PPMI Expands Genetic Cohort to Include Another Mutation

The Parkinson’s Progression Markers Initiative (PPMI) is expanding again. Building on the successful infrastructure of its genetic cohort, initially launched in early 2014, PPMI is now recruiting individuals with a mutation in another gene associated with Parkinson’s: GBA (glucosidase beta acid).

The study of people with genetic variations associated with Parkinson’s disease (PD) can point researchers to proteins and pathways that go awry in the disease. Those proteins and pathways may serve as targets for new therapies or as biomarker measures to track disease progression.

“Insights gleaned from volunteers with genetic mutations will help speed research toward new and improved Parkinson’s therapies, benefitting the greater Parkinson’s community,” said Ken Marek, MD, principal investigator of PPMI and president and senior scientist at the Institute for Neurodegenerative Disorders in New Haven, Connecticut.

PPMI will enroll 125 people with the GBA mutation who have Parkinson’s and 125 carriers (people with the mutation who do not have Parkinson’s). Similar to another genetic mutation linked to Parkinson’s (in the LRRK2 gene), a mutation of the GBA gene is more common among people of Ashkenazi Jewish descent. Therefore, PPMI is asking Ashkenazi Jews with Parkinson’s or with a first-degree relative with Parkinson’s to contact study coordinators for screening and genetic counseling.

People already in PPMI cannot count toward the recruitment goal for this cohort.

PPMI now takes place at 33 clinical sites around the world and completed initial enrollment of 423 recently diagnosed Parkinson’s patients and 196 controls in April 2013. The study also completed enrollment of people without PD but with a risk factor of either smell loss or REM sleep behavior disorder earlier this year. The genetics arm is currently recruiting people (with or without PD) with a mutation in the LRRK2, SNCA (alpha-synuclein) or, now, GBA gene.

Across the cohorts, participants contribute data and samples over five years. PPMI makes the data accessible to the broader research community for further study to speed discovery and validation.
Get to Know your PPMI Coordinator

A profile of Carly Linder, MPH, University of Pennsylvania

Q: Carly, describe your role in PPMI.
A: I am a clinical research coordinator at UPenn, and for PPMI I recruit, inform, schedule, orient, and accompany study participants on the complex journey that is study participation. What I strive to achieve, more than anything else, in my position as a CRC is to make that journey as tolerable, painless, and (if you can believe it) fun as possible for the participants with whom I am fortunate to work.

Q: What is your favorite part of working on PPMI?
A: Truly, my favorite part of my job is meeting, learning about, and spending the study visit time with the participants at our site. Penn’s participants are incredibly dedicated, selfless, and genial. I have laughed and cried alongside them and try to make sure that they know how special they are to not only the study, but to myself and our team.

Q: Why do you think the work being done in PPMI is so important?
A: The obvious reason that PPMI’s research is so important is that it will identify biomarkers that will unlock the mysteries of Parkinson’s disease, both for treatment and preventative purposes. What inspires me the most about PPMI, however, is that it is global effort - collaborative research circumventing the globe and connecting the most brilliant teams available in order to achieve its mission. What’s more is that all of the data and samples are made available for the rest of the smarty-pants in the world to explore and with which to conduct their own research!

Q: Any fun facts you want to share about your time away from PPMI?
A: I recently joined the oldest amateur theater company in the world dedicated to Gilbert and Sullivan last year and it’s been one heck of an old-world-meets-new-world ride on which to be!

What Happens to your Blood and CSF after a PPMI Study Visit?

One of the most important aspects of the PPMI study is that the data and biospecimens are made available in real-time to the broader Parkinson’s research community for further analysis and discovery. To access the biospecimens (blood, urine, CSF, etc.) contributed by PPMI participants, researchers are asked to complete an application form online in which they must explain their proposed specimen analysis plan, rationale, and what kind of samples they need. These applications undergo rigorous review by an independent committee made up of Parkinson’s research experts.

Proposals with a strong rationale that meet the objectives of PPMI are approved to receive samples for their analysis. Once the analysis of the samples is completed, PPMI requires that any results and findings shared back with PPMI study leadership.

For example, a researcher from Italy recently completed her analysis of the serum from PPMI blood samples, and the results have now been posted to the online PPMI database for the research community at-large to view. Dr. Maria Teresa Pellechia examined whether an insulin-like growth factor called IGF-1 that’s found in serum was related to cognitive deficits in people with Parkinson’s disease by comparing the level of IGF-1 to PPMI participant scores on baseline cognitive tests, such as tests of verbal memory and attention. She found that in early PD participants, lower levels of IGF-1 in serum were associated with lower performance on cognitive tasks that assessed attention, verbal memory, and executive function.

PPMI’s model of open-access data sharing is designed to foster Parkinson’s research around the world to increase the number of smart scientists working toward the same problem: finding new treatments and ultimately a cure for Parkinson’s.
PPMI had a large presence at American Academy of Neurology (AAN) 2015 Annual Meeting. The meeting took place in Washington D.C. from April 18 to April 25 and brought together top players in neurology around the world to share the latest in neurological research.

Nine presentations at the conference featured analyses using PPMI data. Notably, John Seibyl, principal investigator of the PPMI Imaging Core, presented two-year longitudinal data on changes in a particular imaging test called a 123-I Ioflupane Single Photon Emission Computed Tomography (or simply, SPECT or DaTScan) performed in all of the study’s Parkinson’s volunteers, at baseline (first visit), and at one and two years following baseline. SPECT scans measure dopamine function in the brain, and all people with Parkinson’s in the study must have had SPECT scans showing dopamine deficit in order to be eligible to participate. Dr. Seibyl’s analysis shows that the rate of SPECT signal change in PD participants is less between year one and year two when compared to the change between baseline and year one. This could suggest that dopamine changes occur more rapidly early in disease progression than later on.

Visit the blog on www.ppmi-info.org to view the full list of AAN 2015 presentations.

In His Genes: PPMI Participant Shares Why He Chose to Get Involved

Jon Gilman, a software engineer in Boston, is into health and fitness. Motivated to learn more about how his body works using data science, Gilman decided to be genetically tested earlier this year through 23andMe. Gilman wasn’t surprised to discover that he has a gene commonly found in sprinters. More surprising was the revelation that he carries a mutation in his LRK2 gene — linked to more cases of Parkinson’s disease than any other gene discovered to date.

“There’s no history of Parkinson’s disease in my family. I didn’t know what to think about it at first,” he recalls. Uncertain what the news meant for his health, he did what any rational person would do — he took to Google.

Through his internet searches, Gilman discovered that LRRK2 is of interest to pharmaceutical companies as a promising drug target in Parkinson’s and that, while only a small percentage of individual Parkinson’s cases are caused by genes, studying them can benefit everyone living with the disease. Motivated by this, Jon enrolled in PPMI. Gilman explains, “Throughout the process, I just felt good contributing to something bigger than myself, hoping that I can play a small part in finding a cure for Parkinson’s.”
Michael J. Fox Discusses PPMI on The Late Show with David Letterman

Michael J. Fox made his last visit to the Late Show with David Letterman on April 15. He joined a star-studded list of guests appearing in the show's final episodes and has shared the stage with David an astonishing 41 times.

After discussing his diagnosis, Michael spoke about the crucial need for a biomarker for Parkinson's and the way PPMI is working to find one.

“What we are doing in our Foundation is we are trying to find biomarkers and ways to identify the disease before its symptoms are present and, in connection to that, we are trying to find genetic links to it,” Michael said.

He then alludes to PPMI’s genetic cohort, which is investigating those genetic links to PD. Michael explains that an area of interest is the LRRK2 mutation which is more commonly carried by people of Ashkenazi Jewish descent than the general population, and he encourages volunteers to get involved.

Visit the blog on www.michaeljfox.org to watch the video clip.

Want to stay informed of the latest scientific developments in PPMI? Visit www.PPMI-info.org. This is the portal for the scientific community to learn more about PPMI and to access the data and samples coming out of the study.