PPMI Launches New Genetics Cohort

As you already know, in early 2013, PPMI leadership decided to leverage the study’s comprehensive infrastructure and expand to include a new prodromal cohort to better identify biomarkers that can be identified before the onset of Parkinson’s. One year later, prodromal recruitment is well underway, and PPMI has expanded again: this time to study two Parkinson’s-related genes focused on the same mission of identifying biomarkers. This new study cohort will require yet another new group of PPMI participants.

“Focusing on PD patients and those at risk for PD with genetic mutations will allow us to track the disease process at the very earliest stages of illness,” said Ken Marek, MD, principal investigator of PPMI and president and senior scientist at the Institute for Neurodegenerative Disorders in New Haven, Connecticut. “A Parkinson’s-related genetic mutation represents the first indicator of PD in an individual. Identifying and studying people with these mutations will teach us even more about the biology of Parkinson’s disease and further accelerate our research toward a PD biomarker and more effective PD therapies.”

Finding Volunteers for the Genetics Cohort

To get a full picture of genetic implications of Parkinson’s, PPMI needs people with PD who carry the mutation as well as people who do not have PD but are related to someone who does and also carries a LRRK2 or SNCA mutation. Studying these two types of individuals in PPMI will help researchers understand why some people with a LRRK2 or SNCA mutation do go on to develop PD and others do not. Because genetic mutations are passed down through families, there are some ancestral groups with a higher prevalence of mutations in the SNCA or LRRK2 genes. In fact, PPMI has expanded to eight new sites around the world to better access populations that are more likely to have these mutations. (Read more about PPMI’s new sites on page 3.)

The SNCA mutation, for example, has only been seen rarely in a few familial groups such as people from the Contursi region in Italy or the Peloponnese islands in Greece.

PPMI is working through established networks in these locations to enroll 50 people with this mutation and Parkinson’s disease and 50 people with the mutation but not Parkinson’s for the genetics cohort.

To date, a mutation in the LRRK2 gene is the greatest known genetic contributor to Parkinson’s disease. A PD biomarker would allow researchers to quickly and objectively measure a therapy’s impact on PD and potentially develop new therapies to benefit everyone with PD, even those with a non-genetic form. The new genetics cohort of PPMI aims to identify biomarkers that scientists can use to test drugs that target LRRK2 and alpha-synuclein.

About PPMI

The Parkinson’s Progression Markers Initiative (PPMI) is a landmark, five-year international clinical study that aims to find reliable and consistent biomarkers of Parkinson’s disease (PD) progression. The study is testing today’s most promising biomarker candidates through neuroimaging, the collection of blood, urine, and spinal fluid, and clinical and behavioral tests. Valid measures could allow scientists to predict, objectively diagnose and monitor diseases as well as definitively determine which medications work and which will not. PPMI is sponsored by The Michael J. Fox Foundation for Parkinson’s Research and funded by a consortium of industry partners and individual donors. To learn more or volunteer to participate in the study, visit www.michaeljfox.org/PPMI or call (877) 525-PPMI.
PPMI Launches Genetics Cohort

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Parkinson’s, accounting for one to two percent of all PD cases. However, in individuals of certain backgrounds — Ashkenazi (Eastern European) Jewish, Basque or North African Berber — that number jumps to 13 to 40 percent, and the LRRK2 mutation accounts for more cases of Parkinson’s in those populations.

In total, PPMI hopes to enroll 250 Parkinson’s patients with a LRRK2 mutation and 250 people without Parkinson’s disease but with a LRRK2 mutation for the genetics cohort. People who meet these criteria are being asked to fill out a simple survey at www.michaeljfox.org/ppmi/genetics to determine if they qualify to participate. PPMI will provide genetic counseling and testing of the LRRK2 or SNCA gene at no charge for people who meet certain study criteria.

Those of you who are enrolled in other groups of PPMI are also contributing to the new genetics cohort. Because each enrolled participant is screened for genetic mutations, including in the LRRK2 and SNCA genes, scientists are already analyzing the genetic data of enrolled volunteers and will use this information to better understand key differences between PPMI groups.

Looking Ahead
The first genetics volunteer enrolled in at the end of 2013, and our goal is to complete recruitment in the next two years. Adding a new cohort to PPMI is a major milestone for the study and one that further confirms PPMI’s role as a new model for biomarker research.

Of course, we realize that we couldn’t have gotten here without you — our partners in research. Your continued study visits are yielding tons of data, resulting in a rich, ever-growing resource for scientists looking to improve the Parkinson’s therapeutic landscape. (See the chart on the right for the impressive stats on just how many researchers are accessing the data coming out of PPMI!)

Thank you, as always, for your continued commitment to PPMI.

Be a PPMI Genetics Ambassador
Recruitment is underway for the genetics cohort of PPMI! There is no better advocate for PPMI than those of you who are already participating in the study and you can play a critical role in spreading the word about this new effort.

How can I help?
Ask your friends and family members to visit www.michaeljfox.org/ppmi/genetics and encourage them to take the genetic screening survey. Through this online survey, PPMI is seeking individuals with or without PD who are of Eastern European (Ashkenazi) Jewish, North African Berber, or Basque ancestry to be screened for the study.

What is the PPMI Genetics Ambassadors team?
PPMI is organizing a group of study participants who are interested in helping spread the word about PPMI Genetics in Eastern European (Ashkenazi) Jewish, North African Berber, or Basque communities. If you are interested in joining this group, please contact a PPMI team member at your local site and let them know you’re ready to get involved.

Participant Profile: Jessi Keavney Shares Her Story

Twelve years ago, at age 52, my dad was diagnosed with Parkinson’s disease. His father had it, too, and last year, I became more interested in finding out more about the disease and whether it could run in my family. First, I decided to get a genetic test. When the results came back that I have the LRRK2 mutation, I was even more determined to do something and I encouraged my dad and my sister to get tested, as well. I even discovered something else. I only learned afterward that my dad is a quarter Ashkenazi Jewish and having that ancestry makes it more probable to have a LRRK2 mutation.

The mutation had been there all along. Now knowing it’s there allows me the opportunity to become more involved. And, if I ever do develop symptoms, I’ll be prepared. But, at 36 and without a Parkinson’s disease diagnosis, what could I do to contribute to the cause?

In January, both my dad and I were some of the first volunteers for the new genetics cohort of PPMI. I’m not scared knowing my genetic status; instead I’m empowered. I don’t want to hide from the disease. I know my data is valuable to researchers. It is particularly gratifying to know that the scientific discoveries made by studying individuals with genetic causes of PD can to benefit ALL people living with the disease and potentially prevent others from developing it in the first place.

- By Jessi Keavney, PPMI Participant

PPMI Statistics

Researchers from all over the world are downloading and analyzing data collected in PPMI. Here are some of the most interesting facts:

Over 200% Increase in the Data Downloads
- 139,135 in 2013 (compared to 46,385 in 2012)

94% Increase in Researchers Who Have Downloaded PPMI Data
- 760 people in 2013 (391 people in 2012)

To date, six articles using PPMI data have been published in scientific journals. Topics include:
- Overview of PPMI study design
- Impulse control symptoms
- Examining Alzheimer’s biomarkers in CSF collected in PPMI
SNCA and LRRK2: A Closer Look

Today, Parkinson’s researchers are looking for a disease-modifying treatment that will stop the disease or prevent it from ever developing. The alpha-synuclein and LRRK2 proteins are viable targets for such a treatment, but researchers need to know more about these proteins and how drugs affect them in Parkinson’s disease. The PPMI genetics cohort is one way to move therapies targeting alpha-synuclein and LRRK2 closer to the market.

Researchers hope that greater understanding of the biology and clinical features associated with LRRK2 and SNCA genetic mutations will point to biomarkers that can speed clinical trials to test new therapies. While mutations in these genes are rare, biomarkers related to these genes could be used to develop therapies that would help everyone living with or even at risk for PD. Below is an informative comparison of the two genes:

<table>
<thead>
<tr>
<th>Parkinson’s-Related Genes Being Studied in PPMI</th>
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<tr>
<td><strong>SNCA Gene</strong></td>
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<tr>
<td><strong>Mutation Discovered</strong></td>
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<tr>
<td><strong>Prevalence of Mutation</strong></td>
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<td><strong>Groups with Increased Prevalence of the Mutation</strong></td>
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<td><strong>Gene Codes</strong></td>
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<td><strong>How Affected in PD</strong></td>
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<td><strong>State of Drugs Targeting</strong></td>
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Where in the World is PPMI?

With the addition of the genetics cohort, the number of PPMI sites is up to 32 centers worldwide. This includes eight brand new sites that were chosen based on their proximity to the ethnic and geographic groups associated with the SNCA and LRRK2 genes. Visit [http://bit.ly/O2UkUo](http://bit.ly/O2UkUo) to view these maps and a full list of PPMI sites online.
A Letter from the PPMI Statistics Core

The PPMI Statistics Core leads the statistical analyses that are performed on all PPMI data and samples. Below is a letter from PPMI Statistics Working Group Chair, Christopher Coffey, PhD.

Dear PPMI participants,

I just wanted to take a brief moment to personally thank you for your participation in the PPMI study. I’m sure you are already aware of this, but important research such as this could not move forward without the efforts of individuals like yourself. Unfortunately, it is not enough to just sign up for the study at the beginning. As a statistician, I have had numerous experiences where great ideas and studies have been derailed by a large amount of missing data. Efforts like PPMI are much more successful when a large number of individuals complete all of the study assessments.

Think of it this way: at the end of the study when we want to ask important questions, it would be much more difficult to find the answers if there are holes in the data. For that reason, I want to stress the importance to you of remaining in the study and participating in as many scheduled visits as possible during the remaining years of PPMI. I fully understand that I cannot put myself in your shoes. Each one of you has a different set of unique circumstances that led to your participation in the study. The time that you are giving to participate in this study is a valuable gift. I can assure you that, on behalf of the PPMI investigators, we will work diligently to make sure that your gift is utilized to the fullest.

Sincerely,

Christopher Coffey, PhD
Director, Statistical and Data Management Center, University of Iowa
Chair, PPMI Statistics Working Group