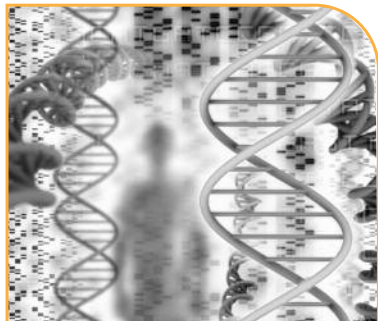


## Genetics: A Foundation for Future Parkinson's Treatments

By Matthew Farrer, Ph.D.

A decade or so ago, medical textbooks and most practicing neurologists held the view that Parkinson's disease (PD) occurred sporadically. Environmental toxins, such as pesticides, were considered the most important risk factors, despite the difficulty in measuring a person's lifetime exposure. In contrast, genetic risk factors were thought unlikely, given that Parkinson's



disease rarely affected identical twins at the same age. Researchers debated the issue for several decades until genetic studies revealed that the DNA we inherit contributes to our susceptibility for Parkinson's disease.

In contrast to environmental exposures, an individual's DNA can be reliably measured. Using modern technologies, scientists are able to study

the genes of families as well as thousands of individuals. More than 20 regions of the human genome have been found to be "associated" with Parkinson's disease, and in many of these, "causal" gene mutations have been identified.

Mutations that are "causal" lead to inherited disease down a family line. These are found in only about one to two percent of people with Parkinson's. By contrast, those variants that are "associated" — also known as "common variants" — do not directly cause Parkinson's but contribute to disease susceptibility. While the contribution is modest for an individual, the risk that may be attributed across a population is considerable.

Together, these genetic discoveries provide a "molecular foundation" on which to build novel treatments for Parkinson's. The rationale is as follows: if we can determine what it is that causes the problem, or what it is that predisposes individuals to disease susceptibility, we can develop more effective medications to tackle the symptoms and to slow — and perhaps to halt — the progression of Parkinson's. >> Read more on page 6

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### Science News |

#### US Food and Drug Administration Holds Hearing on Parkinson's Drug

On October 17, an advisory committee to the United States Food and Drug Administration (FDA) met to hear public commentary on the request by Teva Pharmaceutical Industries, the manufacturer of rasagiline (Azilect®), for a label change indicating that the drug "slows the clinical progression of Parkinson's." The manufacturer based its request on two large-scale research studies that it says indicate the medication does more than ease the symptoms of Parkinson's. The hearing included a day of debate amongst doctors, >> Read more on page 8

#### New Hope For Parkinson's Stem Cell Therapy

Scientists funded in part by the Parkinson's Disease Foundation announced in the November issue of *Nature*, that they have made an important step towards stem cell treatment for Parkinson's disease (PD). Pluripotent stem cells, such as those derived from embryos and more recently induced from adult skin cells, have the potential to develop into nearly any cell type. For this reason, they could potentially serve as unlimited sources of healthy new cells to treat diseases including Parkinson's. However, scientists have had trouble transforming stem >> Read more on page 8

## Letter from the Executive Director

Dear Friends,

There are three points to be made about genetics and Parkinson's. The **first** is that very few cases of Parkinson's — probably less than five percent — are directly determined by genes. The **second** is that although genetic factors in Parkinson's do not cause the disease in most cases, they do shine a powerful spotlight on the pathways that lead

"We urge you to learn more about the exciting potential of genetics and Parkinson's."

Robin Elliott



to Parkinson's. And the **third** is that no area of science has been more astonishingly productive in the modern history of Parkinson's science than the study of genetics.

Just think: a decade and a half ago, scientists did not know of a single gene linked to Parkinson's. Today, we have more than twenty!

It is fitting that we lead off this issue of *News & Review* with a fascinating and comprehensive article by one of the most accomplished leaders in this area of science, Matthew Farrer, Ph.D. We also thought Matt's terrific overview would provide a good opportunity for us to tell our readers about the contributions PDF has made — with your support — to this important area of Parkinson's science.

For many years, PDF has helped support studies of the basic science and clinical genetics of Parkinson's

through its grants to scientific teams and individual investigators, such as Christine Klein, M.D., whose work is featured on page 3.

Early in 2012, PDF is initiating a multi-million multi-year interdisciplinary Parkinson's clinical genetics research program. We will bring together several of the intellectual powerhouses in the New York metropolitan area to create a consortium — named for Lucien Côté, M.D., a beloved Parkinson's doctor — for Parkinson's genetics. Our aim — similar to that expressed by Dr. Klein — is to learn as much as we can about genetics and Parkinson's disease and apply those lessons to improving treatment for those living with the disease **today**. One of our first projects will be to fund the work of some of the brightest young investigators in this field.

We hope you will find these articles of interest. We also invite you this time of year to contact us to order two free seasonal publications. The first, our annual *Creativity Calendar*, features the inspiring work of 13 artists living with Parkinson's. The second is our annual *Parkinson's Awareness Toolkit*, which will help you prepare your own activities during Parkinson's Awareness Month in April 2012.

On behalf of my staff colleagues, Board leaders and scientific collaborators at PDF, may I wish all of our readers a joyful and healthy holiday season and a great start to 2012.

Robin Anthony Elliott  
Executive Director

## In our Inbox

### Readers Respond to Fall 2011 Newsletter

I wanted to express to you how much I enjoyed, "A Note to My Friends About Parkinson's." Mr. Gall managed to describe a rather complex disease in simple terms in approximately twelve paragraphs! He included facts, details, humor and a revealing "self portrait" of a man coping with a serious disease. Very impressive!

Murlowe L. von Stuck, Ph.D., D.Min., via email

Great story by Peter Gall in *PDF News & Review* ... uplifting ... can relate.

Sandra Milner Adams, via Facebook

Mr. Elliott, your article entitled, "The Problem of Failed Trials: One Piece of the Solution," was brilliant! I am totally in agreement with every point on which you elaborated. I like what you said, "engaging people living with Parkinson's in research decision-making is not just a warm and fuzzy idea; it is a vital means to improving the design, conduct and outcomes of clinical research down the road." I have been saying this for years! And I am honored to be a part of this group of "scientists."

Peggy Willocks, PDF People with Parkinson's Advisory Council Member and Research Advocate, via Email

### PDF Research Advocates Use Twitter to Wish Luck to Newest Colleagues

Have a great session [at the Learning Institute]! 27 lucky people will have a transformational experience!

Diane Cook, (@newPWP), via Twitter

Best wishes for a successful Learning Institute that started today. Looking forward to working with the newest group.

Israel Robledo, (@pd2007), via Twitter

*Diane and Israel are PDF Research Advocates who underwent training via the Learning Institute (see page 9 for more information).*

Share comments and suggestions with the Parkinson's Disease Foundation at 1359 Broadway, Suite 1509, New York, NY 10018, info@pdf.org or (800) 457-6676.



www.pdf.org

## Bringing Genetics to the Clinic

Among the most exciting advances in Parkinson's disease (PD) research in the last decade has been the discovery of several genes that are linked to the disease. Yet very few diagnoses of Parkinson's — perhaps only five percent — can be attributed wholly to faulty genes (see the article by Dr. Matthew Farrer on page 1).

The research of PDF-funded investigator Christine Klein, M.D., has helped to translate the fruits of genetic discoveries in the lab to benefit people with Parkinson's disease in the clinic. She received the first of her two PDF International Research Grants in 2001 (the other came in 2003), at a time when she was just establishing herself as an independent researcher. The PDF grants enable scientists at the early stages of their careers to test

*"I'm trying to bridge the gap between clinical findings and research, and then back again."*

**Christine Klein, M.D.**



original ideas and build the preliminary data that are required for larger grants from major funding sources.

Dr. Klein became interested in Parkinson's genetics in the late 1990s, just as the field was opening up. While working as a postdoctoral fellow in a group led by Xandra Breakefield, Ph.D., at Harvard Medical School, she learned of a family in which many members had a form of Parkinson's and found out that it was caused by a newly discovered gene called *Parkin*. It was the second Parkinson's-related gene to be discovered. (The first, alpha-synuclein, was reported in 1997 by a team led by Roger Duvoisin, M.D., the first postdoctoral fellow supported by PDF in 1962.)

At the time Dr. Klein began her PDF-funded work on this family, certain mutations in *Parkin* had already been linked to Parkinson's. Such mutations are a kind of "spelling error" — that is, changes in the sequence of letters that stand for a gene's molecular components.

Dr. Klein found an entirely different set of mutations: deletions and duplications of entire sections of the gene. It turns out that such deletions and duplications make up about 80 percent of all *Parkin* mutations.

Dr. Klein's discoveries did not end there; she helped to develop the first "assay," or small-scale genetic test, that would identify people who have *Parkin* mutations. She published these discoveries in 2001. Her findings led to accurate and sensitive genetic tests for the gene.

Today, Dr. Klein is a professor at the University of Lübeck, Germany, and is building upon these earlier discoveries (being able to identify people whose Parkinson's is caused by *Parkin*), to study the brain changes in Parkinson's and to improve care for her patients.

In one approach, she uses imaging techniques such as MRI and PET scans to compare the brains of people with Parkinson's caused by *Parkin* with those of people who carry *Parkin* mutations but have not yet developed symptoms of Parkinson's. The hope is to identify brain changes that occur early in the disease, before motor symptoms develop. This would allow for early diagnosis and also shed light on how the brains of people with Parkinson's are altered by the disease.

As a clinician, Dr. Klein is always concerned with what her genetics research means for her patients. "Recently I have seen three young women with a diagnosis of *Parkin* mutations," says Dr. Klein. "They wanted answers. Knowing that they had these mutations, they could put a name to the disease, and I could counsel them that this form of Parkinson's disease responds well to medications and rarely leads to dementia."

With these projects and others, she says, "I'm trying to bridge the gap between clinical findings and research, and then back again."

*Dr. Klein is head of the Research Group on Clinical and Molecular Neurogenetics at the University of Lübeck in Germany. Her work was funded through the International Research Grants Program. In FY2012, PDF is supporting the program with \$825,000.*

## Bring the Parkinson's Quilt to Your Community this April!

**April 2012 is Parkinson's Awareness Month.** Display the Parkinson's Quilt to show the impact of Parkinson's on your community.

*Blocks of the quilt are available to rent from PDF for a modest fee.*

**(800) 457-6676 | [www.pdf.org/quilt](http://www.pdf.org/quilt) | [quilt@pdf.org](mailto:quilt@pdf.org)**



# Understanding Pain in Parkinson's Disease

By Jeffrey Wertheimer, Ph.D.

Pain is the most common reason people in the United States visit their doctors each year. Although pain is highly subjective and difficult to describe, a working definition is “an unpleasant sensory and emotional experience associated with actual or potential physical damage.” Its components are physical, cognitive, behavioral, emotional and perceptual.

Among people who have Parkinson's disease (PD), pain is a major complaint. In fact, up to 85 percent of people with Parkinson's report pain as a troubling

*"[Up] to 85 percent of people with Parkinson's report pain as a troubling symptom"*

Jeffrey Wertheimer, Ph.D.



symptom. Some of these people experience pain as an early symptom of Parkinson's, before their disease has even been diagnosed. Yet, pain in Parkinson's disease often re-

mains undiagnosed and untreated. Thus, it is important to understand that pain can be part of the Parkinson's experience and to learn ways to manage it.

## Causes of Pain in Parkinson's

Pain researchers use a classification system that is based on the separation of tissue pain receptors from the nerves that transmit pain signals. Pain can be classified as nociceptive, which relates to tissue damage, implicating the pain receptors in the skin, bones or surrounding tissues; as neuropathic, indicating pain arising in nerves; or as a mixed pain syndrome involving both nociceptive and neuropathic pain.

In Parkinson's, most pain experiences seem to result from tissue that is injured or has the potential to be damaged: causes include persistent tremor, muscle rigidity, dystonia, musculoskeletal injury (i.e., sprains, bruises, bone fractures resulting from a fall etc.), burns and inflammation. The pain is typically well-localized to the affected body part; it may fluctuate with the medication dosing. Pain caused by dystonia can be diagnosed when there is visible twisting, cramping or posturing of the painful body part. The most common areas of the body where people with Parkinson's experience pain are the neck, upper back and extremities.

In Parkinson's, neuropathic pain is less common than nociceptive pain, and includes a number of conditions not directly related to PD, such as shingles,

cancer pain, carpal tunnel syndrome, diabetic neuropathy, and peripheral neuropathy. The pain may present as burning, numbness and tingling, sharp sensations, or electric shock qualities. Pain due to nerve or root disease is most commonly caused by akathisia, an extreme inner restlessness.

Parkinson's specialists gain insight from the perspective of the pain specialist, and often select treatments based on the nociceptive versus neuropathic classification. In practical terms, it often proves helpful to conceptualize the experience of pain in Parkinson's as relating to one or more of the following five categories: pain from the muscles or skeleton, pain from nerves or spinal roots, pain related to sustained twisting or writhing, discomfort from akathisia and pain caused directly by changes in chemicals in the brain due to Parkinson's.

## The Impact of Pain

It is important to address pain because it may interfere with day-to-day activities, mood, sleep and overall enjoyment of life. Specific problems resulting from chronic pain may include sleep disturbance, malnutrition, social withdrawal, physical and functional decline, depression, anxiety and impaired cognition. Pain also accounts for increased overall health care costs.

A person's perception of pain can be affected by emotional factors. Scientists have shown that depression, which affects approximately 40 percent of individuals diagnosed with Parkinson's, plays an important role in the way people perceive pain. Similarly, tension and muscle stress caused by anxiety can compound pain. Cognitive processes — how a person views pain and how he or she pays attention to it — also influence the level of pain a person feels. A person who pays more attention to his or her pain and reacts to pain with a high level of stress will likely experience more pain than someone who tries to ignore the pain and considers it irrelevant to his or her daily life. Feeling helpless to control pain — that is, believing that pain is uncontrollable or that there are no treatment options or health professionals available to assist in managing pain — can also make pain seem worse.

Fortunately, many options exist for treating pain. How can you find which are right for you? The first step is to talk to your doctor who can assess your pain and then help to build a pain management plan.

## Assessing and Managing Pain

Your doctor can assess pain through a clinical inter-

view and neurological examination, sometimes performed in both the unmedicated state and when the Parkinson's medications are working fully.

Your doctor may also ask you to describe the characteristics of your pain. For example, when do you feel pain? Where in the body is your pain? Does the pain feel hot or cold, stabbing or burning? You also may be asked to report how pain impacts your daily activities — for example, walking or sleeping. The more information you can provide about your pain, the better your doctor will be able to diagnose and treat it.

Management options for pain in Parkinson's include both the pharmacological (i.e., medications) and the non-pharmacological. A combination of both may offer the best pain control, and an interdisciplinary model of care can lead to optimal results for pain management. Some treatment options include:

- medications
- exercise
- physical therapy
- acupuncture/acupressure
- massage
- psychotherapy (emphasis on pain management)
- botulin toxin injections
- stretching
- nutrition management

Because of the relationship between dopamine and pain, dopaminergic medications such as levodopa can affect a person's perception of pain. People with Parkinson's who are in the "on" levodopa state, when the medication is at peak effectiveness, report less pain than those in the "off" state. Pain due to rigidity or dystonia can be relieved by dopamine drugs, but on the other hand, may cause dyskinesias. Therefore, effective management of levodopa medication for people with Parkinson's may help to reduce pain.

Because certain thought processes and behaviors can alleviate or worsen pain, some people find psy-

## To Do List

- Tell your doctors as soon as you experience pain. Mention your pain to all doctors involved in your treatment (neurologist, orthopedist, primary care physician, etc.) so that they can work together to relieve your pain.
- Ask about types of treatment.
- Document your pain: when, where, description (burning, aching, etc.), and what has or has not helped.
- Call PDF's HelpLine staff — at (800) 457-6676, from Monday to Friday, 9 AM to 5 PM ET — with your questions about pain.

chotherapy helpful for managing their pain. Techniques such as cognitive-behavioral therapy (helping to control the psychological response to pain; teaching diaphragmatic breathing, visual imagery exercises, relaxation techniques, etc.), and biofeedback may help ease pain, but are unlikely to eliminate it completely.

A physical therapist can help you select and modify appropriate exercise routines. Of course, you should avoid activities or exercises that make your pain worse.

### How Can I Get Started?

If you or a loved one experiences pain, take action with the "To Do List" above. This will put you on a treatment plan that will ease your symptoms, so you are able to live as pain-free as possible.

*Dr. Wertheimer originally presented this topic as a PD ExpertBriefing, which is now available to view at [www.pdf.org/parkinson\\_briefing\\_understanding\\_pain](http://www.pdf.org/parkinson_briefing_understanding_pain).*

## Join PDF for the Next Four PD ExpertBriefings

Free educational programs available online or by phone for people with Parkinson's, family members and health care professionals. Pre-registration is recommended.

**Driving and PD: Balancing Independence and Safety**  
Tuesday, January 31, 2012, 1:00 PM – 2:00 PM ET  
Margaret O'Connor, Ph.D., A.B.P.P., and Lissa Robins Kapust, L.I.C.S.W., Beth Israel Deaconess Medical Center, Boston, MA

**Parkinson's Medications: Today and Tomorrow**  
Tuesday, April 17, 2012, 1:00 PM – 2:00 PM ET  
Cynthia L. Comella, M.D., F.A.A.N., Rush University Medical Center, Chicago, IL

**A Closer Look at Anxiety and Depression in PD**  
Tuesday, March 6, 2012, 1:00 PM – 2:00 PM ET  
Laura Marsh, M.D., Michael E. DeBakey Veterans Affairs Medical Center and Baylor College of Medicine, Houston, TX

**Understanding the Progression of Parkinson's**  
Tuesday, June 26, 2012, 1:00 PM – 2:00 PM ET  
Ronald F. Pfeiffer, M.D., University of Tennessee Health Science Center, Memphis, TN

*This series is made possible by an educational grant from Teva Neuroscience.*

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## What Does Genetics Mean to Your Family?

About 14 percent of people who have Parkinson's have a first-degree relative — a parent, sibling or child — who also lives with Parkinson's. The medical literature includes evidence of many large families in which there are multiple members affected by Parkinson's, often spanning successive generations.

Traditionally, a method called classical genetic mapping allowed us to identify rare mutations in genes that result in disease. The first of these to be described in Parkinson's was in SNCA, a gene that makes a protein named alpha-synuclein. This mutation is the result of a single DNA nucleotide change, "c.209G>A (A53T)" —

"These genetic discoveries provide a 'molecular foundation' on which to build novel treatments for Parkinson's."

Matthew Farrer, Ph.D.



in effect a single spelling error among six billion such nucleotides in the genome (see call-out box below at right). It was first found in a

family from Italy in which many members through several generations developed Parkinson's.

Although the A53T mutation is rare, what we learn from it can be applied to more common cases of Parkinson's. For example, alpha-synuclein was found to be the major component of protein clumps known as Lewy bodies, affecting the nervous system of this family and the majority of people with Parkinson's. The presence of Lewy bodies in the brain is now considered the hallmark of Parkinson's. Alpha-synuclein also led to the discovery of common "associated" variants in this same gene in populations all over the world.

In another example, a mutation in a gene called LRRK2, "c.6055G>A (G2019S)," was found in the DNA of one-third of people with Parkinson's in Northern Africa, one-seventh of people with Parkinson's with Jewish heritage, and one in a hundred people with Parkinson's in North America. It encodes a protein known as leucine-rich repeat kinase 2. Interestingly, the majority of those who carry the G2019S mutation are genetically related to a common ancestor, regardless of current citizenship and geographical location. Recently, many more common LRRK2 variants have been found in populations around the world. Some of these are believed to increase risk for Parkinson's, while others appear to protect against it.

Recent technological advances in a process known as "massively parallel" DNA sequencing have made it

possible to quickly and cost-efficiently conduct family-based genetic discovery and to identify novel, rare mutations. The first discovery in Parkinson's using this method was a mutation in the gene called VPS35, "c.1858G>A (D620N)," and was funded in part by the Parkinson's Disease Foundation. VPS35 encodes a protein known as "vesicular protein sorting 35" (see image on page 7). Its responsibilities within the cell include managing a "recycling system" for membrane-associated proteins. Nerve cells have more membrane and surface area than other cells, which they need to maintain and repair during neurotransmission and aging.

As with all mutations, understanding the role of VPS35 — in this case, as part of a recycling system — could provide clues to what is causing Parkinson's.

## What Does Genetics Mean to Individuals?

The majority of people who have Parkinson's, about 86 percent, do not have a close family member with Parkinson's. Among these individuals, Parkinson's may not have been inherited, but genetic factors have been shown to contribute to their susceptibility.

This discovery has in large part been due to the development of "genome-wide association studies" (GWAS, for short). GWAS involve thousands of people with Parkinson's, and have helped to identify the common genetic variants mentioned above. The technology applied in GWAS cannot meaningfully predict an individual's risk of developing PD. However, findings from these studies have repeatedly demonstrated that among people with Parkinson's, there are relatively common variants within specific genes — and often regions of the genome (or loci) that contain several

## Defining a Gene Mutation

You may notice gene variants/mutations have long names. This is because they are very specific. As Dr. Farrer said, "Genetics pinpoints the precise nucleotide change of the 3 billion pairs (actually six billion, three billion from mom; three billion from dad) we inherit."

### Let's break down SNCA, c.209G>A (A53T)

- SNCA:** tells us the specific gene name or locus
- c.:** stands for the 'coding' sequence
- 209:** tells us the mutation's exact location
- G:** tells us which nucleotide is mutated, in this case guanine
- A:** tells us what the last nucleotide is mutated into, in this case adenine
- (A53T):** the amino acid that is in turn affected by this mutation, in this case the 'A' alanine at position 53 of the protein is substituted for a 'T' threonine

neighboring genes — which contribute to disease risk.

In Caucasian populations, GWAS in Parkinson's have shown that two genes in particular — SNCA, which makes alpha-synuclein and MAPT, which makes the protein tau — are most important. (You may recall that we mentioned SNCA earlier as it may harbor causal mutations in certain families.) GWAS studies in non-Caucasian populations have taught us that the genetic contribution to Parkinson's in different countries, and among various ethnicities while overlapping, may be different. For example, in Japan, a gene region found on chromosome 1, known as PARK16, was found to be more prominently associated with Parkinson's.

Ever-larger GWAS and analyses are being planned to identify additional genetic components associated with Parkinson's risk, albeit playing an ever-diminishing role. Such studies will compare the DNA variability in several hundreds of thousands of people who have Parkinson's with age, gender and ethnically-matched individuals who do not. These findings do not tell us about the risk for Parkinson's that is faced by any one individual. Nevertheless, the findings in aggregate, in a given population, help identify the many molecular components that are disturbed in Parkinson's.

To age "successfully," biological systems must work optimally. The discovery of genetic mutations and variants tell us which parts of the genome, and which molecular components of a nerve cell in a person's brain, are critical to keeping systems working properly and which go awry in Parkinson's.

### Completing the Genetic Puzzle

Through this process of genetic discovery a common theme appears to be emerging in the biology of Parkinson's — just as the picture on a jigsaw puzzle begins to take shape as the pieces are filled in. Each new gene and story the genes tell together are providing the most remarkable, most fundamental, molecular insights into what is happening in Parkinson's disease.

For example, we know that the genes implicated in Parkinson's coordinate interconnected processes. Alpha-synuclein (SNCA) regulates the delivery of certain molecules (including neurotransmitters), responsible for communication between one nerve and another. Within the cell, tau (MAPT) helps regulate the loading/ unloading of these molecules and other "cargo" on both local and long distance highways. Tau manages the back and forth journey of the cargo — the frequent stops and loading/unloading that a delivery van might make.

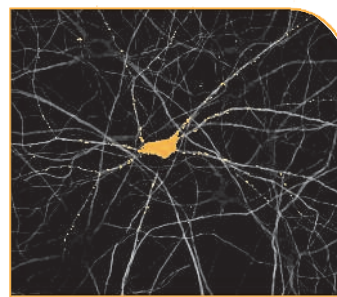
Meanwhile, LRRK2 and VPS35 select and sort cargo like workers in a mail depot, ensuring they are appropri-

ately packaged and addressed to get to the right place.

Through genetic discovery, we are beginning to understand how minor imperfections of very specific and related biologic processes, possibly accelerated by genetic mutations or disease-associated variants, become a chronic and cumulative problem. We must continue to find more pieces of the puzzle, and to understand how they are related. The clearer the picture, the higher its molecular resolution, the more likely we will succeed in future therapeutic development.

### Genetics and New Treatments

In all areas of medicine, genetic discovery is helping



*The distribution of VPS35 (labeled yellow) in a nerve cell.*

to predict and prevent, to make pharmaceutical investment and interventions more successful.

Findings such as the mutations and variants mentioned above point us to specific targets to treat.

Knowing the genetic background for disease susceptibility in individuals will improve the design of clinical trials and the likelihood of success.

In Parkinson's, the slowly progressive course provides the timeframe in which new medications, if appropriately targeted, can be efficacious. Already there are numerous translational research programs focused on turning discoveries such as alpha-synuclein and LRRK2 into medications.

Challenges remain — for example, in the development of biomarkers that will track the progression of Parkinson's and provide benchmarks to measure the effectiveness of treatments. But the pace of progress is quickening. Most encouraging is that the separate pieces of genetics research are now being brought together, providing an undisputable molecular foundation upon which to build the medications of tomorrow. Indispensable to success is the participation of people with Parkinson's and their families in genetic research, their gift to humanity.

As we "join the dots," so the biological network that is perturbed in Parkinson's becomes clearer, each pathway proving additional targets for intervention to ease the symptoms of disease, and to halt progression — in effect, to provide a cure.

*Dr. Farrer is Canada Excellence Research Chair in Neurogenetics and Translational Neuroscience at the University of British Columbia. He received PDF support in 2004 and 2011. Visit his website at [www.can.ubc.ca](http://www.can.ubc.ca).*

**FDA Hearing\*** | Continued from page 1

scientists, and people living with Parkinson's about the scientific evidence presented by the FDA and the study sponsor. PDF Research Advocate Jackie Hunt Christensen, who lives with Parkinson's, served as the committee's patient advocate. Three other PDF Research Advocates contributed written and oral testimony.

PDF and five other Parkinson's organizations prepared written testimony recommending against the proposed label change, which included this passage: *"While we are encouraged by the evidence presented to date, it appears to our community that the data surrounding Azilect as a therapy that slows clinical progression of Parkinson's are not yet definitive, and that additional information is required to completely determine the impact of Azilect on clinical disease progression."*

**Results**

The committee recommended to the FDA that there was not enough scientific evidence provided to show that the medication is effective in slowing the

clinical progression of Parkinson's. The FDA will take this recommendation and other factors into account when making its final decision, though when this will happen is not yet known.

**What Does it Mean?**

All Parkinson's medications currently on the market have been proven to ease the symptoms of the disease. However, none of these has yet been proven to slow or reverse its course. Thus, an action supporting the "clinical progression" indication would have immense implications for people with Parkinson's. While such an indication would be great news for the community, it is the position of PDF and the other organizations that such a decision must be based firmly on the science — and this, we believe, does not yet support this case for Azilect.

We will advise you when the FDA makes its final decision. In the meantime, Azilect will remain on the market, with or without the proposed new indication. People whose doctors have prescribed Azilect to ease their symptoms will be able to continue using this treatment.

**New Hope\*** | Continued from page 1

cells into the neurons lost in Parkinson's. So researchers led by Lorenz Studer, M.D., at the Memorial Sloan-Kettering Cancer Center worked out the precise conditions needed to do so. They also transplanted the neurons into the brains of animals with brain lesions reminiscent of those observed in Parkinson's.

**Results**

- The researchers made cultured human pluripotent stem cells differentiate into dopamine neurons.
- The dopamine neurons produced by this method had the same characteristics as dopamine neurons from the brain region affected by Parkinson's.
- When transplanted into the brains of mice and rats, the neurons survived for at least four and a half months and did not form tumors.
- The transplanted dopamine neurons improved the performance of mice and rats in motor function tests.

- Dopamine neurons transplanted into the brains of rhesus monkeys survived for at least one month.

**What Does it Mean?**

Pluripotent stem cells hold great promise, but scientists have struggled with transforming stem cells into working dopamine neurons. For the first time, Dr. Studer and his colleagues appear to have identified the correct conditions necessary to transform pluripotent stem cells exclusively into dopamine neurons that resemble those lost from the same brain region affected by Parkinson's, that perform well in animals, and that do not produce tumors. The fact that these transplanted neurons reduced some Parkinson's symptoms in animals is a good sign for potential therapeutic applications in people living with the disease. Before stem cell therapy for Parkinson's becomes a reality, significant challenges remain. Until then, this new protocol will be helpful to screen and test new potential drug therapies.

 **More Science News on PDF.org**

- Exposure to Chemical Solvents Linked to Parkinson's
- Study Supports Long-Term Safety of Levodopa Use

[www.pdf.org/science\\_news](http://www.pdf.org/science_news)

\* To read the full summaries of these two stories, visit [www.pdf.org/science\\_news](http://www.pdf.org/science_news).

## Meet the Newest PDF Research Advocates

The Parkinson's Disease Foundation (PDF) congratulates the 27 newest members of Parkinson's Advocates in Research (PAIR). They join 100 others around the country in influencing research and speeding the development of new and effective treatments for Parkinson's. In late October, the group gathered in New Jersey to complete the Learning Institute – Northeastern region, undergoing intensive sessions on the science of Parkinson's and the process that brings new treatments to market. They have returned to their communities to take on research-related activities through which they can share their perspectives as people touched by Parkinson's.

### What is Your Goal as a PDF Research Advocate?



*"My goal is to ensure that every person with Parkinson's in our community has access to the latest research information and the tools to make an informed decision about participation."*

**Bill Brawley, Etna, NH**



*"It is often difficult for people with Parkinson's in Maine to participate in research studies simply because issues like distance and inclement weather make traveling difficult. I'll be working with PDF Research Advocate Gordie Guist (Class of 2010) to provide encouragement and logistical support to people who want to participate in studies."*

**Cameron Weaver, Mount Vernon, ME**



*"I'm working with three Research Advocates in our state and our local Parkinson's specialist to inform people with Parkinson's who live in the rural areas of Vermont, where few support groups exist, about opportunities to get involved in research."*

**Cassie Blanchard, Randolph, VT**



*"There are some impediments to study participation for people with Parkinson's, such as being required stay off medications for a period of time. One of my goals is to discuss this with researchers, so they will adopt criteria that are more compassionate to people with PD, yet still scientifically reliable."*

**Leonard Schwartz, Owings Mills, MD**

### Partner with PDF Research Advocates

If you are a doctor, research professional or support group leader, we invite you to partner with our advocates to influence Parkinson's research and speed new and effective treatments. They are available to: (1) serve on national, regional and local Parkinson's research advisory boards; (2) work with the research community to address gaps in Parkinson's research; (3) speak at conferences and support groups on the importance of clinical study participation. If you are interested in becoming a PDF Research Advocate, see our notice on page 12 or contact us for information about upcoming trainings.

**(800) 457-6676 | [www.pdf.org/pair](http://www.pdf.org/pair) | [info@pdf.org](mailto:info@pdf.org)**



## PDF Carnaval at the Copa Returns

On November 14, nearly 300 guests came together for the return of PDF's Carnaval at the Copa at the legendary Copacabana club in New York City. The event grossed over \$62,000. All proceeds benefit PDF's research programs. Guests enjoyed dinner, open bar, and music from GDO Soul, while a lucky few received salsa lessons on the dance floor. Some competed to win exciting prizes by playing games of chance while others bid on silent auction items ranging from NY Giants box seats to a week in Phuket, Thailand. Amy Sole, a co-chair of the event, said, "I was thrilled to help lead the PDF Carnaval at the Copa for this great cause and in memory of my father. Thanks to everyone who joined us for such a fun event at such an iconic venue!"

PDF thanks Board member and club co-owner Peter Dorn for generously underwriting a portion of the event; Master of Ceremonies Mike Woods of Fox 5's *Good Day New York*; our enthusiastic event co-chairs Bob Benjamin, Jose Cruz, Peter Dorn, Stephanie Goldman-Pittel, Sharon Klein, Amy Sole, Douglas Stern and Jeffrey Zyglar; and the host committee for their hard work in making this event a success. View photos of this event at [www.pdf.org/flickr](http://www.pdf.org/flickr).



Amy Sole and friends at the Copa



## PDF CHAMPIONS

### Paddle Boarder Asks Community to "Stand Up to Parkinson's"

On October 22, Pamela Strom hosted the first Standup to Parkinson's Race, a SUP-o-Run, duathlon and awareness event in Newport Beach, CA. She also became the first PDF Champion to hold an event focused on standup paddle boarding. Ms. Strom became involved with PDF because of her inspiration, her mother-in-law who lives with Parkinson's. Around the same time her mother-in-law was diagnosed, Ms. Strom was becoming an active standup paddle boarder. She decided to use her new hobby to organize an event to honor her mother-in-law and others living with Parkinson's. She coordinated a

daylong event that included paddleboard races, foot races, refreshments, music and prizes. She brought on board corporate sponsors and raised funds online and through t-shirt sales. To find out more, visit her Facebook page at [www.facebook.com/pages/Standup-to-Parkinsons-Race-a-SUP-o-Run/161991927187529?ref=ts](http://www.facebook.com/pages/Standup-to-Parkinsons-Race-a-SUP-o-Run/161991927187529?ref=ts).



## PDF Mourns the Loss of Board Member Daniel Gersen

The Parkinson's Disease Foundation (PDF) mourns the loss of Daniel Gersen, a long-time member of the PDF family, who passed away on September 20 at the age of 94.



Daniel and Adeline Gersen

Mr. Gersen served as an advisor to PDF for more than 30 years, both as a Board member and as its legal counsel. He was well known for his unwavering dedication to PDF's programs of research, education and advocacy.

During his illustrious 70-year legal career, Mr. Gersen worked with clients in the areas of commercial litigation, labor and employment law, banking and finance, corporate law, and trusts and estates. For many years, he was a partner in the firm Blum, Gersen and Stream. More recently he was senior partner of Gersen, Blakeman and Ackert.

PDF Executive Director Robin Elliott noted, "We mourn the loss, and honor the memory of a devoted member and advisor of many years standing. His erudition, curiosity and unfailing loyalty served our mission, elevated our discussions, and warmed our hearts. To his wife Adeline and the family, we extend our personal condolences and our gratitude for the life and friendship of a wise and honorable man."



## PDF CHAMPIONS

### Spence Family Dances to "Ernie's Favorites"

On October 9 in Concord, MA, family and friends celebrated the life of Ernest G. Spence with "Ernie's Favorites," a New England-style contra dance. Ernie Spence lived with Parkinson's for 25 years and according to his family, "despite the devastating effects of Parkinson's, he maintained his love of dance and life until he died." In his honor, his family – including his wife Joan, their children and spouses, Linda D. Spence, Betsy Harlow (Reneé Harlow) and Harlan Spence (Gael Phillips-Spence), eight grandchildren, one great-grandchild and countless friends – brought the community together to dance the Chorus Jig and Money Musk, among others. Mr. Spence's community connections were evident, with several musicians donating their time for the evening. Through "Ernie's Favorites" and additional donations made in Mr. Spence's honor, the family raised \$5,630.

### Join the PDF Champions "30 in 30" Challenge this coming April

April is Parkinson's Awareness Month. PDF Champions plan to hold 30 events in 30 days to benefit Parkinson's research. Will you join them? Events can range from a lemonade stand, to a bake sale to running a marathon!

(800) 457-6676 | [www.pdf.org/pdf\\_champion](http://www.pdf.org/pdf_champion) | [info@pdf.org](mailto:info@pdf.org)

## Community Events |

### April is Parkinson's Awareness Month

Get ready to spread the word, educate yourself and support the cure this April by ordering the PDF toolkit, awareness bracelets, stickers and more! Here are just a few events taking place in April (dates to be determined).

#### Celebrate Spring

**Date:** To Be Announced

**Place:** New York, NY

Enjoy a night of cocktails and dancing with PDF's Young New Yorkers for the Fight Against Parkinson's and help to benefit PDF's research programs.

(800) 457-6676

[www.pdf.org/celebrate\\_spring](http://www.pdf.org/celebrate_spring)

#### Parkinson's Unity Walk

**Date:** To Be Announced

**Place:** Central Park, New York, NY

Join the community for a two-mile walk to increase awareness and raise funds for Parkinson's disease research.

(866) PUW-WALK

[www.unitywalk.org](http://www.unitywalk.org)

Find more ways to get involved during Parkinson's Awareness Month:

(800) 457-6676 | [www.pdf.org/parkinson\\_awareness](http://www.pdf.org/parkinson_awareness)

### PDF is pleased to honor:


#### Isobel Robins Konecky

Secretary of PDF Board of Directors  
President of New Dramatists



This award will be presented at PDF's annual gala, *Bal du Printemps*

**Wednesday, May 16, 2012**  
**at The Pierre Hotel, New York City**

 PDF Event

**Photo Credits:** Page 10 Amy Sole and friends (Credit – Patrick McMullan); Pamela Strom, Susie Prestie (Credit – Cynthia Servais); T-Shirt design – David Ruch and Jeff Warner; Daniel and Adeline Gersen (Credit – Janet Charles); Page 11 Joan and Ernie Spence.



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therapies  
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## Parkinson's Advocates in Research

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Influence research and speed new and effective treatments for Parkinson's by joining Parkinson's Advocates in Research!

Apply to the Learning Institute – Western Region taking place in July 2012

- Learn from experts about the science of Parkinson's and the process that brings new treatments to market.
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Application period opens in February 2012. For more information on this and other trainings and to apply online, visit [www.pdf.org/crli](http://www.pdf.org/crli), call (800) 457-6676 or email [info@pdf.org](mailto:info@pdf.org).

*Applicants must reside in Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington and Wyoming. If selected, attendee expenses will be paid by PDF.*

## Community | Commitment | Impact

Supporting the research and ideas that will improve the lives and futures of people touched by Parkinson's.

### Stay Connected

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### Support Us

[support.pdf.org](http://support.pdf.org)

**Disclaimer** If you have or believe you have Parkinson's disease, then promptly consult a physician and follow your physician's advice. This publication is not a substitute for a physician's diagnosis of Parkinson's disease or for a physician's prescription of drugs, treatment or operations for Parkinson's disease.

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