

Request for Applications (RFA)

Joint Collaborative Program between Genome Canada and the Canadian Institutes of Health Research (CIHR)

Advancing Technology Innovation through Discovery

BACKGROUND

This joint collaborative program was developed by Genome Canada and the Canadian Institutes of Health Research (CIHR) to bring together Genome Canada-funded Science and Technology Innovation Centres (S&T ICs) with Canadian researchers to focus on applying the latest genomics technologies to identify the genetic causes of childhood diseases. This funding opportunity will specifically focus on diseases where such identification can be achieved rapidly with the potential for important novel biological, clinical and commercial discoveries.

It has been twenty years since the official commencement of the Human Genome Project and six years since its completion. Next generation sequencing technologies are well established and third generation sequencing technologies are now being developed and tested. With the introduction of massively parallel next-generation sequencing techniques there is an emerging paradigm shift in our ability to identify disease causing genetic mutations. The Genome Canada-funded S&T ICs need to be able to adapt to this new reality as quickly as possible; equally the Canadian research community should be able to take advantage of these technological advances just as quickly.

Canada is well positioned to take advantage of its many important resources to put us on the leading edge in disease gene discovery. The S&T ICs are among the leaders in the world in the application of technology to scientific problems. There are patient cohorts ready for study, with samples available and consent for research given. Also, Canadian researchers are well-organized and have a proven capacity to work collaboratively.

Other countries, such as the United States, China and the United Kingdom, are moving forward in this area as well. This joint CIHR-Genome Canada program will allow Canada to benefit from its unique advantages to take an internationally leading role in disease gene discovery.

JUNE 2010 PLANNING WORKSHOP

To define the parameters of the collaborative program a one-day workshop entitled “Advancing Technology Innovation through Discovery” was held on June 8, 2010 bringing together leaders from the fields of genetics of childhood diseases and genomics technologies. The recommendations from that meeting have been incorporated into this RFA.

PROGRAM OVERVIEW

The focus of the collaborative program is childhood diseases **for which genes can be identified in a short time frame and with a small number of subjects** to ensure the greatest impact with the funds available; these may include both (i) rare, Mendelian diseases and (ii) some rare pediatric

and adolescent cancers. This collaborative program is not intended to study gene variants in complex diseases. However, should a longer term program be developed, more complex diseases may be considered for study in an expanded program.

Applications are expected to be pan-Canadian and must include multiple research centres. It is expected that geneticists and clinicians will work in partnership with the Genome Canada-funded S&T ICs to develop applications for this collaborative program. Of the three Genome Canada-funded S&T ICs that offer sequencing and data analysis, at least two must be involved in each application. (See Appendix 1 for a list of S&T ICs). Applications can focus solely on rare pediatric and adolescent cancers, on other rare Mendelian diseases or, if appropriate, can combine both disease areas/streams in a single application.

The program has three stages:

Stage 1: Establishment of National Disease Consortia and Development of Applications

Stage 2: Application of Next-generation Sequencing Technologies for Gene Discovery

Stage 3: Validation of proposed mutations

Stage 1

Establishment of National Disease Consortia and Development of Applications. It is envisaged that national disease consortia will bring together clinicians, geneticists and the S&T ICs to allow the rapid assembly of patient resources across Canada and the development of an application for funding. It is expected that no more than one national consortium will be established in each stream: (i) rare pediatric and adolescent cancers and (ii) other rare Mendelian diseases. This collaborative program is short-term in nature and intended to capitalize on patient resources already available for study, so the consortia will need to demonstrate that the necessary experimental materials and appropriate consents are already in place.

Each consortium would be responsible for prioritizing the diseases and samples for study. It is recommended that the consortium establish a selection committee to undertake the prioritization process using appropriate criteria, such as:

- i. Likelihood of rapid, successful identification of disease related genes (e.g. based on inheritance pattern, consanguinity, number of patients/families, additional biochemical information, quality of clinical diagnosis); and
- ii. Benefit to patient, family and/or healthcare system.

Patient consent and Research Ethics Board (REB) approvals will have to either exist or be likely to be obtained in a timely manner. In this context and, given the involvement of vulnerable populations (children) and the central role of consent, confidentiality and other important issues, all applicants must consider the ethical, environmental, economic, legal and social (GE³LS) implications of their proposals and integrate plans to effectively address them beginning in stage 1.

The CIHR Institute of Genetics is in the process of catalyzing the creation of a Canadian Rare Diseases Consortium. In addition, the CIHR Institute of Cancer Research is engaging their community to develop a Pediatric and Adolescent Cancer Consortium. Those interested in learning more about these efforts, should contact Stephanie Robertson (Institute of Genetics) for the Canadian Rare Diseases Consortium, or David Hartell (Institute of Cancer Research) for the Pediatric and Adolescent Cancer Consortium. Contact information is below.

Stage 2

Application of next-generation sequencing technologies for gene discovery by targeted enrichment, including whole-exome, or whole-genome sequencing. The sequencing and preliminary bioinformatics analysis (calling bases and variants) will be undertaken by Genome Canada-funded S&T ICs. During this stage of the program early results identifying genetic mutations for rare childhood diseases should be expected with minimal follow-on validation efforts.

Stage 3

Validation of proposed disease mutations. It is expected that many of the results from sequencing small cohorts will require follow-on validation to identify the mutations causing disease. We anticipate that validation will take up to 12 months to achieve. Precise methods of validation will depend upon the nature of the specific genes identified but could involve sequencing the specific gene from a larger cohort of patients and their relatives, functional studies in animal models, gene expression analysis, and other approaches. Validation will therefore require multiple disciplines and expertise, including bioinformatics, molecular biology, genetics, cell biology, GE³LS experts, etc. and will require active collaboration between the S&T ICs and the geneticists and clinicians.

APPLICATION AND PEER REVIEW PROCESS FOR STAGE 2 & 3

Genome Canada will manage the review process. Consortium leaders must submit completed applications for funding by October 15, 2010 to:

Name: Kim Corbett
Title: Program Manager, Genome Canada
Phone: 613-751-4460 ext 120
E-mail: kcorbett@genomecanada.ca

Funding applications must:

- summarize the demonstration work related to the formation of the consortium;
- address the review criteria;
- describe the key activities to be undertaken in stages 2 and 3, as well as potential follow-on activities funded through other mechanisms; and
- provide a detailed budget.

The application form, including a budget template, will be made available through Genome Canada.

The applications will be reviewed by a small expert panel to identify the proposals that best respond to the RFA. In addition to the overall quality of the research, the evaluation criteria will include (note that these descriptors are not all inclusive):

- Are the diseases well selected with respect to the potential for rapid identification of the causative genes based on information from a relatively small number of subjects, and is there an efficient downstream validation process proposed?
- Will identification of the causative genes for these diseases make a significant impact on the field?
- Are the priorities assigned to diseases/resources well justified?
- Is the most appropriate technology for the proposed work being put forward?
- Is the community of researchers comprising the team appropriate (e.g., both geographic and disciplinary representation)?

- Have the applicants made a convincing case for the timely availability of patient material, including receiving the appropriate consent?
- Have applicants considered GE³LS implications of their proposals and integrated plans to effectively address them?
- Is the proposed budget reasonable relative to the proposed project activities?

Results will be made available by November 30, 2010.

POTENTIAL FOLLOW-ON STAGE

Given that one of the key outcomes of any investment should be translation into benefits and impact, it is expected that the findings arising from this program will be taken forward for further study using funding programs of other organizations, such as CIHR Operating Grants competitions or Institute-led strategic initiatives, other Genome Canada or regional Genome Centre funding opportunities, competitions launched by other non-profit organizations or opportunities to access institutional funds. In particular, the following two CIHR Strategic Initiatives represent opportunities for continued support:

- *Rare Diseases Emerging Teams: Translating Basic Biology to Enhanced Patient Care* (October 2010 program launch) co-led by the CIHR Institute of Genetics and the CIHR Institute of Nutrition, Metabolism and Diabetes
- *Pediatric and Adolescent Cancer – Prevention or Mitigation of the Adverse Consequences of Treatment* (launched June 2010) <http://www.researchnet-recherchenet.ca:80/rnr16/vwOpprtntyDtIs.do?prog=1024&tag=1> led by the CIHR Institute of Cancer Research

These two RFAs, that represent a combined total funding commitment of close to \$20 million, could provide up to five years of follow-on funding to build on the successes of the CIHR/Genome Canada program.

FUNDING AVAILABLE

CIHR and Genome Canada will contribute equal amounts, up to \$2 million each, to this collaborative program. It is expected that additional funders will be sought by all participants (both funders and applicants) to help augment the scale of the program and speed development of results. There is no requirement for co-funding.

TIMELINE

July 28, 2010	RFA Released
October 15, 2010	Applications submitted
November 30, 2010	Announcement of results of review
December 2010	Initiate sequencing and primary data analysis
January 2011- December 2011	Validation of variant list

CONTACTS:

CIHR Contacts

Institute of Genetics

Name: Stephanie Robertson

Title: Assistant Director

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E-mail: Stephanie.robertson@cihr-irsc.gc.ca

Institute of Cancer Research

Name: David Hartell

Title: Associate, Institute Strategic Initiatives

Phone: 613-941-4329

E-mail: David.hartell@cihr-irsc.gc.ca

Genome Canada Contact

Name: Kim Corbett

Title: Program Manager

Phone: 613-751-4460 ext 120

E-mail: kcorbett@genomecanada.ca

ABOUT THE FUNDERS

The Canadian Institutes of Health Research (CIHR) is the Government of Canada's agency for health research. CIHR's mission is to create new scientific knowledge and to catalyze its translation into improved health, more effective health services and products, and a strengthened Canadian health-care system. Composed of 13 Institutes, CIHR provides leadership and support to more than 13,000 health researchers and trainees across Canada.

CIHR Institute of Genetics supports research on the human and model genomes and on all aspects of genetics, basic biochemistry and cell biology related to health and disease, including the translation of knowledge into health policy and practice, and the societal implications of genetic discoveries.

CIHR Institute of Cancer Research fosters research based on internationally accepted standards of excellence, which bear on preventing and treating cancer, and improving the health and quality of life of cancer patients.

Genome Canada is a not-for-profit Corporation that acts as the primary funding and information resource relating to genomics research in Canada. Its main objective is to position Canada as a world leader in genomics research. Dedicated to developing and implementing a national strategy in genomics research for the benefit of all Canadians, it has received \$915 million in funding from the Government of Canada since 2000 to which has been added close to \$1.0 billion in partnered co-funding and interest earnings. Genome Canada will work closely with its regional Genome Centres (Genome British Columbia, Genome Alberta, Genome Prairie, Ontario Genomics Institute, Genome Quebec, and Genome Atlantic) to facilitate the interaction between the genetics community and its technology providers as well as ensuring effective collaborations between S&T ICs.

Appendix 1

Genome Canada-funded Science and Technology Innovation Centres that offer sequencing and data analysis

Genome Sciences Centre

675 West 10th Avenue
Vancouver, British Columbia
<http://www.bcgsc.ca/platform>

Contact: Robyn Roscoe
Head, Strategic Planning & Project Management
rrscoe@bsqsc.ca

McGill University and Genome Quebec Innovation Centre

740, Dr. Penfield Avenue, Room 7104
Montreal, Quebec
<http://www.gqinnovationcenter.com/index.aspx>

Contact: Alexandre Montpetit
Assistant Scientific Director
Alexandre.montpetit@mail.mcgill.ca

The Centre for Applied Genomics

The Hospital for Sick Children
MaRS Centre - East Tower
101 College Street, Room 14-706
Toronto, Ontario
<http://www.tcag.ca/>

Contact: Jo-Anne Herbrick
Facilities Manager
jherbrick@sickkids.ca