Backgrounder

Genome Canada investments drive cutting-edge R&D in health, environmental sustainability and agricultural resilience

This milestone investment marks the 100th project funded through Genome Canada's Genomic Applications Partnership Program, which has invested in late-stage research and development (R&D) projects addressing real world opportunities and challenges for the last decade.

Genome Canada is proud to announce the launch of 13 new projects within its Genomic Applications Partnership Program (GAPP) that will mobilize cutting-edge genomics research and innovation to deliver real world impact for Canadians. The GAPP program leverages world-leading expertise and diversified partnerships to accelerate the translation of scientific knowledge into broad economic and societal benefits for Canada.

These 13 applied genomics research projects represent $18.1 million in federal support through Genome Canada to deliver tangible benefits to Canadians. In collaboration with industry, healthcare organizations, as well as provincial and other federal partners—who collectively bring co-funding valued at $38.6 million—this represents a total investment of $56.7 million.

The projects in this backgrounder are listed by the regional Genome Centre leading on the work, and within those groupings, alphabetically by project name.

FUNDED PROJECTS

GENOME BC

Title: Parent-of-Origin Aware genomic analysis
Academic Leader / Institution: Steven Jones and Peter Lansdorp (The University of British Columbia)
Receptor Leader/ Organization: Kasmintan Schrader (BC Cancer)
Genome Centre: Genome BC
Total Funding: $6,102,150

Around 300,000 unidentified Canadians are at high risk for developing hereditary cancers. This is a missed opportunity for preventing or catching cancer early. Although current genetic testing can inform a patient's inherited risk for disease, it does not predict which

side of the family an autosomal variant comes from. This limitation can lead to costly and ineffective genetic counselling and testing of multiple family members from both sides (known as cascade genetic testing). This project will validate a new technology, Parent-of-Origin-Aware genomic analysis (POAga), in real-world hereditary cancer patient samples in British Columbia and the Yukon. Preliminary data demonstrates that this technology offers 99% accurate prediction of the parent-of-origin, using only the blood sample of the child. Once in clinical use, the anticipated benefits of POAga include a 50% increase in the efficiencies in cascade genetic testing, in the number of carriers identified, and in mutation detection rates, as well as reduced financial and emotional benefits for patients and their families. Success will position BC Cancer as a global centre of excellence for POAga. The technology can then potentially be expanded to other hereditary cancer syndromes and non-cancer related genetic diseases.

Title: RapidOmics 2.0: Long-read genomic sequencing for urgent genetic disease diagnosis
Academic Leader / Institution: Jan Friedman (The University of British Columbia)
Receptor Leader/ Organization: Craig Ivany (Provincial Health Services Authority)
Genome Centre: Genome BC
Total Funding: $3,645,141

Genetic disorders are a leading cause of major illness and death in infancy. Although precise diagnosis is necessary, access to genome-wide sequencing is limited in British Columbia. This is a particular problem in the fetal and neonatal period, when making a genetic diagnosis can profoundly influence clinical management and have lifelong consequences. Long-read genome sequencing offers the promise of greater diagnostic sensitivity and shorter turn-around-time for urgent diagnosis of genetic disease. Over three years, RapidOmics will use rapid long-read sequencing to test 100 patients, either acutely ill infants or pregnant women with a fetus at very high risk of genetic disease, in BC Children's Hospital or BC Women's Hospital & Health Centre.

The project will assess the clinical value, limitations, costs and benefits of this type of sequencing as a diagnostic test. If successful, it may lead to establishing a provincially funded clinical reference laboratory for rapid long-read sequencing. Such a laboratory would also create a robust environment for training graduate and health professional students and postdoctoral fellows. The research will ultimately improve the quality of genetic healthcare provided to babies with genetic diseases and their families in BC, with the hope to one day extend this service to more than 3,000 pregnancies or infants annually across Canada.

GENOME ALBERTA

Title: Genomic testing of wastewater to promote public health and safeguard economic performance
Academic Leader / Institution: Casey Hubert (University of Calgary)
Receptor Leaders / Organizations: Alex Alexander (Alberta Health)
Genome Centre: Genome Alberta
Total Funding: $6,000,001

The COVID-19 pandemic has demonstrated the urgent need for early warning surveillance systems that can provide information to public health authorities on emerging COVID-19

variants and other infectious diseases. Wastewater-based epidemiology (WBE) is a non-invasive, comprehensive and cost-effective early warning system that enables population-level monitoring independent of clinical testing. The research team has already developed an innovative platform for field-based sampling of wastewater followed by optimized nucleic acid purification in the lab. They have partnered with Alberta Health and municipal end-users to demonstrate that COVID-19 case numbers can be predicted with a six-day lead time, mirroring results from other teams globally. This project will leverage existing wastewater surveillance activities to analyze other high priority disease targets in Alberta municipalities and First Nations communities. As well as mitigating infection transmission and supporting the early detection of outbreaks, WBE can potentially create economic benefits by minimizing indirect effects of increased disease burden on employment, family structure, mental health, and education.

Title: Transcriptional and epigenetic events underpinning Navacim-Induced TR1 cell formation and expansion
Academic Leaders / Institutions: Pere Santamaria (University of Calgary)
Receptor Leaders / Organizations: Jord Cowan (Parvus Therapeutics)
Genome Centre: Genome Alberta
Total Funding: $2,880,000

More than 100 autoimmune diseases have complex immune responses to autoantigens. Nanoparticles coated with autoimmune-disease-relevant peptide-major histocompatibility complexes (Navacims) have the potential to halt and cure autoimmune disease by restoring immune tolerance without compromising normal immunity to infections and cancer. They are currently the only technology that can activate internal generation of disease-specific regulatory T cells within the host. This project aims to understand the types of changes in the structure of the nuclear DNA of the cells that are re-programmed by Navacims, to expand the commercial and clinical potential of Parvus Therapeutics' proprietary platform. It seeks to precisely define the cellular identity of the initial, transitional and final T cell types of this cellular re-programming process, and to identify biomarkers to monitor effectiveness and efficacy of treatment. This information will then be used to define, validate and develop a clinical/biomarker strategy for Phase 2 and Phase 3 trials, potentially revolutionizing the treatment of autoimmune diseases, many of which are multi-billion dollar per year markets.

GENOME PRAIRIE

Title: Clinical implementation of oncogenomic testing and synoptic reporting for improved ovarian cancer patient care in Saskatchewan
Academic Leader / Institution: John DeCoteau (University of Saskatchewan)
Receptor Leaders / Organizations: Marilyn Kinloch (Saskatchewan Health Authority)
Genome Centre: Genome Prairie
Total Funding: $3,921,377

Women with ovarian cancer have an overall survival rate of only six years, with the first of multiple recurrences happening between 12 and 18 months after detection. That is because ovarian cancer commonly presents at an advanced stage and has biologic resistance to conventional therapy. Once ovarian cancer is detected, there is an urgent need to better identify precision treatment options for each patient, based on their unique tumour characteristics. This pilot implementation project will use a suite of genomics testing— Comprehensive Genomic Profile—to more efficiently identify patients with one type of

profile, homologous recombination deficiency, which are specific for the recently developed Poly(ADP-ribose) polymerase inhibitors (PARPi) treatment. It will integrate testing with an upgraded clinical and diagnostic reporting solution for genetic profiling of patient tumour information. As well as enhancing testing capacity, clinical implementation will improve treatment of cancer patients, optimize their care and enable more efficient use of resources in Saskatchewan's healthcare system.

Title: Development and clinical implementation of an omics assay for the diagnosis and treatment of *Helicobacter pylori*
Academic Leaders / Institutions: David Alexander (University of Manitoba)
Receptor Leaders / Organizations: Sara Christianson and Aleisha Reimer (National Microbiology Laboratory, Public Health Agency of Canada)
Genome Centre: Genome Prairie
Total Funding: $1,715,276

*Helicobacter pylori (*Hp) is the main cause of peptic ulcer disease and a major risk factor for gastric cancer. Around 13 million Canadians are infected with Hp, a bacterial pathogen. Hp infections and related gastric cancers disproportionately affect Indigenous and new arrival to Canada populations. Treatment can cure Hp infections and prevent gastric cancer. The standard treatment is complex, requiring up to four different medications, and some types of Hp are now resistant to this treatment. Antimicrobial susceptibility testing can improve Hp treatment, but it is technically demanding and not routinely done in Canada. Therefore, an effective alternative to diagnose Hp infections and identify antimicrobial resistance (AMR) is urgently needed. This project will develop an end-to-end metagenomics-based pipeline prototype for Hp identification and AMR detection directly from clinical specimens. The team will also create a reference database for Hp AMR and develop national reports, in the form of antibiograms. Potential benefits include more rapid and accurate testing, leading to more successful treatment of Hp infections and fewer cases of gastric cancer. Data from this project will also fill current gaps in Hp monitoring, thus allowing the clinical, public health and scientific communities to better understand Hp diversity in Canada. The ultimate impact will be to reduce the social and economic burden of Hp infections on Canadians.

ONTARIO GENOMICS

Title: Biopesticide with new modes of action for control of highly polyphagous mite agricultural pests
Academic Leader / Institution: Vojislava Grbic (Western University)
Receptor Leaders / Organizations: Ken Narva (GreenLight Biosciences, PBC), Niki Bennett (Ontario Greenhouse Vegetable Growers)
Genome Centre: Ontario Genomics
Total Funding: $4,087,687

Pest management is a top priority for Canada's horticulture greenhouse sector (with farm gate value of $3.9 billion), which provides Canadians with fresh produce year-round. The two-spotted spider mite (TSSM) presents a particular threat to crop security due to its well-documented resistance to pesticides. This project will develop, register and commercialize RNAi biomiticide (dsRNA biopesticides specific for mites) against the TSSM to effectively manage its outbreaks. Project researchers—the first to demonstrate that RNAi-based silencing operates in TSSM—have already developed protocols for high-throughput

screening of RNAi targets, provided proof-of-principle that sprayable RNAi works against TSSM, and identified effective TSSM RNAi targets. The project benefits from the experience of GreenLight Biosciences, PBC in designing, developing and manufacturing targeted RNA-based biopesticides and the Ontario Greenhouse Vegetable Growers' first-hand knowledge of the needs of Canada's horticulture greenhouse growers. A potential game-changer for mite control, RNAi biomiticide will not only provide the sector with potential economic benefits of ~$600 million per year, it will also provide growers with an alternative to synthetic chemical insecticides, thus reducing their environmental footprint.

Title: Developing novel bioleaching process for Ni recovery from pyrrhotite streams
Academic Leaders / Institutions: Krishna Mahadevan (University of Toronto)
Receptor Leaders / Organizations: Jan Van Niekerk (Metso-Outotec)
Genome Centre: Ontario Genomics
Total Funding: $6,054,674

Current methods of mining and processing ores for metal recovery are energy intensive. They lead to significant waste streams, tailings and energy-related greenhouse gas emissions, exacerbating the climate crisis. However, (re)processing existing tailings containing metals value is not energy intensive as the energy to extract the minerals has already been spent. In addition, electrification of the transportation sector is a key part of Canada's climate strategy. Bioprocessing offers energy-efficient and environmentally friendly methods for recovering critical minerals, such as nickel, that are key components in batteries and electric vehicles. The project will use genomics technologies to characterize and engineer microbial populations and test bioleaching process strategies to treat pyrrhotite tailings, waste streams of current mining practices, for nickel extraction. Bioleaching technologies are already commercially used for mining, mainly extracting gold, and copper from sulfidic ores. The team will use genomic solutions to enable the widespread application of bioleaching technology, aiming at achieving faster bioleaching kinetics, improved residue quality, selectivity for Ni extraction and developing process monitoring methods. Metso-Outotec and BacTech work with Glencore and Vale to implement the technology on pyrrhotite tailings from the Sudbury, ON, basin mines. The extraction of nickel from pyrrhotite tailings in Canada has a potential value of $26 billion, can provide a source of critical minerals for the production of electric vehicle batteries, and enable significant (>75%) reduction in waste generation from local mining activities.

Title: Enabling personalized genomics in health with the CanPath data safe haven
Academic Leaders / Institutions: Philip Awadalla (Ontario Institute for Cancer Research)
Receptor Leaders / Organization: John McLaughlin and Trevor Dummer (Canadian Partnership for Tomorrow's Health), Anne-Renee Hartman (Adela)
Lead Genome Centre: Ontario Genomics
Total funding: $6,149,537

Personalized healthcare programs require the collection and integration of high-quality data and biosamples from a vast number of individuals to capture the complex factors that can shape an individual's health over the course of their lifetime. To enable discovery, evidence generation and policy change, the data must be accessible to both researchers, as well as public and commercial health decision makers. In Canada, the sharing and combining of data across jurisdictions, rather than collecting the data itself, is a major barrier to progress

in precision medicine. The promise of personalized medicine is within reach through the Canadian Partnership for Tomorrow's Health project (CanPath): Canada's largest population health cohort. CanPath has made major strides towards integrating clinical, environmental, and population-level health data across all provinces and providing a national access point to deeply characterized and longitudinal health and lifestyle information, more so than any other entity in Canada. Here, the team will build upon CanPath's existing national infrastructure to democratize access to the CanPath platform to better enable Canadian-led innovation and discovery. They will develop and pilot a data safe haven (DSH), a secure environment within which researchers, clinicians and industry in Canada can access deeply characterized population health and biobank data. In partnership with Adela, they will generate genomic data that will be hosted alongside clinical and population data of consented CanPath participants from across Canada within this secure digital framework. The DSH holds the potential to launch Canada to the forefront of genomic medicine globally. It will also support the development of Canada's biotechnology sector and industry research as well as creating the ability to harmonize with leading precision medicine programs. The ultimate result will be earlier diagnosis of disease, advances in medical interventions, and improved health system performance for Canadians.

GÉNOME QUÉBEC

Title: Genomics tools for the prediction of antifungal resistance in clinical samples
Academic Leader / Institution: Christian Landry (Université Laval)
Receptor Leader/ Organization: Philippe Dufresne (Le Laboratoire de santé de publique du Québec)
Genome Centre: Génome Québec
Total Funding: $3,440,067

Fungal infections and resistance to antifungals are on the rise worldwide, with 14.9 million cases and 1.7 million deaths every year. Nearly 2% of Canadians have serious fungal infections and spikes in frequency have been associated with COVID-19, particularly in the most vulnerable patients. This project will develop faster and more accurate tools to identify fungal species and antifungal susceptibility from DNA sequencing directly from clinical samples. The deliverables will include a database of pre-validated resistance mutations, a procedure for generating multilocus sequencing from clinical samples, and a bioinformatic pipeline for species identification and prediction of antifungal resistance. The project will implement the diagnostic tools in Laboratoire de Santé Publique du Québec, Public Health Agency of Canada, Public Health Ontario and Alberta Precision Laboratories - Public Health Laboratory. These three organizations have vast experience in the development of diagnostic tests and play key roles in regulatory organizations and committees that set standards in the field. Implementing faster and more targeted and sensitive testing will reduce the number of deaths and morbidity of Canadians with invasive fungal infections.

Title: MutaQuant: A powerful proteogenomic phenotyping tool for precision medicine
Academic Leader / Institution: Christoph Borchers (McGill University)
Receptor Leader/ Organization: René Zahedi (MRM Proteomics)
Genome Centre: Génome Québec
Total Funding: $3,109,506

In precision oncology, the current method of screening for specific genomic mutations, even using transcriptomics (the complete set of all RNA molecules), has only moderate success in predicting the success of targeted therapies for cancer. In Canada, precision oncology genomic testing costs around $40 million per year for response rates of ~52%. Because proteins are the main drug targets, genomics alone can often not clarify which mutations are biologically relevant in an individual tumour. It is, therefore, important to determine three key things: i) how mutations affect protein expression levels; ii) which are actually expressed on the protein level in relevant amounts rather than just being encoded in the genome; and iii) to what extent these mutations are expressed in a given sample. This project will develop mass spectrometry kits that decipher the impact at the protein level of ~1000 known cancer mutations, which represent the main cancer drivers and drug targets. MRM Proteomics and Agilent Technologies will commercialize novel, validated "MutaQuant" kits, provide education on use, as well as offering a sample analysis service. There is potential for significant cost savings by preventing non-effective cancer treatment and improving patient outcomes.

Title: RosHAB: Rapid on-site detection of harmful algal blooms
Academic Leader / Institution: Jérôme Comte (Institut national de la recherche scientifique), Roger C. Levesque (Université Laval)
Receptor Leaders / Organizations: Daniel Verreault (Ministère de l'Environnement, de la Lutte contre les changements climatiques, de la Faune et des Parcs, Québec; MELCCFP)
Genome Centre: Génome Québec
Total Funding: $5,461,850

The frequency of cyanobacterial harmful algal blooms (cHABs) in water bodies worldwide is increasing due to climate change and expanding urbanization. Exposure to toxins produced by some cHABs can lead to acute and chronic health problems for humans and animals. Early diagnostic tools that effectively detect and identify cHABs are urgently needed. This project will develop an innovative metagenomic tool for in-the-field surveillance of cHABs in Quebec. It will implement on-site sampling and analytical procedures that enable its rapid detection in water bodies; and a bioinformatic platform at MELCCFP that includes a user-friendly sequence database of cyanobacteria species. Local municipalities across the province will validate and implement the tool, which can potentially reduce the identification time for cHABs from four days in some cases to less than 24 hours. The overall project goal will be to expand use to other jurisdictions. A comprehensive rapid cHAB observing and forecasting information system would potentially represent a value of at least $130 million annually to Canada.

Title: Validation of the use of the EcoToxChip test system for regulatory decision-making
Academic Leader / Institution: Niladri Basu (McGill University)
Receptor Leader / Organization: Rebecca Dalton (Environment and Climate Change Canada)
Genome Centre: Génome Québec
Total Funding: $4,739,793

Environmental pollution is a significant threat globally but efforts to reduce the risks posed by chemicals are challenged by the time and cost of toxicity testing, as well as the large number of chemicals that need data. There is a need for improved toxicity testing tools that

are more efficient and affordable, less dependent on animal studies, and better able to accelerate the throughput of chemical screening. This project aims to advance the existing EcoToxChip Test System so that it can be accessible, while also being consistent and reliable for informing regulatory decisions.

The goal is, in partnership with Environment and Climate Change Canada's Science and Technology Branch, to validate these tools for use in a range of prioritization and assessment activities under Canada's **Chemicals Management Plan**. Ultimately, the project will deliver version 2 EcoToxChips for three commonly used test species (fathead minnow, rainbow trout, zebrafish) and an updated data evaluation tool (EcoToxXplorer.ca). Post-project we envision that project results will be communicated to the international regulatory community through the OECD Integrated Approaches to Testing and Assessment Case Study Project. This new made-in-Canada tool will reduce the cost and time for chemical testing as well as boost Canadian leadership in this area.