

Spring 2005

Parkinson Research Consortium Blooms at Last

The official launch of the Parkinson's Research Consortium as part of the Ottawa Health Research Institute, the research arm of The Ottawa Hospital and the Faculty of Medicine at the University of Ottawa was held on October 5, 2004. The two leadership gifts in support of the Consortium from the Parkinson Society Ottawa and the Kiwanis Medical Foundation were recognized.



DAVID GRIMES and DAVID PARK – co-directors of the PRC with ALAN RICCARDI (president) and Ruth Vant (executive director) from the Parkinson Society Ottawa.

Parkinson's disease is the most common neurodegenerative disease after Alzheimer's, affecting at least 100,000 Canadians with the number of cases expected to double by the year 2050. The typical symptoms consist of slowness of movement, stiffness and tremor. However, a wide variety of other difficulties can occur such as depression and memory loss. The typical symptoms are mainly due to a loss of a chemical in the brain called dopamine. Why the cells that normally produce dopamine are dying faster than they should is currently unknown. There are presently no proven treatments available that can slow the relentless progression of the disease. Only through a better understanding of the basic mechanisms that cause it can effective disease-altering treatments be developed.

The Parkinson Research Consortium (PRC) was formed this past year in Ottawa to bring together scientists with the common goals of understanding the mechanisms which cause the death of these specific brain cells and applying this knowledge to the treatment of those with the condition. It is composed of a select group of scientists from the Ottawa Health Research Institute (OHRI), the National Research Council and the University of Ottawa with diverse scientific talents and expertise in genetics, molecular biology, neuroscience and patient care. Our overall vision is to bring together a comprehensive group of individuals whose purpose is to eradicate a disease that currently follows an unremittingly, disabling course.



"Organizations like the PRC are important to the entire region, and we are able to provide them the resources they need thanks to community organizations like the Kiwanis and the Parkinson Society," said Dr. Peter Walker, Dean of the Faculty of Medicine at the University of Ottawa.

Meet the PRC

We benefit from the expertise and efforts of the following group of elite researchers:

- Dr. DAVID PARK: an expert in neuronal death using mouse models of Parkinson's disease
 - Dr. DAVID GRIMES: neurologist, specializing in Parkinson's disease and molecular genetics
 - Dr. ANTONIO COLAVITA: molecular biologist and an expert in *C. elegans* worm genetics and development
 - Dr. DENNIS BULMAN: geneticist, an expert at the identification of human disease genes
 - Dr. MARK EKKER: internationally renowned developmental biologist who uses zebra fish as a model to study cell death mechanisms
 - Dr. RUTH SLACK: an expert in stem cell biology and neuronal death
 - Dr. ROBIN PARKS: a scientist with research expertise in gene therapy using viruses
 - Dr. PAUL ALBERT: an expert in dopamine signaling within the brain
 - Dr. JOHNNY NGSEE: an expert in the processes that determine information traffic among brain cells
 - Dr. JOHN WOLFE: neuropathologist, exploring why abnormal inclusions form within dying brain cells
 - Dr. TILAK MENDIS: neurologist with expertise in cognitive dementia who performs clinical research in neurodegenerative disease
 - Dr. MARIO TIBERI: scientist exploring how dopamine signaling works in the brain
 - Dr. MARGARET SONNENFELD: geneticist and developmental biologist who uses drosophila fly's as a model to study human diseases
 - Dr. VANCE TRUDEAU: expert in biology
- And our most recent associates: DR. MARIANNA SIKORSKA, DR. JAGDEEP SANDHU and DR. MOSSA GARDANEH from the National Research Centre.

Our Vision

To build a comprehensive Center focused on the science of understanding the genetic susceptibility factors and cell biological processes that contribute to Parkinson's disease progression.

To provide a scientific forum which will readily link the goals of basic and clinical scientists in the treatment of Parkinson's disease.

To use this virtual center of excellence in Ottawa as a springboard to build a cohesive national Canadian effort in Parkinson's disease research.

To date, Parkinson's Society of Ottawa has partnered with the Ottawa Kiwanis Medical Foundation to provide an initial grant of \$150,000 [\$100,000/PSO and \$50,000/KMF]. The PRC is striving to raise a minimum of \$900,000 in funding to provide the initial support for new parkinson research.

All donations are welcome.

Four Projects – a start...

- 1 Identification of genetic determinants of dopaminergic neuron development and death in the *C. Elegans* worm.
- 2 Zebra fish as a powerful vertebrate genetic model for the study of PD
- 3 Delineation of the molecular mechanisms of dopaminergic loss in mammalian models of PD
- 4 Identification of novel genes or gene mutations in individuals with Parkinson's disease

Events

- April 7, 2005: Paul Anka Evening sponsored by the Thomas C. Assaly Charitable Foundation and Parkinson Society Ottawa.
- June 10, 2005: Kiwanis Club of Ottawa, guest speakers David Park and David Grimes.

"The Michael J. Fox Foundation for Parkinson's Research applauds the launch of the Parkinson Research Consortium at the University of Ottawa. It is exciting to hear about the dynamic team of scientists and physicians who have been meeting to generate research ideas around Parkinson's... Thank you for all your excellent work. Like you, we are confident that a cure will be found as we steadfastly move the Parkinson's research effort forward."

The PRC is dedicated to funding important projects centered around three very important questions.

Questions and understanding

What are the genetic causes of familial form of PD?

Understanding the cause(s) of PD is complicated by the fact that it appears to have both genetic and environmental causes. A few rare forms of familial PD are caused by single gene mutations. Several have been identified and there are ongoing efforts to identify additional genes. While all forms of familial PD are uncommon, identification is important since it provides insight into how dopamine neurons ultimately die, even with non-familial cases.

The PRC scientists have made the exciting discovery of a new locus for familial PD. They are currently working with a French-Canadian family to identify the exact gene located at this locus linked to PD. They have collected blood samples from 65 individuals from this large Parkinson's family where 14 have been affected with Parkinson's. When the identification of this new gene is made, this knowledge will provide important clues into how PD is initiated and progresses in patients.

Are there susceptibility genes which may contribute to idiopathic PD?

While the identification of familial PD genes is important, the vast majority of PD patients do not have a simple direct link to one gene. In this regard, it is likely that there is a complex series of susceptibility genes, which might predispose individuals to PD with an appropriate (and unfortunate) environmental insult. These genes likely influence how dopamine neurons function. Therefore, fundamental efforts must be made to not only identify these susceptibility genes, but to also identify potential environmental insults.

The PRC scientists are addressing this important question by setting up a sophisticated biological screening system using more simple animals (worms and fish) to identify which genes might make one more susceptible to dopamine neuron loss. By harnessing the power of genetic screens only possible in these lower animals, we can identify genes that are potentially critical for dopaminergic function. Once identified, we can then assess how these genes may potentially make individuals more susceptible to PD.

How do these genes control how dopamine neurons die in PD?

Once factors are identified as described above, it is critical to then understand the mechanisms by which these genes cause death. Several genes that provide a direct link to PD have already been identified. These include recently identified PD genes, DJ-1, PINK1 and LRRK2. How these genes actually cause PD is unknown. The scientists of the PRC have expertise in a wide variety of model animal systems to study these genes in dopamine neuron loss. These systems include the well known mouse system. However, the PRC scientists can also examine these genes in a manner that cannot be readily performed in mice. By using a variety of simpler and surprisingly elegant animal systems including the drosophila fruitfly, the zebra fish, and the *C. elegans* worm, we can more quickly unravel the mysteries of how these genes provoke the onset of PD. The scientists, by use of a wide variety of genetic and biochemical approaches are dedicated to understanding how these genes may lead to PD.