May 30, 2024

Backgrounder

Genome Canada announces investment in eight new Genomic Applications Partnership Program projects

Genome Canada is proud to announce the launch of eight 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.

This announcement represents more than $11 million in federal support to cutting-edge genomics science and innovation funded by Genome Canada. Provincial governments, business and research partners are also investing another $23 million in co-funding, for a total investment of more than $34 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: Prospective epitope matching for renal transplant patients in British Columbia as a test bed for national implementation
Academic Leaders/Institutions: Dr. Paul Keown (University of British Columbia)
Receptor Leaders/Organizations: Dr. Robert Liwski (Canadian Blood Services)
Genome Centre: Genome BC
Total Funding: $5,885,587

Almost a million Canadians suffer from progressive disease of a vital organ, leading to premature debility and death. The complex care these patients need creates some of our most demanding health challenges, with the economic burden exceeding $10 billion per year. Recent medical advances in transplanting cells and organs have extended the lives and improved the health of many patients. However, transplant is still a high-risk, high-cost procedure. Only around 5,000 patients receive new transplants each year, of which most grafts fail prematurely.

Researchers are working with Canadian Blood Services, the national coordinator of transplant services, to propose a visionary genomics-based solution for better matching donors and recipients for kidney transplants. This solution implements a world-first epitope-based program and aims to reduce patients' risk of organ rejection, minimize toxic immune suppression, and eliminate the need for lifelong immunosuppressive therapy. The project will be tested in British Columbia, building on previous Genome-Canada-funded work exploring the role of antibody-mediated rejection in graft failure and the key epitopes (the part of an antigen molecule that our immune systems recognize) on the donor human leukocyte antigen molecules responsible. When extended to all of Canada, the project conservatively estimates a benefit of $100 million through preventing hospitalization, premature graft loss and death.

ONTARIO GENOMICS

Title: A synthetic biology platform to support fungal drug discovery
Academic Leaders/Institutions: Dr. Gerard Wright (McMaster University)
Receptor Leaders/Organizations: Dr. Eric Brown (Kapoose Creek Bio)
Genome Centre: Ontario Genomics
Total Funding: $2,268,417

Fungi have been the source of some of the most effective medicines in history, such as penicillin. However, producing the active medicinal ingredients at scale for R&D has been a key challenge to further fungal drug discovery. This project aims to create a flexible, scalable and cost-efficient synthetic biology platform that supports the synthesis of diverse fungal molecules and produces sufficient compound. It will leverage Kapoose Creek Bio's (KCB's) proprietary AI-enabled drug discovery platform (unEarth Rx), which mines nature for new therapeutic drug leads. The platform will use genomics and metabolomics solutions to develop a biosynthetic expression system for genetically-encoded fungal compounds.

The implementation of an in-house synthetic biology platform at KCB will provide a significant competitive advantage, both to accelerate the drug discovery program and enable future clinical-stage partnerships. The project is anticipated to catalyze KCB's growth and position the company to bring new therapies to market with the potential to counteract cognitive impairment, a major health burden for Canadians, particularly as they age.

Title: Advancing patient care in oncology: Integrating multiscale transcriptomics for sarcoma classification, and beyond
Academic Leaders/Institutions: Dr. Adam Shlien (The Hospital for Sick Children)
Receptor Leaders/Organizations: Dr. Brendan Dickson (Mount Sinai Hospital) and Dr. Rose Chami (The Hospital for Sick Children)
Genome Centre: Ontario Genomics
Total Funding: $6,061,850

Cancer is responsible for more than 1 in 4 deaths in Canada, with more than 600 new cases diagnosed daily. Sarcomas – tumours of the bone and soft tissue – are the most challenging cancers to diagnose. The many sarcoma types all have intrinsically different molecular pathogenesis (the process by which a disease develops). Patients with sarcomas, which are proportionately more common in children, face delays of weeks to months until they can be referred to a specialist centre and there are few clinical trials. Current histomorphology and immunohistochemistry approaches to diagnosis are also extremely subjective, requiring clinicians to order 10-20 tests per patient. These challenges lead to ultimately higher health system costs and lower patient survival rates.

Pathologists need a comprehensive approach with better tools to diagnose sarcoma. Project researchers have recently developed a platform to accurately diagnose (with 85-95% accuracy) any sarcoma using its ribonucleic acid (RNA). The highly scalable RNA-Seq-based tumour classification system has been trained on >13,000 tumours and normal samples, and improves with every sample analyzed. This project will validate and implement the platform at two major Toronto hospitals, which together treat around 1,000 patients with tumours of soft tissue and bone each year. The team will implement the initial web platform and will work with two commercial partners: DNAstack to expand the platform to the cloud; and Illumina to expand access to this platform outside of Ontario. It will also compare the platform to World Health Organization classifications to support future global adoption of the platform. In 3-5 years, the platform will be expanded to other types of cancer and altogether better streamline the diagnosis of sarcomas of cancer patients.

Title: Streamlined care for Canadians with mismatch repair deficient cancers through full-service genetic and epigenetic DNA sequencing
Academic Leader/Institution: Dr. Trevor Pugh (Princess Margaret Cancer Centre)
Receptor Leader/Organization: Dr. Hilary Racher (Dynacare)
Genome Centre: Ontario Genomics
Total Funding: $795,393

Inherited mismatch repair (MMR) deficiency (also known as Lynch Syndrome, LS) affects at least 1 in 300 Canadians. It is a feature of families with heightened risk of colon, brain and gynaecological cancer. Despite a tenfold increased risk, the majority of LS patients are not well identified by the Canadian health system, which takes a piecemeal and overly complex approach to testing, including an excessive use of often-limited tumour tissues. As a result, the length of time to diagnosis is currently 1-3 years in Ontario and up to 6 years in other provinces. While they wait, many Canadians are developing advanced cancers. There is an urgent need for a more efficient, comprehensive MMR screening protocol to identify and treat high-risk patients earlier.

MMR tumours all display a biological feature (microsatellite instability, MSI) that leads to the accumulation of 10,000s of DNA mutations. The project aims to commercialize a MultiMMR tumour test previously developed by the researchers involved. In a single cost-efficient test, this comprehensive DNA sequencing method queries the MMR genes for germline and somatic mutations, MSI status and promoter methylation. MultiMMR conserves tissue,

eliminates the need for serial molecular testing and helps differentiate LS from other hereditary cancers.

In partnership with the health solutions company Dynacare, the team will test and clinically validate the MultiMMR panel through a pilot study with various clinics nationally, and validate a new application of MultiMMR to blood cell-free DNA for proactive cancer screening in LS and constitutional mismatch repair deficiency (CMMRD) carriers. Within 3-5 years of completion, the project will reduce LS/CMMRD diagnosis time from 1-6 years to 4 months, saving 50-75% of patients from lifelong cancer screening. It will also reduce healthcare spending on molecular testing by more than 10%, and ultimately improve patient experiences and outcomes.

GÉNOME QUÉBEC

Title: ApiOmic, honeybee breeding using genomics
Academic Leader/Institution: Dr. Pierre Giovenazzo (Université Laval)
Receptor Leader/Organization: Ségolène Maucourt and Andrée Rousseau (Centre de recherche en sciences animales de Deschambault, CRSAD)
Genome Centre: Génome Québec
Total Funding: $3,254,079

Each year, the Canadian beekeeping industry produces nearly 75 million pounds of honey worth $253 million and offers pollination services that make an annual contribution to agricultural crops, such as canola and blueberries, worth an estimated $4.5–6.1 billion. Unfortunately, over the last 15 years, beekeepers have suffered an average winter colony loss of 26%. The highest ever recorded loss occurred during winter 2022, when beekeepers across Canada lost 46% of their 800,000 colonies and imported 360,000 queens and 60,000 packages of bees from various countries to rebuild their honeybee livestock. Supporting Canadian honeybee queen rearing and breeding is a sustainable solution to help ensure Canadian honeybee stock self-sufficiency.

The ApiOmic project will implement the use of genomic tools to produce honeybee stock that is winter hardy, productive and disease resistant, thus ensuring efficient pollination services, superior honey production and increasing sustainability of the Canadian beekeeping industry. ApiOmic will use the novel Illumina Honeybee SNP array that provides a cost-effective genomic tool for breeding and selection. ApiOmic will develop a routine estimation of genomic breeding values by maintaining reference honeybee selected lines at the Centre de recherche en sciences animales de Deschambault and by monitoring the performance of selected lines in commercial queen breeding operations of the Apiculteurs et apicultrices du Québec and of those in other provinces. The genomic and pedigree database will be available to all via the non-human genomics data valorization center, Genovalia.

Title: Crowdsourcing the analysis of environmental metagenomic data for biodiversity and antimicrobial resistance genes through a AAA video game
Academic Leader/Institution: Dr. Jérôme Waldispühl (McGill University)

Receptor Leader/Organization: Sébastien Caisse (Gearbox Studio)
Genome Centre: Génome Québec
Total Funding: $4,502,256

The accuracy and reproducibility of genomic studies rely on the quality of available data. When possible, manual curation is the gold standard for preparing these resources. However, the large volume of metagenomic data, especially in environmental and public health, outpaces human processing capacities. In a previous GAPP project, Gearbox showed that commercial video games can provide access to massive human processing resources for curating multiple sequence alignments for genomic research. Over a 3-year period, Borderlands Science, a mini game, became the largest citizen science initiative in the world with 4 million participants and 135 million puzzle solutions collected for human microbiome research.

The project team will now develop a citizen science framework to process metagenomics and metabolomics data sets from the Earth Microbiome Project for identifying antibiotic resistance genes in metagenome-assembled genomes. The team will also develop a mobile version to increase accessibility and user engagement, and open new channels of communication with the public.

The integration of citizen science projects in video games could bring the equivalent of millions of dollars in advertisement and sustain the expansion of Gearbox's Canadian studios. The video game industry in Canada, now worth $3.4 billion, has grown by 20% since 2019 and ranks among the largest in the world. The project will also leverage ESG (environmental, social and governance) as a workforce strategy for the industry, increasing the attractiveness of jobs in Canada in a competitive landscape. Increased public understanding of biodiversity and awareness of antimicrobial resistance will reinforce public trust in the need for public policies to address sustainability challenges.

Title: Establishing therapeutic cord blood-derived NK cells for hard-to-treat cancers through omics based and pharmacological activators
Academic Leaders/Institution: Drs. Michel Tremblay and David Langlais (McGill University)
Receptor Leader/Organization: Dr. Pierre Laneuville (McGill University Health Centre)
Genome Centre: Génome Québec
Total Funding: $5,907,187

Cancer immunotherapies, such as modified T-cells with Chimeric Antigen Receptors (CAR-T), can elicit strong responses and even cure some blood cancers such as acute myeloid leukemia (AML). However, the drawbacks of CAR-T therapies include poorer responses against solid tumours, autologous cell requirements, high manufacturing costs, and potentially fatal toxicities. These limitations can be overcome with natural killer (NK) cells. These innate immune cells can efficiently kill cancer cells, allowing the development of non-genetically modified NK cells to treat both blood and solid tumour cancers. The anti-tumour activity and response to stimulation of primary cord blood-derived NKs (CB-NK) are superior to those of NK cell lines and are being used in clinical trials in the U.S. and China.

This project will use genomics solutions to improve the clinical management of hard-to-treat cancers like AML through CB-NK cell therapy. It will establish a comprehensive resource for "off-the-shelf" NK cell immunotherapy. Its unique methodologies will enable the processing, storage and recovery of CB-NK cells; optimisation and simplification of their clinical use; and national distribution of the therapeutic CB-NK cell bank to treat a larger cohort of cancer patients.

The acceleration of CB-NK cell therapies will place Canada at the forefront of this fast-moving and strategically important field. Canadian patients will benefit from safer, more effective immunotherapies with the potential to tackle diverse hard-to-treat cancers, while their "off-the-shelf" nature will significantly lower healthcare costs. Economic benefits include increased revenues associated with licensing and development of commercial products, as well as economic growth and job creation due to innovation in the cell therapy sector, where the global market is growing rapidly.

Title: Whole-genome embryo sequencing for improved IVF outcomes
Academic Leader/Institution: Dr. Sophie Petropoulos (Université de Montréal)
Receptor Leader/Organization: Dr. Jeremy Grushcow (Juniper Genomics)
Genome Centre: Génome Québec
Total Funding: $5,658,042

Around four million people use in vitro fertilization (IVF) every year, but only 34% of IVF cycles succeed. Patients in Canada and the U.S mostly pay out of pocket for this expensive procedure, with the average patient undergoing 2-3 cycles at a total cost of C$40,000-$60,000. At least 85% of the time, the genetics of the embryo itself cause the high rate at which transferred embryos fail to implant or to carry to term. However, patients and clinicians currently do not have the technology to perform comprehensive embryo genetic testing. IVF is the only human genetics area that still uses low-resolution approaches (chromosome counting, genotyping) instead of high-resolution next-generation sequencing (exome or whole genome).

This project aims to develop a comprehensive single-cell whole-genome sequencing-based genetic test for embryos to give IVF patients and clinicians as much certainty as possible that the first embryo they choose to transfer will be successful. Its specific goal is to deliver a scalable biopsy processing workflow for cell handling and sample preparation that delivers optimal sequencing results in a cost-effective manner.

By reducing the financial and mental health burden of IVF, the project will transform IVF – improving outcomes and increasing access for Canadian patients – without changing clinical workflows. The project will accelerate the development of Juniper's pre-implantation embryo genetic test (PGT), which will replace existing PGT products ($8 billion annual market). To bring this test to market, Juniper has already secured partnerships with 35 IVF clinics. The project's success will establish Juniper as a world leader in embryo genetics, allowing it to raise additional funds, create new research jobs, and partner with additional IVF clinics.