal
Co-Leader: Gerard Wright, McMaster University
Administrative Lead Genome Centre: Génome Québec
Co-Lead Centre: Ontario Genomics
Total Funding: $249,358

Antibiotics, drugs and biologic agents costly to manufacture, store and deliver to patients, whether human or animal. Antibiotics can also contaminate the environment, leading to antibiotic resistance. Drs. Michael Tyers of Université de Montréal and Gerard Wright of McMaster University propose to create a cell-microfactory and delivery system that will radically transform the way drugs are deployed. They will engineer a non-toxic yeast that is biocompatible with the gastrointestinal (GI) tract and that will produce any desired bioactive agent. Introducing the yeast into a human patient or animal will result in the production of the bioagent. Local production and delivery in the gut will be in much smaller amounts than typically needed for whole-body doses of antibiotics and will therefore help mitigate the problem of antibiotic resistance.