

## The Huntington Society of Canada's Research Investments

The universal goal for international Huntington disease (HD) research is to find treatments that reverse, slow or prevent the progression of HD. The Huntington Society of Canada (HSC) and Canadian HD researchers are 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 that will positively influence the direction of HD research in Canada and globally.

Currently our research program involves two research competitions that are normally launched the beginning of each calendar year for funding in June.

### NAVIGATOR RESEARCH COMPETITION

The long-standing NAVIGATOR Research Program supports basic scientific research within Canada of direct and immediate relevance to HD with the aim of providing 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 provides funding up to \$75,000 per year for one or two years.

### NEW PATHWAYS RESEARCH 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 and are open to all researchers.

## We Fund Excellence

At the Huntington Society of Canada, all research proposals are reviewed by a panel of peer review experts. We only fund excellent proposals and in many cases cannot fund all of those that are submitted.

In 2012, HSC had an external reviewer evaluate the quality of the research that HSC had funded to date. A summary of the conclusions are as follows:

- Overall, looking at the success of HSC funded research over the years 1998 to present, the reviewer was struck by the quality of the program and the research achievement. HSC can be, and is, very satisfied with its accomplishments. This success has been achieved at a modest cost. Looking at the overall research program of HSC, the reviewer could clearly see a steady increase in quality research from 1998 to the present and the growth of Huntington disease research in Canada.
- One interesting question that the reviewer examined was if there was other excellent research in HD in Canada that was not supported by HSC. A brief survey of the literature revealed that there was not. In other words, information about HSC appears to have reached the right places and the right people in Canada.
- The overall conclusion of the review was that HSC has received an excellent return on investment in HD research.

HSC has been part of the development of a number of centres for HD research in Canada that are producing high quality results. HSC has also been the driver behind building a critical mass of HD researchers across Canada.

## Recent HSC Funded Research Breakthroughs

### 2011-2012

*Dr. Ray Truant, McMaster University*

Dr. Truant discovered a common link between Alzheimer's and Huntington disease. This could lead to a treatment for Alzheimer's disease once we find the treatment for HD.

### 2012-2013

*Dr. Ray Truant, McMaster University*

Using highly sophisticated FLIM-FRET microscopy, Dr. Truant was able to see that the huntingtin protein produced by the disease-causing HD gene folds into a different shape than the protein produced by the normal gene. This research leads to interesting questions like "Are there drugs that could reshape the disease-causing protein and if so will they halt HD." This discovery will be significant in understanding treatments for HD and how they work.

*Dr. Simonetta Sipione, University of Alberta*

Administering GM1 (a substance that naturally occurs in humans) to mice, Dr. Sipione was able to reverse the symptoms of HD in two mouse models of the disease, bringing them back to normal. GM1 induced changes in the shape of the huntingtin protein that made it less toxic. In a third HD mouse model, GM1 was able to slow down death of brain cells and to increase the lifespan of mice with the disease.

### 2013-2014

*Dr. Jeff Carroll, Western Washington University*

By examining liver cells in HD mice, Dr. Carroll discovered that where the mutant HD protein severely affects metabolism in brain cells it affects metabolism in liver cells even more. This is critical information when looking for other biomarkers in the body to identify the early onset of HD symptoms and the efficacy of potential drugs to treat HD. The link between the liver and the brain in individuals with the HD mutation could very well lead to early treatments. The promise of this exciting research is supported by CHDI (a major HD-focused research funder) who has committed to the ongoing funding of Dr. Carroll's research.

*Dr. Stephen Ferguson, University of Western Ontario*

In healthy humans, mGluR5 (a glutamate receptor found in the membrane of brain cells) is an essential part of the machinery that transmits signals from one brain cell to the next, but not in an HD mouse. Dr. Ferguson and his team discovered that when mGluR5 receptor was genetically knocked out in an HD mouse, it ran and kept on running long after the other HD mice that were not given the glutamate receptor. There was also a big difference inside the brain cells. When Dr. Ferguson and his colleagues looked at the nucleus, they found 90 per cent less of the huntingtin protein aggregates in the HD mouse given the glutamate receptor blocker. These protein aggregates are a hallmark of HD. This has resulted in HD clinical trials in humans. The pharmaceutical industry has already created mGluR5 blockers to treat other diseases, and tested them in humans. It is reasonable to assume that this could go straight to Phase III clinical trials for the treatment of HD.

To learn more about Huntington disease or to sign up for one or more of our publications, visit [www.huntingtonsociety.ca](http://www.huntingtonsociety.ca).

## Promising HSC Funded Research in 2014-2015

*Dr. Vanessa Wheeler, Massachusetts General Hospital, Boston*

Dr. Wheeler is exploring genetic modifiers in HD mice by knocking out specific genes in the brain in order to understand early disease mechanisms.

*Dr. Rona Graham, University of Sherbrooke, Quebec*

Dr. Graham is exploring olfactory dysfunction in early HD.

The work in this study will provide a link between olfactory dysfunction and the striatal degeneration in HD. Importantly this study will identify novel, early biomarkers for therapeutic trials.

*Dr. David Stellwagen, McGill University, Quebec*

Neuroinflammation occurs early during HD, but the contribution of inflammation to disease progression of HD is unclear. Dr. Stellwagen and his team will examine the impact of the inflammatory response on the function of the striatum, a key brain region that degenerates during HD. They have evidence that inflammation may be an early adaptive response to HD pathology that initially acts to stabilize striatal function, but later contributes to cell death. They will examine the process and attempt to rescue striatal synaptic function, while limiting the damage that inflammation can cause.

*Dr. Stephen Ferguson, University of Western Ontario*

In his previous study, Dr. Ferguson demonstrated that genetic deletion of mGluR5 resulted in improved motor skills in an HD mouse. Dr. Ferguson will continue his study blocking the glutamate receptors to see if there are improved cognitive responses in mutant HD mice.

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