



## BACKGROUND

### Seven Genomic Applications Partnership Program Projects Funded

Genome Canada is proud to announce the launch of seven projects within its [Genomic Applications Partnership Program](#) (GAPP). GAPP funds translational research and development projects that address real-world challenges and opportunities as identified by industry, government, not-for-profits, and other receptors of genomics knowledge and technology.

This backgrounder includes an eighth project called the *All for One* Policy Toolkit that will establish a data sharing framework for three of the GAPP projects included in this announcement (although the Toolkit itself is not a GAPP project).

Together, the seven GAPP projects and the *All for One* Policy Toolkit project represent a total investment of \$38.6 million in research funding, of which \$12.1 million is from Genome Canada and \$26.5 million is from co-funding partners including provincial governments, private sector and not-for-profit organizations.

The projects are listed by order of the GAPP round (15 or 16) to which they belong, then by province (West to East) within each round, and the *All for One* Policy Toolkit project is listed at the end of this document.

#### GAPP ROUND 15

##### British Columbia

**Title:** Implementation of Diagnostic Whole Genome Sequencing for Rare Diseases in British Columbia

**Academic Leader:** Anna Lehman (University of British Columbia)

**Receptor Leader:** Pam Ramsay (Provincial Health Services Authority)

**Genome Centre:** Genome British Columbia

**Total funding:** \$8.1 million

In the province of British Columbia, each year thousands of patients with genetic disorders require access to complex genetic tests that currently must be performed in laboratories outside of Canada. Building genomic diagnostic capacity within Canada will improve our understanding of these and other genetic disorders, as well as enhance the care of impacted patients and families. This project aims to evaluate the feasibility of integrating whole genome sequencing into standard of care for BC's rare disease patients while facilitating the system changes necessary to achieve this anticipated future state. To accomplish this, the Provincial Health Services Authority's Genome Diagnostics Laboratory and Provincial Medical Genetics Program, based at BC Children's and BC Women's Hospitals, will collaborate to introduce clinical whole genome sequencing diagnostics to a subset of patients with rare

diseases under a pilot project, as well as collaborate with UBC to perform the necessary health economic assessment to inform this feasibility study. This project will also identify and support the development of processes requiring further resources and education while outlining policies involving inter-laboratory knowledge sharing, clinic-lab collaboration and stakeholder engagement. This project is made possible through the support of the Provincial Health Services Authority, Genome Canada, Genome BC, and Illumina, Inc. The deliverables of this project will support implementation of BC's broader genomic strategy.

## **Ontario**

### **Title: Beyond Genomics: Assessing the Improvement in Diagnosis of Rare Diseases using Clinical Epigenomics in Canada (EpiSign-CAN)**

**Academic Leader:** Bekim Sadikovic (Lawson Health Research Institute/Western University)

**Receptor Leader:** Mike Kadour (London Health Sciences Centre)

**Genome Centre:** Ontario Genomics

**Total funding:** \$4.8 million

This project will be validating a test, called EpiSign, a proprietary machine learning algorithm built on rare genetic disease datasets (EpiSign Knowledge Database) which analyzes data obtained from whole-genome methylation arrays. This approach is expected to increase diagnostic yield above that of current genetic analyses. This project will validate the conditions for maximizing patient and health system impact and assess the evidence for first-visit and reflex scenarios for adoption of genome-wide DNA methylation testing within Canada. Future clinical adaptation would see EpiSign implemented as a bioinformatics service with tertiary genetic centres engaging with their patients and performing the wet lab methylation array data production locally. These centres would then utilize a secure web-based portal to have their data interpreted by the EpiSign Knowledge Database. Expected benefits to Canada include improved quality of life to patients and families who will receive a long-awaited definitive diagnosis. Providing patients with a diagnosis sooner will also have cost benefits, as many tests will be avoided in addition to reducing the reliance on out-of-country commercial laboratories.

### **Title: Targeting fungal stress responses to provide first-in-class treatment for drug resistant fungal pathogens**

**Academic Leader:** Leah Cowen (University of Toronto)

**Receptor Leader:** Dominic Jaikaran (Bright Angel Therapeutics)

**Genome Centre:** Ontario Genomics

**Total funding:** \$6.0 million

The impact of fungal infections on human health in Canada is profound, with recent epidemiological reports of approximately 3,000 invasive fungal infections annually, resulting in approximately 1,000 deaths, with immunocompromised individuals being the most vulnerable. Only three major classes of antifungal drugs are currently available and resistance to each class is increasing at an alarming rate. This team has established that fungal stress responses are critical for fungal drug resistance and virulence traits and has identified potential antifungal inhibitors of the molecular chaperone and stress response regulator Hsp90. This project couples Schrödinger's computational drug discovery expertise with the Cowen lab's expertise in fungal genomics and Hsp90 to enable Bright Angel Therapeutics to rapidly translate existing data supporting the benefit of targeting fungal Hsp90 into an IND-ready drug candidate. The project will pursue a 3-task development approach based on computational design, targeted medicinal chemistry, and biological verification/validation. The project gives Canada a chance

to be a global leader in antifungal research. The drug coming to market would be expected to reduce morbidity and mortality due to fungal infections and provide significant savings to the Canadian health care system, which currently spends \$345 million on invasive fungal infections.

## **Québec**

**Title: Rapid Whole-Genome Sequencing in Acute Care Neonates and Infants**

**Academic Leader:** Jacques Michaud (CHU Sainte-Justine)

**Receptor Leader:** Denis Ouellet (Ministère de la Santé et des Services sociaux)

**Genome Centre:** Génome Québec

**Total funding:** \$6.2 million

Rare genetic disorders and congenital malformations indicating a possible genetic syndrome affect 1-2% of live births and are the leading cause of hospitalization and death in infants in Canada. A genetic diagnosis in the first few months of life can have critical implications on the clinical management of newborns and infants as well as on a child's health for their entire life. With upwards of 8,000 rare genetic conditions combined with very young patients presenting with non-specific or different symptoms than are observed in older patients, the precise diagnosis of a rare genetic disorder is often very difficult. The ultimate objective of the project is to offer rapid clinical genome-wide sequencing (GWS) to all critically ill newborns and infants who may benefit from this test in the province of Quebec. The first phase of this project will develop and study the impact of a rapid GWS program for the investigation of these children. The second phase will implement this program in the Quebec health care system.

## **GAPP ROUND 16**

### **Alberta**

**Title: TIGeR: Translational Implementation of Genomics for Rare diseases**

**Academic Leader:** Francois Bernier (University of Calgary)

**Receptor Leader:** Carolyn O'Hara (Alberta Precision Laboratories)

**Genome Centre:** Genome Alberta

**Total funding:** \$6.2 million

Alberta patients with rare genetic diseases continue to face lengthy and expensive diagnostic odysseys, estimated at over \$500 million in the past decade. In recent years, clinical genome-wide sequencing (GWS) has emerged as a rapid and cost-effective approach to diagnosis, providing a molecular diagnosis in 25-60% of patients. To date, Alberta Precision Laboratories has relied on international commercial laboratories to provide GWS. The volume of GWS has been increasing 30% per year, resulting in an unsustainable expense to the health care system. To address this, Alberta Precision Laboratories' vision is to develop, evaluate and implement a large scale clinical GWS service and a governance framework that integrates genomics data provincially, nationally and internationally using a learning lab system that will continually optimize and improve performance. This is expected to begin a transformational change to health care in Alberta, enabling physicians to order a single comprehensive test and ensuring accessible, cost-effective and integrated GWS. The increased number of timely and cost-effective diagnoses will have an immeasurable impact on the physical and mental health of both rare disease patients and their families.

## Ontario

**Title: Strain development for butanol process addition to existing biodiesel plants**

**Academic Leader:** Lars Rehmann (University of Western Ontario)

**Receptor Leader:** Nak Paik (World Energy, Hamilton Facility)

**Genome Centre:** Ontario Genomics

**Total funding:** \$795,500

Biodiesel production from agricultural crops generates a considerable amount of crude glycerol as a by-product each year. The purification costs for this crude glycerol are high and market demand for refined glycerine is low, resulting in a large fraction of the crude glycerol being incinerated, adding to climate emissions and production costs. World Energy intends to commercialize the production of bio-butanol, a superior biofuel and chemical commodity, from this waste glycerol. A process has previously been developed for the conversion of glycerol to butanol using *Clostridium pasteurianum*, however the genetic changes that have occurred and the stability of the new strains are not well understood. The aim of this project is to improve the continuous fermentation process by gaining a better understanding of the genetic changes that have occurred in the engineered bacterial strains as well as enhance bio-butanol production and fatty acid tolerance through additional genetic modifications. Process scale up is also planned. World Energy generates approximately 66,000 MT of glycerol annually that can be used for bio-butanol production. With initial goals of 30% of the carbon from waste glycerol being converted to bio-butanol, up to \$3.7 million additional revenue could be incurred per facility per year.

## Quebec

**Title: Detecting Ovarian and Endometrial Cancer Early Using Genomics (DOvEEgene)**

**Academic Leader:** Lucy Gilbert (McGill University)

**Receptor Leader:** Guy Rouleau (OPTILAB - McGill University Health Centre)

**Genome Centre:** Génome Québec

**Total funding:** \$6.2 million

Ovarian and endometrial cancer-related deaths are within the top four causes of cancer deaths in North American women. Because of the lack of symptoms in early stage, these cancers continue to be diagnosed in Stage III/IV with metastasis outside the gynecologic organs making cure unlikely. The project will develop DOvEEgene, a genomic uterine pap test that aims to screen and detect these cancers while they are confined to the gynecologic organs and curable. The test will use next generation sequencing to interrogate 23 genes involved in the development of sporadic and hereditary ovarian and endometrial cancers in women between 45-70 years. Currently the direct costs of treating the 10,000 Canadian women diagnosed with these cancers every year is over \$1 billion. It is expected that with DOvEEgene and diagnosis in earlier stages these expenditures could be decreased by up to \$250 million per year.

## **GAPP-related but not part of a specific GAPP round**

### ***ALL FOR ONE POLICY TOOLKIT***

**Title:** *All for One Policy Toolkit*

**Academic Leader:** Bartha Maria Knoppers (McGill University)

**Receptor Leader:** n/a

**Lead Genome Centre: Génome Québec**

**Total funding: \$329,715**

With rare diseases, sufficient patient numbers are not available at any one site; data needs to be centralized, integrated and broadly accessible to drive rare disease research for gene identification and understanding. To do so, a broad, actionable and ethically grounded policy toolkit will be developed, and made available to the different *All for One* stakeholders, including institutions, and provincial and federal regulators. The development of these policy tools will require a three-stage approach: 1) assessment of the rare disease policy ecosystem to identify commonalities, differences and limitations to inter-provincial data sharing; 2) consensus-building activities to identify the policy needs of the rare diseases research community; and 3) development of an overarching governance framework. Resulting resources aim to be interoperable and standardized to meet the needs of different clinical and research sites – for approval and use in the clinical implementation stage, as well as future sites. Through tailored to the rare disease clinical research community, the tools developed by *All for One* Policy Toolkit can be adapted and used as models for more common diseases as precision medicine advances.