

Two Davids against a Goliath: University of Ottawa researchers David Park and David Grimes are the leaders of a unique group with a huge challenge: Finding a cure for Parkinson's disease

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David Simmonds holds a piece of paper in his trembling right hand. The soft fluttering creates a light crackling sound. The murmur deepens when a bouncing leg dances up alongside the dining room table where he's seated.

He has lived with Parkinson's disease for so long, it seems he no longer takes notice of his turbulent limbs. But the 51-year-old, a former lawyer forced into early retirement, is keenly aware of the affliction he's had for 12 years and shares with 100,000 Canadians.

It is an incurable disease, where progress towards a cure is measured in inches and there are yards to go before its cause is understood. Even greater distance must be travelled before the creation of treatments that address the condition rather than ease the symptoms.

"Research is the most effective drug you can prescribe," says Mr. Simmonds. "Hope is the most potent drug ... Hope gives you self-esteem, which gives you energy, which gives you life."

The paper in Mr. Simmonds' hand heralds the creation of the Parkinson's Research Consortium (PRC), a unique venture spearheaded by the Ottawa Health Research Institute (OHRI), the research arm of the University of Ottawa and the Ottawa Hospital.

"This gives hope," says Mr. Simmonds.

That's why he has volunteered to help raise funds for the PRC, a one-of-a-kind collaboration between 11 Ottawa scientists from various fields who aren't specifically studying Parkinson's. But by pooling their research and expertise, they're reaching for better treatments for Parkinson's and, ultimately, to discover a cure. Not only will the PRC put more people to the task of solving Parkinson's, it will make the Ottawa region more attractive for clinicians to move here and offer better service to patients.

While many researchers worldwide are studying Parkinson's, the PRC is unique. Each of its scientists possesses a different specialty -- neurology, genetics, stem cell biology, gene therapy -- giving each individual a unique perspective on the disease.

This isn't just a team where more players wear the same-coloured jersey. Each player is capable of playing a different position. It's the synergy that exists between them that could thrust Ottawa to the forefront of Parkinson's research, both nationally and internationally.

"I don't know of anywhere else in this country where scientists and clinicians, spanning the spectrum from molecule all the way to the community, have come together," said Dr. Antoine Hakim, director of the neuroscience research program at the health institute.

"Frankly, I don't know of another place in the country where that spectrum of expertise exists in people who are willing to come together and work towards a single goal -- helping patients with Parkinson's."

The disease results from the degeneration of neurons in a region of the brain that controls movement. The breakdown creates a shortage of the brain-signaling chemical known as dopamine and causes involuntary movement. Sometimes you can't move when you want to, and other times you move when you don't want to.

It is a progressive disease that affects people at different rates. Medication will only manage the symptoms -- it won't halt the course or cure the condition. The disease won't kill you, but it will shave a few years off your life expectancy and wither your ability to function independently.

Although the PRC was established a year ago and the group already meets every month or two, the official launch is scheduled for Tuesday at the university, where donations of \$100,000 by the Parkinson Society of Ottawa and \$50,000 by the Ottawa Kiwanis Medical Foundation will be recognized.

The group is soliciting \$900,000 over three years. The money will help develop projects, support the training of post-doctoral and graduate students, and provide equipment and laboratory materials.

The consortium was developed by two Parkinson's specialists at the university's faculty of medicine, David Park, 37, and David Grimes, 38 -- a formidable pair some have dubbed "Two Davids battling Goliath."

After moving to Ottawa in 1998 from the United States, Dr. Park noticed a tremendous level of expertise in the capital region, just waiting to be "knitted together."

The sales pitch, he insists, was easy to make: "the scientists came together of their own accord. They just needed a little catalyst and there was tremendous interest in pursuing the scientific program."

"Not a whole lot of effort was needed, just a spark."

There's a sense of camaraderie amongst scientists in Canada, which is fairly unique and makes this easier to do than if we were in the States," Dr. Park says. "The atmosphere in Canada is really conducive to this type of effort."

The concept behind the group is really quite simple, says Dr. Grimes -- it's about bringing together scientists who wouldn't normally swap ideas with one another.

"We're so far advanced in terms of different molecular techniques that not any one scientist can know them all or be an expert in them all," he says.

"Scientists can get really focused on trying to figure out one pathway, which might take five or 10 years of hard research," he says, adding they may know where their research is going, but they lose sight of the bigger picture. "This (consortium) gives them the big picture."

It's a picture his own father, Dr. J. David Grimes, would have loved to see. The elder Dr. Grimes, who died in 2001, was the founder of the Ottawa Parkinson's Disease Research Laboratory at the Civic Hospital and of the LOEB Health Research Institute -- both of which also received grants from the Kiwanis Medical Foundation.

When the lab opened in 1983, Dr. Grimes Sr. dreamed of establishing bench-to-bedside research programs, where basic scientists and physicians worked in tandem to translate laboratory discoveries into cures.

But his dream fizzled after a colleague moved away to the States.

His son now heads that lab, which today bears the name Parkinson's Disease and Movement Disorders Clinic at the Ottawa Hospital. And two decades later, his son is helping to realize that dream, with Dr. Park.

"I think he'd be very proud," says Dr. Grimes of continuing his father's legacy. It is a fitting tribute to the father who sparked his own interest in Parkinson's.

"He'd certainly be very happy to see that Parkinson research is growing in Ottawa."

With the formation of a consortium, the wealth of research will only grow, he predicts, since funding agencies tend to award grants to larger research groups.

"Granting agencies realize things are complicated. And if you're trying to study just one aspect of a disease, you might get nowhere, versus if you have 10 people studying multiple little aspects of the disease, they can link it all together much easier."

And the number studying Parkinson's will likely grow. Researchers in Toronto and Vancouver have already been contacted about doing collaborative work with the consortium, he says. "We want to extend it to a national level. The more people you have bouncing ideas off each other, hopefully, the more quickly the research will progress along.

"We have a real chance of being very successful and very prominent ... Over the next five or six years we'll definitely see Ottawa grow as a real recognized force in Parkinson's research."

Research and hope: That's exactly the kind of medication Mr. Simmonds needs. A fundamental bargain exists between patient and researcher, explains Mr. Simmonds. The patient presents the researcher with the inspiration of dignity in coping with affliction. And the researcher offers the patient hope.

But if researchers can't do the necessary research, it violates the bargain and turns hope to despair.

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Parkinson's Research Consortium - The team

The University of Ottawa's Faculty of Medicine is home to two highly regarded Parkinson's specialists: David Park is a researcher whose efforts to delineate the signaling pathways causing neuronal death are aimed at helping devise treatments for neuronal diseases. David Grimes studies the role of molecular genetics in Parkinson's and related movement disorders.

Dr. Park and Dr. Grimes have enlisted the services of the following scientists to participate in the Parkinson's Research Consortium; all of whom are passionate about bringing their expertise to new projects that will create more opportunities to treat Parkinson's disease.

All are members of the University of Ottawa's faculty of medicine.

Tilak Mendis

Dr. Mendis is a consultant in neurology at the Ottawa Hospital and an assistant professor of medicine at the University of Ottawa and Queens University in Kingston. He supervises residents in clinical situations and is a guest lecturer teaching family physicians about movement disorders. He also conducts clinical research related to movement disorders, Lewy-body disease and Parkinson's dementia, attends to patients at Saint-Vincent chronic care hospital, The Ottawa Hospital (Parkinson's Clinic) and his office.

Dennis Bulman

Dr. Bulman is a geneticist and expert at the identification of human disease genes. His laboratory is focused on identifying the cause and understanding the pathophysiology of genetic disorders. Dr. Bulman is using Linkage analysis and positional cloning strategies, attempting to identify the genes for various disorders. He is also involved in a study of Parkinson's, with Dr. Grimes, looking at the genetic and physical map of a family with members affected by the disease.

Paul Albert

Dr. Albert is a senior scientist, neuroscience, OHRI. His interests are in the areas of molecular mechanisms of autoreceptor desensitization, and successful therapy of major depression (as well as generalized anxiety, obsessive-compulsive, and other mental disorders). He established a research collaboration with the Royal Ottawa Hospital to apply this work in the area of schizophrenia.

Antonio Colavita

Dr. Colavita is a molecular biologist and expert in *C. elegans* genetics and development. His research interests include genetic analysis of Axon Branching in *C. elegans*: studies mechanisms involved in axon branching by studying axon branching in the simple nervous system of *Caenorhabditis elegans*. This work is aimed at the development of new drug targets or therapies that promote axon regeneration following brain injury or neurodegenerative disease.

Johnny Ngsee

Dr. Ngsee is an expert in the processes that determine information traffic among brain cells. He investigates the molecular mechanism that governs synaptic transmission, the fundamental activity of the brain that is the process through which one neuron makes contact with another through neurotransmitter fluid. He is also investigating this by studying proteins that control this process, and also what regulates VAMP, with aim of having a better understanding of motor disorders.

Marc Ekker

Dr. Ekker is an internationally recognized developmental biologist. His major research activities include the evolution of genetic cascades involving Dlx homeobox genes in the forebrain, brachial arches and inner ear of zebrafish and other vertebrates. Mapping of the zebrafish genome with a collection of radiation hybrids. Genetic analysis of inner ear development in the zebrafish using an organotypic culture system.

Ruth Slack

Dr. Slack is an expert in stem cell biology and neuronal death. Her interest lies in tumor suppressor proteins (p53 and retinoblastoma), as previous studies by her show that p53 may function as a molecular switch leading to neuronal cell death following ischemia. This research is a first step towards gene therapy approaches for the treatment of ischemia, hoping that in the future, these strategies will reduce the rate of neuronal cell death, reducing disability resulting from stroke.

Mario Tiberi

The research activities of Dr. Tiberi's laboratory are focused on the molecular mechanisms underlying the dopaminergic neurotransmission in the mammalian brain, and more specifically the signal transduction elicited by the activation of specific receptor proteins for dopamine. A better understanding of dopamine receptor function may serve to clarify the mechanisms by which dopamine exerts its physiological effects and lead to a more detailed knowledge of the role played by the dopaminergic system in the etiology and management of several brain dysfunctions such as schizophrenia and Parkinson's disease.

John M. Woulfe

Dr. Woulfe is an accomplished neuropathologist. He has research activities in neuronal intranuclear inclusions in Health and Disease, and aberrant proteolysis in neurodegenerative disease. Dr. Woulfe won the Menek Goldstein Research Scholar Award, from the National Parkinson Foundation.

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