April 26, 2022

Backgrounder

All for One: New pan-Canadian initiative will increase equitable access to genome-wide sequencing for diagnosis and treatment of genetic disease

The Genome Canada-led All for One precision health partnership is advancing a new standard of health care for Canadians, expanding access to genome-wide sequencing for diagnosis and treatment of life-threatening genetic diseases.

The $39 million All for One initiative includes $13 million in federal investment through Genome Canada and $26 million in co-funding from industry, health-care organizations, provincial and other partners brought in through six regional Genome Centres.

All for One is:

- Now deployed across six implementation projects serving nine provinces, funded through the **Genomic Applications Partnership Program** (GAPP).
- Unified by the **All for One Policy Toolkit**, to ensure ethical, equitable collection of genomic and clinical data.
- Bolstered by the development of a **Pan-Canadian Health Data Ecosystem**, which will connect and leverage genomic and clinically generated data to improve patient care and fuel life saving scientific breakthroughs.

GENOME BC

Title: Implementation of Diagnostic Whole Genome Sequencing for Rare Diseases in British Columbia
Academic Leader / Institution: Anna Lehman (University of British Columbia)
Receptor Leader / Organization: Pam Ramsay (Provincial Health Services Authority)
Lead Genome Centre: Genome BC
Total funding: $8,124,794

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.

GENOME ALBERTA

Title: TIGeR: Translational Implementation of Genomics for Rare diseases
Academic Leader / Institution: François Bernier (University of Calgary)
Receptor Leader / Organization: Carolyn O'Hara (Alberta Precision Laboratories)
Lead Genome Centre: Genome Alberta
Total funding: $6,089,492

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.

GENOME PRAIRIE

Title: Canadian Prairie Metabolic Network
Academic Leader / Institution: Cheryl Rockman-Greenberg (University of Manitoba)
Receptor Leader / Organization: Petr Kresta (Shared Health)
Lead Genome Centres: Genome Prairie, Genome Alberta
Total funding: $6,068,618

Inborn errors of metabolism (IEM) are genetic diseases caused by mutations in either the nuclear or mitochondrial genome. Although each of the more than 600 known IEMs is individually rare, together they affect more than 6,400 patients in the Prairies—primarily children. Throughout the Prairie provinces, there is a limited local capacity for next-generation sequencing causing delays which limit the benefits of early diagnosis, early treatment, and improved outcomes. These delays result in adverse outcomes in patients. This project will combine clinical and laboratory approaches to ensure patients have timely

access to new diagnostics, new therapies, and clinical and specialty supports. The Canadian Prairie Metabolic Network (CPMN) will provide access to a full range of multidisciplinary expertise, develop best practice approaches, and provide, as needed, clinical specialist coverage for generalist physicians and their patients. It will also ensure the timely and more cost-effective delivery of innovative and relevant genomic testing in the Prairies, including rapid, inexpensive mitochondrial DNA testing not available elsewhere; generate genomics data that will stay in Canada; and contribute to knowledge and expertise in Canada across multiple disciplines and specialties. The result will be the timely treatment and improved outcomes for IEM patients.

ONTARIO GENOMICS

Title: Optimization and Implementation of a Clinical Genome-Wide Sequencing Service for Rare Disease Diagnosis in Ontario
Academic Leaders / Institutions: Kym Boycott (CHEO Research Institute, University of Ottawa) and Martin Somerville (SickKids Research Institute, University of Toronto)
Receptor Leader / Organization: Neeta Sarta (Ontario Ministry of Health)
Lead Genome Centre: Ontario Genomics
Total funding: $6,000,000

Currently, more than one third of Ontarians with a rare disease lack a genetic diagnosis, despite lengthy and costly investigations. Fortunately, genome-wide sequencing (GWS), in the form of exome sequencing (ES) and genome sequencing (GS), has transformed our ability to achieve a timely diagnosis for rare disease patients. Prior to April 2021, clinical GWS for Ontario patients was only available via an exceptional access program (EAP) and completed in laboratories outside Canada. The EAP program was designed as a 'safety net', rather than a regular service delivery model, and presented significant challenges including lack of oversight of turnaround time, diagnostic yield and impact, timing, and outcome of exome vs. genome. To address these challenges, CHEO and The Hospital for Sick Children (SickKids), in collaboration with the Ontario Ministry of Health, developed and is delivering an optimized clinical GWS service as a two-year pilot for individuals with rare diseases that is equitable, accessible, sustainable and performed in Ontario. The pilot project will provide GWS in the form of both ES (n=325 trios) and GS (n=325 trios) to 650 families from CHEO and SickKids. This work will enable robust assessment of diagnostic utility, cost effectiveness, and timeliness of ES and GS to inform provincial and cross-provincial policy related to the long-term organization, delivery, and reimbursement of genome-based diagnostics for rare disease.

GÉNOME QUÉBEC

Title: Rapid Whole-Genome Sequencing in Acute Care Neonates and Infants
Academic Leader / Institution: Jacques Michaud (CHU Sainte-Justine Research Center)
Receptor Leader / Organization: Denis Ouellet (Ministère de la Santé et des Services sociaux)
Lead Genome Centre: Génome Québec
Total funding: $6,165,460

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.

GENOME ATLANTIC

Title: Implementation of Clinical Exomes in a Pre- and Peri-Natal Setting
Academic Leaders / Institutions: Karen Bedard and Anthony Vandersteen (Dalhousie University)
Receptor Leaders / Organizations: Jo Ann Brock and Sarah Dyack (IWK Health Centre)
Lead Genome Centre: Genome Atlantic
Total funding: $4,758,489

Rare genetic disorders affect approximately 500,000 children in Canada and constitute 30% of the pediatric inpatient population. These children often undergo lengthy and expensive diagnostic procedures and may be subject to uninformed care while waiting for a correct diagnosis. The introduction of genome wide sequencing as a diagnostic tool has been shown to be effective, with a diagnostic yield of 30-40% for patients with undiagnosed genetic disorders. Adoption into clinical practice has been slow, however, due to insufficient evidence surrounding cost savings, inconsistent description of patient phenotypic data, insufficient integration of clinical and laboratory systems, data sharing difficulties and concerns among patients about potentially significant incidental findings. The project aims to develop and assess the clinical utility and cost effectiveness of the implementation of genome wide sequencing for clinical exomes in order to begin to adopt this testing as standard of care for pediatric and prenatal populations in Atlantic Canada.

PAN-CANADIAN TOOLKIT

Title: All for One Policy Toolkit
Academic Leader / Institution: Ma'n H. Zawati (formerly Bartha Maria Knoppers) (McGill University)
Receptor Leader / Organization: n/a
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 develop a data governance framework for clinical consent and genomic data sharing in Canada. It is funded as part of the All for One initiative, the goal of which is to improve the health and wellness of Canadians with serious genetic conditions by enabling access to a timely and accurate genomic-based diagnosis. Moreover, All for One will enable patients to benefit while helping others through the sharing of their clinical and genomic data within a learning health system. It lays a foundation for precision health in Canada.

The development of this project's 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.

PAN-CANADIAN HEALTH DATA ECOSYSTEM NEEDS ASSESSMENT

Title: Defining a Canadian Data Solution That Will Deliver Precision Health for Rare Genetic Disease
Academic Leader / Institution: Kym Boycott (CHEO Research Institute)
Receptor Leader / Organization: n/a
Lead Genome Centre: Ontario Genomics
Total funding: $950,000

Clinical genome-wide sequencing (GWS), which includes exome and genome sequencing, has become standard of care for the diagnosis of complex rare genetic disease (RD). Until recently, all provinces across Canada have been sending clinical GWS to private, mostly US-based, labs for sequencing, analysis and interpretation. With the support of Genome Canada's Genomics Applied Partnerships Program (GAPP), provinces are patriating clinical GWS and integrating it into the diagnostic care pathway for complex RD. Six GAPP projects (British Columbia, Alberta, Prairie, Ontario, Québec, Atlantic) share a vision to deliver on the promise of precision health for RD. To realize this vision, the GAPP projects identified two goals: facilitate high-quality clinical GWS as standard-of-care and provide access to precision health research for Canadians with RD.

Significant barriers to achieving these goals include a lack of comprehensive databases for analyzing and interpreting sequencing data, and the resource-intensive processes for inviting Canadians living with RD to participate in research. Given the Canadian context of healthcare as a provincial responsibility with relatively low clinical GWS volumes and a variety of clinical data custodians, a comprehensive national approach is needed that accommodates the challenges of sharing data across jurisdictions. This project will engage with end-users and stakeholders to perform a robust needs assessment and develop a detailed plan for a health data ecosystem.