Donor Report

Fall 2015

Huntington Society of Canada **Société Huntington du Canada**

"Energy and persistence conquer all things." – Benjamin Franklin

For more than four decades, the Huntington Society of Canada (HSC) has strived for excellence by providing practical help for families impacted by Huntington disease (HD) and investing in research to slow and prevent this disease that destroys both mind and body. Your leadership support of the Huntington Society of Canada is an integral component of that excellence and tells a powerful story: a story of a community of caring people who pull together and change the reality of families living with HD.

Research

The $2 million match

Earlier this year we were approached by a donor who asked "If I donated $1 million to the Society would you know where to spend it in research and do you know a donor that will match the amount?"

In February, we invited global thought leaders in HD research to a round table discussion and asked how we should spend $2 million in order to have the most impact on the global understanding of treatments for HD. Subsequent to that meeting we submitted a proposal to Brain Canada and a request to match the donor investment.

Brain Canada was open to our proposal and we are now working together on a transformative research initiative. This initiative will connect clinicians, basic scientists and the HD community to ensure ongoing collaboration with a focus on expediting discovery to treatment, and to slow or prevent Huntington disease and other related neurological diseases.

This is an exciting, collaborative initiative that will transform HD research in Canada. We are proud to partner with Brain Canada and look forward to the launch of a research initiative that will enrich the overall understanding of potential treatments for HD and other neurological conditions like Parkinson's, Alzheimer's and ALS.

Funding world-class research

This year we received 10 letters of intent for our NAVIGATOR program and 10 for our NEW PATHWAYS program. All had potential to create significant insights into HD and pave the way to treatments. Ultimately, based on the recommendations of HSC's Research Council, we selected three outstanding projects to fund.

NAVIGATOR RESEARCH PROGRAM 2015 COMPETITION - The long-standing NAVIGATOR Research Program supports basic scientific research of direct and immediate relevance to HD in Canada. The aim is to provide a platform for the recruitment of outstanding investigators to HD research, to facilitate research collaboration nationally and internationally, and to support research that is relevant to other neurodegenerative disorders. The competition is run once per year and will provide funding of up to CDN $75,000 per year, for one or two years.

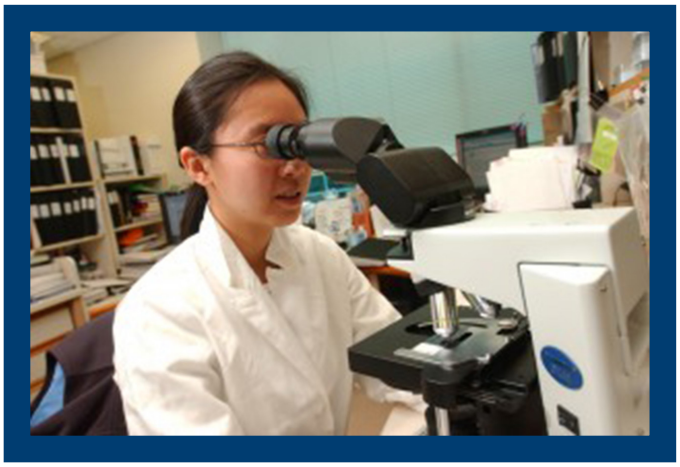
Dr. Michael Hayden, University of British Columbia, Vancouver, British Columbia is a recipient of the one year 2015 NAVIGATOR Research Grant competition, for his project called: *Pre-clinical therapeutic evaluation of allele-specific mutant huntingtin suppression by antisense oligonucleotides.*

Dr. Hayden's lab has identified DNA sequence variations that are more common in mutant huntingtin genes than normal huntingtin genes. His team has generated a mouse model of HD that recapitulates these DNA variations and develops HD-like symptoms and uses them to identify therapeutic reagents called antisense oligonucleotides, or ASOs, targeted to these DNA variations that can selectively silence the mutant huntingtin gene in the living brain without adverse effects. They have seen up to 90% reduction of mutant huntingtin protein with negligible reduction of normal huntingtin protein and determined that a single administration of ASO is sufficient to reduce mutant huntingtin in the entire brain for greater than 36 weeks.

Dr. Hayden's team is currently evaluating candidate ASOs in a pre-clinical trial in HD model mice and have found that treatment prior to symptom onset can prevent or delay motor and cognitive deficits and anxiety. Studies to determine if this treatment can prevent physical changes in the brain are ongoing. Additionally, Dr. Hayden's team is investigating if treatment after symptom onset can restore normal function. If successful in mice, this therapy can be rapidly translated to human applications.

Dr. Blair Leavitt, Centre for Molecular Medicine and Therapeutics, Vancouver, British Columbia is the recipient of a 2015 NAVIGATOR Research Program two-year grant ($75,000 per year), for his project called: *Contribution of microglia and neurons to HD pathogenesis.*

Dr. Leavitt and his team will examine the effects of mHTT on microglia, a type of immune cell in the brain. Microglia support neurons, regulate brain immune responses, and act as scavenging cells to remove dying cells. Microglia respond to changes in the brain, and can increase inflammation (harms neurons) or decrease inflammation (protects neurons). His lab has previously shown that brain microglia from HD mice have increased inflammatory responses compared to normal microglia.



Dr. Leavitt predicts that mHTT increases microglial inflammation accelerating brain cell death in HD. In this project he and his team will study the effects of mHTT in isolated microglia and look for changes in cellular signals. They will also generate novel HD mice that express mHTT only in microglia and not in other brain cell types to see how this affects brain cell death in HD.

NEW PATHWAYS RESEARCH PROGRAM 2015 COMPETITION - Introduced in 2007, this program is targeted to fostering innovative lines of inquiry that will eventually lead to the next generation of targets for the treatment of HD. This global competition will provide funding up to CAD $150,000. Projects are expected to run for up to one year.

Dr. Marta Biagioli, University of Trento, Italy is the recipient of the 2015 NEW PATHWAYS Research Program competition, for one year, for her project called: *Alternative splicing and circRNA alterations in Huntington disease pathogenesis.*

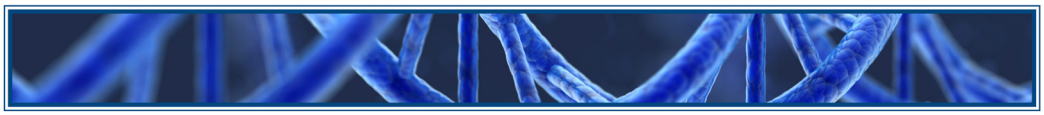
Recent findings revealed that the process of alternative splicing (AS), which contributes to generate different proteins from the same DNA information, might be compromised in HD.

Dr. Biagioli's project proposes a comprehensive study to identify changes in AS happening early during development and affecting not only the protein-coding potential of the cells, but also the production of regulatory, non-coding transcripts, important players in neuronal homeostasis and survival.

Dr. Biagioli and her team will investigate the potential regulatory role of alternative splicing (AS) process, locally at the Htt locus where a short, highly pathogenic fragment is produced, and more globally at genome-wide level. They will search for changes presenting more severe alterations with increasing DNA expansion in a manner that totally recapitulates the human HD mutation. These molecular consequences, thanks to the HD genetics criteria utilized for their identification, are expected to be proximal to the mutation, thus likely more relevant for the disease pathological process.

Dr. Biagioli's team proposes that these findings will unveil early pathways altered by the mutation and ultimately responsible for cell death, thus offering important clues for the quest of new, effective drugs.

Be Brave · Be Bold · Be Ready



Be Brave, Be Bold, Be Ready: Accelerating Clinical Trials

We continue to work with the HD Clinical Trials Consortium to accelerate clinical trials in Canada. The Society is spearheading the Consortium and working to complete the HD National Clinical Trial Strategy. The Consortium has finalized the HD specific Clinical Trials Readiness Checklist, to help clinicians get involved in HD research. At the same time, we are developing an HD Best Practices Guide to present at the Consortium workshop this fall. With the input of researchers, clinicians and families we will have the HD Best Practices Guide completed by the end of year, a first in Canada.

Simultaneously, we have developed, with input from clinicians in Canada, an HD Clinical Mentorship Program. This program will roll out this fall after being launched at the fall workshop and will match seasoned clinicians with more junior colleagues. This program sets the stage to help substantially increase the number of clinical trial sites in Canada, especially outside major urban centres.

Finally, to help those thinking of participating in clinical trials, we launched an HD Clinical Trials Map on the HSC website at www.huntingtonsociety.ca. This simple and straightforward map makes it easy for families to find their closest sites, learn more about the trials currently underway and obtain the contact information of each site hosting an HD clinical trial. It will be a useful centralized resource for families who are considering participating in clinical trials.

Advocacy

PUSHING FORWARD FOR GENETIC FAIRNESS

Genetic fairness has gained considerable attention over the past 12 months, thanks to two different federal bills.

Senator James Cowan's very comprehensive *Bill S-201, An Act to prohibit and prevent genetic discrimination*, was tabled by Conservative senators, but the Senate before it reached third reading. However, fortunately for us, Senator Cowan is committed to continue advocating for genetic fairness in Canada, and we will continue to support his sterling efforts.

Meanwhile, the federal government introduced Bill C-68 in June, following through on its 2013 Throne Speech commitment. The bill would have protected genetic test results under the Privacy Act and the Personal Information Protection and Electronic Documents Act. It would also have amended the Canadian Human Rights Act, making it illegal for government departments and federally regulated companies to discriminate on the basis of someone's genetic predisposition to a disability.

Unfortunately, the bill did not address the issue of insurance: one the biggest sources of concern for individuals at-risk for Huntington disease. We were also disappointed that it was introduced too late to be passed before Parliament rose on June 19th.

After the federal election this fall, we will work with the government to re-table Bill C-68 and launch a provincial strategy to ensure that provincial and territorial governments across Canada protect genetic test information and prohibit genetic discrimination.

L to R: Alex Munter, CEO of CHEO, Dr. Christine Armour, Honourable Peter MacKay, Bev Heim-Myers, CEO of HSC & Chair of CCGF, Richard Marceau, Senior Government Advisor of CIJA

We are pleased to introduce our new Canadian Coalition for Genetic Fairness website, www.ccgf-cceg.ca. This interactive website will allow us to gather real life examples from Canadians who have experienced genetic discrimination so we can share with our governments the impact this issue is having on Canadians.

Youth

Yes, I Believe!

Plans for our 2015 Fall "Yes, I Believe" National Symposium are shaping up, with 15 sites now confirmed across the country. On October 17, families will come together to learn about potential HD treatments, discover how drugs move from the lab bench to the medicine cabinet and find out what is involved in volunteering for a clinical trial. Those interested can either live-stream the event at home or head to the host site in their area.

Our national web presentation speakers include CHDI's Joe Giuliano and Dr. Mark Guttman, Director of the Centre for Movement Disorders in Toronto, Ontario. Many symposium sites will also offer local programming.

Visit www.huntingtonsociety.ca/symposium for detailed information.

Believe

2015 HSC National Symposium

Services

Strengthening our team

The cumulative impact of working to support clients is a serious issue within the social work field. This year, we invested in compassion fatigue training to ensure our Family Services team members are equipped to continue providing top-quality service to our families. We also created a new position: the Family Services Coordinator. This position will be responsible for gathering information, disseminating resources and coordinating projects for our Family Services team, allowing them to work more efficiently and effectively.

Connecting youth

We are pleased that our Youth Mentorship Program continues to strengthen and grow. The interest at the 2014 HSC National Conference was incredible and in response we launched a second round of mentor recruitment, selection and training in 2015. All seven first-round mentors have been paired up with young Canadians seeking support from their peers, while five of our eight newest mentors have been similarly matched. Meanwhile, we have received queries about the program from around the world. We are excited about how our program has grown, and are proud to bring this unique program to our Canadian youth.

To foster international youth connections, we provided funding for two Young People Affected by Huntington Disease (YPAHD) members to attend the Huntington's Disease Society of America (HDSA) convention in Texas in June. They will sharing what they learned with their peers and to support HSC Conference development. Later in the summer, seven Canadian youth and two counsellors headed to Maryland for the first North American HD Youth Camp organized by the Huntington's Disease Youth Organization (HDYO).

Meanwhile, based on feedback from our pre-conference YPAHD Day last fall, we will hold our first-ever standalone YPAHD Regional Days on November 21, 2015. To make it accessible to as many youth as possible, we are organizing simultaneous events in Toronto, Calgary and Halifax and linking the sites by web conference.

Thank You

On behalf of families living with HD, thank you for your continued partnership and generous support. Your donations make all the difference as we reach out to families who are not yet connected to HSC, continue to support and advocate for families from coast to coast, invest in world-class research, and play a leadership role in the international Huntington's community.

With your help, we are continuing to improve the quality of life for people with HD, cultivating strength and resilience in the Huntington's community and providing substantive reasons for hope by investing in globally recognized research leading to treatments that will slow or stop Huntington disease.