



Canada's national platform for
genome sequencing and analysis

Annual Report 2023-24

CGEn is committed to continually enhancing genomic sciences in Canada through the provision of high-quality data to the research community and by leading pioneering Canadian projects, helping to elevate Canada's global position in genomics research.

Contents

| | |
|---|-----------|
| About CGEn | 4 |
| Vision and Mission | 6 |
| Message from the Board Chair | 7 |
| Message from the CEO | 8 |
| Executive Summary | 9 |
| Impact 2023-24 | 10 |
| Technology and Consultations | 12 |
| CGEn: Advancing Canadian Science | 15 |
| Supporting Genomic Sciences | 16 |
| Key CGEn Projects | 18 |
| Empowering Canadian Research | 25 |
| Developing Talent | 32 |
| Engagement and Outreach | 33 |
| Financial Highlights | 35 |

About CGEn



CGEn is Canada's national platform for genome sequencing and analysis. Established in 2015, CGEn employs over 200 staff and is funded primarily by the Canada Foundation for Innovation (CFI) through its Major Science Initiatives Fund (MSIF), leveraging investments from the provincial governments of Ontario, Quebec, and British Columbia, Genome Canada, and others. CGEn operates as an integrated national platform with nodes in Toronto ([The Centre for Applied Genomics](#) at The Hospital for Sick Children [SickKids]), Montréal, ([McGill Genome Centre](#) at McGill University) and Vancouver ([Canada's Michael Smith Genome Sciences Centre](#) at BC Cancer), leading large-scale projects and providing advanced genomic services to enable research in the health sciences, agriculture, forestry, fishery, the environment, biodiversity, and other sectors of importance in Canada.

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Scientific Director CGEn-Toronto, SickKids and University of Toronto

Vision and Mission

Our Vision

Serve as Canada's engine for genomics-enabled research and discovery, supporting a healthier and more sustainable future for all Canadians.

Our Mission

Enhance Canada's national capacity for genome sequencing and informatics analysis; **Accelerate** next-generation scientific solutions underpinned by large-scale data generation, and **Support** Canadian national and international projects in sequencing, databasing and open science collaborations.

Message from the Board Chair

CGEn continues to serve as a pivotal organizing platform for genomics research in Canada. From supporting individual researchers to leading nationwide projects, CGEn is instrumental in bolstering Canada's global presence in genomics.

CGEn's achievements are laying the groundwork for its ongoing success. By enabling comprehensive and high-quality data generation and analysis and fostering collaborations across diverse domains of genomics research, CGEn is supporting excellence in research which will lead to important downstream impacts and support a better future for all Canadians.

The maintenance and growth of major research infrastructures like CGEn necessitate commitment across the enterprise. CGEn's skilled, dedicated staff and scientific leadership remain at the forefront of the field and are key to CGEn's role as a driver of genomic science in Canada. CGEn also appreciates the sustained support from its funders (including federal and provincial governments and agencies), host institutions, and other invested partners. We look forward to your continued partnership in advancing CGEn's mission. I would also like to thank the members of the CGEn Board of Directors and Scientific Advisory Board for their invaluable contributions that help to shape CGEn's strategic direction.

Among many other activities, CGEn is building on the success of the HostSeq initiative, which created Canada's largest genomic health databank. In partnership with others in the ecosystem, CGEn is establishing robust frameworks for large-scale research that will be paramount to realizing Canada's aspirations in human genomics and precision medicine. In both health and non-health realms, these research frameworks also enable our country's participation in expansive worldwide projects, such as the Earth BioGenome Project, and ensure that Canada continues to leverage CGEn's expertise and resources to enhance its global presence in the field of genomics.

There are many exciting opportunities on the horizon. CGEn's infrastructure and expertise position us well to support Canada's diverse research community and by fostering collaborations, engaging in international initiatives, and advocating for Canadian projects, CGEn will remain committed to innovation and excellence in genomics research.



A handwritten signature in black ink that reads "Gordon C McCauley".

Gordon C McCauley
Chair, CGEn Board of Directors

Message from the CEO

Since its inception, CGEn has been critical in the advancement of genomic science in Canada. Our recent success in securing a second round of funding as a Major Science Initiative (MSI) of the Canada Foundation for Innovation (CFI) (2023-29) is based on CGEn's commitment to supporting the Canadian research community with top-tier data generation and a track record of scientific excellence built on expert staff, state-of-the-art infrastructure, and continuous technological innovation. CGEn also has world-renowned scientific leadership: members of CGEn's founding Executive Team have been recognized [among the top five genetics scientists](#) in Canada (Steven Jones, Stephen Scherer, Mark Lathrop, and Marco Marra). We continue to benefit from the expertise and contributions of world-renowned advisors from CGEn's Board of Directors and Scientific Advisory Board.

Key Canadian projects led or supported by CGEn this year exemplify its far-reaching impact on Canadian science. HostSeq, Canada's leading genomic health databank formed as a part of Genome Canada's Canadian COVID-19 Genomics Network (CanCOGeN), continues to fuel research projects across various health domains and has laid a robust foundation for Canada's future population genomics initiatives. The Canada BioGenome Project, funded by Genome Canada, is advancing biodiversity research in Canada and around the world by generating reference genomes for species of ecological, cultural, and economic importance. Through this project, CGEn's Vancouver node joined the Earth BioGenome Secretariat to bring Canadian expertise to this important initiative that aims to sequence all of Earth's plants and animals. Involvement in global partnerships such as these will continue to position our country as a significant contributor to genomics research and further solidify Canada's global position in the field.

Through 2023-24 CGEn engaged with over 1,100 research groups, acting as a critical partner for genomic science in Canada and beyond. Together, CGEn nodes have yielded nearly 13 petabases of sequence data to date, encompassing over 125,000 whole genome sequences from human, animal, plant, and microbial samples. This vast reservoir of CGEn-generated data, used domestically and internationally in the public and private sectors, helps to train the next generation of genomic data scientists and serves as a catalyst for groundbreaking research endeavours that ultimately equip end-users and decision-makers with the insights needed to benefit Canada and Canadians.

As we embark on the upcoming year, CGEn remains committed to pushing the boundaries of genomics research and innovation. CGEn's track record of scientific and service excellence has helped to attract new funding to sustain and grow both critical internal projects and other research initiatives. We anticipate another year of impactful contributions, both within the Canadian genomics landscape and on the global stage.



A handwritten signature in black ink that reads "M. McLaren".

Dr. Meredith McLaren
CEO, CGEn

Executive Summary

This 2023-24 annual report showcases CGEn's pivotal and continuing role in advancing genomic research across Canada. This year, CGEn served 1,158 principal investigator laboratories from all 10 provinces, across critical Canadian sectors including health and human studies (950+ of the userbase), conservation and sustainability (120+ of the userbase), and agriculture, commercial and other sectors (70+ of the userbase). CGEn produced an impressive 2.6 petabases of data – the highest data output since its inception – and sequenced over 16,000 genomes from human, animal, plant, and microbial samples. CGEn also acquired, deployed and upgraded new genome sequencers to further enhance its capacity to generate high-quality data in the future. With over 200 highly qualified staff members, CGEn remains at the forefront of data generation and analysis services, evaluating and implementing emerging technologies, and inter-institutional collaboration.

With sequencing activities concluding in 2022-23, CGEn continued its data governance of HostSeq, Canada's foremost genomic health databank, which contains more than 10,000 whole genome sequences and matched metadata and is accessible broadly for research. HostSeq continues to fuel approved research projects across health domains and has laid a solid foundation for future population genomics projects in Canada. Importantly, CGEn is working toward establishing HostSeq as the foundational dataset for the newly launched CIHR-funded Pan-Canadian Human Genome Library (PCGL). The ongoing Canada BioGenome Project, collaboratively supported by all CGEn nodes and affiliated with the Earth BioGenome Project, has now provided 63 assembled and 8 annotated reference genomes for species of ecological, cultural, and economic importance in Canada. These high-quality genomes will play a crucial role in research supporting conservation efforts in Canada and beyond.

CGEn continues to support the largest genomics projects in Canada, including the Marathon of Hope Cancer Centres Network, PRrecision Oncology For Young peopLE (PROFYLE), MSSNG, Forward-In-Time Natural Experimental Study of Selection (FITNESS) project, and the Silent Genomes Project. Additionally, CGEn empowers many other Canadian and international research projects by generating high-quality genomic data and supporting diverse projects across many sectors, some of which are highlighted in this report.

CGEn-generated data are strengthening the skills of highly qualified personnel representing the next generation of genomic data scientists, who will be critical for enhancing Canada's future genomic research activities. CGEn also remains dedicated to advancing Inclusion, Diversity, Equity & Accessibility (IDEA), with notable achievements this year including the development of an IDEA Strategic Action Plan and participation in the [50-30 Challenge](#).

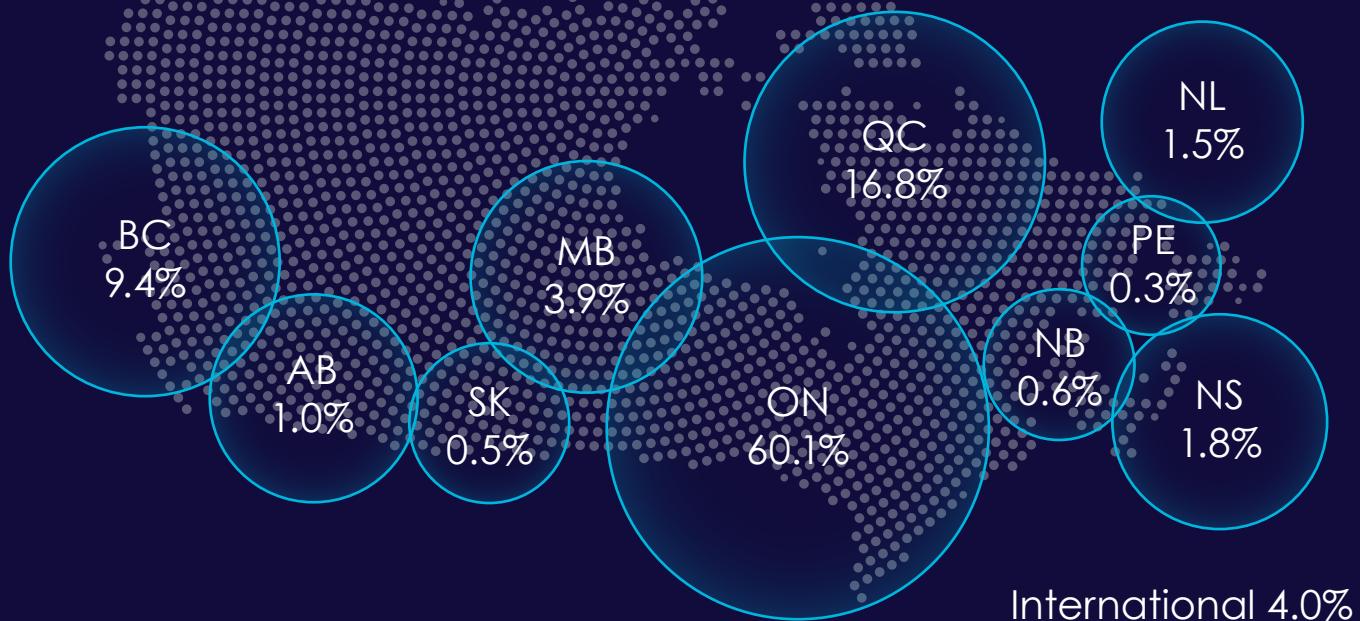


Impact 2023-24

User Base

Research groups across Canada and beyond

1,158



User Research Categories

950+ Health and human studies

120+ Conservation, ecology, and sustainability

70+ Agriculture, commercial and other sectors



User Satisfaction

Proportion of users satisfied

98% Quality of service

95% Expertise of the staff

97% Quality of data

97% CGEn service is essential/important for research



Estimated HQP Supported

300+ Master's students

100+ College and undergraduate students

650+ PhD students and postdoctoral fellows

1,600+ Scientific and technical personnel

Data Generation

Terabases of data produced by CGEn



>16,000 genomes were sequenced in 2023-24.

Since 2015, **125,000+ genomes** have been generated,
>65% of which were human.



=



Data from human whole genomes
sequenced in 2023-24

over 30,000 4k movies

which would take close to
7 years to binge watch

Advancement of Research



Organizations Supported

Over 450+ organizations supported from 2017-24, the majority year-over-year, typically with multiple users per organization.

Academic Institutions

140+ Canadian **40+** International

Government Agencies/Not-for-profit

60+ Canadian **20+** International

Companies

140+ Canadian **40+** International



Research Outputs

Since 2017 CGEn users and staff have contributed to scientific advancements via:

2,900+ Publications and book/chapters
(925+ from CGEn staff)

800+ Conference contributions

*The 2020-21 drop is largely due to research activity slowdown resulting from the COVID-19 pandemic.

Technology and Consultations

Drawing on the collective knowledge and experience of our three centres, CGEn has been at the forefront of accessible genomics research for over 15 years, and served more than 1,100 Principal Investigator laboratories this year. CGEn's skilled technical team collaborates with various vendors to evaluate and implement the best technologies in order to deliver cost-effective and timely genomics services.

"The CGEn facility stands out for their proactive approach and willingness to experiment, always striving for optimal results. It's crucial to collaborate with a provider open to adaptation, as protocols aren't always one-size-fits-all, particularly when dealing with diverse species." - **CGEn User**

CGEn nodes actively engage with platform users, providing expert guidance on genomics approaches and issues. Genome sequencing, for example, can be fraught with challenges such as low DNA quality, complex biochemistry (especially in non-human samples), and a lack of reference genomes. Consultations with CGEn expert staff and collaborative engagement between users and nodes are crucial for successful genome sequencing and high-quality data generation.

"In most projects where I have worked with a CGEn node, I've come to them with a broad idea and asked their advice on what specific technology and what depth of technology I should apply to a system. And they've been vital in answering both of those questions. For me, they really make the difference between doing this easily or struggling to do it and maybe not doing it."

- **CGEn User**

Our Fleet of Sequencers

CGEn plays an important role in evaluating and implementing emerging sequencing technologies. With optimization, the nodes can significantly increase sequencing throughput, speed, and quantity, all while reducing costs. CGEn offers the most up-to-date, cutting-edge sequencing technologies by continuously upgrading existing systems and acquiring the latest innovations in the field. In the past year, CGEn has acquired and deployed two of the newest genome sequencers: the Illumina NovaSeq X Plus Series for short-read applications and the PacBio Revio for long-read sequencing, while also upgrading the Oxford Nanopore Technologies PromethION sequencer. CGEn's infrastructure covers a range of services, including:

- Whole genome, exome and targeted sequencing
- RNA sequencing
- Methylation sequencing
- ChIP sequencing
- microRNA sequencing
- Hi-C and ATAC sequencing
- Metagenomics
- Single-cell DNA and RNA sequencing

Visit our [website](#) for more information on the available infrastructure that support these services.



Oxford Nanopore Technologies PromethION sequencer



Illumina NovaSeq X Plus Series



PacBio Revio

Technical Heads at CGEn's Nodes Share their Perspectives:



"At CGEn-Toronto, we are committed to excellence in genome sequencing services. Located at one of Canada's leading hospital-affiliated research centres, our sequencing capabilities have been pivotal in advancing complex research in medicine and precision health. We also engage in ongoing technical development to overcome challenges, leveraging our expertise to refine sequencing technologies."

Jo-Anne Herbrick, Senior Manager, The Centre for Applied Genomics



"At CGEn-Vancouver, we take pride in our collaborative efforts. Our team is dedicated to providing exceptional support and expertise to ensure the success of research endeavours. We offer consultations on sequencing strategies to optimize sequencing yield and data quality on hard-to-extract samples (e.g. novel species of ecological importance), and leverage our technical expertise to ensure seamless operation of the latest genome sequencing technologies."

Dr. Andy Mungall, Interim Co-Director, Genome Sciences Centre



"At CGEn-Montreal, we are excited to keep pace with advancements in genome sequencing. Our commitment to continuous training and workshops equips our team with the latest knowledge, allowing us to offer top-notch sequencing services. Through sustained development and collaboration with CGEn, we stay at the forefront of genomics, ready to meet the evolving needs of the research community."

Dr. Tony Kwan, Project Manager, McGill Genome Centre

CGEn: Advancing Canadian Science

Supporting Genomic Sciences

Since its inception in 2015, CGEn has been enabling Canada to make significant advances in genomics, facilitating research across health, conservation and sustainability, and agriculture, commercial and other sectors. Through its nodes in Toronto, Vancouver, and Montreal, CGEn has sequenced over 125,000 human and non-human genomes and generated more than 12 petabytes of data. In 2023-24 alone, CGEn generated 2.3 petabytes of data and sequenced over 16,000 genomes, with more than 65% of these being human genomes.

This year, CGEn users (total 1,158) came predominantly from academia (80% Canadian), with international users, industry and government agencies representing the remaining user base. Among CGEn's high-throughput service users, 950+ focused on health and human studies, 120+ on conservation, ecology, and sustainability, and 70+ on agriculture, commercial and other sectors.

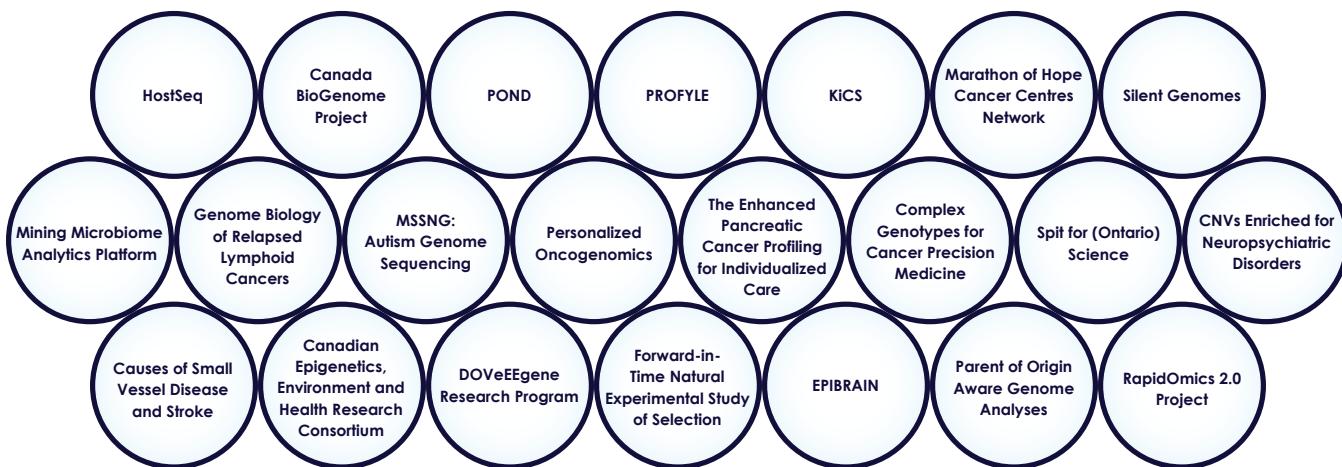
CGEn plays a critical role in the provision of high-quality genomic data to the research community. CGEn enables research projects both large and small, and also has the necessary capacity and expertise to support large-scale sequencing programs (see select projects below, and in the following narrative sections).



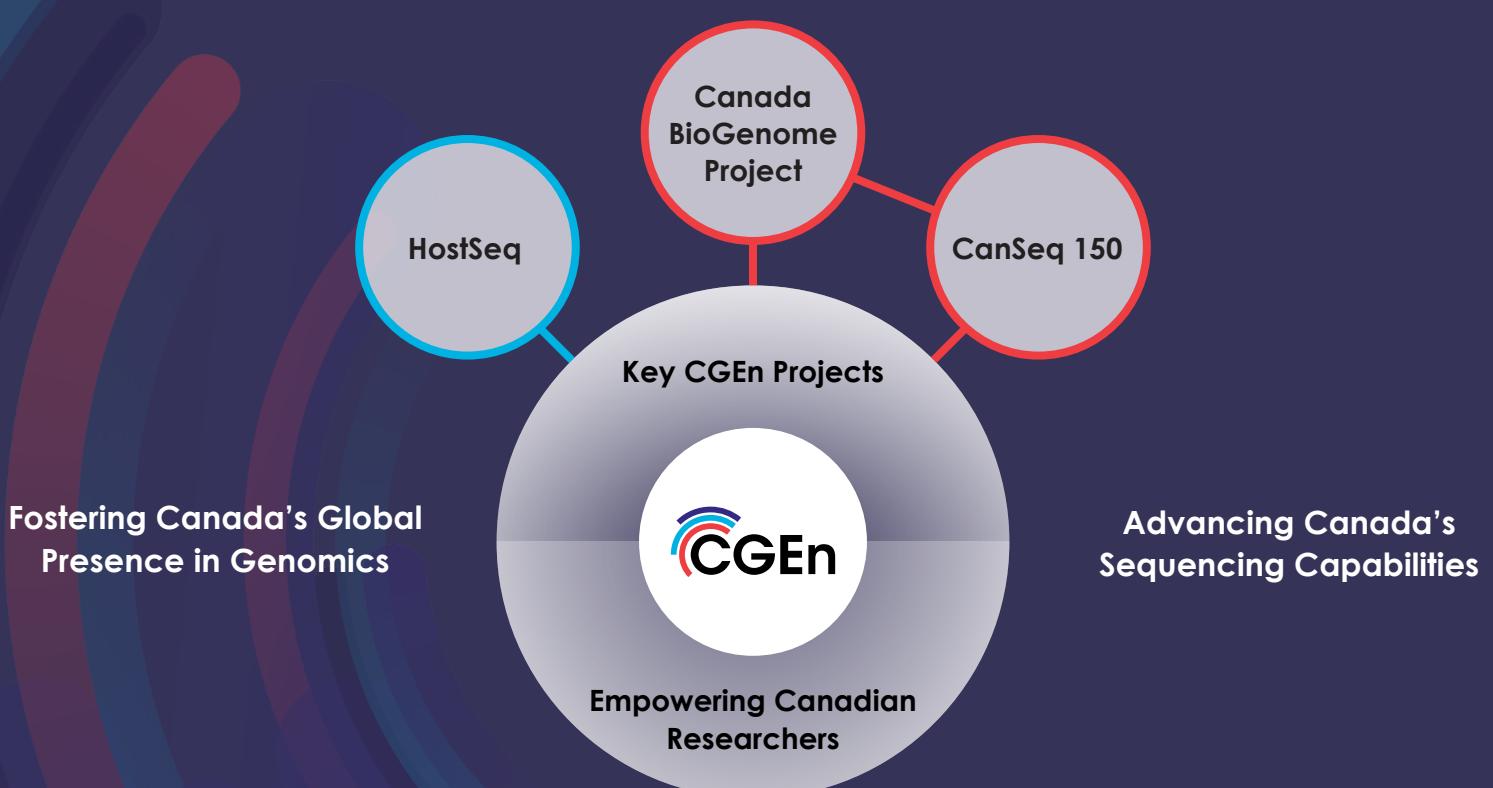
"CGEn is a cornerstone of Canada's genomic advances, supporting crucial research in health, conservation, sustainability, and agriculture. By generating vast amounts of high-quality genomic data and enabling large-scale studies, CGEn is positioning Canada as a leader in global genomic initiatives and ensuring impactful contributions to science."

Dr. Mark Lathrop, Scientific Director of CGEn-Montreal

Large-scale Sequencing Programs Supported by CGEn



Supporting Genomic Science in Canada



Supporting
Large-scale Data
Generation Initiatives

Health and Human Studies

Conservation, Ecology and Sustainability

Agriculture, Commercial and Other Sectors

Supporting User
Research Projects
of All Sizes

Overview of Select Projects Highlighted in this Report
Click on the project titles to learn more

- Forward-In-Time Natural Experimental Study of Selection
- Blue Whale Genome for Conservation
- American Eel Population Dynamics

- Marathon of Hope Cancer Centres Network
- Silent Genomes
- Genetic Markers of Cardiomyopathy
- Genetic Contribution to Cerebral Palsy
- Cost-Effective Whole Exome Genome Sequencing

- Mining Microbiome Analytics Platform
- Genomic Tools for Leaf Fungus
- Genomic Solutions for Invasive Species Management

Key CGEn Projects

HostSeq

Project website: www.cgen.ca/project-overview

In the growing landscape of genomics, comprehensive datasets serve as the bedrock for pioneering research and innovation. HostSeq, established in 2020 with federal support under Genome Canada's Canadian COVID-19 Genomics Network (CanCOGeN), stands as a testament to this ethos. HostSeq marks an important milestone in Canadian genomic research – creating the largest genomic health databank in Canada by consolidating data from more than 10,000 participants enrolled across 16 diverse Canadian studies to unravel the genetic underpinnings of COVID-19. Central to HostSeq's success is its commitment to broad consent and data sharing, a cornerstone of responsible genomic research. The HostSeq databank, containing whole-genome sequences and health data (COVID-related and other health outcomes) from a diverse cohort of people living in Canada, is accessible to researchers from both the public and private sectors for health research broadly. Hence, its significance extends far beyond its initial scope, serving as an important model for study design, data governance, and broad consent in genomic medicine in Canada.



HostSeq has enabled more than 100 researchers and trainees across 32 research projects to work with large-scale genomic data.

HostSeq has enabled more than 100 researchers and trainees from 18 institutions across 5 provinces to work with large-scale genomic data, contributing to [32 research projects](#) across various health domains. HostSeq data has demonstrated its broad utility by supporting 9 non-COVID-19 research projects thus far (these include mapping genetic diversity in the Canadian population, studying conditions such as cardiac issues and idiopathic scoliosis, and serving as a population control for Canadian studies on Autism and pediatric cancers), as well as supporting 23 COVID-19 projects. HostSeq access requests are increasingly related to non-COVID health research projects and it is expected this trend will continue, supporting HostSeq's utility beyond pandemic research.

HostSeq Data Access Projects

HostSeq is supporting 31 ongoing research projects (1 project has been completed). Those initiated in 2023-24 are listed below. For a complete list of research projects, please see the CGEn [website](#).

COVID-19 Research Projects

| Lead PI | Title |
|--|---|
| Nathan Yaganathan & John Gillard (both from, JN Nova Pharma Inc.) | Genomic Assessment of Pulmonary and Renal Complications During COVID-19 Hospitalization |
| Gerald Pfeffer , University of Calgary | Solving the Genomics of Unsolved Rare Life-threatening COVID-19 Using Genome Sequencing |
| Stuart Turvey , University of British Columbia | Host Genomic Determinants of Severe COVID-19 |
| Jennifer Brooks , University of Toronto | Post-acute COVID-19 in the Province of Ontario: Estimation of Prevalence and Identification of Risk Factors |
| Andrew Doxey , University of Waterloo | Comprehensive RNA-seq Profiling of COVID-19 Patients: Combining Microbial Diagnostics with Host Genetics Determinants of Disease Severity |
| Jessica Dennis , University of British Columbia | Characterizing the Role of Human Endogenous Retroviruses in COVID-19 Severity Via the HostSeq Databank |

Other Health Research Projects

| Lead PI | Title |
|---|---|
| David Malkin , SickKids | Characterizing and Navigating the Landscape of Genomic 'Secondary Findings' in Pediatric Cancer Patients of Diverse Backgrounds |
| Ziv Gan-Or , McGill University | Understanding the Genetic Background of Synucleinopathies and Their Progression |
| Guillaume Bourque , McGill University | Characterizing the Human Virome in European and Japanese Cohorts Using Unmapped Reads from Whole Genome Sequencing |
| Raymond Kim , SickKids | Improved Understanding of the Genetic Etiology of Cardiac Conditions Using HostSeq as a Control Dataset |
| Kamran Shazand , Shriner's Children's Genomics Institute & Steve Scherer , SickKids | HostSeq as a Canadian Population Control for Studying the Genetics of Adolescent Idiopathic Scoliosis |
| David Malkin , SickKids | The Clinical Utility of Integrative Genomics in Childhood Cancer Extends Beyond Targetable Mutations |

On the international stage, HostSeq was involved with the COVID-19 Host Genetics Initiative (HGI) – a worldwide effort to share and analyze data to learn the genetic determinants of COVID-19 susceptibility, severity, and outcomes. Recent HGI research identified 51 genetic locations significantly associated with COVID-19, mapped to three major biological pathways ([The COVID-19 Host Genetics Initiative, Nature 2023](#)). Notably, a more recent analysis of the HostSeq dataset replicated two genetic loci reported to be associated with COVID-19 severity through the HGI, and identified associations with two additional genes to be further investigated (see research highlight below; [Garg et al., PLoS Genet. 2024](#)).

As the only existing Canadian genomic health dataset that is broadly consented for sharing, storage and use, HostSeq also represents the inaugural cohort for the CIHR-supported [Pan-Canadian Genome Library \(PCGL\)](#), launched in October 2023. The aim of the PCGL is to develop a responsibly governed infrastructure that unites human genome sequencing efforts across Canada, and acts as a key resource for the integration of genomics as a core component of learning health systems. Looking ahead, CGEn will continue to work with the PCGL to build its centralized dataset and explore opportunities for data linkage with HostSeq enabled through broad consent.

HostSeq Data Research Highlights

Conducting a Genome Wide Study and Building a Polygenic Risk Score for COVID-19 Severity Using the HostSeq Dataset

Principal investigator: Lloyd Elliott, Simon Fraser University

Dr. Lloyd Elliott, member of the HostSeq Genetic Epidemiology Sub-Committee and Assistant Professor at Simon Fraser University, embarked on COVID-19 pandemic response research, initially focusing on epidemiological inquiries before transitioning to genetic studies. Leveraging access to HostSeq data, this project aimed to validate disease severity HGI loci. Beyond investigating the evidence for replication of loci reported by the HGI, the research team (with technical work led by Elika Garg, at SickKids) analyzed the X chromosome, conducted rare variant gene-based analysis and polygenic risk score testing. Their results confirmed two HGI-identified loci (*LZTFL1/SLC6A20* on chromosome 3 and *FOXP4* on chromosome 6) and uncovered two new significant associations: *MRAS* and *WDR89*. Their study also constructed a polygenic risk score, explaining 1.01% of severe COVID-19 variance, offering insights into potential treatment targets and long COVID. Innovative methodologies, including gene-based analyses and stringent quality control measures, were employed to overcome challenges like sample size constraints, resulting in robust findings.

"Access to the HostSeq data was crucial for our GWAS of COVID-19 severity on a Canadian cohort. In planning this research methodology, we aimed to develop an analysis strategy inclusive of all available individuals, including related ones and those from diverse ancestries, even within smaller cohorts. This approach represents a significant stride towards enhancing diversity and inclusivity in genomic dataset analyses."



Dr. Lloyd Elliott, Assistant Professor, Simon Fraser University

Relevant publication: Garg E., et al., Canadian COVID-19 host genetics cohort replicates known severity associations. PLOS Genetics (2024) 20(3): e1011192. <https://doi.org/10.1371/journal.pgen.1011192>

Establishing the Link Between COVID-19 Severity and Human Leukocyte Antigens (HLAs) Using the HostSeq Dataset

Principal investigator: Inanc Birol, Canada's Michael Smith Genome Sciences Centre, and the University of British Columbia

Amid the COVID-19 pandemic, Dr. Inanc Birol's team at the Michael Smith Genome Sciences Centre delved into the genetic factors influencing COVID-19 disease severity. Led by René L. Warren, they focused on Human Leukocyte Antigens (HLAs), key players in human immunity. They explored how HLA variants might affect COVID-19 susceptibility and outcomes. HLAs present viral fragments to the immune system at the cell surface, and certain variants, like HLA-C*04:01, may limit the immune response to the SARS-CoV-2 virus, the etiological agent of COVID-19. The team analyzed HostSeq data and other genomic datasets from COVID-19 patients, uncovering associations between specific HLA alleles and disease severity. These findings, including the potential of alleles like C*04:01 as markers for severe COVID-19, could inform disease prognosis and public health strategies for more effective pandemic responses.

"Very early on during the pandemic, we heard about asymptomatic individuals and populations. It begged the question: what is unique about these populations that makes them largely immune to the effects of this virus? This question intrigued me, especially considering how HLA allele frequencies and compositions vary among different populations. Throughout the pandemic, cohort data was being collected in real-time to understand COVID severity. Despite it not being our group's primary focus initially, any genomics-related question within reach interested us. We were particularly excited about the launch of the HostSeq project as it provided us with a Canadian dataset to explore our research question."



René Warren, Michael Smith Genome Sciences Centre

Relevant publication: Warren, R.L., et al., Establishing association between HLA-C*04:01 and severe COVID-19. HLA (2024), 103: e15355. <https://doi.org/10.1111/tan.15355>

Using the HostSeq Dataset as a Control Population to Map X Chromosome-wide Common Variants in Autism Spectrum Disorder

Principal investigator: Stephen Scherer, SickKids and the University of Toronto

Autism Spectrum Disorder (ASD) shows a notable male bias in prevalence, suggesting that females may require a higher genetic burden to exhibit symptoms similar to males. Whole-genome sequencing (WGS) can potentially unravel such observations in ASD and related neurodevelopmental disorders by detecting genetic variants. The HostSeq dataset provides a much-needed and relatively uncommon population control with WGS for such analyses.

Dr. Stephen Scherer, Scientific Director CGEn-Toronto, investigates the genetic contributions to autism. In this study, his research team used the HostSeq dataset in conjunction with patient cohorts with ASD (82% males) across Autism Speaks MSSNG, Simons Simplex Cohort (SSC), and Simons Foundation Powering Autism Research (SPARK) to conduct an X chromosome-wide association study (XWAS). They analyzed 400,000+ X-chromosome variants and identified over 50 associated markers and 14 genes with significant ASD-associated variants. Among these, six genes – *DMD*, *HDAC8*, *PCDH11X*, *PCDH19*, *FGF13*, and *PTCHD1-AS* – had been previously associated with ASD, and 8 are novel findings: *ASB11*, *ASB9*, *ENOX2*, *HTR2C*, *LOC124905257*, *PABPC1L2A*, *PDHA1*, and *TXLN*.

"Despite the well-recognized 'female protective effect' in ASD, large-scale X chromosome association studies have been limited due to technical complexities. We overcame these challenges, revealing significant new insights into X chromosome biology in ASD and identifying genes and pathways for further investigation. Access to the HostSeq data as a WGS control cohort was important for this research."

HostSeq is Canada's first accessible genomic health resource. The sample collection and sequencing were executed under unprecedented circumstances and in a short timeframe, enabling crucial advances in precision medicine, pandemic preparedness, and health studies. HostSeq continues to empower researchers through controlled access to its databank. It serves as a blueprint for large-scale genomics programs in Canada and has strengthened its international positioning."

Dr. Stephen Scherer, Scientific Director of CGEn-Toronto



Relevant publication: Mendes M., et al., Chromosome X-Wide Common Variant Association Study (XWAS) in Autism Spectrum Disorder. medRxiv (2024)v07.18.24310640. [doi:<https://doi.org/10.1101/2024.07.18.24310640>](https://doi.org/10.1101/2024.07.18.24310640)

Canada BioGenome Project

Project website: www.earthbiogenome.ca

Led by Dr. Steven Jones (Scientific Director of CGEn-Vancouver), and Maribeth Murray, (Executive Director, Arctic Institute of North America; Professor, Anthropology and Archaeology, University of Calgary), the Canada BioGenome Project (CBP) strives to ascertain the genetic diversity of Canada's plants and animals through genomic sequencing, furnishing reference genomes for species of ecological, cultural, or economic importance to the nation. As part of the Earth BioGenome Project, the CBP continues its effort in providing high-quality reference genomes to research groups, and partnering with the public, and local communities. The CGEn-Vancouver node, the Genome Sciences Centre, [joined the Earth BioGenome Secretariat in December 2023](#), marking a milestone in Canada's contribution to advancing genomic-informed biodiversity conservation.



The Canada BioGenome Project is deepening the understanding of Canadian biodiversity's relationship to food security, Indigenous ways of life, and ecological benefits.

Over the past year, CBP has increased its species acquisition and sequencing activities through its 32 taxonomic committees, ranging from mammals to birds to insects. These committees have facilitated the acquisition of 1,670 samples from 156 species in total. CBP is enabled by CGEn's national sequencing infrastructure and technical collaboration to devise appropriate sequencing strategies for challenging samples or genomes. The three CGEn nodes have contributed 89 PacBio Long Read sequences, 42 HiC sequences, and 39 RNA sequences to the CBP. The project has released 50 assemblies on NCBI and annotated 8 genomes with EMBL-EBI, six of these were released in the last year: Greenland Cockle, Musk Turtle, Wood Turtle, Daubed Shanny, Arctic Surfclam, and Copper Redhorse.

Samples for sequencing efforts have also come from three case study species workshops: Muskoxen, Eastern Massasauga Rattlesnake and Long Toed Salamander. All three case studies have held at least one workshop, engaging with end-users including conservation interest groups, Indigenous groups, Parks Management, and other organizations. These workshops were held in areas of conservation significance for example, Waterton, Alberta, and the Canadian High Arctic Research Station, Nunavut, and aimed to educate participants on genomics and its applications in conservation, including disease monitoring and conservation breeding. Additionally, project team members presented four talks at the

Canadian Herpetological Society 2023 meeting, covering project overviews and discussions on snake and turtle species for conservation management. The project also participated in the Biodiversity Genomics Conference 2023, alongside other Earth BioGenome affiliated projects globally.

The CBP project is committed to deepening the understanding of Canadian biodiversity's relationship to food security, Indigenous ways of life, and ecological benefits. To support this, the project is developing a knowledge mobilization platform to bridge the gap between genomics and local communities. Prototypes, including a click-through mock-up, are nearing completion to facilitate better data sharing for non-specialists.



"The Canadian BioGenome Project is a vital initiative for our nation, positioning Canada as a leader in genomics and conservation. By participating in the global Earth BioGenome Project, we are not only unlocking the genetic secrets of our diverse species but also fostering international collaboration and innovation in biodiversity conservation."

Dr. Steven Jones, Scientific Director of CGEn-Vancouver

Application Showcase

The CBP aims to provide reference genomes for various applications, including research, park management, conservation, and zoo breeding. Recently, an aquarium contacted the project to conduct a paternity test for a Steller Sea Lion pup using the CBP generated Stellar Sea Lion genome for reference. Sampling a trio family (pup and both parents) allowed for a haplotype-resolved assembly, enhancing breeding information for the aquarium and other zoo associations for zoological species survival plans.



Arctic Surfclam and Muskoxen.

Empowering Canadian Research

Health and Human Studies

Marathon of Hope Cancer Centres Network

Project website: www.marathonofhopecancercentres.ca

The Marathon of Hope Cancer Centre Network (MOHCCN) was inspired by Terry Fox's determination and vision to unite Canadians in the fight against cancer. Spearheaded by the Terry Fox Research Institute and collaborating with partners nationwide, including the Government of Canada, this initiative aims to implement precision medicine for cancer across the nation.

MOHCCN researchers investigate a great diversity of cancer sites including but not limited to blood, brain, breast and liver, and are working towards an ambitious target of generating 15,000 genomic profiles, along with matched clinical data, from participants across Canada. This MOHCCN Gold Cohort dataset will enable researchers to access large-scale, high-quality, standardized data to inform precision medicine cancer applications. For two MOHCCN regional consortia, genome sequencing is being conducted at CGEn nodes: BC Cancer Consortium at CGEn-Vancouver and Marathon of Hope-Quebec at CGEn-Montreal. So far, 2,296 of genome profiles have been completed at CGEn nodes.

Silent Genomes Project

Project website: www.bcchr.ca/silent-genomes-project

The Silent Genomes Project, funded by Genome Canada from 2018-24, sought to tackle barriers to precision healthcare for Indigenous peoples in Canada. Led by Dr. Laura Arbour, with co-leads Dr. Nadine Caron and Dr. Wyeth Wasserman, the project focuses on access to genetic and genomic healthcare and research while respecting Indigenous governance and data sovereignty. In the summer of 2023, CGEn-Vancouver completed whole genome sequencing (>40X average coverage) for 596 Indigenous people. This genomic data was combined into an Indigenous Background Variant Library (IBVL), which marks an important step in addressing health related technology access inequalities for Indigenous populations of Canada. It provides variant frequencies in a healthy Indigenous population that clinicians can use as reference to assist in genetic/genomic test interpretation when a genetic condition is suspected.

The Indigenous Rare Disease Diagnosis Steering Committee oversees the release of genomic variants within the IBVL. This ensures ongoing Indigenous governance and aims to improve healthcare outcomes for Indigenous communities. The project has provided training to increase cultural awareness in clinical genetics units across Canada, while offering genome analysis to Indigenous patients with rare genetic disorders.

Genetic Marker Discovery: Insights into Cardiomyopathy



Principal investigators: Seema Mital, SickKids and University of Toronto; and Ryan K.C. Yuen, SickKids and University of Toronto

Whole genome sequencing has unveiled a new genetic marker for cardiomyopathy. Research led by Drs. Seema Mital and Ryan Yuen, SickKids, sheds light on the genetic mechanisms underlying this inherited condition, which affects up to one in 500 individuals and can lead to heart failure. The sequencing ($n=1,216$) for this study was carried out at CGEn-Toronto.

The study reveals that tandem repeats, a form of genetic variation, are expanded in the DNA of some patients with cardiomyopathy, potentially contributing up to 4% of cases. Tandem repeats contain many copies of the same short sequence over and over, and sequencing such stretches is technically challenging. By identifying tandem repeats in the gene *DIP2B* as a significant risk factor, the researchers have laid the groundwork for future precision therapies. These findings not only enhance our understanding of cardiomyopathy but also offer promising avenues for targeted interventions to improve patient outcomes.

Relevant publication: Mitina A., et al., Genome-wide enhancer-associated tandem repeats are expanded in cardiomyopathy. *eBioMedicine* (2024), Volume 101, 105027. <https://doi.org/10.1016/j.ebiom.2024.105027>

Genetic Insights into Cerebral Palsy Unveiled



Principal investigators: Stephen Scherer, SickKids, Maryam Oskoui, Research Institute of the McGill University Health Centre (RI-MUHC) and Darcy Fehlings, Holland Bloorview Kids Rehabilitation Hospital

A pioneering Canadian-led study, with Dr. Darcy Fehlings as the lead co-author, has uncovered genetic contributions to cerebral palsy (CP), shedding new light on this complex condition that affects motor skill development in children. By comparing whole genome sequence data generated from 327 children with CP and their parents to control sequences, this seven-year study revealed that more than one in ten children had a genetic variant associated with their condition. The whole genome sequencing for this

study was carried out at CGEn-Toronto. The control population subset used in this study has since been extensively utilized.

Led by scientists from Holland Bloorview Kids Rehabilitation Hospital, SickKids, and RI-MUHC, the research suggests that CP may result from a combination of genetic and environmental factors. These findings represent a significant advancement in our understanding of CP and offer hope for improved diagnosis and treatment through precision medicine approaches. Moreover, the study's open data initiative, hosted on the Brain-CODE analytics platform, provides a valuable resource for future research, aiming to identify new genes and pathways involved in CP and ultimately transform treatment options for affected children and their families.

Relevant publication: Fehlings D.L., et al., Comprehensive whole-genome sequence analyses provide insights into the genomic architecture of cerebral palsy. *Nat Genet* (2024) 56, 585–594. <https://doi.org/10.1038/s41588-024-01686-x>

Cost-Effective Whole Exome Genome Sequencing (WEGS) for Genetic Studies



Principal investigator: Daniel Taliun, McGill University

In a recent collaborative study led by McGill University, researchers introduced Whole Exome Genome Sequencing (WEGS), a cost-effective approach combining low-depth whole genome sequencing (WGS) with high-depth whole exome sequencing (WES). By multiplexing up to eight samples, WEGS achieves a 50% cost reduction compared to standard WES, enabling high-depth sequencing of twice the number of exomes while providing valuable genome-wide insights into genetic variants associated with human health and diseases.

Using existing open-source software tools, WEGS data processing pipelines were efficiently developed, offering comparable performance to standard WES in detecting coding variants while uncovering more population-specific variants in non-coding regions. Application of WEGS to 862 patients with peripheral artery disease demonstrated its ability to assess known disease-associated variants and reveal thousands of non-imputable variants per disease-associated locus. This innovative method not only revolutionizes sequencing methodologies but also holds promise for advancing precision medicine and genetic research initiatives. The sequencing runs for this study were conducted at CGEn-Montreal.

Relevant publication: Bhérer, C., et al. A cost-effective sequencing method for genetic studies combining high-depth whole exome and low-depth whole genome. *npj Genom. Med.* (2024) 9, 8 <https://doi.org/10.1038/s41525-024-00390-3>

Conservation and Sustainability

Forward-In-Time Natural Experimental Study of Selection (FITNESS)



Principal investigators: Catherine Peichel, Universität Bern, Switzerland and Rowan Barrett, McGill University

The FITNESS project tracks the evolutionary trajectories of phenotypes and genotypes in the wild using Threespine Stickleback fish. Led by Catherine Peichel (Universität Bern, Switzerland), the FITNESS project is the first forward-in-time, highly replicated, whole-ecosystem study of parallel genetic and phenotypic evolution. The project plans to sequence the genomes of 11,000 stickleback fish, with over 9,000 genomes already completed by CGEn-Montreal. This will be followed by developing a custom genotyping array of 50K markers from the identified variants. Through this comprehensive approach, the FITNESS project will provide novel insights into the roles of historical contingencies and deterministic selective forces in shaping evolutionary paths.

Unraveling the Blue Whale Genome for Conservation



Principal investigator: Mark Engstrom, Royal Ontario Museum and University of Toronto

Dr. Mark Engstrom's team focuses on North Atlantic Blue Whale conservation in Canada. A rare opportunity to collect samples presented itself in 2014 when nine blue whales perished after being trapped by ice near Newfoundland. The team embarked on the task of sequencing and assembling (for the first time) the Blue Whale reference genome. They worked closely with the CGEn-Toronto node on this challenging step. The genome sequencing for this project also fell under the purview of another CGEn initiative, the [CanSeq150](#) project, and the resulting annotated genome was made publicly available on NCBI.

The team's research uncovered surprising findings, including resilience to the impact of past whaling, and evidence of interspecies mating with fin whales. This interdisciplinary effort not only reshapes our understanding of the blue whale but can also inform crucial conservation strategies for their survival in an ever-changing world.

Relevant publication: Jossey S., et al., Population structure and history of North Atlantic Blue whales (*Balaenoptera musculus musculus*) inferred from whole genome sequence analysis. *Conserv Genet* (2024) 25, 357–371. <https://doi.org/10.1007/s10592-023-01584-5>

Understanding American Eel Population Dynamics



Principal investigators: Louis Bernatchez, Universite Laval and Jiannis Ragoosiss, McGill University

The American Eel (*Anguilla rostrata*), once abundant in Canadian habitats, has seen rapid population decline, especially in Lake Ontario and the upper St. Lawrence River. As part of the CGEn's [CanSeq150](#) initiative, the American Eel genome was sequenced at CGEn-Montreal and the resulting data were deposited on NCBI to enable researchers working on the genomics of this species.

Using genomic data generated through CanSeq150, generated in collaboration with CanSeq150 co-lead Dr. Jiannis Ragoosiss at CGEn-Montreal, the late Dr. Louis Bernatchez from Université Laval led a study investigating panmixia in American Eels across their range, from northern to tropical habitats. Panmixia, indicating genetic homogeneity, was confirmed through genetic analyses of 460 eels from 21 diverse sites, spanning Canada to Trinidad and Tobago. Employing rigorous genetic analyses, including ADMIXTURE-like clustering and multivariate analyses, the study revealed an absence of population structure. This supports the species' panmictic nature, suggesting that a uniform conservation strategy may be effective. Additionally, two genomic regions with putative inversions were identified, hinting at potential evolutionary significance.

Relevant publication: Ulmo-Diaz G., et al., Panmixia in the American eel extends to its tropical range of distribution: Biological implications and policymaking challenges. *Evolutionary Applications* (2023), 16, 1872–1888. <https://doi.org/10.1111/eva.13599>



Agriculture, Commercial and Other Sectors

Genomic Supports for Combating Leaf Rust Fungus for Sustainable Wheat Crop Protection



Principal investigator: Guus Bakkeren, Agriculture and Agri-Food Canada

Leaf Rust Fungus poses a significant threat to wheat crops in Canada and globally, causing yield losses and impacting food security. Dr. Guus Bakkeren's team studies the genetic mechanisms underlying plant pathogen evolution and host resistance, offering insights into developing more resilient wheat varieties and sustainable crop protection strategies.

Leveraging expertise and specialized infrastructure at CGEn-Vancouver, including consultations with the team and advanced long-read sequencing technologies, Dr. Bakkeren's team tackled the challenges posed by non-culturable biotrophic fungi. This project is done in collaboration with Terramera, an industry partner that focuses on developing natural product-based crop protection compounds as eco-friendly alternatives to traditional fungicides, and is supported through Canada's Digital Supercluster Program.

Relevant publication: Wang, X., et al., The analysis of *Puccinia triticina* field populations in Canada between 2018 and 2020 using restriction site-associated DNA genotyping-by-sequencing. *Plant Pathology* (2024), 73, 157–169.
<https://doi.org/10.1111/ppa.13805>

Protecting Forests: Genomic Solutions for Invasive Species Management



Principal investigator: Gwylim Blackburn, Canadian Forest Services

Dr. Gwylim Blackburn's research is focused on developing genetic tools for combating invasive species. One target species is the Pinewood Nematode which has caused widespread devastation to pine trees outside of its native range. As a scientist within Canada's forestry sector, Dr. Blackburn's work is integral to safeguarding Canadian forests and ensuring the sustainability of the forestry industry. Collaborating with experts like Dr. Caren Helbing at the University of Victoria, Bakkeren's research forms part of the ongoing iTrackDNA project, funded by Genome Canada. This initiative aims to develop genetic tools for the detection of invasive species and species of conservation concern, based on 'environmental' tissue samples collected in nature.

Supported by genomic data generated at CGEn-Vancouver, Dr. Blackburn and his team analyze tissue samples to assess the presence and viability of the Pinewood Nematode in wood that has been heat treated. The destructive impact of the Pinewood Nematode on pine forests, particularly in regions like Japan, underscores the urgency of effective detection and control measures.

Related publication: Helbing C.C., et al., Progress in national standards development to support the use of environmental RNA for the detection of live pinewood nematodes and to assess the efficacy of phytosanitary measures. [20th meeting of the International Forestry Quarantine Research Group \(IFQRG\) \(2023\)](#).

Mining Microbiome Analytics Platform (M-MAP)

Project website: www.m-map.ca

The mining industry grapples with mounting challenges: the scarcity of accessible, high-quality ore deposits drives up costs and emissions, while stricter environmental regulations compel a shift toward sustainability. Microbes offer a promising solution, aiding in the identification of potential mining sites through surface microbial signatures via bioprospecting, enhancing metal extraction efficiency via bioleaching, and facilitating the cleanup of contaminated sites through bioremediation. These microbial interventions present sustainable alternatives to address environmental concerns within the mining sector.

One of the biggest obstacles in developing innovative microbial-based technologies is that microbes are complex. Springing from Canada's Digital Supercluster Program is M-MAP. This project has built an online analysis platform and library housing genomic and environmental information about thousands of microbes. M-MAP leveraged genomic capabilities provided by CGEn-Vancouver to sequence 300 samples and build a basis for the platform. The sequencing phase of the project is now complete, with data analysis and compilation of the bacterial genomes ongoing. The extensive library of genomic and environmental data from mining-related sites will lay the groundwork for innovative microbial solutions for the mining industry.

Developing Talent

CGEn remains steadfast in its commitment to nurturing the next generation of Canadian genomic scientists, to help feed a talent pipeline that will be critical for the future.

Genomic applications will be crucial to Canada's health, environment, and economy, and cultivating home-grown talent will bolster Canada's competitive advantage. By continually augmenting its infrastructure and supporting groundbreaking projects, CGEn significantly enhances sequencing and computational genomics capabilities across the country, thereby playing an important role in retaining researchers and Highly Qualified Personnel (HQP).

The impact of CGEn's commitment to HQP is underscored by the substantial number of individuals utilizing CGEn-generated data for their research. In 2023-24, CGEn is estimated to have helped shape the careers of more than 100 college and undergraduate students, more than 950 graduate students, and at least 650 postdoctoral fellows. It is also estimated that at least 1,600 scientific and technical personnel have also benefited from the facility's resources and expertise.

Empowering HQPs through the HostSeq Initiative

Canada's renowned research enterprise and innovation economy rely on top talent, yet historically, Canada has struggled to attract and retain STEM talent due to factors like the allure of leading companies abroad and higher pay. A critical area needing attention is genomics, where global research is advancing towards creating vast resources of genome sequences and data, enabling significant social and economic benefits.

Large-scale genomic datasets, like CGEn's HostSeq databank, provide an excellent resource for training of the next generation of genomic data scientists. HostSeq data has been utilized by over 100 researchers and trainees from 18 institutions across 5 provinces. This includes 30 students and postdoctoral fellows as well as 50 staff members.



"Working with HostSeq data was my first experience with joint calling and whole genome sequencing data, which presented significant challenges. This was exciting to navigate. The collaborative spirit across Canada made it a rich learning environment, providing access to experts across various fields, from genomics to epidemiology."

Elika Garg, Biostatistician, SickKids



"HostSeq stood out as remarkably accessible compared to other datasets I've pursued. The approval process took only about two weeks. The infrastructure at CGEn-Toronto supports seamless data sharing, which is incredibly helpful for someone like me, especially considering my tight timeline and priorities in training. Time spent on acquisition isn't always the most crucial aspect for my research goals."

Safa Majeed, MD/PhD Student, University of Toronto

Engagement and Outreach

CGEn makes significant, ongoing efforts to support and inform our staff, affiliated scientists, users as well as the public with pertinent information, events and communications. These activities are designed to enhance staff experiences, further enable high-quality genomic science in Canada, support appropriate implementation of research outcomes, and inform the public.

As CGEn moves forward to strengthen its commitment to Inclusion, Diversity, Equity & Accessibility (IDEA), we have made notable advancements this past year. A key achievement has been the development of the [IDEA Strategic Action Plan](#). Based on current and relevant literature and resources, best practices at CGEn node host institutions, and the results of a CGEn-wide staff survey, the IDEA Strategic Action Plan, and consultation with the CGEn IDEA Committee, guide our ongoing IDEA actions and activities.

To continue promoting diversity on the CGEn team, CGEn has signed up for the 50-30 Challenge, which encourages equity and diversity on governance boards and in senior management positions. CGEn also developed and delivered a number of IDEA-focused education sessions to enhance staff and trainees' understanding of the important role that IDEA plays in research and the workplace. Education topics included Introduction to IDEA, Sex and Gender in Science and the Workplace, and Implicit Bias. A number of frameworks and toolkits were also developed to support more inclusive and equitable research.



CGEn hosted a panel discussion at CSPC 2023 on 'The Role of Artificial Intelligence in Delivering Precision Medicine' (left) and organized a CIHR-funded Café Scientifique exploring 'Breaking Down Barriers: Exploring Equity's Role in the Future of Precision Medicine' (right).

In 2023, CGEn hosted two events to encourage dialogue and collaboration within the scientific and wider community. A CIHR-funded Café Scientifique in September 2023 called "[Breaking down barriers: Exploring equity's role in the future of precision medicine](#)," featured diverse experts and moderated discussions for an audience of researchers,

clinicians and the public. A second event, at the Canadian Science Policy Conference (CSPC) 2023, focused on [“The role of artificial intelligence in delivering precision medicine,”](#) and facilitate insightful discourse among leaders in AI and precision medicine.

CGEn employs a multifaceted communication strategy to disseminate impactful findings and promote its services. This includes producing focused research stories and a bi-monthly newsletter, as well as sharing relevant information on social media channels.

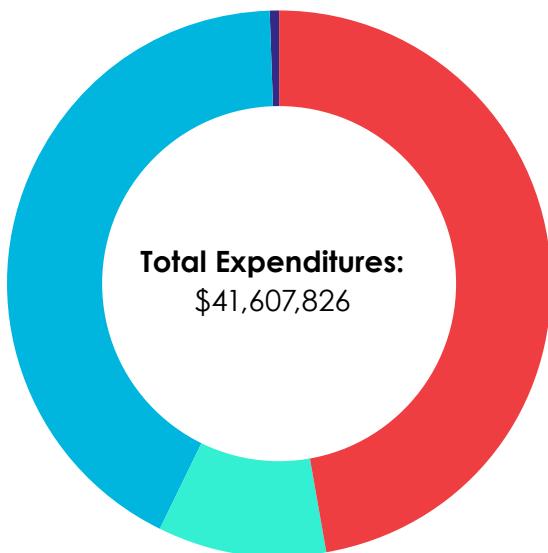
The image displays three electronic devices showcasing CGEn's communication efforts:

- Laptop Screen:** Shows a Twitter post from the official CGEn account (@CGEn). The post reads: "Happy International Women's Day! Today we celebrate and recognize the amazing women working to advance genomics research. Join us in championing and empowering the women of CGEn." It includes a photo of several women and the hashtags #internationalwomensday and #iwd2024.
- Tablet Screen:** Displays a news article titled "Whale Tales: Blue Whale Genomes, Resilience to Genetic Bottleneck, and Interbreeding Insights". The article discusses research by CGEn scientists. It includes a photo of a blue whale breaching.
- Smartphone Screen:** Shows the cover of the "SEQUENCE" newsletter, Vol. 3, Issue 1, February 2024. The cover features a blue and white DNA pattern background and the title "SEQUENCE" in large white letters. It also includes a "Note from CGEn" section and a "Welcome" message.

Financial Highlights

CGEn's cutting-edge facilities and scientific expertise, crucial for genome sequencing, are made possible by the support of our partners and funders. Our cornerstone funding comes from the Canada Foundation for Innovation (CFI) Major Science Initiatives Fund (MSIF 2023-29), which, along with provincial governments and host institutions, supports the operation and maintenance of research facilities vital to the nation.

Additionally, in 2023-24, CGEn received funding from CFI's Innovation Fund and from Genome Canada's Technology Development program for MSIF facilities. These funds enable CGEn to continue to assess and implement strategic infrastructure upgrades and perform leading edge genomic science, while leveraging provincial funding and private-sector in-kind contributions. CGEn's revenue and expenditures balance over multi-year funding cycles.



- **47.4%** Infrastructure: \$19,717,688
- **10%** Maintenance – (extended warranties, parts, upgrades, services, supplies/consumables): \$4,175,690
- **42.1%** Salaries and Benefits: \$17,533,475
- **0.4%** Professional Development, Non-Salary Administrative and Outreach Expenses: \$180,973



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