PROGENI News

NEWSLETTER FOR PARKINSON'S RESEARCH:
THE ORGANIZED GENETICS INITIATIVE

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Parkinson's Research: The Organized Genetics Initiative, also known as PROGENI, is a research effort between several research groups across North America. The PROGENI and PROGENI Cares studies are sponsored by the National Institutes of Health. To be eligible to participate in the PROGENI study, individuals must be affected with, or suspected of having, PD and have a history of another first degree relative with PD. The PROGENI Cares study is currently only being conducted in Indianapolis, IN, Toledo, OH, Memphis, TN and Iowa City, IA. Anyone with PD is eligible to participate in PROGENI Cares.

If you would like more information about these studies, please contact us.

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DNA SEQUENCE VARIANTS IN GBA

By Tatiana Foroud, PhD, Indiana University
and William C. Nichols, PhD, Cincinatti Children's Hospital Medical Center

Sometimes hints to the genes important in Parkinson disease come from unlikely sources. The link between Gaucher disease and Parkinson disease is just such an example.

Gaucher disease is a rare inherited disorder in which individuals with the disease have a host of symptoms, including skeletal deterioration, anemia, and organ dysfunction. The disease is caused by defects in both copies of a gene called glucocerebrosidase (GBA). Gaucher disease has been found in nearly all populations around the world, but it is most common among individuals of Ashkenazi Jewish ancestry. As early as 1939, it was reported that patients with Gaucher disease were coming to their doctor with parkinsonian symptoms. However, it was not until recently that researchers hypothesized that a deficiency of glucocerebrosidase (such as is found in patients with Gaucher disease) might contribute to an increased risk of parkinsonism. To test whether there was a link between Gaucher disease and Parkinson disease (PD), researchers examined the gene defective in Gaucher disease (called GBA) to determine whether alterations in the DNA sequence of this gene were found at higher frequency among individuals with PD as compared to those who did not have PD (called controls). Initial studies suggested that

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10 COMMON SYMPTOMS OF PD (AND SOME YOU MAY NOT KNOW)

By Claire E. Wegel, MPH, CCRP
Indiana University

1. Tremor
2. Rigidity (stiff muscles)
3. Bradykinesia (slow movement)
4. Postural instability (poor balance)
5. Shuffling gait
6. Depression
7. Reduces facial expression
8. Changes in handwriting
9. Speech changes
10. Personality changes

These symptoms are caused by the death of dopamine-producing cells in the brain. Dopamine is an important chemical messenger which is used to send information to the parts of the brain that control movement. If you or someone you know has PD, you are likely very familiar with these symptoms.

There are, however, many other less well recognized symptoms that are very common in individuals with PD. One symptom which is believed to begin very early in the onset of PD is the loss of the sense of smell. Some individuals report losing the ability to smell even before the onset of other PD symptoms.

Another symptom that is commonly experienced but less commonly discussed is constipation. Almost all individuals with PD experience problems with slowed digestion and constipation as their PD progresses. This may be due to the improper functioning of the autonomic nervous system. The autonomic nervous system is responsible for regulating smooth muscle activity. If this system is not working properly, the intestinal tract might operate slowly, causing constipation. In addition, some medicines used to treat Parkinson's disease can cause constipation, particularly the anti-cholinergic agents such as trihexyphenadyl (Artane) and benztropine (Cogentin). Improper function of the autonomic nervous system also causes the excessive salivation and bladder problems that some people with PD experience.

In some cases, as the disease progresses, the degeneration of brain cells caused by PD also occurs in areas of the brain that control emotion and cognitive ability. As a result, some individuals with PD may experience anxiety, sleep disturbances, and dementia.

If you or a loved one are experiencing any of these symptoms, it is important to discuss them with your primary physician or neurologist. They may have recommendations to help you better manage these symptoms. And, always, talk with your doctor before you take any over-the-counter medication.

DNA SEQUENCE VARIANTS IN GBA

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particular sequence changes in the GBA gene did, in fact, appear to be at higher frequency among people with PD as compared with controls.

The researchers in the PROGENI study decided to test this hypothesis in our families who have multiple members with PD. We looked for DNA sequence changes in the part of the GBA gene that makes the protein. We found multiple DNA sequence changes in the GBA gene in these families; five of the DNA sequence changes have also been reported by other researchers. We then looked for these five DNA sequence changes in all PROGENI participants. We found that PROGENI participants with PD were nearly three times more likely than controls to have one of these five GBA sequence changes. We also found that PROGENI participants who had one of these five DNA variants in the GBA gene reported showing PD symptoms six years earlier than participants who did not have one of these five variants. These results have just been published in the journal Neurology.

We find these results very exciting and hope that these data will shed new light on the causes of PD. However, we must include a word of caution. DNA sequence changes in GBA appear to act as a risk factor for Parkinson disease. That means that some individuals who inherit one of the DNA sequence changes may never develop PD, and many individuals with PD do not have any of these sequence changes in GBA. Therefore, we believe it is very important that researchers continue to test the GBA gene in individuals of all races and ethnicities to identify changes in the DNA sequence of this gene.

We found that PROGENI participants with PD were nearly three times more likely than controls to have one of these five GBA sequence changes.

We believe that through these studies, researchers will be able to better understand how this gene acts to affect the risk for PD. With this information, we hope that researchers can provide better estimates of whether each DNA sequence change in GBA increases the risk of PD. More importantly, we hope to understand how much the risk of PD is increased in people with GBA gene sequence changes over that of the general population.

In the meantime, the PROGENI researchers will continue our search to identify additional genes that increase or decrease the risk of Parkinson disease.

PROVIDING INFORMATION TO US ABOUT A FAMILY MEMBER

By Cheryl A. Halter, MS, CCRC, Indiana University

The PROGENI study continues to gather information each year about the research participant's symptoms of Parkinson disease and about the family's history of Parkinson disease. Sometimes, over the course of the study, an individual may no longer be able to provide information. This may happen because of the individual's increased physical or cognitive disability, or in some cases due to the death of the individual. When this occurs, the PROGENI staff will often ask other family members, typically a spouse or offspring, to continue to provide information about the participant's PD or family history. When a family member begins to provide information about others, that family member also becomes a PROGENI study participant.

What are we going to ask you to do?

If you are a person who provides information about a member of your family, we will be asking you to also sign an Informed Consent form. We will ask you to sign this document (along with a HIPAA, privacy form) for yourself, not for your family member. We feel that by asking everyone who provides information to the study to sign an IC, we are better informing them about the study.

What is an Informed Consent form?

Individuals are required to sign an Informed Consent document before they can take part in a clinical research study. The Informed Consent form (IC or ICF) is a document that provides the potential research participant with specific information about the study. The Federal government dictates what information should be contained in the document. Among other things, people should be informed about the purpose and procedures of the study, how many people will be taking part in the study; any risks, benefits, or costs associated with taking part in the study and information about who to contact if they have questions or concerns about the research.

Participants must also be told that the research is voluntary, and that they can stop their participation at any time. They should also be informed about steps taken to maintain the confidentiality of information they provide, as well as information learned about them as a result of taking part in the study.

While the IC is a document, it is also a process that continues throughout the individual's participation in the research study. When an individual is enrolled into a research study they are given an IC form to read, review and sign. The investigator and coordinators conducting the study are available to answer and address any questions or concerns the person might have about the research. This process of answering questions and addressing concerns continues throughout the individual's participation. So, by signing an Informed Consent form, you will be confirming that you understand the research and are willingly providing information to us for our research.

We always welcome your questions about the PROGENI Study. If you are a person providing information about another member of your family, please contact us if you have questions when you receive the study documents. We will answer your questions and walk you through the process of signing the forms.

> You can contact us at 1-888-830-6299 (toll-free) or by email at PROGENI@iupui.edu.

AUTOPSY IS AN IMPORTANT PART OF OUR RESEARCH

By Tatiana Foroud, PhD and Cheryl A. Halter, MS, CCRC, Indiana University

The word "autopsy" is derived from the Greek word autopsia, which means to see with one's own eyes. An autopsy is the examination of brain tissue by a pathologist with special training in the area of neurological disorders, such as Parkinson disease. The pathologist looks for changes in brain tissue that would only occur in an individual with Parkinson disease.

While it is often difficult to decide to pursue an autopsy of a family member, there are several important reasons to consider this option. First, a post-mortem examination of the brain is the only way to definitively diagnose Parkinson disease. Second, information obtained through an autopsy may provide family members with essential information, particularly in the case of hereditary diseases. Third, the autopsy procedure provides additional tissue samples for research into the causes and mechanisms of the disease.

PROGENI and PROGENI Cares participants who have not been diagnosed with Parkinson disease may also take part in our autopsy programs. We have much still to learn about how the brain changes as we age. It is important that we not only understand the changes in the brain which are caused by Parkinson disease, but we also need to understand how the normal aging process affects brain tissue.

Many families are reluctant to discuss an autopsy and wait until the last moment to do so. The time when a family member passes away is filled with many emotions as well as the need to carry out any arrangements and notify the necessary individuals. By having the autopsy planned well in advance, this time will not have the added stress of deciding whether or not to have an autopsy done, contacting all of the individuals needed to make the decision, and alerting the appropriate physicians. Planning ahead allows a family peace of mind during the grieving process and ensures that the autopsy will be properly performed. Planning ahead does not obligate you or your family to have an autopsy; you can change your mind at any time.

Coping with a degenerative illness affecting a family member is emotionally difficult as is the decision to prearrange an autopsy; however, it is important for both the family and the community. We will pay all costs associated with the autopsy such as transportation of the body, brain tissue removal, and neuropathological examination of the tissue.

PROGENI staff members can discuss autopsy with you and answer any questions that you might have. We can work together to plan the autopsy and ensure that the opportunity to gain this valuable family medical information is not lost.

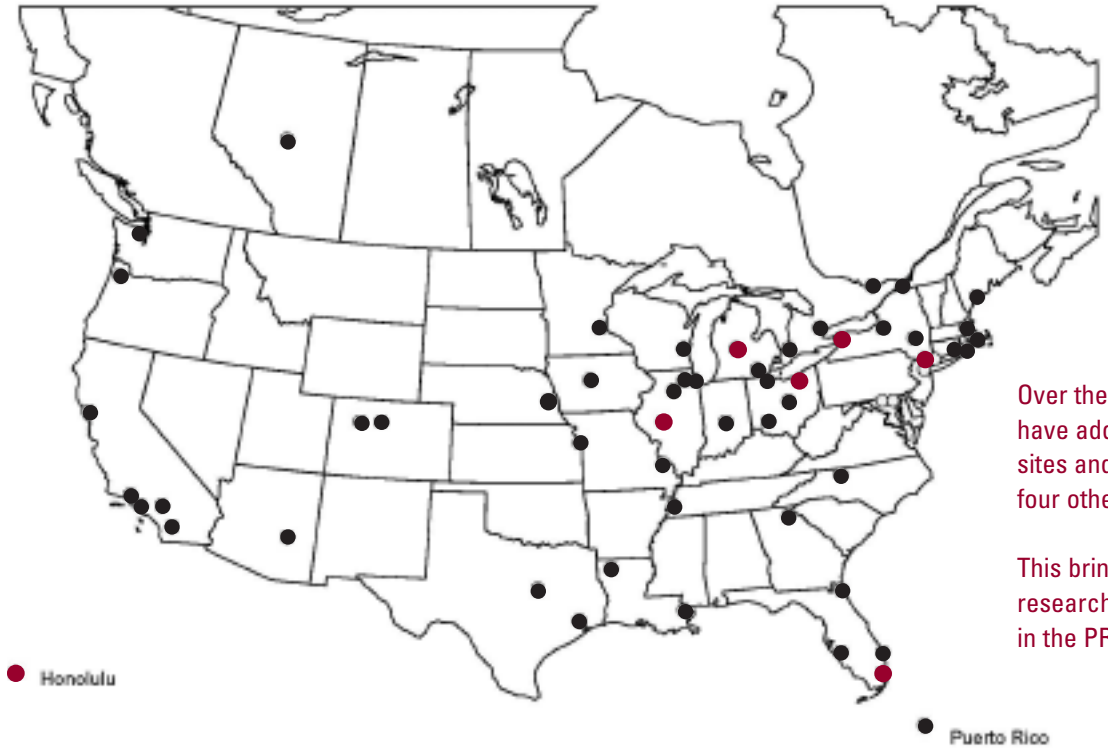
> For further information, please contact - Sue Fox (PROGENI) or Claire Wegel (PROGENI Cares) at 1-888-830-6299.

DID YOU KNOW?

- Parkinson disease is a chronic neurological condition named after Dr. James Parkinson, a London physician who was the first to describe the syndrome in 1817.
- According to the National Institute of Neurological Disorders and Stroke, about 50,000 Americans are diagnosed with Parkinson disease each year, with more than half a million Americans affected at any one time.
- PROGENI enrolled its first family in 1998 and has collected information from more than 900 families.
- To date, 2,500 people have completed a study visit for PROGENI or PROGENI Cares.
- We have gathered information on participants from all 50 U.S. states, the District of Columbia, and Puerto Rico. Additionally, we have participants from seven of the ten Canadian provinces.

MAJOR EXPANSION OF THE PROGENI STUDY TO NEW SITES

By Tatiana Foroud, Ph.D., Indiana University



Over the past year we have added seven new sites and welcomed back four other sites.

This brings the number of research centers participating in the PROGENI study to sixty.

We are pleased to announce a major expansion in the number of research facilities participating in the PROGENI study. Over the past year we have added seven new sites and welcomed back four other sites. This brings the number of research centers participating in the PROGENI study to sixty. See the map for all the sites in North America.

● The new sites are shown in red.

The impact of the addition of these investigators and coordinators is already being felt in increased recruitment and less travel for subjects to undergo a Study Visits. Please join us in welcoming the following:

Dr. Laura Marsh and
Ms. Melissa Gerstenhaber
John Hopkins, Baltimore MD

Dr. Thomas Guttuso
University of Buffalo, Buffalo, NY

Dr. James Sutton and Ms. Margarita Ramos
Pacific Neuroscience Medical Group, Oxnard, CA

Dr. Christopher Hyson
and Ms. Julie Megens
London Health Sciences Center, London ONT

Dr. Anwar Ahmed and Ms. Patty St. Marie
Cleveland Clinic, Cleveland, OH

Dr. Peter Lewitt and
Ms. Patricia Kaminski
Henry Ford Hospital, Southfield, MI

Dr. Alessandro DiRocco
and Dr. Sara Varanese
NYU Parkinson & Movement Disorder, Center, New York, NY

Dr. Roger Elble and Ms. Dolly Kelley
Southern Illinois University, Springfield, IL

Dr. Webster Ross and
Ms. Stephanie Terashita
Pacific Health Research Institute, Honolulu, HI

Dr. John Goudreau and
Ms. Dossie Snider
Michigan State University, East Lansing, MI

Dr. Stuart Isaacson
and Mr. Robert Delaney
Parkinson's Disease & Movement Disorders Center, Boca Raton, FL

Remember, the PROGENI study is now recruiting any individual with Parkinson disease who has a parent, sibling or child who has or had Parkinson disease. The other family member does not need to be living in order for the family to qualify for the study. We welcome new referrals to the study.

Useful Sources for Information and Support

The American Parkinson Disease Association (APDA)
http://www.apdaparkinson.org
Tel: 718-981-8001 or 800-223-2732

The Michael J. Fox Foundation for Parkinson's Research
http://www.michaeljfox.org
Tel: 800-708-7644

National Parkinson Foundation
http://www.parkinson.org/
Tel: 305-243-6666 or 800-327-4545

Parkinson's Disease Foundation (PDF)
http://www.pdf.org
Tel: 212-923-4700 or 800-457-6676

Parkinson Disease Information and Resources
http://www.pslgroup.com/PARKINSON.htm

The Parkinson Study Group (PSG)
http://www.parkinson-study-group.org/

World Parkinson Disease Association
http://www.wpda.org/
Tel: [39] 02 667.13.111 (Italy)

Parkinson's Action Network (PAN)
info@parkinsonsaction.org
http://www.parkinsonsaction.org
Tel: 800-850-4726 or 202-638-4101
Fax: 202-638-7257

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