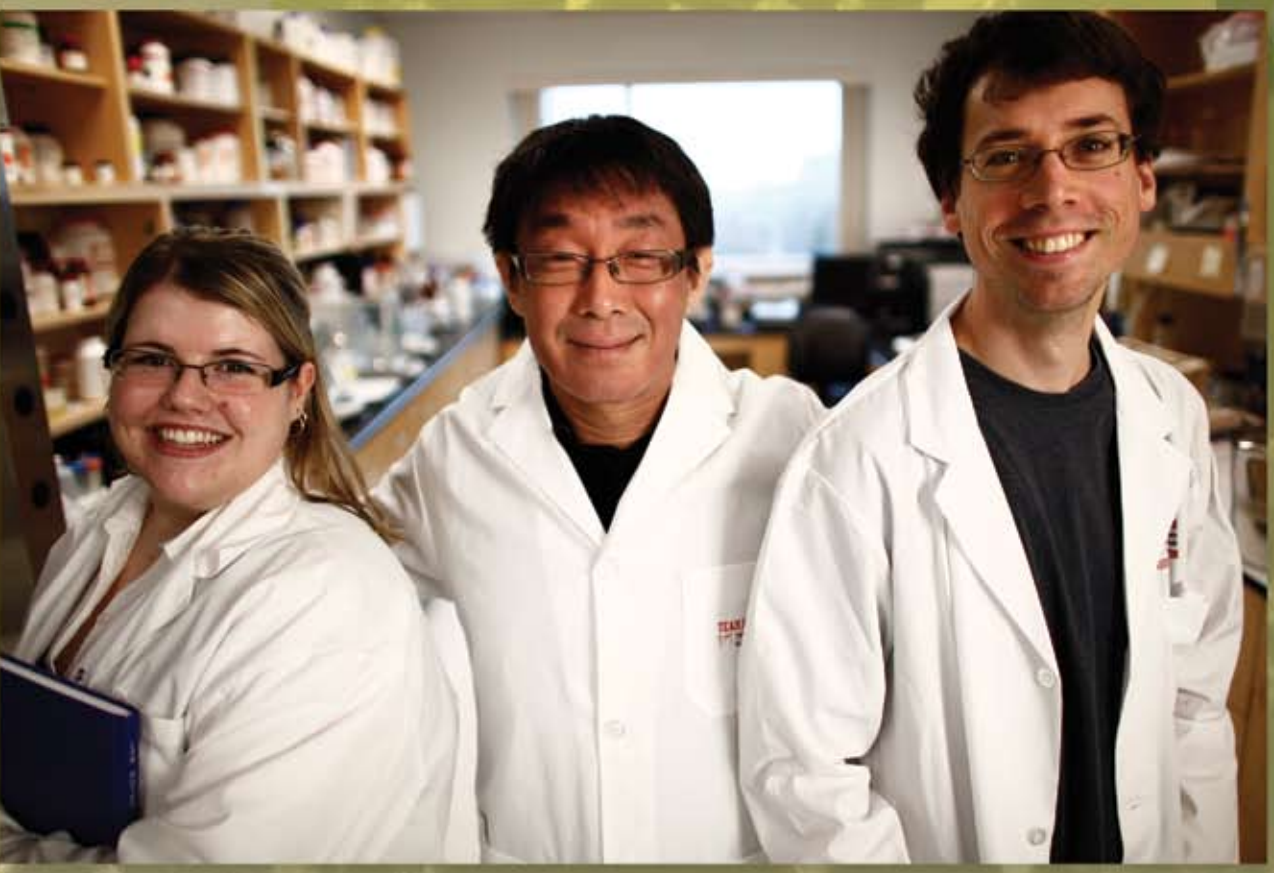
Research

HIGHLIGHTS 2009-2011

Parkinson
Society
Canada



Parkinson Society Canada
Société Parkinson Canada

Research
HIGHLIGHTS 2009-2011

Message from the Chair and President & CEO

Bruce Ireland
Chair

Joyce Gordon
President & CEO

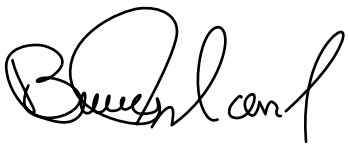
We are delighted to introduce to you the second edition of Research Highlights which focuses exclusively on Research, one of our four pillars of Parkinson Society Canada.

We have a long-standing legacy of supporting Canadian researchers, who have become world renowned. We are particularly proud to contribute to the science of discovery in Canada by supporting emerging young scientists from their earliest beginnings and we continue to build a solid Canadian research community.

A complicated disease, Parkinson's requires research in many broad areas, and Parkinson Society Canada's research program focuses on this approach. Currently we are funding projects in the causes of Parkinson's; biomarkers; neuroprotection; dopamine development; cognition and complications of Parkinson's. In addition, Parkinson Society Canada values and supports research into quality of life issues in order to help people living with Parkinson's and their families. Although researchers have not yet found the cure, they have unraveled some of the mysteries of Parkinson's.

Investing in young scientists with promising futures in neuroscience and Parkinson's related work is the backbone of our research and clinical programs. Our researchers are future neurologists and movement disorders specialists. They are new investigators involved in basic research. They are post-doctoral fellows embarking on exciting careers. They are graduate students. They are engaged in both basic science and the increasingly important psychosocial research to explore the impact this disease has on Canadians living with Parkinson's every single day. They seek to find the causes of Parkinson's and to address the complications of the disease.

Parkinson Society Canada's **National Research Program** *provides an essential resource to Parkinson's researchers in Canada that ensures that Parkinson's research continues to be encouraged and supported in a competitive market for research funding. Our program is made possible through the support of our regional partners, generous donors, volunteers and partnerships with other funding organizations which allow us to maximize our resources and expand our reach in the Parkinson community. The year 2010 marks 45 years that Parkinson Society Canada has supported Canadians living with Parkinson's through advocacy, research, education and support services.*



Bruce Ireland, Chair
Parkinson Society Canada

Joyce Gordon, President & CEO
Parkinson Society Canada

Message from the Chair, Research Policy Committee

Dr. Anne-Louise Lafontaine
Chair, Research Policy Committee

Dr. Pierre Blanchet
Incoming Chair, Research Policy Committee

The Research Policy Committee promotes the relevance, credibility and viability of the research program to Parkinson Society Canada Board members, the scientific community and other stakeholders.

The National Research Program is a cornerstone of PSC and the Research Policy Committee strives to promote research that is meaningful to people with Parkinson's and their care partners. To that end, the research program was revamped at the start of my term in 2003 and our focus was to ensure the greatest impact on the Canadian Parkinson's research community.

In response to the evolving nature of research and our growing understanding of Parkinson's, the Research Policy Committee created a psychosocial research stream directed towards closing the gap in understanding and treating non-motor symptoms of Parkinson's. We developed a new category of award for graduate students to foster the development of young Parkinson's researchers at the start of their research careers. We also expanded our mandate to encourage applications for related disorders including: Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP) and other Parkinson's conditions.

I am proud to have had the opportunity to participate and to contribute to the growth and the success of the National Research Program. I am confident that Dr. Pierre Blanchet, in his capacity as new Chair, will continue to build on past success and bring new insight and ideas to advance the research mandate.

Dr. Anne-Louise Lafontaine, Chair
Research Policy Committee

Message from the Chair, Scientific Advisory Board

Dr. Jon Stoessl
Chair, Scientific Advisory Board

Dr. Edward Fon
Incoming Chair, Scientific Advisory Board

The Scientific Advisory Board is responsible for the peer review process to determine scientific excellence and relevance to Parkinson's disease. It provides the highest quality of objective adjudication and is made possible through the significant efforts of a diverse volunteer panel of experts from the neurosciences field. Each year has seen an increase in the number and quality of applications received through the National Research Program's annual competition cycles. This year in particular yielded the highest number of exceptional applications meritorious of funding.

Through the research program, PSC invests in innovative pilot projects, supports researchers with novel ideas and builds capacity in Parkinson's research by encouraging new investigators and supporting research training. These individuals have leveraged this support in order to obtain further funding, and have developed into independent researchers, continuing the cycle of revitalization and growth of the Parkinson's research field. This is a sure indication of the positive direction and success of the program and speaks to the importance of supporting creativity and excellence.

I am proud to have been Chair of this panel for the past six years and an SAB member for 10 of the 12 previous years. I have taken particular joy in the ability to promote some of the most promising emerging young researchers in the country. I leave the SAB secure in the knowledge that it has superb leadership in Dr. Ted Fon, an outstanding clinician-scientist who is passionate about Parkinson's research, and the support of Ivy Lim-Carter, the Director, National Research & Clinical Programs. Thanks to the SAB members, to Joyce Gordon, CEO, Dr. Anne-Louise Lafontaine, outgoing Chair of the Research Policy Committee, and the PSC Board for their unflagging support of the research program, even during difficult times. With everyone's collective help, we can make a difference.

Dr. Jon Stoessl, Chair
Scientific Advisory Board

Research Program at Parkinson Society Canada

Parkinson Society Canada (PSC) understands the importance of investing in Canada's talented Parkinson's disease researchers. PSC supports the highest standard of excellence in research to enable progress in the effort to "ease the burden and find a cure". Through new discoveries and treatments, research improves the quality of life of all Canadians and reduces the economic burden of illness on the economy. Today's investment will go directly to research that is aimed at improving the health and lives of Canadians living with Parkinson's now and in the future.

In Canada, we are very proud to have some of the best Parkinson's researchers in the world. Canadians and visitors to Canada have contributed a disproportionate amount of knowledge to our understanding of the aetiology, progression and treatment of Parkinson's. Very few other countries in the world, if any, can make such a claim. As well Parkinson Society Canada is a national organization in Canada that specifically supports Canadian Parkinson's research and researchers.

PSC's Research Funding Philosophy

Parkinson Society Canada strives to make an impact on the Canadian Parkinson's research community by working as investors in Canadian Parkinson's research potential. By funding meaningful and innovative projects and promising young researchers in their professional development, PSC aims to encourage continued growth and revitalization in the fields of Parkinson's research in Canada. Our "seed money" plants the seeds that will bear fruit tomorrow, ensuring that today's fresh ideas and innovative researchers become tomorrow's research breakthroughs and leaders in the field.

PSC awards research grants, fellowships and studentships on an annual basis. Grants are used to fund expenses associated with conducting a project and fellowships support the salary of a researcher who has completed doctoral training (an MD or a PhD) and who is pursuing specialized training in Parkinson's. Studentships support the salary of a graduate student at the masters or doctoral level who is at the start of their research career and has chosen to focus on Parkinson's research. PSC grants, fellowships and studentships range from one to two years in duration, creating a funding leap-frog pattern where two research cycles are funded at any given time.

PSC's Research Program is modelled on the Canadian Institutes of Health Research's four pillars of research and encourages a broad range of applications from biomedical, clinical, health services and systems research and population studies. PSC supports these four pillars of research with 75% of funding dedicated to biomedical research and 25% of funding directed to clinical, health services and systems and population studies.

A proud funding tradition

Since 1981, PSC has invested more than $16.8 million into Canadian Parkinson's research granting over 330 basic research, clinical movement disorders and clinical research fellowships, pilot project grants, graduate studentships, new investigator and psychosocial awards.

In July 2009, Parkinson Society Canada announced its commitment to fund seven research grants, six fellowships and three studentships over the July 2009 - June 2011 Research Program cycle, for a total of $907,886 over the next two years. This is in addition to the $355,000 already committed to support existing 2008-2010 cycle awards in their second year.

Research Policy Committee

Dr. Anne-Louise Lafontaine, Chair	Quebec
Mr. Barry Johnson	Alberta
Dr. Jim Emmett	Alberta
Dr. Pierre J. Blanchet	Quebec*
Dr. Edward Fon	Quebec
Dr. Mark Guttman	Ontario
Dr. Douglas Hobson	Manitoba
Dr. Jon Stoessl	British Columbia
Dr. Fran Squire	Ontario

*Incoming Chair – commencing July 2009

Scientific Advisory Board (2008-2009)

Dr. Jon Stoessl, Chair	University of British Columbia*
Dr. Richard Camicioli	University of Alberta
Dr. Francesca Cicchetti	Laval University, QC
Dr. Edward Fon	McGill University, QC**
Dr. Susan Fox	University of Toronto
Dr. Douglas Hobson	University of Manitoba*
Dr. Zelma Kiss	University of Calgary
Dr. Martin McKeown	University of British Columbia
Dr. David Park	University of Ottawa
Dr. Alex Rajput	University of Saskatchewan
Dr. Harold Robertson	Dalhousie University, NS

*Completed Terms on SAB June 2009

** Incoming Chair – commencing July 2009

New Scientific Advisory Board Members 2009-2010

Dr. Anurag Tandon	University of Toronto
Dr. Louis-Eric Trudeau	University of Montreal

Donald Calne Lectureship

The Donald Calne Lectureship recognizes a distinguished neurologist of international reputation, whose work is primarily in the area of Parkinson's disease. Awarded annually, the recipient will deliver a "state of the illness" lecture on Parkinson's disease to the Parkinson community. This lectureship was established in 2002 to honour Dr. Donald Calne for his outstanding service to the Parkinson's community as Professor of Neuroscience, University of British Columbia and past chair and long time member of the Scientific Advisory Board, Parkinson Society Canada.

Donald Calne Lectureship Awardees

2009 Dr. Andrés Lozano, Toronto Western Hospital, Toronto, Ontario

2008 Dr. J. William Langston, Scientific Director of the Parkinson's Institute in Sunnyvale, California, U.S.A.

2007 Dr. Anthony Lang, Director of the Morton and Gloria Shulman Movement Disorders Centre, Toronto Western Hospital, Toronto, Ontario

2006 Dr. Jon Stoessl, Director of the Pacific Parkinson's Research Centre at the University of British Columbia, Vancouver, British Columbia

2005 Dr. Zbigniew Wszolek, Mayo Clinic Jacksonville, Florida, U.S.A.

2004 Dr. Oleh Hornykiewicz, The Brain Research Institute at the University of Vienna, Vienna, Austria

2003 Dr. Yoshikuni Mizuno, Neurology Department, Juntendo University Medical School, Tokyo, Japan

Research Programs

PILOT PROJECT PROGRAM

Duration **1 year**
Funding Amount **Maximum $45,000**

Through its Pilot Project grants, PSC aims to fund professionals engaged in novel, emerging, or innovative research in areas relevant to the cure, cause, prevention, improved treatment and/or understanding of Parkinson's disease and its impacts on society. This program is a strategic initiative to encourage established investigators to enter into the study of Parkinson's disease and to perform research in new, specifically targeted, high priority areas.

PSC is a committed supporter of Canadian research potential. PSC anticipates that funded projects in this program may lead to subsequent substantial grants from larger granting institutions. This critical "seed money" fosters new development and promises to "grow" new ideas and approaches to Parkinson's research.

NEW INVESTIGATOR AWARD PROGRAM

Duration **2 years**
Funding Amount **Maximum $45,000 /year**

During the initial period of their independent careers, new investigators are in a good position to formulate innovative and fertile research projects. New Investigator Awards provide researchers who have recently completed research training with an early opportunity to develop and demonstrate ability to initiate and conduct independent health research. This program is part of an active investment in the future of Canadian Parkinson's research, supporting promising individual researchers in their professional development.

PSYCHOSOCIAL RESEARCH GRANT

Duration **2 years**
Funding Amount **$50,000 /year**

This strategic initiative to encourage researchers specifically in the area of psychosocial research in Parkinson's disease helps PSC to better serve Canadians with Parkinson's, to foster Canadian Parkinson's research leadership internationally, and to support efforts to ease the burden and find a cure.

Research is directed towards closing the gap in understanding and treating non motor symptoms of Parkinson's.

Research topics identified as priority issues by Parkinson's Society Canada are:

1. Investigating the Psychological Well Being of People Living With Parkinson's, Partners and Families
2. Evaluating the Benefits of Standardized care
3. Assessing Medical Services
4. The Economic Burden of Parkinson's

BASIC RESEARCH FELLOWSHIP PROGRAM

Duration **2 years**
Funding Amount **$40,000 - $50,000 /year based on CIHR salary scale**

The basic research fellowship program is a strategic initiative to encourage promising young scientists to enter the field of biomedical research into Parkinson's disease. Through the provision of this salary support, Parkinson Society Canada aims to attract new scientists to the field and to invest in their research training, offering promise for future work in the area of Parkinson's disease.

CLINICAL RESEARCH FELLOWSHIP PROGRAM

Duration **2 years**
Funding Amount **$50,000 /year**

Relative to the needs of Canadians with Parkinson's, there is currently a shortage of leaders involved in Parkinson's service and clinical research programs in Canada. PSC believes that this shortage of medical specialists, neurologists or neurosurgeons with experience both in the critical management of Parkinson's and in its clinical research, has the potential to worsen in the next few years.

The clinical research fellowship program is a strategic initiative that redresses physician shortages by encouraging promising young scientists to enter the field of Parkinson's clinical research while simultaneously investing in research training that offers promise for future work in the area of Parkinson's disease.

CLINICAL MOVEMENT DISORDERS FELLOWSHIP PROGRAM

Duration **1 year**
Funding Amount **$50,000**

Parkinson Society Canada wants to ensure that each Canadian with Parkinson's receives appropriate medical expertise, drug treatment, support services, continuous care, educational resources, respect, dignity, help and hope. This fellowship represents the first step in achieving part of our goal of ensuring that these critical elements in the day-to-day management of Parkinson's are accessible and available.

The Clinical Movement Disorders fellowship program is a strategic initiative to encourage promising young clinicians to enter into clinical training in the subspecialty of Movement Disorders, which will include Parkinson's disease. The purpose of this post-residency training is to provide expertise in the diagnosis and management of Parkinson's disease and may include other movement disorders. Clinical training is the largest component of this hands-on program but it could include an element of research.

In this initiative, Parkinson Society Canada is also capitalizing on the potential of partnerships to support new programs and increase overall funding for our research program.

PSYCHOSOCIAL DOCTORAL AWARD

This strategic initiative encourages researchers specifically in the area of psychosocial research in Parkinson's. It helps PSC to better serve Canadians with Parkinson's, to foster Canadian Parkinson research leadership internationally, and to support efforts to ease the burden and find a cure.

Doctoral Awards provide support to students who are pursuing a PhD. The Psychosocial Doctoral Award Program is intended to encourage emerging young scientists to enter the field of Parkinson's and to invest in psychosocial research training specifically directed toward closing the gap in understanding and treating non motor symptoms of Parkinson's.

GRADUATE STUDENT AWARD

Duration **2 years**
Funding Amount **$15,000/ year***

The Graduate Student Award Program is a strategic initiative to encourage promising young scientists to enter the field of Parkinson's research and to invest in research training that offers promise for future work in the area of Parkinson's disease. PSC wishes to encourage continued growth and revitalization in the fields of Parkinson's research in Canada by supporting talented young scientists and providing students with an opportunity to enter into the area of Parkinson's research during the early stages of their training.

*Additional $5,000 /year is contributed by the student's supervisor for a total award amount of $20,000 per year.

Pilot Project Grant

Quantitative assessment of the efficacy of treatment strategies to avoid levodopa-induced dyskinesia: focus on every-day-life mobility

One Year Award $44,882

Dr. Christian Duval
Dr. Duval is an Associate Professor at the University of Quebec at Montreal in the Department of Kinanthropology. Prior to his move to Quebec, from 2003-2005, he was an Assistant Professor at Brock University in St. Catharines, Ontario. Dr. Duval received his PhD in Neuroscience from McGill University in 2003.

Dr. Patrick Boissy
Dr. Boissy is currently an Associate Professor of Kinesiology at the University of Sherbrooke. Following his PhD in Biomedical Sciences at the University of Montreal, he undertook his post-doctoral training at Boston University in the Health Service Research field.

Dr. Mandar Jog
Dr. Jog is currently the Director of the Movement Disorders Program at the London Health Sciences Centre and Professor of Neurology at the University of Western Ontario. He received his Medical Degree from the University of Toronto and completed a fellowship in movement disorders with Dr. Anthony Lang. A four year post-doctoral fellowship in Computational Neuroscience at the Massachusetts Institute of Technology followed.

One of the most difficult things for neurologists treating people with Parkinson's disease to assess is the effect of medications on their patients' mobility.

Unlike people who have had a stroke, whose condition stabilizes once they have been treated and recovered, people with Parkinson's may experience vast changes in mobility from hour to hour. That means when they come to a clinic to be assessed, they might be moving well. But when they go home, they have more trouble. The opposite can also be true.

Unfortunately, neurologists can only work with what they see when assessing the effect of medications that induce uncontrollable movements, known as dyskinesia, says Dr. Mandar Jog, Director of the Movement Disorders Program at the London Health Sciences Centre in London, Ontario.

That's why Jog went to colleagues Christian Duval and Patrick Boissy for help designing a way to measure people's mobility objectively.

Dr. Duval, a neuroscientist at the University of Quebec at Montreal, and Boissy, a kinesiologist at the University of Sherbrooke, specialize in evaluating and measuring mobility. Using a lycra suit embedded with sensors that people with Parkinson's wear for up to four hours inside their homes, and a GPS-based movement tracker and wearable sensors they can fix to their wrist or their body, they will measure people's movements at home and in the community. Analyzing that data and comparing people's mobility before and after a change in the levels of levodopa they are taking will then allow Jog to better assess the optimal level of the medication.

"When we find out the different changes that occur with different treatments, we will build a database," explains Duval. "The idea is to generalize the results."

The researchers hope to pinpoint when dyskinesia hinders someone's ability to perform their daily tasks.

Ultimately, Jog hopes the research will tell clinicians whether the changes they make in people's treatment actually affect the quality of their lives.

Dr. Boissy was attracted to the project because of the direct results it will produce. "Most neurologists rely on self-reports," he says. "We can provide a better and more representative picture of the effects of these medication changes."He also knows first-hand the effects of Parkinson's, having watched the disease affect his mother's partner's mobility.

For Duval, pushing the boundaries of research into Parkinson's disease is an extension of his addiction to skydiving, as a former Canadian national champion. "I basically transferred my interest from one thing to the next," he says with a laugh.

And for Jog, this project could have a lasting impact for his patients, many of whom will participate in the study. "All of my patients are like family to me," he says.

Pilot Project Grant

Sensorimotor priming for improving swallowing function in patients with Parkinson's disease.

One Year Award $31,500

Dr. Mandar Jog

Dr. Jog is currently the Director of the Movement Disorders Centre, a National Parkinson Foundation Centre of Excellence, at the London Health Sciences Centre and Professor of Neurology at the University of Western Ontario. He received his Medical Degree from the University of Toronto and completed a fellowship in Movement disorders with Dr. Anthony Lang. A four year post-doctoral fellowship in Computational Neuroscience at the Massachusetts Institute of Technology followed.

Ms. Angela South

Ms. South is a Speech Language Pathologist at the London Health Sciences Center, University Hospital. She received her BA and MA in Speech Pathology from the University of Tennessee. She is a PhD candidate at the University of Western Ontario.

Ms. Stephanie Somers

Ms. Somers is a Speech Language Pathologist at the London Health Sciences Center, University Hospital. She received her BA in Linguistics: Communication Disorders from Brock University in 2000 and her MCISc in Communication Sciences and Disorders from the University of Western Ontario in 2003.

Dr. Mandar Jog was returning from his dentist when the advice he'd received about chewing gum to remove food particles in his teeth struck him as a possible solution to the swallowing difficulties people with Parkinson's disease endure.

Jog, a neurologist and Director of the Movement Disorders Clinic at the London Health Sciences Centre, knew that as their disease progresses, all people with Parkinson's have trouble swallowing. In Parkinson's, the natural tendency to swallow frequently is slowed, causing excess saliva to build up in the mouth. This puts people at risk of choking, and saliva can seep onto their chin because their brain is not prompting them to swallow often.

None of the Parkinson's medications are particularly effective in treating this problem, which affects people's ability to socialize, their relationships with their partners, and their health, since aspirating saliva can result in pneumonia.

It occurred to Jog that chewing gum – a normal, socially acceptable activity – might serve as a sensory cue. "In the same way we use a laser light for Parkinson patients as a cue for them to step out to improve their gait, maybe chewing gum will improve their swallowing function," he thought.

Jog and speech and language pathologists Angela South and Stephanie Somers began asking people with Parkinson's who came to Jog's clinic to chew gum for half an hour before meals. The results were astonishing.

"Close to a dozen patients over a period of a dozen weeks said they didn't choke even once after doing this," says Jog.

Jog, South and Somers are now studying the effects of chewing gum on the swallowing sensory motor integration functions of people with Parkinson's disease. They have already shown, in a small sample, that even after people stopped chewing gum their swallowing function improved. Chewing gum seems to act as physiotherapy for the tongue, jaw and pharynx, improving sensory motor memory.

"We're having clients coming back in saying they are swallowing better with meals and they are able to socialize and speak without worrying about drooling," says South.

Jog and South are particularly excited about this therapy because it's simple, cost-effective and patients can manage it on their own. Their pilot project will assess how long the improvements in swallowing and secretion control last, if patients chew gum for several hours a day.

For Jog, this project exemplifies the importance of clinicians who are also researchers, and can apply their research directly to their patients' problems.

As for South, who has returned to the University of Western Ontario as a PhD candidate in communication science and disorders, the study exemplifies the applied research she wants to conduct to improve people's quality of life quickly.

"We can't cure (Parkinson's) right now, but if we can make life easier, then we owe that to them," South says of her patients.

Pilot Project Grant

Role of a PINK1-BAG2 pathway in regulating dopaminergic loss

Dr. David Park

Dr. Park received his PhD from Rutgers University in New Brunswick, New Jersey and obtained his post-doctoral training with Dr. Lloyd Greene at Columbia University in New York. He is currently Full Professor in the Department of Cellular Molecular Medicine at the University of Ottawa. He is the Co-director of the Ottawa Parkinson Research Consortium and a Senior Scientist at the Ottawa Health Research Institute. Dr Park is a well established and extremely productive scientist with numerous personal awards, including a Career Scientist Award from the Heart and Stroke Foundation.

One Year Award $45,000

At the University of Ottawa, biochemist David Park is doggedly trying to pinpoint all of the steps that lead to the neurodegenerative process that ends in Parkinson's disease.

It's exciting yet frustrating work, Park confesses.

The exciting part is that researchers have already identified several genes, such as PINK1, which begin the process that causes the familial form of Parkinson's disease. That's the first step in understanding the chain of interaction that kills dopamine-producing cells in the brain.

The frustration comes from the fact that no one yet understands what the genes and their proteins are actually doing to result in the disease.

"We don't know Step 2," says Park. "If you know Step 2, then you can proceed and march down and understand the bigger picture of all the steps that occur. And if you understand all the steps, you can understand which steps are best to interfere with."

In his quest for that second step, Park is currently studying the interaction between PINK1 and a protein known as BAG2. He's trying to understand whether PINK1 modifies BAG2, or vice versa.

Once Park can determine this molecular relationship, he will be one step closer to understanding the entire process. That's critical to being able to devise a new drug or therapy that could eventually prevent Parkinson's disease.

"It's important to gain a bigger understanding of the steps, because a lot of times, the steps are redundant, and halting one is not going to halt the entire process," Park explains. "You block one pathway and another pathway picks up the slack and you still get degeneration."

Unlike his father, who is a surgeon, Park cannot just isolate the problem and cut it out. He wishes he could. Instead, he has to continue to work on this piece of the Parkinson's puzzle. Eventually, the work of different researchers may fit together to produce a clear picture.

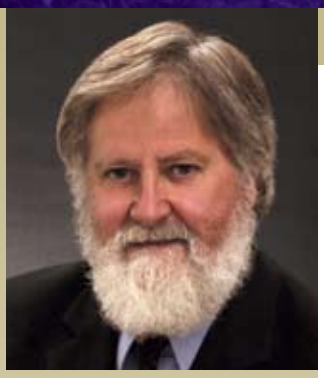
"People have to be patient. It's amazing to think that it's only been 150 years since we understood that a cell was a cell – and now we're doing this," says Park.

When he first began his research into Parkinson's disease, Park also assumed it would be relatively straightforward to work out the process of what causes these key brain cells to die.

"Turns out, Parkinson's is an incredibly complicated disease, and I was completely wrong," he says, with a laugh. "But my passion and interests continue, nonetheless, for Parkinson's disease research."

Pilot Project Grant

Clinical Trial of a diagnostic procedure for early stage Parkinson's disease



Dr. Harold Robertson

Dr. Harold Robertson is Professor Emeritus of Pharmacology, Scientific Director and Co-founder of the Brain Repair Centre at Dalhousie University. His research is currently focused on the diagnosis and treatment of Parkinson's disease. He has published over 170 papers on neurotransmission, gene expression in the brain, dopamine and dopaminergic drugs in schizophrenia and Parkinson's disease, and molecular neurobiology of Huntington's disease. Dr. Robertson was part of the team that carried out the first neural transplantations for Parkinson's disease in 1991 and is a pioneer in the field of neurological research in Atlantic Canada.

One Year Award $43,024

Losing the sense of smell is one of the most common symptoms people with Parkinson's disease experience – and often, the first. But until now, that loss has never formed the basis for early detection.

Harold Robertson, an emeritus professor of pharmacology at Halifax's Dalhousie University, thinks coupling a new form of diagnostic imaging with a "scratch and sniff" test will enable him to create a test that will not only diagnose Parkinson's years earlier, it may help people get earlier treatment.

"By the time it (Parkinson's) shows up clinically, about 60-70 percent of dopamine neurons are already lost," Robertson says. "The damage is largely irreparable. If we can diagnosis earlier, we can begin treatment earlier."

Currently, researchers do not have established treatments that are effective for people in the early stages of Parkinson's. There is widespread belief in the Parkinson's research community, however, that neural transplantation or stem cell transplantation will work better if applied earlier, and there is some evidence that deep brain stimulation works better if applied earlier, Robertson says.

That's why he has begun a program using a form of magnetic resonance imaging called diffusion tensor imaging, or DTI, to scan the brains of people who have lost their sense of smell. DTI enables researchers to probe the anatomical structure and chemical makeup of the brain externally, using a large magnet that maps the direction of water molecules vibrating in the brain. The computer images can highlight changes in the olfactory bulb and the brain's substantia nigra. By combining those brain maps with the results of a series of 40 smell identification tests, Robertson hopes he will get an accurate predictor of which patients have or will develop Parkinson's disease.

Robertson's study will enrol patients in the early stages of Parkinson's disease, and compare the results of their sniff tests and imaging with those of their spouses, partners and/or siblings who do not have Parkinson's.

The pharmacologist became interested in identifying people with Parkinson's early through his work in Dalhousie's neural transplantation program.

"It became apparent … that the reason we weren't having the success we hoped for was that we were trying to treat patients whose dopaminergic systems were perhaps too far gone to give us a good result," says Robertson.

He wondered how to find a marker that would show up in patients before their clinical symptoms appeared, to try to find people to treat before the disease develops. That line of inquiry led Robertson to the olfactory system.

"It's as reliable a symptom as tremour is for Parkinson's disease, and it can occur around five years before the clinical symptoms of Parkinson's disease show up," Robertson says.

Pilot Project Grant

Role of parkin in the turnover of defective mitochondria

Dr. Eric Shoubridge

Dr. Shoubridge is a professor in the Department of Neurology, Neurosurgery, and Human Genetics at McGill University. He received a PhD in biochemistry in 1981 from the University of British Columbia and went on to do postdoctoral research in the United Kingdom at the University of Oxford. In 2003, he was awarded a James McGill Professorship and was elected a fellow of the Royal Society of Canada in 2004.

One Year Award $38,480

Dr. Eric Shoubridge may have his PhD in genetics, but he has long been a biologist at heart. That's why he finds research into cellular systems and how they may be implicated in Parkinson's disease so fascinating.

"The discovery of the workings of the cell constantly amazes me," says Shoubridge, a professor at the Montreal Neurological Institute.

For almost 20 years, Shoubridge's laboratory has been studying mitochondrial diseases – diseases that have their basis in damaged or mutated mitochondria, the powerhouses that generate the energy a cell needs to survive.

Recent studies have shown that a gene called parkin that is mutated in some people with Parkinson's disease could play a central role in the death of dopamine-producing neurons.

Parkin binds to the outside of damaged mitochondria, to direct them to a natural process that disposes of damaged material within cells. But if Parkin is itself damaged or mutated, it may not recognize the "bad" mitochondria, allowing them to avoid the cellular "recycling bin." Such an interruption in that natural process would allow damaged mitochondria to accumulate and may be responsible for killing valuable brain cells.

Shoubridge wants to test this theory, using cell lines with different genetic defects that his lab has developed. By using fluorescent dyes, he will be able to spot parkin under a microscope and see whether it can recognize and distinguish between mitochondria containing defective copies of mitochondrial DNA and those that are normal.

If he can prove that parkin is indeed directing the genetically defective mitochondria to the cell's disposal system, researchers will gain greater insight into parkin's function. That knowledge will help them develop a way to encourage defective mitochondria to enter the disposal system, thus preventing dopamine-producing cells from dying.

Eventually, researchers would use their knowledge of parkin's role and the signals it uses to identify the damaged mitochondria to develop a new drug that would either increase the way parkin is supposed to function, or could bypass the entire system. Either way, knowing the detail of how parkin works and being able to duplicate its function would preserve vital dopamine-producing neurons.

Shoubridge is motivated to tackle this work by his knowledge of mitochondrial diseases and the expertise he and his colleagues have developed.

"I thought we could probably make a contribution here," he says.

Pilot Project Grant

Neurotransmitter phenotype plasticity in monoamine neurons in the context of Parkinson's disease

Dr. Louis-Eric Trudeau

Dr. Trudeau is a Full Professor of Pharmacology and Neuroscience with cross-appointments to the Departments of Psychiatry and Physiology at the University of Montreal. He received his PhD in Neuroscience from the University of Montreal and completed his post-doctoral training at Iowa State University.

Dr. Salah El Mestikawy

Dr. Salah El Mestikawy is Full Professor and Canada Research Chair in Psychiatry at McGill University. He received his PhD from the Pierre & Marie Curie University in Paris and pursued his post-doctoral training at Duke University. Dr. El Mestikawy moved to Quebec in 2008 to direct an international research team based both in Quebec, at the Douglas Hospital Research Institute, and in France, at INSERM (Institut national de la santé et de la recherche médicale) and at the Pierre & Marie Curie University in Paris.

One Year Award $45,000

Researchers studying the brain cells that produce dopamine have recently discovered that their basic properties appear to change in the face of Parkinson's disease.

Dr. Louis-Eric Trudeau, a professor in pharmacology at the University of Montreal, and his colleague Dr. Salah El Mestikawy, a neuroscientist and Canada Research Chair at McGill University, already know, thanks to Trudeau's earlier work, that some dopamine neurons have the ability to release glutamate. Like dopamine, glutamate is a neurotransmitter, a chemical messenger, which helps transfer information swiftly.

Now Trudeau and El Mestikawy, a specialist in the study of neurons that produce glutamate, are studying its relationship to Parkinson's disease.

"Nobody has any idea of the role of this glutamate used by dopaminergic neurons to communicate," says El Mestikawy. "Is it increased or decreased in Parkinson's disease? Is it responsible for some of the symptoms?"

The researchers believe this second neurotransmitter may help dopamine-producing brain cells reconnect with other neurons once they are faced with a traumatic event – like the impact of Parkinson's disease. But it's also possible too much glutamate contributes to the death of other brain cells.

"Either way, figuring out glutamate's role could ultimately help people with Parkinson's disease," says Trudeau.

When dopamine-producing neurons die, the circuits in the brain become disorganized, causing the motor symptoms that occur for people who have the disease.

"We hope our work will help us understand exactly how these circuits are disorganizing, and this may help us come up with better ideas to normalize the activity of the circuits," Trudeau says.

Using mouse models, the researchers will analyze what glutamate does, or how much of it is produced, when dopamine-producing neurons die. Eventually, they hope to provide a new drug target or other therapy for treating it.

Trudeau approaches this research from a fresh angle, since he is new to Parkinson's disease research. His collaboration with El Mestikawy, who has long worked with colleagues pioneering dopamine studies, provides a unique outlook on the disease.

"Not a lot of people are paying attention to the question of the basic functioning of dopamine neurons and how their contacts with other cells in the brain are organized," says Trudeau.

The Garden Centre Group Co-op
New Investigator Award

Understanding impulse control disorders in Parkinson's disease

Dr. Stephanie Borgland

Dr. Borgland is currently an Assistant Professor in the Department of Anesthesiology, Pharmacology & Therapeutics at the University of British Columbia. She received her PhD in Pharmacology/Neuroscience from the University of Sydney, Australia in 2002 and then went on to complete her Post-Doctoral training at the University of California, San Francisco ending in 2006.

Year 1 $45,000 Year 2 $45,000 Total Award: $90,000

University of British Columbia professor Dr. Stephanie Borgland has long been interested in investigating motivation and impulse control and the psychological aspects associated with these problems.

Impulse control problems such as gambling, hyper-sexuality and other addictive behaviours are among the most disturbing side-effects that can occur when people with Parkinson's disease take drugs that activate dopamine receptors in their brain cells.

"Drug addiction and these other impulse control disorders are really devastating disorders," says Borgland, who is an electrophysiologist and Assistant Professor at the University of British Columbia. "People are aware they have them, and they would like to change, but for some reason they just can't do it."

Dr. Borgland is specifically investigating the role that dopamine plays in the orbitofrontal cortex, a region of the brain involved in impulse control. Dopamine neurons located in a group of neurons at the centre of the brain, known as the ventral tegmental area, communicate with the orbitofrontal cortex, and can release dopamine into this region. Researchers believe dopamine in that region regulates impulsive behaviours.

Dopamine neurons located in this area, part of the midbrain, are relatively unspared by Parkinson's disease. But when between 8-10 percent of people with Parkinson's take drugs to treat motor control problems, those drugs affect the dopamine release in the orbitofrontal cortex. By altering the way the neurons in this area communicate, that may cause impulse control and addiction problems.

Before researchers can adapt existing drugs or design new ones, they need to understand more about how the dopamine-producing neurons in this part of the brain regulate behaviours.

"The research that I'm doing is setting out to understand more about the neurobiological mechanisms underlying these impulse control disorders," says Borgland.

Dr. Borgland was drawn to UBC after a post-doctoral fellowship at the University of California in San Francisco because of the group of researchers there involved in dopamine research.

"It's an amazing academic environment for me to be in, as a lot of people share my interests," she says.

The results of the UBC researchers' work will, they hope, translate into better therapies that could have applications for Parkinson's disease and other problems, including schizophrenia and learning and memory disorders.

Parkinson Society Canada –
Canadian Institutes of Health
Research/Institute of Neurosciences
Mental Health and Addiction
Psychosocial
Research Grant

Improving detection and management of non-motor features of Parkinson's Disease – Development of a knowledge translation outreach strategy

Year 1 $49,454 Year 2 $49,454 Total Award: $98,908

Dr. Ron Postuma

Dr. Postuma is an Assistant Professor in the Department of Neurology at McGill University and a staff Neurologist at Montreal General Hospital. He obtained his MD in 1995 from the University of Manitoba and completed his Neurology Residency at McGill University in 2002. Dr. Postuma is a past recipient of a PSC Clinical Research Fellowship and trained under the supervision of Dr. Anthony Lang at the Toronto Western Hospital, Movement Disorder Center.

People with Parkinson's disease often experience a wide variety of symptoms that they may not know are related to the illness that is causing them to shake or that is disrupting other aspects of their motor control.

Because people are unaware that the anxiety, depression, hallucinations, lightheadedness, insomnia, constipation, dementia or impulse control issues they are experiencing are related to Parkinson's, they may not mention them to their doctor. Many doctors may not understand the relationship either, or how to treat the symptoms. That's why Dr. Ron Postuma is testing aids to help patients and doctors detect and treat the non-motor symptoms of Parkinson's disease.

"On average, patients have not discussed half of their non-motor symptoms with a physician," says Postuma, a neurologist and movement disorders specialist, as well as an assistant professor at McGill University in Montreal.

"Most of them are treatable. That's why it's so important that they be detected."

As a first step, Postuma is testing the reliability of a screening questionnaire to help people identify their symptoms. After having 60 patients complete the questionnaire, he is following up with in-depth evaluations to see if it caught all the non-motor symptoms people are experiencing.

In addition, Postuma is developing a patients' guide and a physicians' guide that describe these symptoms, help people recognize them and advise doctors about how to treat the problems.

Finally, with the help of Parkinson Society Quebec, Postuma is going to have a wider group of people, who have filled out the questionnaires, take them to their doctor. He and his colleagues will have contacted those same doctors to make sure they have a physicians' guide in hand. They will then evaluate what difference the guide and questionnaire made in helping people with the disease and their doctors detect non-motor manifestations of the disease.

In the future, if this project proves successful at increasing detection and treatment, Postuma would like to see his questionnaires and guides implemented on a national level.

Although the neurologist began his work on neuro-degenerative diseases with Alzheimer's patients, he switched to working with people with Parkinson's because he found it more encouraging, he says.

"People really do get a lot better after they see you," Postuma says. "I like doing practical research. That way I know I'm making a difference in the end."

Basic Research Fellowship

Mitochondrial Dysfunction in the Etiology of Parkinson's disease

Dr. Jonathon Burman

Dr. Burman obtained his BSc in 2001 from the University of Western Ontario and recently completed his PhD in neurosciences at the Montreal Neurological Institute. Dr. Burman will continue with his studies and will undergo post-doctoral training at the University of Washington under the supervision of Dr. Leo Pallanck.

Year 1 $40,000 Year 2 $40,000 Total Award: $80,000

To create more effective treatments for people with Parkinson's disease, researchers need to understand exactly how the disease works, down to the finest detail.

That's why Jonathon Burman, a 33-year-old post-doctoral fellow in neuroscience at the University of Washington, is exploring the role that two particular proteins play in interacting with the mitochondria in dopamine-producing brain cells.

"You need to know what's going wrong at a mechanistic level before you can really find a long-lasting cure," says Burman.

Working in the laboratory of Dr. Leo Pallanck, Burman is studying the proteins known as PINK1 and parkin. Damaged copies of these proteins have been genetically linked to early-onset Parkinson's disease. Using the fruit fly model system as a subject, Burman is investigating how PINK1 and parkin interact with mitochondria, the energy powerhouses of cells.

He plans to test a theory that PINK1 and parkin, when working properly, help to keep brain cells healthy by being part of the machinery that removes unhealthy or damaged mitochondria from the cells, clearing the way for healthier mitochondria to thrive.

If the proteins are themselves damaged, however, as is the case in people with early-onset or familial Parkinson's disease, they can't perform their task of clearing away dysfunctional mitochondria. That, in turn, somehow causes the neurons that produce dopamine to die.

"The goal of this type of research is really to look at why these cells are dying and to stop them from dying," Burman says.

Eventually, these proteins and the mechanism involved in having them attach to mitochondria could be the target for new drug therapy.

Long interested in how science can explain the complex nature of the world, Burman was drawn to the world of Parkinson's research when he studied with a leader in the field, Professor Robert Edwards, in San Francisco.

During that time his grandmother, Jeanine Rosen, was diagnosed with Parkinson's disease. Before his grandmother died, at 83, he often talked to her about what he was learning and discovering.

"With research, there are lots of ups and downs, and you need time," Burman says. "In that way, her memory continues to inspire me to stay the course."

Basic Research Fellowship

Neuronal cell death/Autophagy

Dr. Marc Germain

Dr. Germain is presently a post-doctoral fellow at the University of Ottawa in the Department of Cellular & Molecular Medicine training under the supervision of Dr. Ruth Slack. Prior to his move to Ottawa, he was a post-doctoral student at the University of British Columbia. Dr. Germain received his PhD in Biochemistry from McGill University in 2004 and his Masters in Molecular and Cellular Biology from Laval University in 1999.

Year 1 $50,000 Year 2 $50,000 Total Award: $100,000

Marc Germain has always liked finding out how things work. That's why the biochemist has turned his attention to the genes and proteins involved in the death of the dopamine-producing cells that are central to Parkinson's disease.

At the University of Ottawa lab where Germain is conducting his research as a post-doctoral fellow, he is focused on a protein known as MCL-1, which helps to regulate the process of autophagy. Autophagy, which is a naturally occurring process, allows cells to recycle their components and generate energy during periods of starvation. However, autophagy can also result in the death of cells when they are under prolonged stress.

"There have recently been several links between autophagy and Parkinson's disease," Germain says.

Researchers do not yet completely understand the role that MCL-1 and autophagy play in Parkinson's disease – that's what Germain is investigating. One theory is the proteins that aggregate in the dopamine-producing neurons cause them to die, and the autophagy process is somehow blocked. In other words, explains Germain, blocking autophagy means the cells "can't get the garbage out" – the garbage being the clumped proteins.

Alternatively, damaged or mutated genes may be failing to regulate the autophagy process so that cells are eating themselves and dying that way.

Using mice with MCL-1 and other genes knocked out will enable Germain to begin answering the questions about how the autophagy and other forms of cell death affect the dopamine-producing neurons, at the molecular level.

Originally, Germain was working in the cancer field, studying ways to turn on a second MCL-1-regulated process, called apoptosis (cell suicide), in order to kill cancer cells. He was drawn to Parkinson's disease because of the critical mass of research involved in trying to understand the neuroscience and underlying mechanisms that cause the degenerative illness. The complexity of the problem, and the quality of other researchers at the University of Ottawa, drew him there.

Germain hopes his basic research will help to illuminate the reasons that Parkinson's disease occurs, and show a pathway for future treatment.

"Eventually, if we show that this process of autophagy is really important, that could provide new drug targets for Parkinson's disease," says Germain.

Basic Research Fellowship

The influence of 5HT1A and 5HT2A serotoninergic receptors in the generation of psychosis in Parkinson's Disease

Year 1 $50,000 Year 2 $50,000 Total Award: $100,000

Dr. Philippe Huot

Dr. Huot is currently a Movement Disorders Fellow pursuing his PhD at the Toronto Western Research Institute under the supervision of Drs. Jonathan Brotchie and Susan Fox. He obtained his FRCPC in Neurology in 2008, an MSc in Neurobiology in 2006 and his MD in 2003 all from Laval University, Quebec.

One of the most difficult aspects of treating people with Parkinson's disease is the disturbing level of side-effects that accompany the only long-term drug therapy currently available for them. Among those side-effects are vivid visual hallucinations that up to 60 percent of people experience.

Those hallucinations appear to result from an interaction between the administration of dopamine drugs and the effects on the brain of advanced Parkinson's disease, says Dr. Philippe Huot, a neurologist and PhD candidate in neurobiology at Toronto Western Hospital.

"The problem is that it's hard to control the hallucinations without changing the drug regimens people take," says Huot. Stopping or reducing Levodopa therapy can alleviate the hallucinations – but then the patient's other neurological symptoms are untreated.

That's why Huot is exploring the involvement of serotonin Type 2A receptors in the brains of people who are experiencing these hallucinations. He hopes that by better understanding the role these serotonin receptors play in Parkinson's disease, he will eventually provide an avenue for new compound drugs that will act as tools against the debilitating effects of the illness.

"These symptoms can be very debilitating for the patients," says Huot. "It impairs their quality of life, which is already impaired by the disease itself."

Huot, who treated Parkinson's patients during his neurology residency, is drawn to research because he wants to give larger numbers of patients hope that there is a better treatment on the horizon, he says. He was first inspired to work in the area after studying with Dr. André Parent, a neuroanatomist at Laval University who was studying the basal ganglia.

"I was very interested in how so many aspects of behaviour can be regulated by very small structures in the brain," says Huot. "When their functioning is impaired, it can lead to very serious diseases like Parkinson's or Huntington's chorea."

During his residency, Huot was frustrated by the number of treatments available for people with Parkinson's disease that become limited, eventually, by the severity of their side effects. He hopes a part-time clinical fellowship in movement disorders, as well as his research, will allow him to help people with Parkinson's in both the short-term and the long-term.

"It's important for me to help the patients directly, not just through a long-term perspective," Huot says.

Clinical Movement Disorders Fellowship

Clinical Movement Disorders Training

Dr. Manon Bouchard

Dr. Bouchard received her MD from Laval University in 2004 and recently completed her Neurology residency in Quebec. She is currently training as a movement disorders specialist under the supervision of Dr. Oksana Suchowersky at Foothills Hospital in Calgary, Alberta.

One Year Award $50,000

Dr. Manon Bouchard believes that when it comes to treating people with Parkinson's disease, book learning can only take her so far.

That's why, despite having finished five years of medical residency where she treated a few people with Parkinson's, the neurologist wanted a fellowship that would give her more hands-on experience. So she will spend the next year at the Foothills Hospital in Calgary, working with Dr. Oksana Suchowersky at the Movement Disorders Clinic there, and with other colleagues at the hospital's sleep lab. She is particularly interested in helping people with the non-motor symptoms of Parkinson's that plague them, like difficulty sleeping.

Often, those non-motor symptoms emerge at different stages in the disease, but during her residency, the people with Parkinson's that Bouchard saw were usually in the beginning of their illness.

"We read about how to treat them as it progresses, but I did not feel comfortable enough just by reading it in the books," she says. "Some problems need to be recognized just by seeing them."

At Foothills, Bouchard will also learn how to select patients who are good candidates for deep-brain stimulation surgery. By applying electrical stimulation deep in the brain, this surgery can relieve the dyskinesia, or uncontrollable movements, that is often the side-effect of Parkinson's medication.

Selecting the appropriate patients for this kind of surgery, and providing their follow-up care, is experience no one at the Hotel Dieu de Levis possesses. Once trained, Bouchard will return there, and work with the surgeons who will then be able to provide that program.

"I will also learn to program and re-program the machine that goes with it (deep brain stimulation), so that after I come back I will be able to do that," Bouchard says.

Bouchard was drawn to patients with movement disorders, and Parkinson's in particular, because treating them requires "basic old neurology," she says. Unlike other fields of medicine, where new diagnostic tools like special imaging machines are important, diagnosing and assisting patients with Parkinson's relies on taking a comprehensive history, examining the patient and observing him or her, she says.

She also finds the field rewarding, because there is so much she can offer her patients to relieve their symptoms, unlike people suffering from muscular dystrophy or other degenerative neurological diseases.

"Of course we can't cure people, but we can help people feel better and live better with their disease," she says.

Clinical Research in the area of Multiple System Atrophy (MSA)

Dr. Amitabh Gupta

As the recipient of a Clinical Research Fellowship, and a past recipient of a Clinical Movement Disorders Fellowship, Dr. Gupta is working under the supervision of Dr. Tony Lang at the Morton & Gloria Shulman Movement Disorders Centre. Dr. Gupta completed his Residency in Adult Neurology at Johns Hopkins Hospital in Baltimore in 2008. He obtained his PhD from Harvard Medical School in Biological and Biomedical Sciences following a postdoctoral fellowship at the Harvard School of Public Health. Dr. Gupta received his MD from Ruprecht-Karls-Universitaet Heidelberg, Germany in 1995.

One Year $50,000

Every day, Dr. Amitabh Gupta sees someone at the Morton & Gloria Shulman Movement Disorder Clinic at Toronto Western Hospital who has been misdiagnosed with Parkinson disease but actually has a rarer and more serious illness.

About one in 10 people initially thought to have Parkinson's actually have Multiple System Atrophy - MSA. Although people with MSA often have Parkinson-like symptoms, such as stiffness, shakiness and difficulty moving, they also have some unique issues, including bowel and bladder problems, erectile dysfunction in males, dizziness and hypotension. Unlike most people with Parkinson's, those with MSA do not respond to medications that mimic the actions of dopamine, the chemical that regulates nerve cells in the brain.

"Parkinson's disease can be fairly well managed over decades, but MSA people usually die in 10-12 years," says Gupta.

That's why the neurologist is focusing on finding ways to diagnose patients with MSA earlier. He will spend the next year, during a clinical research fellowship at Toronto Western Hospital, reviewing the hospital's large database of brain tissue and examining the charts of patients with MSA, as well as treating them. By also using MRI machines to scan people's brains, Gupta hopes to develop definitive clinical criteria for diagnosing people with this devastating disease. In addition, he will study sleep disturbances and apply neuro-psychological tests to see if MSA affects people's cognitive abilities.

Gupta will also conduct basic research in this area, to investigate whether there is a different path of destruction in the brains of people with MSA. He is concentrating on the accumulation of a protein alpha-synuclein in the glial cells of those patients.

If he is able to develop a definitive clinical criteria, or find a genetic marker for MSA, doctors could diagnose it sooner. Eventually, Gupta hopes this will open a pathway for neuro-protective drugs that people could receive earlier in the progression of their disease.

"We have many neuro-protective drugs that have been tried right now, and they don't work," he says. "Maybe one of the reasons they don't work is because they have been tried too late."

If researchers could prescribe a drug early in the onset of this degenerative disease, it could protect millions of neurons before the disease destroys them. That early intervention could modify or even stop the MSA.

"It's like the difference between having a sore throat and having full-blown pneumonia and starting the antibiotics earlier," Gupta says. "If you're an 80-year old woman with full-blown pneumonia, you'd obviously rather have started the antibiotic when you have a sore throat."

Gupta was drawn to medicine by his desire to help people, and to neurology and the study of movement disorders by his fascination with the brain. MSA is under-studied, and Gupta sees his work as an opportunity to make a difference for people who at the moment have little hope.

"Research is aimed at improving their lives," he says.

Clinical Research Fellowship

Maladaptive neuroplasticity in Parkinson's disease

Dr. Michael Sidel

Dr. Sidel is currently a Clinical fellow training at the Lady Davis Institute for Medical Research at the Sir Mortimer B. Davis – Jewish General Hospital in Montreal under the supervision of Drs. Alexandre Thiel, Calvin Melmed and Anne-Louise Lafontaine. He received his Doctor of Medicine and Master of Surgery (MD.CM) from McGill University in 2004 and recently completed his Neurology Residency in May 2009.

One Year Award $50,000 Year Two Award $50,000 Total Award: $100,000

Dr. Michael Sidel hopes that something as simple and non-invasive as a powerful magnet will help researchers find ways to prevent and treat the uncontrollable movements that affect some people with Parkinson's disease.

That's why Sidel will spend the majority of his clinical research fellowship at Montreal's Jewish General Hospital working with another neurologist who specializes in a new technology that could eventually open up another area for Parkinson's treatment.

Dr. Alexander Thiel, with whom Sidel will be training, uses a powerful electro-magnet to manipulate patients' brains without even touching them, a technique called transcranial magnetic stimulation. The magnet is positioned above a patient's skull. Currently, Thiel is using the magnet to determine what areas of people's brains are activated as they begin recovering from strokes.

Sidel will work with him to use the magnet to send rapid electrical pulses to the brains of people with Parkinson's, to determine which connections and passageways in the brain are involved when they experience dyskinesia – the uncontrollable movements that are often side-effects to drugs treating the disease.

"We're trying to understand what brain pathways are actually involved in the creation of these things," says Sidel. "No one's ever looked at it quite in this way before."

In addition to the magnetic tools and experience that Thiel has brought to Canada from Germany, Sidel will also have access to imaging tools, like the hospital's high-resolution PET scanner. Combining the detailed images of people's brains that the PET scanner will provide with the electro-magnetic stimulation will provide Sidel with a map showing where neurons are activated or inhibited in the brain.

"We know a lot about the circuits that are involved as we generate movement, but we don't understand how people with Parkinson's disease generate these movements and how they are perpetuated," Sidel says.

Finding the specific pathways involved would allow researchers to develop drugs or new surgical interventions to prevent or treat the dyskinesia, or to develop new drugs that would avoid these side-effects.

Although 80 percent of Sidel's time during the fellowship will be spent on research, he's glad that the other 20 percent will involve seeing patients.

"What drew me to medicine was patient interaction and patient diagnosis, not sitting in front of a computer all day," he says.

Parkinson Society Canada –
Canadian Institutes of Health
Research/Institute of Neurosciences
Mental Health and Addiction
Psychosocial
Doctoral Award

Awareness of deficit in Parkinson's disease – Understanding patient reality

Ms. Christine Cullion-Hicks

Ms. Cullion-Hicks is currently a PhD student training under the supervision of Drs. Andrew Johnson and Linda Miller in the Faculty of Health Rehabilitation Sciences at the University of Western Ontario. She received her Masters degree in Counselling Psychology with a focus on the diagnosis of children with developmental disabilities and high-risk youth populations, from the Adler School of Professional Psychology in Toronto in 2006, and an Honours BA in Psychology from the University of Guelph in 2002.

Year 1 Award $22,000 Year 2 Award $22,000 Total Award: $44,000

Christine Cullion-Hicks believes that professionals treating people with Parkinson's disease are too focused on the way the symptoms of the disease restrict their patients' lives.

Instead, the University of Western Ontario graduate student in the School of Health and Rehabilitation Sciences thinks professionals need to consider whether people with Parkinson's feel as disabled as the textbooks say they should.

"People with Parkinson's can exceed the expectations that the diagnosis puts on them," Cullion-Hicks says.

That's why her research will try to identify the difference between the neurological, cognitive, functional, and biomechanical deficits that Parkinson's disease results in, and the way people with Parkinson's actually perceive those deficits.

For example, although people with Parkinson's may have a slow or halting gait, that deficit or disability might be perceived as more restrictive by a doctor or physiotherapist than by the person experiencing it, who might simply attribute their slowness to age.

That perception can, in turn, alter the way a person deals with their reality. Someone who accepts the medical model of the severity of their symptoms might find them more restrictive than someone who takes their symptoms in stride.

"I think people still believe that they are not as sick as what the doctor says," Cullion-Hicks explains. "I want to focus on the individual's voice versus the professional's voice and look at any discrepancies in how they're actually experiencing the deficit."

Cullion-Hicks' research will examine whether people with Parkinson's are living within the confines of their diagnosis, or not.

She will see about 50 people in her London, Ontario laboratory to measure their gait, the way they can perform activities of daily living, such as self-care, and their cognitive abilities. She will also spend time with the individuals in her study to talk to them and their caregivers, assessing the way they feel about their abilities, rather than just using a standard questionnaire that is one of the common tools health care professionals use to arrive at a description of people's deficits.

"That method may be too restrictive," Cullion-Hicks says. "We need to take time to talk to patients about what they actually feel."

Cullion-Hicks expects that her research will find that people consider themselves much less restricted than do the professionals. She hopes her findings will help improve the assessment, treatment and counselling that people with Parkinson's disease receive.

Cullion-Hicks, whose background is in psychology, has always been interested in the psychosocial domain of illness – how it affects the people experiencing it and their caregivers and family members. She brings that background to this project.

"People's reality is what's really important to them, and what they believe they can do is way more important than what the health professionals told them they can do," she says.

Harrison McCain Foundation
Graduate Student Award

Understanding the role of DJ-1 in Parkinson's disease: Role of VDAC1

Ms. Sarah Hewitt

Ms. Hewitt obtained her BSc, Honours in Biochemistry at the University of Ottawa and is currently a Master of Science student in Neuroscience. As the recipient of a Graduate Student Award, Ms. Hewitt will be training under the supervision of Dr. David Park.

Year 1 $15,000 Year 2 $15,000 Total Award: $30,000

Sarah Hewitt is a self-proclaimed science geek. As a child, she watched Popular Mechanics for Kids; as an adult, she is trying to decipher the genetic process involved in familial forms of Parkinson's disease.

The research that Hewitt, 24, conducts with a team at the University of Ottawa is a natural outgrowth of her childhood curiosity about how things work – in particular, the brain.

"It's the regulator of your entire body and the thing that defines who you are. I just find it really cool," she says.

Hewitt is exploring the relationship between a protein known as DJ-1, which has been linked to familial Parkinson's disease, and a protein called VDAC-1. She is pursuing a theory that DJ-1 plays a protective role in reducing cell death, particularly in certain dopamine-producing cells in the brain, the area most severely affected in Parkinson's disease.

In healthy people, DJ-1 appears to affect the mitochondria, the structures inside cells that convert energy, to help protect neurons and reduce cell death. People who have mutations in DJ-1 lose its protection. Mitochondria are also responsible for many other intricate processes such as the regulation of cell death. VDAC-1, a channel that sits on the outside of the mitochondria, appears to be an activating switch for cell death. Hewitt hopes to connect the dots between loss of DJ-1 and increased cell death through VDAC-1.

"The whole point of my research is to see if this interaction between DJ-1 and VDAC-1 has any merit," says Hewitt. "What I hope to find is an explanation of how DJ-1 protects the cell and its loss can in turn lead to Parkinson's disease."

Hewitt's results may suggest a new drug target or treatment for Parkinson's disease, or even the ability to prevent it. If researchers can determine how cell death occurs and then prevent that death, using targeted gene therapy, it would be a major advance.

Currently, about 10 percent of people who have Parkinson's disease have the familial form. Even if stem cell therapy were able to generate new cells in the affected region of the brain, people with mutations in DJ-1 would still eventually experience the degeneration of those new stem cells, without this gene's protection.

Hewitt, who hopes to enter a PhD program in neuroscience, did not know any people with Parkinson's disease when she began her studies. But she has been inspired by Shelby Hayter, a woman with Parkinson's who works with scientists to educate school children about the disease and help them participate in fund-raising for research directed at a cure. Hewitt has helped Hayter demonstrate projects for students in the University of Ottawa lab.

"The more people you can recruit to research, the better," Hewitt says.

IBM Employees Charitable Fund
Graduate Student Award

Exploring lysosomal cathepsins as candidate 'synucleinases'

Mr. Piotr Kolodziej

Mr. Kolodziej received his BSc from Carleton University in 2002 and is currently completing his Master of Science in Neurosciences. As the recipient of a Graduate Student Award, he will be training under the supervision of Dr. Michael Schlossmacher at the Ottawa Health Research Institute.

Year One Award $15,000 Year Two Award $15,000 Total Award: $30,000

Sometimes, researchers working on basic science problems that underpin the mechanisms of diseases can lose sight of the impact of those diseases on the people they're trying to help.

But not Piotr Kolodziej.

Kolodziej, a Master's student in neuroscience at the University of Ottawa, can put a personal face on his research into the roles that proteins play in Parkinson's disease. Several neurodegenerative diseases run in his family, and before he died, Kolodziej's grandfather was diagnosed with Parkinson's.

"Having the (family) connection makes the work more personal," Kolodziej says.

Kolodziej's research centres around a protein called alpha-synuclein, which is found within neurons. Having too much alpha-synuclein can kill brain cells, especially those producing dopamine, and strongly increases the chance of developing Parkinson's disease and affects its severity.

"It's broadly accepted to be a bad player in Parkinson's disease," Kolodziej says.

His work revolves around trying to encourage enzymes operating within vulnerable brain cells to degrade alpha-synuclein, clearing the protein out of the cells before it can kill them.

As part of a natural process, these enzymes digest proteins like alpha-synuclein, thereby lowering concentrations of the substrate protein within the cell. Kolodziej is trying to identify the exact enzymes and mechanisms involved in clearing out the troublesome alpha-synuclein. He hopes that in the future, researchers will be able enhance enzyme activity—through drugs or enzyme replacement therapy—to speed up or augment this process, so as to prevent the death of brain cells and slow or halt the onset of Parkinson's.

"We're identifying which (enzymes) are the most important within the human brain, and which are the most important within the substantia nigra," Kolodziej says.

So far, his team has found two enzymes that can reduce alpha-synuclein levels in cultured, dopamine-producing cells. Now he plans to examine how these enzymes work both on a molecular level and in mouse models. Ultimately, Kolodziej hopes his work will be able to help the growing numbers of people living with Parkinson's disease and other neurodegenerative disorders.

"As you get fewer and fewer communicative/contagious disorders and our population ages, the long-term chronic neurodegenerative disorders are going to take a greater and greater toll on our health care system. I think it's important to address," he says.

Graduate Student Award

Effect of dopaminergic medication on a finger-moving task in Parkinson's patients: an fMRI study

Ms. Kristina Martinu

Ms. Martinu obtained her BSc in Physiology from McGill University in 2006. She is currently pursuing her PhD, training under the supervision of Dr. Oury Monchi at the University of Montreal and Research Centre, Institut Universitaire de Gériatrie de Montréal.

Year 1 Award $15,000 Year 2 Award $15,000 Total Award: $30,000

One of the persistently perplexing challenges of treating people with Parkinson's disease is that the medication used to restore their mobility does not usually improve their cognitive symptoms.

Researchers are not sure why the drugs used to mimic the effects of dopamine affect only certain areas of the brain damaged by Parkinson's disease. But at the University of Montreal, PhD student Kristina Martinu is conducting research to try to find out more about how the brain circuitry affecting motor function responds to the medication.

Martinu is using magnetic resonance imaging to scan the brains of people with Parkinson's disease as they perform three different tasks, involving pressing coloured buttons in different sequences with their fingers.

By contrasting the brain scans as people with Parkinson's disease press buttons continuously, then press buttons as directed, and finally press buttons in a self-generated order, Martinu hopes to understand how externally triggered and self-initiated movements are processed differently in the brain of patients compared with those of participants who do not have the disease.

"We're also looking at the effect of medication on these tasks," Martinu says.

Finally, Martinu will also be trying to assess how different areas of the brain are activated by people whose Parkinson's disease affects one side of their body more than the other.

The eventual goal of the research is to see if researchers can tailor medication differently so that it affects one area of the brain more than another. The results of Martinu's analysis of the brain scans she collects might also be able to help researchers position electrodes as they conduct deep brain stimulation.

"If we can understand more about what the medication does and how it changes these (brain) activation patterns, we might be able to target the medication better to certain things," Martinu says.

Martinu, who is a physiologist, is intrigued by Parkinson's disease because it enables her to work directly with patients and try to make a difference in their lives.

"I enjoy the interaction with the patients," she says.

Funded by Parkinson Society of Southern Alberta

Graduate Student Award

Neural mechanisms for the therapeutic effects of posterior hypothalamic nucleus deep brain stimulation

Mr. Calvin Young

Mr. Young is currently pursuing his PhD at the University of Calgary. He received BSc's (Honours) in Biochemistry and Psychology in 2001 and 2002, as well as an MSc in Psychology in 2004 from the University of Otago, New Zealand. As the recipient of a Graduate Student Award, Mr. Young is training under the supervision of Dr. Brian Bland.

Year 1 Award $15,000 Year 2 Award $15,000 Total Award: $30,000

By inserting electrodes and stimulating the areas deep in the brain that Parkinson's disease affects, surgeons can often offer people relief from the tremors and rigidity that affect them. But for as many as 40 percent of people in the advanced stages of the disease, deep brain stimulation is less effective at helping them initiate or maintain movement.

At the University of Calgary, graduate student Calvin Young, 29, is experimenting with placing electrodes in a different part of the brain, to see if stimulating the neurons there can produce better symptom relief for more people with Parkinson's disease.

Working with rat models, Young has demonstrated that inserting electrodes into the posterior hypothalamic nucleus in the brain instead of the subthalamic nucleus, as is traditional, can produce spontaneous and increased levels of movements in the rodents. He uses two different rodent models – one with drug-induced Parkinson's symptoms, and one with brain lesions.

This type of deep brain stimulation is already used in people to relieve cluster headaches, and there are so far no side-effects of the continuous, long-term stimulation. But no one is yet stimulating this area of the brain to relieve symptoms of Parkinson's disease in people.

Young, who came to Canada from New Zealand in 2006, uses a form of functional brain imaging combined with the electrical stimulation to determine exactly what biological mechanisms in the brain are involved, and how the stimulation works to relieve the motor symptoms.

"If you look at more traditional stimulation, a lot of people report depression and gambling problems (that result)," says Young. "That's why it's important to do the basic science and find out how it works, to apply it better so we don't get some side-effects that come with just passing current through the brain."

Young hopes that his work will help determine the best placement of electrodes for the maximum benefit of people with Parkinson's disease, without causing some of the impulsive control or emotional reactions that may result from placing the electrodes in other parts of the brain.

Parkinson's disease has always frustrated Young, an electrophysiologist, because of its effects on people who develop it, and on their families.

"Their health is otherwise intact, but they have this problem being mobile and functional, which has a lot of impact, not only on families but on society as well," he says.

The John Woodley
New Investigator
Award **

Understanding the action of the mitochondrial rhomboid protease in Parkinson's disease

Dr. Angus McQuibban

Dr. McQuibban obtained his PhD from the University of British Columbia and completed his Post Doctoral training under the supervision of Dr. Matthew Freeman at the MRC-Laboratory of Molecular Biology, Cambridge, UK. Dr. McQuibban is currently an Assistant Professor at the University of Toronto in the Department of Biochemistry.

** Year 2 of two year award 2008-2010

Year 1 $45,000 Year 2 $45,000 Total Award: $90,000

Deep inside each cell, tiny powerhouses known as mitochondria provide the energy the cell needs to move, divide and grow. In a laboratory at the University of Toronto, molecular biologist Dr. Angus McQuibban is delving into the role that mitochondria play in the genes involved in Parkinson's disease.

Researchers already know that Parkinson's is caused by the degeneration of nerve cells inside the substantia nigra, the part of the brain that controls movement. They don't yet know exactly what causes those neural cells to degenerate, and they haven't identified all of the genes involved in the disease.

"The cell is a complicated place," says McQuibban. "It's uncommon for there to be a single (genetic) cause for a single disease. We do know that the mitochondria, as a sub-cellular engine, are very important in Parkinson's disease. That's one place to really start looking."

So that's what McQuibban is doing. He's focusing on one particular gene that makes a protein called rhomboid, that is found in the mitochondria of brain cells. Specifically, McQuibban is trying to uncover the role that rhomboid plays in interacting with another protein, the PTEN-induced putative kinase 1 (PINK) gene.

Other researchers have already identified mutations in the PINK gene that can cause the inherited, or familial form of Parkinson's. In animal models, fruit flies without a working PINK1 gene have defects in mitochondria. That results in muscle problems, and degeneration of the brain cells that produce dopamine.

The rhomboid protein cuts the PINK protein into two pieces and alters its activity. By unlocking the role that each of these proteins plays in the signalling cascade, or chain reaction that occurs within the brain of people with Parkinson's, McQuibban and other researchers hope to determine the exact genetic causes of the disease. If they can locate defects in the genes that lead to Parkinson's, they may eventually be able to produce new drugs.

"We think rhomboid will be one of these genes that can contribute to the disease but we have to prove it," McQuibban says.

McQuibban is motivated by his constant desire to understand how things work – from the bicycle he rode to work to the mitochondria in cells. His work on the mitochondrial rhomboid led him towards Parkinson's disease, but it may also eventually pay off for other neuro-degenerative diseases, including Alzheimer's.

Eventually, he hopes drugs will be able to "turn off or turn on" the genes and proteins needed to repair neural damage, or to prevent it.

Psychosocial Research Grant **
Co-funded by CIHR Institute of Neurosciences, Mental Health and Addiction.

MRI and virtual navigational strategies in Parkinson's disease

Dr. Veronique Bohbot

Dr. Bohbot received her BA in Psychology from McGill University and obtained both her MA and PhD in the area of Experimental Psychology from the University of Arizona. She undertook her Postdoctoral training in Neuropsychology at the Montreal Neurological Institute. Dr. Bohbot is currently an Assistant Professor, Clinical Research at the Douglas Hospital Research Centre and is also a lecturer for the Departments of Psychology and Neurosciences, McGill University.

** Year 2 of two year award 2008-2010

Year 1 $48,388 Year 2 $51,622 Total Award: $100,010

Psychologist Veronique Bohbot is an expert in how people use their brains to help them navigate the world.

She hopes to put that expertise to work to help people with Parkinson's strengthen one area of their brain.

Bohbot has used Magnetic Resonance Imaging (MRI) scans to discover that people use two different strategies, involving two different areas of the brain, to navigate. Some people create a mental map that shows them the relationship between where they are and where they are going. They visualize that map before they head home from work, for example. That spatial strategy involves using the part of the brain known as the hippocampus.

Imaging scans have demonstrated that people who use spatial strategies have more grey matter in their hippocampus than people who don't, Bohbot says.

Other people use what's called a stimulus response strategy to navigate – they simply memorize a series of left and right turns, and depend on travelling the same route. Stimulus-response strategies use the part of the brain called the caudate nucleus, located in the basal ganglia. People who rely on stimulus response strategies have more grey matter in the caudate nucleus than those who use spatial strategies.

Ideally, people should be able to shift between one strategy and the other, Bohbot says.

"Both areas of the brain are important and we have to use them both," she says.

But often, people are so accustomed to relying on one strategy they don't know how to shift to another one. That's why Bohbot has developed a program to teach people who rely on stimulus response strategies (the caudate nucleus) how to shift to spatial strategies, giving their hippocampus some exercise. The program involves having people look at different landmarks, or details in their environment, estimate distances between them and visualize the relationships among them.

Bohbot is now using MRI scans to see if Parkinson's patients use these two different strategies – which she suspects they do. In some people with Parkinson's their hippocampus may have atrophied, because they are not using a spatial strategy to navigate.

Bohbot hopes to eventually train Parkinson's patients to use spatial strategies, thus strengthening their hippocampus, the same structure in the brain that's involved in building the relationships needed for good episodic memory, and for making associations among people, objects and places.

"If we have two different strategies, and we can train them (people with Parkinson's) to use one that is not dependent on the caudate nucleus, maybe we can help them have better lives," Bohbot says.

Bohbot became a researcher because she was inspired by Marie Curie, a role model who sparked Bohbot's interest in both physics and psychology. Eventually, psychology won out because Bohbot decided she wanted to work with people, rather than isolating herself in a laboratory. She was drawn to research involving memory because of her fascination with stories about patients with amnesia who learned complex tasks by repetition and automatic behaviour.

Recently, her father's diagnosis of Parkinson's has lent an additional poignancy to Bohbot's work. Although too late to help him, she hopes her plans to help people with this disease, by training and regaining the use of part of their brain, will make a difference in their lives.

Basic Research Fellowship **

Characterization of a novel interaction between parkin and puromycin-sensitive aminopeptidase in Parkinson's disease

Dr. Antoine Duquette

Dr. Duquette obtained his MD from the University of Montreal in 2002. He continued immediately with his education and studied for his MSc in Neurological Sciences simultaneously with a residency in Neurology which he completed in 2005 and 2008 respectively. Dr. Duquette is currently a Post Doctoral Fellow training under the supervision of Dr. Edward Fon at the Montreal Neurological Institute.

** Year 2 of two year award 2008-2010

Year 1 $50,000 Year 2 $50,000 Total Award: $100,000

Dr. Antoine Duquette recently had to tell the father of a close friend that he was in the early stages of Parkinson's disease. He remembers it vividly.

"It was hard," says Duquette, a neurologist who is working on his PhD during a basic research fellowship at McGill University. "It gets very frustrating to know that, when you're with a patient, you can help a lot with the symptoms, but you can't change the whole process that is active in those patients."

That frustration is one of the reasons Duquette turned to research into the causes of Parkinson's disease. The research provides both him and his patients with room to hope, even if a cure remains elusive.

Duquette's investigations focus around a poorly understood protein known as puromycin-sensitive aminopeptidase – PSA. Other researchers have already concluded that another protein – parkin – is responsible for inherited forms of Parkinson's disease. Duquette is looking at PSA because of its suspected interaction with parkin in brain cells affected by Parkinson's disease.

"What makes this protein very interesting is that it may also play a role in Alzheimer's disease and in another family of diseases which includes Huntington's disease," says Duquette. "It would be interesting and quite surprising if it was also implicated in Parkinson's disease."

PSA has been shown to play a protective role in fruit flies that have been genetically altered to display symptoms of Alzheimer's disease, by destroying toxic compounds in cells.

"Since it (PSA) possibly binds with parkin, which has been implicated in Parkinson's, maybe the toxicity that's associated with parkin can also be rescued by PSA," Duquette explains.

If that's true, researchers might then be able to design a drug that would increase the expression of PSA, to protect against the toxicity that appears to be killing dopamine-producing brain cells in people with Parkinson's.

Proteins are a critical focus of Parkinson's research because they are essential to every aspect of the human body's function. If a single protein in a cell or group of cells is damaged or stops working, the chain reaction among connected proteins can affect the entire system.

That's why Duquette's research into PSA is important to understanding – and eventually halting – the progression of Parkinson's disease.

"If we can demonstrate that it does play a role, it could be a therapeutic target," he says.

Basic Research Fellowship **

Evolution of cognitive impairments in Parkinson's disease

Dr. Thomas Jubault

Dr. Jubault received his MSc and PhD in Cognitive Sciences from L'Université Pierre et Marie Curie in Paris, France. He is currently a Post Doctoral Fellow at the PCAN laboratory at the Centre de Recherche de L'Institut Universitaire de Gériatrie de Montréal studying under the supervision of Dr. Oury Monchi.

** Year 2 of two year award 2008-2010

Year 1 $40,000 Year 2 $50,000 Total Award: $90,000

One of the enduring mysteries surrounding Parkinson's disease is why some people with this illness develop dementia, while the cognitive functions of others are not affected. At the Institut Universitaire de Gériatrie de Montréal, Dr. Thomas Jubault is using new imaging techniques to try to answer this question.

"There clearly exist different subtypes of Parkinson's disease," says Jubault, a post-doctoral fellow in neuro-imaging. Those subtypes would include the 30-40 percent of patients who eventually develop dementia, and the other patients who do not.

"We know it has to be related to some kind of different evolution of the illness," he says. But researchers don't yet know which pathways in the brain are involved in the various subtypes.

Jubault will follow a group of people with Parkinson's for three years, using two new kinds of brain imaging techniques to map the pathways, or communication channels, among cells in the substantia nigra, the region of the brain where Parkinson's occurs.

The first technique is called Diffusion Tensor Imaging – DTI – and the second is Magnetization Transfer Imaging – MTI. The new techniques will give Jubault access to data about the health of brain cells at the micro-structural level, so he can analyze whether cell membranes are intact or beginning to deteriorate.

Along with the non-invasive brain scans, Jubault's team will also administer a battery of neuropsychological tests to assess the memory, language, and executive brain functions of the people in his study, to see how well they plan and strategize. Combining those test results with the brain imaging scans will help to separate the subtypes and relate them to different types of deterioration in the brain, Jubault says.

Eventually, Jubault hopes the imaging techniques can be used as a tool to diagnose Parkinson's earlier before the onset of the tremors, rigidity or other motor function problems that are actually later symptoms of the disease, but are usually the ones that first trigger a diagnosis.

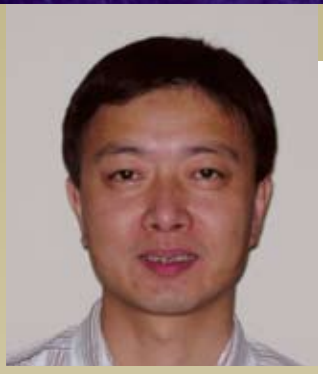
The researcher also hopes his findings will contribute to the growing body of knowledge about Parkinson's that will eventually lead to a cure.

Jubault, who has a cousin with Parkinson's disease, is motivated by his dedication to help people with this illness.

He's also encouraged by the speed with which research in Parkinson's is progressing, he says. "I'm quite optimistic."

Basic Research Fellowship **

Role of DJ-1 in Nrf2-Cdk5-Prx2 signaling



Dr. Dianbo Qu

Dr. Qu received his BSc from Wuhan University, and his MSc in Molecular Biology at the Institute of Biotechnology in China. He completed his PhD in Neurobiochemistry at the National University of Singapore and is currently a Post Doctoral Fellow training under the supervision of Dr. David Park at the University of Ottawa.

** Year 2 of two year award 2008-2010

Year 1 $37,500 Year 2 $50,000 Total Award: $87,500

Unlocking the puzzle of Parkinson's disease is all about relationships – the relationships among genes, proteins and pathways in the brain. At the Ottawa Health Research Institute, neuroscientist Dianbo Qu is examining the relationship between proteins that may protect against the death of critical brain cells.

The targets of Qu's investigation are two proteins: cdk5 and Prx2, and their relationship with a gene called DJ-1, whose mutation results in early onset Parkinson's disease.

Qu, a specialist in neurobiochemistry and neuropathology, is trying to determine how cdk5 and Prx2 regulate each other and work with DJ-1 to rescue the dopamine-producing brain cells whose death contributes to Parkinson's disease.

In animal models, over-expressing the protein Prx2 can stop the death of brain cells affected by MPTP, a chemical known to induce Parkinson-like symptoms.

Qu believes Prx2, working with DJ-1, is part of a natural repair process in cells that is triggered when they come under stress. If the dopamine-producing neurons that are under stress cannot remove all of the toxicities, then the neurons die. That results in Parkinson's disease. That stress might come from the cells' response to neurotoxins, or to mutations in genes. Researchers don't yet know the exact mechanism is that triggers each part of the process that reacts to the stress and produces the repair function.

"We hope if we can identify the relationship between Prx2 and DJ-1, we can find the exact pathway to regulate neurodegeneration," Qu says.

Mapping the mechanisms and the relationship might also give the researchers the clue to how to trigger the repair process when they need to turn it "on."

Their hope is to find a potential target for drug therapy in the future.

Qu came to Canada from Singapore, where he had done initial research on cdk5, which plays an important role in neurodevelopment and neurodegeneration. He was interested in why cdk5, like Jekyll and Hyde, plays opposite roles. When he discovered that Dr. David Park – another Parkinson's grant recipient – was working on cdk5's function in Parkinson's disease, he came to Canada and joined him for a post-doctoral fellowship to unravel the mysterious cdk5.

His interest in biology and in understanding the nature of human beings led him to his work on the brain and to Parkinson's disease research.

"To know the nature of ourselves – that is what I like," Qu says.

Basic Research Fellowship **

Investigation of how a-synuclein forms Lewy bodies and how mutations in a-synuclein gene promote PD pathology

Year 1 $40,000 Year 2 $40,000 Total Award: $80,000

Dr. Hamid Qureshi

Dr. Qureshi obtained his BSc and MSc at the University of the Punjab and an MPhil at the University of Agriculture in Pakistan. Dr. Qureshi was a visiting scholar in Dr. Hemant Paudel's laboratory at the Lady Davis Institute for Medical Research in the Departments of Neurology and Neurosurgery and completed his PhD at the University of Montreal with Dr. Zafarullah. He is currently a Post Doctoral Fellow training under the supervision of Dr. Paudel.

** Year 2 of two year award 2008-2010

Dr. Hamid Qureshi's inspiration for researching the causes of Parkinson's disease comes from the public struggles of two celebrities grappling with the illness: former World Heavyweight Champion Muhammed Ali, and actor Michael J. Fox.

Even in Qureshi's native Pakistan, Ali is well-known, and he learned about Fox when he came to North America. Both men, who have spoken publicly about Parkinson's and, particularly in Fox's case, worked hard to raise money for research, made Qureshi want to focus his skills on defeating the disease, he says.

At the Lady Davis Institute, housed in Montreal's Jewish General Hospital, Qureshi is exploring the way that two proteins, tau and alpha-synuclein, interact to contribute to the death of dopamine-producing brain cells in people with Parkinson's. He's particularly interested in the role the proteins play in the formation of Lewy bodies, the abnormal clumps of fibrous structure found inside the neurons of people with Parkinson's.

One of the components of the Lewy bodies is the alpha-synuclein protein. Qureshi's goal is to determine how mutations in the genes that regulate these proteins promote the formation of Lewy bodies in animal and cell models, by observing three different mutations of alpha-synuclein as they occur.

"To understand the molecular mechanism is very important," Qureshi says. "Then we will be able to design some new therapies."

Those new therapies would be designed to disrupt the reaction that produces the Lewy bodies, which could be either a protective response to damage to the cells, or the cause of the cell death itself.

Qureshi came to Canada to earn his PhD in biomedical sciences and to pursue research.

"I've always been fascinated by medical science. I wanted to help people suffering from disease," Qureshi says.

Basic Research Fellowship **

Characterizing Parkinson's-linked SNCA gene expression by GATA transcription factors

Year 1 $40,000 Year 2 $40,000 Total Award: $80,000

Dr. Julianna Tomlinson

Dr. Tomlinson completed an Honours BSc and PhD in Biochemistry at the University of Ottawa. She is currently a Post Doctoral Fellow at the Ottawa Health Research Institute in the Division of Neurosciences training under the supervision of Dr. Michael Schlossmacher.

** Year 2 of two year award 2008-2010

Never underestimate the influence of a co-operative learning placement. That's what sparked Dr. Julianna Tomlinson's interest in a career in biochemistry and neuroscience.

Tomlinson was still in high school when she accepted a placement in Robert Haché's laboratory at the University of Ottawa. There, as she ran small experiments and helped other scientists with their projects, Tomlinson began her first research into the mechanisms that regulate gene expression. She's particularly interested in transcription – the process of turning on a gene to express more of that gene product.

Today, at the Ottawa Health Research Institute, Tomlinson is putting that expertise to work to identify the mechanisms in the brain that regulate the expression of alpha-synuclein, a critical protein that has been linked to the development of Parkinson's disease.

"There's a strong genetic link between how many copies of that gene an individual carries and the development of the disease," says Tomlinson. The more alpha-synuclein that a person's brain produces, the greater chance they have of developing Parkinson's disease, she adds.

"But very little is known about how the gene is regulated – how it's turned on or off."

Tomlinson's current research builds on work her supervisor, Dr. Michael Schlossmacher, and his colleagues did to identify a family of proteins that regulate the production of alpha-synuclein. These proteins are called the GATA proteins.

Working with a bank of brain tissue from Parkinson's patient and comparing that to tissue from the brains of people who did not have Parkinson's, Tomlinson will try to better characterize the role of the GATA proteins and their relationship to alpha-synuclein. It's an excellent use of the gene transcription skills she first began to develop as a high school co-op student.

"If we can understand how the expression of alpha-synuclein is regulated, then we may be able to interfere with this process and reduce alpha-synuclein production. Targeting the players involved in this pathway could potentially lead to new therapeutic approaches designed to lower alpha-synuclein production in patients with Parkinson's disease."

Since coming to work on this project with Dr. Schlossmacher, Tomlinson has met people with Parkinson's disease and learned about the realities of their lives. That has solidified her determination to use her skills to work toward the challenge of finding a cure.

"It's been really rewarding," she says.

Basic Research Fellowship **

Partially supported by the Catherine and Maxwell Meighen Foundation

The role of the interaction between feritin and alpha synuclein (α-syn) in Parkinson's disease

Year 1 $50,000 Year 2 $50,000 Total Award: $100,000

Dr. Naomi Visanji

Dr. Visanji received her Honours BSc in Neuroscience at the University of Nottingham in the UK in the Department of Biomedical Science. She completed her PhD in Pharmacology at the University of London. From 2004-2007 she was a Post Doctoral Fellow at the Toronto Western Research Institute. Dr. Visanji is currently training under the supervision of Dr. Anurag Tandon at the University of Toronto.

** Year 2 of two year award 2008-2010

When Dr. Naomi Visanji was eight years old, living in her native Winchester, England, her favourite toy was a chemistry set. Today, as a post-doctoral fellow at the University of Toronto, she's still preoccupied with chemistry – the chemistry of the brain.

Visanji, now a neuroscientist, is investigating the interaction between two proteins considered important to understanding the cause and progression of Parkinson's disease. The first protein is alpha-synuclein, which is always present in brain cells, but clumps together in the neurons of people with Parkinson's disease.

"The jury is still out on whether the clumps themselves are toxic, or whether the cells have put them into these clumps to help deal with the excess of the synuclein," says Visanji.

Researchers at the University of Toronto have recently discovered that alpha-synuclein binds to other proteins, including feritin, the second protein on Visanji's agenda. Feritin stores iron, to release it when a cell needs it. But too much iron is dangerous – and the dying dopamine-producing cells implicated in Parkinson's disease have also been found to be much richer in iron than the average cell.

"A major theory at the moment is that the amount of iron in those cells is what makes them vulnerable and what makes them die," Visanji explains.

By figuring out how feritin and alpha-synuclein interact, Visanji hopes to find a common pathway that leads to the death of the dopamine-producing cells.

"By doing that, we may be able to find ways to stop that happening," she says.

Along the way, Visanji may uncover mechanisms that shed light on another disease that produces symptoms similar to Parkinson's. Neuroferitiniopathy is a movement disorder caused by a genetic mutation in the feritin protein. The disease, which is rare, provides more evidence of the important role of iron metabolism in these kinds of neurodegenerative diseases.

Visanji believes the interaction between alpha-synuclein and feritin may be key to unlocking both diseases.

Longterm, Visanji is hoping to uncover a mechanism that can be targeted to prevent the degenerative process that is Parkinson's disease. She is fascinated by Parkinson's – just as she was by her chemistry set – because of the scope of the problem. The small, relatively specific area of the brain that degenerates and the relatively small cell population involved make it seem possible to figure out and prevent the cause or causes of the disease.

"It feels like it's curable," she says.

Catherine and Maxwell Meighen
Graduate Student Award **

How Parkin mutations result in Autosomal Recessive Juvenile Parkinson's disease

Ms. Ventzislava Hristova

Ms. Hristova obtained her Honours BSc in Chemistry and Biochemistry in 2004 from the University of Western Ontario and is currently a PhD student studying under the supervision of Dr. Jane Rylett and Dr. Gary Shaw in the Department of Biochemistry also at the University of Western Ontario.

** Year 2 of two year award 2008-2010

Year 1 $15,000 Year 2 $15,000 Total Award: $30,000

Ventzislava Hristova was just four years old when her grandfather died from Parkinson's, back in her native Bulgaria. The knowledge that the disease affected her family prompted Hristova's determination to discover its origins – and spawned a promising research career.

Hristova, 26, is working on her doctorate in biochemistry at the University of Western Ontario in London, Ont. She's concentrating on characterizing a protein called parkin that is implicated in the cause of Autosomal Recessive Juvenile Parkinson's (ARJP), a type of Parkinson's disease that appears in people at an early age.

Many people with ARJP, who may begin experiencing the tremors, muscle spasms and rigidity that are symptomatic of Parkinson's in their 20s, have a mutation in the park2 gene. That gene is responsible for producing parkin.

Proteins are three-dimensional structures. Hristova's research involves learning about the physical structure of parkin, and how mutations affect its three-dimensional fold, which then prevents it from carrying out its normal activity in a cell.

"The question is what this (mutated) parkin protein does to cause the death of the neurons in a certain region of the brain (the substantia nigra)," says Hristova.

"If we learn more about how the protein is folded and what it does in neuronal cells, we will have an idea of how the various mutations affect protein structure and activity."

When researchers figure that out, "we will learn how the neural degeneration begins and how the death of these cells is triggered," Hristova says. "Once we learn the cause and the mechanism of the neural degeneration behind AJRP, we can learn how to treat and manage it and hopefully even prevent it."

The structure of the protein is critical, because that will eventually become the target of any new drug, says Hristova. Any drugs that are developed and tested will target the pathways with which the parkin protein is involved.

For Hristova, whose family moved to Canada when she was 14, joining the legions of researchers working on Parkinson's is a way of contributing to the illness that has affected her family. Although she doesn't know what form of Parkinson's her grandfather had or whether it is an inherited type, the possibility that one day she or someone else in her family could be affected is always in the back of her mind. She hopes her work will help solve the puzzle and eventually lead her into clinical trials and drug-testing.

"I realize thousands of people are working on Parkinson's disease, but in the long run my little contribution will contribute to bettering the lives of those people affected by Parkinson's disease," she says.

Parkinson Post Subscriber Graduate Student Award **

The role of Pitx3 in the survival of midbrain dopamine neurons that are afflicted in Parkinson disease

Mr. Khanh Nguyen

Mr. Nguyen received his BSc in Physiology and Neuroscience, and his MSc in Neurological Sciences both from McGill University. He is currently a PhD student in Neurological Sciences at McGill University studying under the supervision of Dr. Abbas Sadikot.

** Year 2 of two year award 2008-2010

Year 1 $15,000 Year 2 $15,000 Total Award: $30,000

Ken Nguyen has always believed that to truly understand something, he must first take it apart and learn the function of each component. Only then can he put it back together and know how each part works in unison.

It's a principle Nguyen used to fix his bicycles. Now he's applying the same method to understand the human brain.

Nguyen, a doctoral candidate in neurological sciences at the Montreal Neurological Institute, is studying the reason that dopamine-producing neurons die in Parkinson's disease. He's doing that by "taking apart" a component in those neurons: a protein known as Pitx3.

"This protein is expressed only in the dopamine neurons and not in any other neurons in the brain," says Nguyen. "This piques our interest."

The Pitx3 seems to control other proteins that help the dopamine-producing brain cells survive, says Nguyen. Researchers theorize that Pitx3 may be activating survival systems specifically in these brain cells. Mutations in Pitx3 may fail to activate the survival systems, causing the dopamine-producing brain cells to die, and resulting in Parkinson's.

If Nguyen can help to establish Pitx3's importance, it could become an important target for drug or gene therapy. Increasing the amount of Pitx3 that is expressed, or boosting its function, might then protect the dopamine neurons.

"Several papers have shown that Pitx3 in humans is genetically related to Parkinson's disease and increases the susceptibility to Parkinson's disease," Nguyen says. His goal is to establish that relationship more firmly, to decipher the workings of the Pitx3 and the survival systems in dopamine-producing neurons, and to find a highly specific avenue for treatment.

Nguyen was motivated to study Parkinson's disease because of his desire to take apart and repair things, starting with the brain, the most vital of human organs. Because in Parkinson's one main area of the brain – the substantia nigra – is involved, Nguyen was drawn to the well-defined scope of the research.

"It seems that we have a firm understanding at least of where the major problem lies, and we can (already) fix it to some extent," Nguyen says. "I believe that with this research we are doing we can fix it in a more targeted manner."

Just like his bicycle.

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Every year, individuals, foundations, corporations and employee groups generously support the best Parkinson's research and researchers across Canada.

Parkinson Society Canada and our 12 regional partners gratefully acknowledge these generous contributions. With the support and funding of committed Canadians, together we provide hope for the future for people living with Parkinson's and their families.

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