

Brain Canada-Huntington Society of Canada Multi-Investigator Research Initiative (MIRI) Creating HD Clinician-Scientist-to-Patient Virtual Networks Request for Applications (RFA)

About Brain Canada

Brain Canada is a national non-profit organization that enables and supports transformative, original and outstanding brain research in Canada. For more than a decade, Brain Canada has made the case for the brain as a single, complex system with commonalities across the range of neurological disorders, mental illnesses and addictions, brain and spinal cord injuries. Looking at the brain as one system has underscored the need for increased collaboration across disciplines and institutions, and a smarter way to invest in brain research that is focused on outcomes that will benefit patients and families.

The Canada Brain Research Fund is a public-private partnership established between Brain Canada and Health Canada to encourage Canadians to increase their support of brain research, and maximize the impact and efficiency of those investments. Brain Canada is raising \$120 million from private and non-federal sources, which is being matched by the Government of Canada on a 1:1 basis. The Fund supports “the very best Canadian neuroscience, fostering collaborative research and accelerating the pace of discovery, in order to improve the health and quality of life of Canadians who suffer from brain disorders.”

About Huntington Society of Canada

The Huntington Society of Canada is a not-for-profit organization with the goal of maximizing the quality of life for people living with Huntington disease (HD) by delivering services, enabling others to understand the disease, and furthering research to slow and prevent HD.

The universal goal for HD research is to find treatments that reverse, slow or prevent the progression of HD. The Huntington Society of Canada (HSC) is a key part of this effort and the Society has a unique role to play. We invest in the most promising peer-reviewed research, leading to viable treatments for HD. Since 1973, the Society has partnered with world-class organizations to leverage the best resources and expertise to positively influence the direction of HD research in Canada and globally.

HSC has been successful in developing a critical mass of HD research excellence in Canada. Our Canadian investments and international research collaborations have led to a better understanding of Huntington disease and contributed to expediting processes, from discovery to treatment, to slow and prevent HD.

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Rationale

Brain health is one of the most pressing health challenges facing Canadians. One in three individuals – over 11 million people – will face a psychiatric disease, a neurological disorder or a brain or spinal cord injury at some point in their lives. Advances in brain research are leading to an improved understanding of the etiology of these disabilities, better diagnostics and screening, therapeutic interventions, and improved frontline care and social support services.

Huntington disease (HD) is caused by a CAG trinucleotide repeat of variable length in the *Huntingtin* gene (*HTT*), leading to the expression of a mutant protein that exhibits pathophysiological properties. This autosomal dominant disease overtly affects one in 7,300 people (Fisher & Hayden, 2014) who show debilitating motor, cognitive, and psychiatric disorders. Quality of life for patients and those providing support for affected individuals is severely impacted and declines during the course of the disease. Current management of the disease relies solely on treating symptoms as there are no effective disease-modifying therapies to date.

There remains a significant need to elucidate the key underlying HD pathogenic processes for the purposes of developing therapies to slow, prevent, and reverse HD. Several key areas remain poorly understood, such as: the effects of the mutation relevant to the disease process that leads to physiological changes and clinical diagnosis; modulating factors that alter the rate of disease progression; discovery and validation of biomarkers to track the onset and progression of HD, before and after treatment; and novel clinical trial design.

The known genetic cause of HD presents a unique opportunity to study HD on its own, or HD relative to other neurodegenerative diseases, such as ALS, Alzheimer’s, and Parkinson’s disease. Introducing new disciplines to HD research will enrich the overall understanding of HD, and thereby bring to light new insights into neurodegenerative diseases.

In order to advance our understanding of all aspects of these disorders but with a primary focus on HD, **Brain Canada is partnering in a joint-funding initiative with the Huntington Society of Canada that aims to create Huntington disease (HD) Clinician-Scientist-to-Patient Virtual Networks**. By connecting researchers, clinicians and HD patients, the network intent is to ensure ongoing collaborations focused on expediting the discovery-to-effective-treatment cycle in humans in order to slow or prevent HD and other relevant neurodegenerative diseases. This initiative will facilitate multi-disciplinary and multi-investigator collaboration by engaging experts (e.g. geneticists, computational biologists and others) in the application of emerging technologies. Collaboration with other neurological disease researchers, including but not limited to ALS, Alzheimer’s, and Parkinson’s disease, will enrich the overall understanding of potential treatments for HD and other neurodegenerative disorders.

Grant details

This competition has an overall envelope of \$900,000 over three years allowing to fund one multi-disciplinary grant.

Three-year MIRI research projects are to connect clinicians, scientists and the HD community in a manner that can be demonstrated to create a collaborative HD Clinician-Scientist-to-Patient Virtual Network. For the purposes of this grant, the HD community comprises HD patients with clinically diagnosed symptoms and their family members, individuals at risk of inheriting the HD mutation as well as those individuals who have died of the disorder.

More specifically, the application should address the following points:

- Enhancing our understanding of HD to ultimately lead to, for example, the development of therapeutics, better clinical trials, or improved patient care, to slow or prevent the disease processes responsible for the onset and progression of HD;
- Including basic and clinical research aspects equally in order to move the discovery to an effective treatment. Projects can be at any stage of the discovery-to-effective-treatment cycle but the clinical support has to be clearly described;
- Focusing on human biology beyond animal models of HD and human HD cell models;
- Depending on the stage of effective treatment, using a more “patient-oriented” approach that values the input and involvement of the HD community;
- Demonstrating a clear strategy to connect HD researchers, HD clinicians and the HD community. Research teams must be multi-disciplinary and may involve another relevant neurodegenerative disorder where this strengthens the overall HD research approach. This can include a wide range of experts, for example: geneticists, computational biologists, and others who can build disease models from clinical, molecular, genomic, drug-response and other datasets; or bioengineers and others who can foster collection of refined standardized data in HD carriers; or trialists with access to genetic, genomic and drug-response data.

Use of Funds

The funds must contribute towards the direct costs of the research for which the funds were awarded, and the benefits should be directly attributable to the MIRI grant.

MIRI grants are non-renewable.

Eligible costs

MIRI grants may be used to support any aspect of the operating costs of the research project, including:

- Supplies and materials;
- Provision of special services and user fees;
- Maintenance of essential equipment;
- Travel of team members and trainees for collaboration and presentation of results;

- Publication costs;
- Salaries for technical personnel;
- Stipends of trainees, patients and carers that are part of the research team;
- New equipment that is currently unavailable but essential for the project.

Ineligible costs

- Salaries and consulting fees of any investigators (including the principal investigator and co-investigators applying for the MIRI).
- Indirect costs or overhead costs associated with managing the research project.

Note that this list is not exhaustive, and Brain Canada and Huntington Society of Canada may rule any other expenditure eligible or ineligible. Please contact Brain Canada about the eligibility of expenditures not listed here.

Eligibility

- This competition is open to teams of two or more investigators in any scientific discipline who are eligible to apply for research grants from the Canadian federal granting agencies (CIHR, NSERC, and SSHRC) and who have the experience and expertise required to create a multi-disciplinary HD Clinician-Scientist-to-Patient Virtual Network team;
- The teams must comprise a Principal Investigator and at least one Co-Investigator, and may include one or several Collaborators:
 - A Principal Investigator is an individual responsible for communication between the members of the Virtual Network, as well as communication with the funding partners. He/she is also accountable for the team's research activities and use of funds that will be reported on an annual basis with a progress and financial report;
 - A Co-Investigator is an individual who contributes directly to the proposed research activities;
 - A Collaborator is an individual who contributes indirectly to the proposed research activities by providing a specific service such as access to equipment, provision of specific reagents, training in a specialized technique, statistical analysis, access to a patient population, etc. Collaborators from government, the private sector and other nations are welcome in order to strengthen teams and facilitate the uptake of the team's research results.
- The teams must be multi-disciplinary and the investigators may be based at one or several research institutions. The team must include the range of expertise and experience required to carry out the proposed research including, at minimum, a research scientist and a clinician;
- The teams are encouraged to include researchers at all stages of their careers, as well as researchers within and outside the neurosciences who wish to apply their expertise to problems of neurodegeneration;
- The teams must be primarily Canadian. However, it is possible to include one (and only one) international investigator working in a non-Canadian institution when his expertise or skills

are not available in Canada but are needed to successfully carry out the proposed research. Please note the following:

- An international investigator is defined as an investigator spending more than 50% of working time outside of Canada.
- Brain Canada funds will only support the portion of the work conducted in Canadian institutions eligible to receive funding from the federal granting agencies. However, the Brain Canada funds can be used for the procurement of goods and services outside of Canada, when necessary for the advancement of the project, if such goods and services are not available in Canada;
- Funds provided by the Huntington Society of Canada can be used to support the portion of the work by the international investigator when conducted at a non-Canadian institution;
- Principal Investigators can contact Brain Canada or the Huntington Society of Canada to inquire about the limitations of compensation for an international investigator.

Criteria for Assessment

Innovation (in the sense of being transformative)

Proposals that are solidly-based in scientific fact and technically feasible that offer new knowledge that is designed to expedite the HD discovery-to-effective-treatment cycle. The research conducted includes sex and gender considerations if relevant.

Strength of the HD Clinician-Scientist-to-Patient Virtual Network that is created

The team has the necessary expertise and the requisite organizational structure to build a network that will achieve the goals of the project.

Strength of involvement of the HD community

Inclusion of HD community members at all points in the project's research cycle. Projects can be at any stage of the discovery-to-effective-treatment cycle and can take on one or multiple segments of this cycle. The focus must be on human biology beyond animal models of HD.

Potential for impact

The likelihood that the team's research efforts will lead to novel treatments that slow or prevent disease processes that lead to the onset and progression of the clinical symptoms of HD and thereby, potentially for other disorders, such as ALS, Alzheimer's, and Parkinson's disease. Areas of impact can include, but are not limited to:

- Better therapeutic targets through understanding of the underlying disease processes and modulation in HD;
- Better clinical trials through understanding of the disease process and natural history of HD with suitable validated endpoint measures, biomarkers, and novel trial design;
- Better disease management through understanding of the natural history of HD leading to better decision making around patient care.

Review process

All Full Applications will be reviewed by at least two expert reviewers as well as two members of a full application Selection Committee composed of Canadian and International members with broad experience and expertise in the brain sciences, who are not applicants, to ensure that all funded proposals are assessed against similar standards of excellence.

Brain Canada and Huntington Society of Canada will invite applicants to provide suggestions for the membership of the Selection Committee, and for the selection of the expert reviewers who will provide the Selection Committee with expert advice on specific applications. The Selection Committee will provide a merit score for each full application, and recommend to Brain Canada and Huntington Society of Canada those applications that have received a sufficiently high merit score to deserve funding.

Applicants will receive anonymized written comments from the expert reviewers and the Selection Committee, but if considered uncompetitive by all reviewers, certain applications will not be discussed in detail at the meeting of the Selection Committee and will not receive notes of the Committee discussion. Brain Canada and Huntington Society of Canada will not entertain appeals against the assessment of the Selection Committee.

How to apply

Principal Investigators should contact Brain Canada (programs@braincanada.ca) if they have enquiries about the application process. Full applications must be submitted using Brain Canada’s electronic grant management system (<https://braincanada.smartsimple.ca/s/Login.jsp>). The Principal Investigator must complete all required application fields in the Brain Canada’s electronic grant application system before 16:00 ET on the deadline dates listed below.

Timeline

Request for Applications	December 1 st , 2016
Workshop/Teleconference Q&A session	December 22 nd , 2016
Submissions of Applications	February 2 nd , 2017 at 16:00 ET
Peer Review for Applications	End of March, 2017
Funding Decisions Made and Notifications	Mid-April, 2017
Start Date of Funding	Mid-June, 2017

Workshop/Teleconference Q&A session

There will be an information workshop that will be held on December 22, 2016 via teleconference that will address any questions applicants may have pertaining to the RFA. The workshop will facilitate the opportunity for applicants to consider collaboration with other neurological disease researchers and, therefore, we strongly encourage applicants to participate in this beneficial teleconference workshop. Principal Investigators will be required to submit the title of their project and a 200-word project summary to Brain Canada (programs@braincanada.ca) by **16.00 ET December 18, 2016** in order to participate in the workshop.

Full Application Components

The Full Application will need to be formatted using 12 point Arial or Georgia font, single-spaced, on a letter-size page with 1" minimum margins. The font size for figures and legends has to be a minimum of 10 points. Use of a condensed font and spacing is not permitted. It is the sole responsibility of the applicant to ensure their submission is acceptable and received before the deadline. Those received in any other format, exceeding the page limits, incomplete, or late, will be rejected.

Project summary (*maximum 1000 words*)

- Project title;
- Project start and end dates (note: choose dates within a 36-month window);
- Keywords (including freeform): up to 10 words;
- A summary of the research project and its goals, emphasizing its innovative features and technical feasibility as well its position in the HD discovery-to-effective treatment cycle. It is also important to explain how the project is feasible within the time and funding available from the requested MIRI grant.

Project Team details

- If not registered already, please have your co-applicants register with the Brain Canada grant management system (<https://braincanada.smartsimple.ca/s/Login.jsp>). Registered applicants will receive a Brain Canada PIN found under their "Personal Profile" and have access to co-write the application with the Team Leader;
- Add up to ten key co-applicants using their Brain Canada PIN and last name;
- If there are more than ten key co-applicants, select those most essential to the project;
- Principal and co-investigators publications: For each of the up to ten investigators, cite up to five of their publications, of which at least three must have been published in 2010 or later. "Publications" means any type of document or medium, print or electronic, which best illustrates the member's relevant research experience, expertise and achievement. Ideally, these describe paradigm-shifting ideas and findings, or examples of effective application and knowledge translation of research findings, and demonstrate the applicant's ability to contribute to the proposed research project. Each item should be annotated with a brief reason for its selection. Include the DOI, URL or PMID of publications where applicable so that

reviewers can access them or Dropbox link of publications where applicable so that reviewers can access them. “Publications” refer to any type of document or medium, print or electronic.

- Explain the role of any trainees in the project and the unique learning opportunities they will experience (separate attachment).

Lay Summary (*maximum 300 words*)

Suitable for publication and understandable by non-scientists.

The Proposal (*maximum 15 pages including figures and legends*)

Proposals should include the following information, structured so as to best address the criteria for assessment (innovation, strength of the HD Clinician-Scientist-to-Patient Virtual Network that is created, strength of involvement of the HD community, and impact).

1. The specific objectives to be achieved by the end of the funding period.
2. The rationale for undertaking the study now, including:
 - A clear statement of the unique and innovative features of the project and how it includes the HD community;
 - An explanation of how the approach will maximize the opportunity for discovery and translational research that will expedite the discovery-to-effective-treatment cycle, while expanding the overall understanding of HD treatments in humans;
 - An explanation of how the project will introduce new disciplines to HD research and lead to collaboration with other neurological diseases if that is the case;
 - A brief review of previous results obtained by team members and others that support the rationale for the project.
3. The work plan, including:
 - The approaches, methods and techniques that will be used to connect clinicians with scientists and scientists with the HD community in a manner that can be demonstrated to create a collaborative HD Clinician-Scientist-to-Patient Virtual Network;
 - Anticipated milestones: Key intermediate stages in achieving the final objectives, and the projected dates for their achievement;
 - Potential pitfalls or obstacles, and how they will be overcome;
 - Methods to be used to show how the results of the project will slow or prevent the HD processes that lead to the onset and progression of the clinical symptoms of HD and possibly other disorders;
 - The expected outputs from the project, and how its findings will be disseminated to those who need to know about them;
 - The expected impacts of the HD Clinician-Scientist-to-Patient Virtual Network.

CVs of Principal investigators and co-investigators – up to 10: (maximum 2 pages each):

- Note training and employment history, honours and distinctions, experience working in collaborative projects, titles and dates of major grants held in the past five years and key publications relevant to the current application;
- Provide a URL link to a full CV on an institutional website, or equivalent (e.g. Google Scholar profile, CCV);
- Indicate the average hours per week that the member will devote to this project;
- For other team members, provide only name, position and affiliation, and URL or Dropbox link to full CV.

Budget

- A yearly budget must be provided and the total budget should be equally distributed across the three years of funding;
- Provide costs for major categories only:
 - Salaries for technical personnel;
 - Stipends of trainees. If funding for trainees is requested, an additional page should be provided, explaining the precise role of the trainees in the project, and justifying this as an outstanding training opportunity;
 - Maintenance of essential equipment; equipment that is currently unavailable but essential for the project;
 - Supplies and materials;
 - Provision of special services and user fees, payments to subjects;
 - Travel of team members and trainees for collaboration and presentation of results;
 - Publication costs.
- Each amount for a category as well as the sum of all categories must be rounded to a multiple of \$1,000.

Brain Canada-Huntington Society MIRI grants may not be used for: salary payments to any non-technical or non-trainee team members, payment to clinicians for recruiting subjects, or any institutional overhead.

Attachments:

- References;
- List of >10 team members, if applicable;
- Support letters, if applicable.

Optional information:

- Provide the names and contact information for up to three individuals who are not in conflict and would be competent to review the full application;
- Provide the names and contact information for up to three individuals who should not be contacted to review the full application.

Reviewers will be selected by Brain Canada, taking these and other suggestions into account.

Certification and Signatures

- Signatures of the Principal Investigator and all key members of the team are mandatory for the application to be considered and have to be submitted before the deadline;
- Institutional signatures: Signatures of the responsible officials of each institution where the team members conduct their research are required and the applicants should ensure to obtain these signatures early enough to meet the deadline.

Data Sharing Plan:

- Application must include a plan outlining how data generated under the MIRI grant will be shared with the HD and broader communities.

Confidentiality and Ownership

Brain Canada and Huntington Society of Canada will keep all materials submitted to it for this funding opportunity confidential, and will take reasonable steps to keep these materials confidential, and divulge them only to reviewers, Selection Committee members and observers, and Sponsors, who have signed confidentiality agreements. Funded applications will be retained for comparison of intended and actual outcomes, as part of the final evaluation of the Canada Brain Research Fund.

Brain Canada and Huntington Society of Canada do not claim ownership of intellectual property (I.P.) arising from research funds, and expect that its funds will be used to create I.P. that is developed and commercialized according to the policies of the research institutions in which the research is performed. The Principal Investigator and co-investigator(s) must resolve I.P. ownership issues with funding partners before submitting an application.

Reporting, Communications, and Evaluation

As a condition of continued annual funding of MIRIs, Brain Canada and Huntington Society of Canada require a brief yearly progress report narrative and financial report from the Principal Investigators, outlining use of funds, project achievements and impacts realized, as well as difficulties encountered and steps taken to overcome them. Continued funding will be based upon a satisfactory review of the progress report and financial report by Brain Canada and Huntington Society of Canada. If Brain Canada and Huntington Society of Canada considers that a progress report is questionable, after discussion with the team, the funding partners may agree to extend the period over which the funds are available, or cancel further funding. Details of the reporting process will be provided to the awardees.

In order to demonstrate to Canadians the ongoing value of the Canada Brain Research Fund, the team members must contact Brain Canada and Huntington Society of Canada in advance of the publication, release or public presentation of research results obtained with the awarded grant, so that a press release or other publicity can be prepared. Embargoes will be strictly respected. Acknowledgment of funding provided by Brain Canada and Huntington Society of Canada (as

agreed upon between Brain Canada and the Huntington Society of Canada) must accompany all publication, release or presentation of such research results.

At the end of the current Canada Brain Research Fund, Brain Canada wants to show that exceptional value was received for the investments of the federal government and Huntington Society of Canada. It is important for Brain Canada to ensure that each grant and award has delivered on its expected outputs and proposed impact. For this reason, ten percent of the final year's funding will be withheld and released on receipt of a satisfactory final progress report that describes the current and estimated future outputs and impacts of the MIRI research project.

For Further Information

For any other information or questions:

- About the Brain Canada-Huntington Society of Canada MIRI competition and application process, please contact programs@braincanada.ca
- Brain Canada will acknowledge receipt of the full application within two working days. Please contact programs@braincanada.ca if you do not receive acknowledgement.
- About Brain Canada and the Canada Brain Research Fund: go to <http://braincanada.ca/>
- About Huntington Society of Canada: go to <http://www.huntingtonsociety.ca/>
- Questions to Huntington Society of Canada, please contact info@huntingtonsociety.ca