When Jeff Carroll, a graduate student at the Centre for Molecular Medicine and Therapeutics (CMMT), learned he carried the mutation for a degenerative genetic disorder that would eventually rob him of his personhood by the age of 50, his drive to wipe out all traces of this devastating disease for good only intensified.

“For me, it was confirmation of what I already felt was true because of my family history. Obviously, I would rather have received different news but it didn’t change my life because I already had enough of a taste for the research and science that I felt I could make a contribution, regardless of the results,” says Carroll.

Carroll isn’t waiting around to accept the grim fate that awaits him. At CMMT, he is aggressively conducting potentially life-saving research in a race against time to alter his fate as a result of Huntington’s disease (HD), a neurological disorder that slowly and progressively renders its victims unable to move, talk or think. In fact, Carroll has first-hand knowledge of what to expect: He witnessed HD transform his mother from a vibrant parent of six into an incontinent shell of her former self, prone to violent, involuntary spasms. Unfortunately, stories like these are not rare: The Huntington’s Society of Canada estimates that over 3,000 Canadians currently have the disease and another 20,000 are at risk.

Those at risk have only to look into their genetic make-up to determine whether they carry the mutant gene, as children from a parent with HD have a 50-50 chance of developing the disease. The mutant gene originates on the fourth chromosome where the letters of the genetic alphabet C-A-G typically repeat as many as 35 times in a row. Those with 36 repeats or more will develop HD. The greater the number of repeats, the earlier in life the disease will manifest.

Identifying the gene sequencing involved in HD has helped scientists develop predictive testing for HD, which was offered for the first time at UBC in 1986. Today, predictive tests at CMMT can confirm, with 100 per cent certainty, if an individual has inherited the HD mutation. But despite this progress and more than 100 years since its official
scientific documentation by US physician and namesake George Huntington, there is still no treatment and no cure.

Recent advancements at CMMT, partnered with UBC and the Child and Family Research Institute (CFRI), however, are swiftly turning the tide on HD research. CMMT Director Dr. Michael Hayden, who founded the first HD clinic in Canada that provides multidisciplinary support and care for patients, has been tracking HD for over 30 years but only recently uncovered the compelling evidence needed to offer a glimmer of hope in the fight against the disease.

The landmark finding materialized when Hayden and his team began to piece together an understanding of what happens to cells when a destructive enzyme cleaves the mutant huntingtin protein that is responsible for HD. Through cleavage, the enzyme known as caspase-6 unleashes a toxic fragment that invades the nucleus of a healthy cell and causes it to die through over-excitement. But by inhibiting the cleavage in mice, the team made a remarkable discovery: “We found that if we prevent the protein from being cleaved at one site, you can prevent the illness,” Hayden explains. “The beauty for us is that if we develop inhibitors to the enzyme that cleaves it, you may be able to provide a treatment for HD.”

The discovery is the first time that scientists prevented the development of HD in a mouse that expressed the human HD mutation. As a consequence, the CMMT team is actively involved in developing a drug that will effectively prevent caspase-6’s cleavage or significantly impair its frequency to do so. Carroll, himself, is testing a compound that so far, has resulted in reducing caspase-6’s effects by half in mice over a four-week course of treatment, with results remaining constant even after ceasing to administer the compound after the four-week period.

Results like these have given the CMMT team much to be optimistic about and Hayden believes the research developed in mice models will translate to novel approaches to treatment in approximately five years. He foresees that more than one drug will be involved, producing a multi-dimensional treatment approach much like with cancer therapy.

“There’s a sense of urgency around us. What we learn from HD is likely to have a direct relevance to other diseases of a similar nature like Alzheimer’s,” Hayden says.

“We believe that what we’re learning here will have a broad relevance. This is not esoteric research.”

For Carroll, the day when HD treatment is readily available could not come any sooner. While pre-implantation genetic diagnosis that combines genetic screening with in-vitro fertilization has allowed him to ensure his children will never share his fate, Carroll’s research at CMMT is now being propelled by the prospect of a future where he, and others destined to HD, will evade the oppressive grip of this degenerative disease: “I’d like to see HD become an academic exercise where people will study it to learn about molecular biology and neuron function and not because we’re trying to save lives.”

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