

What is PROGENI?

Parkinson's Research: The Organized Genetics Initiative, also known as PROGENI, is a research effort between several research groups. Many families have been referred to the project by The Parkinson Study Group, a group of neurologists from throughout the United States and Canada, who conduct clinical drug trials for the treatment of PD. Scientists involved in the study are also located at Indiana University, the University of Rochester, Cincinnati Children's Hospital as well as the University of California in both San Diego and Irvine.

The PROGENI study is sponsored by the National Institutes of Health and currently involves approximately 450 pairs of brothers and sisters throughout North America who are affected, or possibly affected, with Parkinson's disease. To be eligible to participate in this study, families must have two or more living siblings (sisters and/or brothers) affected with, or suspected of having, PD.

We would like to thank the many families who have participated in PROGENI by providing family history information and completing a Study Visit. Our hope is that through the efforts of our participants, we will one day unravel the mystery of devastating diseases, like PD. We are always eager to accept new families to help us reach this goal.



**PARKINSON'S RESEARCH:
THE ORGANIZED
GENETICS INITIATIVE
(PROGENI)**

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PROGENI News

NEWSLETTER FOR PARKINSON'S RESEARCH:
THE ORGANIZED GENETICS INITIATIVE

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PROGENI: Parkinson's Research: The Organized Genetics Initiative

By Tatiana Foroud, Ph.D. - Indiana University



The goal of the PROGENI study is to identify the genes that contribute to Parkinson disease. During the past four years, researchers at Indiana University have been working with the neurologists from the Parkinson Study Group (PSG) to identify and enroll families with multiple members diagnosed with Parkinson disease.

As a result of this effort, we have now have had over 1,000 individuals complete the PROGENI study!

Through the active involvement of so many families who have generously participated in this research study, we have been learning a great deal about Parkinson Disease. Our focus remains the identification of the genes contributing to Parkinson disease. It is our hope that through the identification of the genes that increase or decrease the risk of Parkinson disease, better treatments might be developed that could delay or reduce the severity of disease symptoms.

Our studies of the PROGENI families have allowed us to identify several regions on different chromosomes, which may contain genes that contribute to the risk of Parkinson disease. These include regions of DNA on chromosomes 2 and X. During the past few months, we have performed additional analyses to more carefully study the region on chromosome 2. Through this process, we have learned that we find the

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Genetic Definitions

The following definitions were obtained from the Human Genome Project Information Website (http://www.ornl.gov/TechResources/Human_Genome/project/info.html)

Cells are the fundamental working units of every living system. All the instructions needed to direct their activities are contained within the chemical DNA (deoxyribonucleic acid).

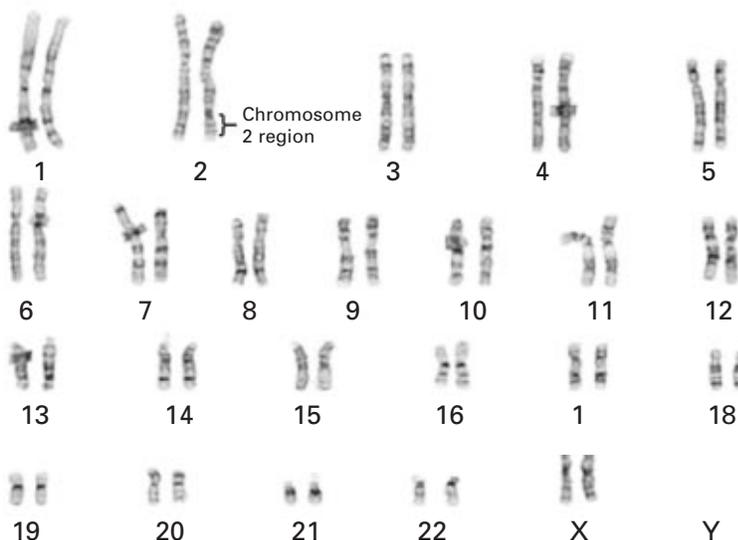
DNA (Deoxyribonucleic Acid) from all organisms is made up of the same chemical and physical components. The DNA sequence is the particular side-by-side arrangement of bases along the DNA strand (e.g., ATTCCGGA). This order spells out the exact instructions required to create a particular organism with its own unique traits.

The **genome** is an organism's complete set of DNA. Genomes vary widely in size: the smallest known genome for a free-living organism (a bacterium) contains about 600,000 DNA base pairs, while human and mouse genomes have some 3 billion. Except for mature red blood cells, all human cells contain a complete genome.

DNA in the human genome is arranged into 24 distinct **chromosomes**—physically separate molecules that range in length from about 50 million to 250 million base pairs. A few types of major chromosomal abnormalities, including missing or extra copies or gross breaks and rejoinings (translocations), can be detected by microscopic examination. Most changes in DNA, however, are more subtle and require a closer analysis of the DNA molecule to find perhaps single-base differences.

Each chromosome contains many **genes**, the basic physical and functional units of heredity. Genes are specific sequences of bases that encode instructions on how to make proteins. Genes comprise only about 2% of the human genome; the remainder consists of noncoding regions, whose functions may include providing chromosomal structural integrity and regulating where, when, and in what quantity proteins are made. The human genome is estimated to contain 30,000 to 40,000 genes.

Genetic susceptibility is the state of being more likely than the average person to develop a disease as a result of genetics.



Chromosomes 1-22 and the two X chromosomes of a female

Parkinson Research

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greatest evidence for a gene on chromosome 2 when we study those families with the strongest family history of Parkinson disease.

Chromosome 2 is one of the longest chromosomes and therefore contains many genes. We now have a great deal of work ahead of us and must begin to examine the DNA sequence of hundreds of genes located in this particular region of chromosome 2. We would expect that in individuals with Parkinson disease, a gene that contributes to the development of Parkinson disease might have a change in the DNA sequence. The study of the DNA sequence of a gene is a slow process and requires the comparison of many samples from individuals with Parkinson disease as well as individuals who have not developed symptoms of disease.

To help us better understand Parkinson disease we always keep in contact with families who have participated in our study. It is important that we learn about new family members that may be showing signs of Parkinson disease so that we can ask them if they would like to participate in this important research project. We look forward to keeping you informed of the important scientific information we are learning from this study. We also want to thank you again for your willingness to help us better understand the genetics of Parkinson Disease.



Getting to Know The PSG Coordinators

What is a Clinical Research Coordinator?

By Cheryl Halter, M.S. - Indiana University

The coordinators of the PROGENI study come from a variety of backgrounds to work on the study. While most are nurses and many have advanced degrees, a nursing degree is not required. What is required is the ability to communicate well with people, put people at ease and manage many tasks, often all at the same time. For most coordinators, the PROGENI study is only one of many research projects they conduct.

The main coordinator responsibilities for the PROGENI study include recruiting subjects and scheduling and conducting study visits. Recruiting subjects may involve discussing the study with clinic patients, writing articles for newsletters, speaking at support group meeting and following up on “leads” provided by patients and co-workers. The coordinator will contact subjects to schedule the study visit and will provide information about location and access to the clinic. They may also provide information about lodging and airport access to subjects who are traveling to undergo their visits. During the study visit, the coordinator will complete several questionnaires with subjects, draw or arrange for the draw of blood samples, and assist the Investigator with her/his portion of the visit. After the visit is complete the coordinator must complete additional paperwork and ship

the blood sample. They are also responsible for reviewing the data collected during the study visit and correcting that data as necessary.

While coordinators balance many tasks, they say that they enjoy the PROGENI study. Subjects also report that they enjoy the study visit and are excited to participate. This may be because PROGENI only requires a single visit and allows the coordinators and subject’s time to get to know each other. Perhaps you had a memorable interaction with a PROGENI coordinator. If so, we would love to hear about it. We are glad to have the support of the coordinators for the study for, without them, the project could not succeed. As an ongoing feature, we would like to highlight some of the PROGENI coordinators and see what being a coordinator is like at the various PSG sites.

Theresa Shirley

University of Saskatoon Royal University Hospital,
Saskatoon SK, Canada

How long have you and Dr. Rajput been doing PD research?

5 1/2 years.

How many PD patients do you see in a day? a week?

Averages about 2 a day or 10 - 15 a week.

How many PROGENI Study Visits have you done?

42 visits

What is your favorite part of the Study Visit?

Often, when patients are asked to provide the different residences and careers over their lifetime, they usually take a trip down memory lane, and very interesting stories are shared, which wouldn't happen at a routine clinic appointment.

What do you like most about your involvement with PROGENI? Why?

From a coordinators perspective, it is an 'easy' study to do. The project leaders are very approachable and helpful. As we approach the numbers of sibling pairs, I try to keep tabs on these subjects since we have

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Did You Know?

- PROGENI enrolled its first family in 1998 and currently has close to 600 families actively participating.
- PROGENI has gathered information on subjects from 48 U.S. states and Puerto Rico (only Delaware and Vermont are not represented). Additionally, we have subjects from seven of the ten Canadian Provinces (New Brunswick, Nova Scotia and Prince Edward Island are not represented)
- We have done a study visit on a subject in Italy and have collected blood samples from individuals in England and Ireland.



A Personal Story...

Anonymous

I had been sick for several days with bronchitis, sinusitis, fever, and an inner ear infection. Having Parkinson's disease and an inner ear infection that gave me dizzy spells had been especially challenging. The form of Parkinson's I have does not cause me to tremble and shake. My muscles stiffen, tense up, and refuse to move. My

medication doesn't work as well as it once did. I spend hours unable to relax or get into a comfortable position. On good days rising from a sitting position to standing or getting up and out of bed are struggles. Rolling over in bed at night has become a forgotten art! I usually plan my days around the times I can move somewhat easily and I hadn't been able to do

anything for days. On this day, even though I wasn't having the dizzy spells any longer, movement had been more difficult. I believed nothing in the world was going right for me or ever would again. I wondered why me. I had even missed getting to see my newborn nephew for "fear of giving him something." I had a major case of the "poor me." I was really feeling sorry for myself.

It was an unusually warm beautiful evening in January. Dave suggested I join him and sit on the back porch steps. I was reluctant at first because I didn't believe I would be able to get myself through the house. Dave had me put my hands on his shoulders and walk

behind him. One step at a time he got me through the house, out the back door and seated on the back porch steps. The fresh air felt good. (Dave and I came together at a time in our lives when we both were dealing with medical problems. We had a common bond of understanding even though his problems are quite different from mine. He is robbed of much of his strength and energy. He generously uses much of what he has left helping me).

“We danced and laughed until we both were winded.”

We sat on the back porch and watched a group of children as they rode in the street on scooters and skateboards and played with a boom-a-rang. The sunset was beautiful. I said a silent prayer and asked God to let me relax for “just a little while”.

When we decided to go inside I was able to move a little better. Parkinson’s often makes me unaware I am stooped over and walking on my toes. When this happens Dave acts as my coach. He tells when I am standing straight. I concentrate on keeping my feet flat. It feels totally wrong and like I am going to fall backwards. I have learned to trust him on this and believe him and not my body! This was one of those times. Dave got me started. I took a deep breath and took a step. I was able to get myself into the living room on my own power.

Dave had stayed in the kitchen to cook us something to eat. I heard music and decided to join him. I made my way a step at a time from the living room to the kitchen and sat down at the table. Dave told me not to sit down but to stand up instead. He put his arms around me and indicated he wanted to dance. I thought to myself, “yeah right”,

but I went along with it. The first steps were wobbly but became easier after a few moments. We were dancing together! We were not “Fred and Ginger” by any stretch of the imagination. We did managed not to fall or step on each other’s feet. We even managed a few twirls! We danced and laughed until we both were winded.

I was able to return to the living room walking naturally without coaching or concentrating. Dave brought our food into the living room to eat. We ate and relaxed on the sofa to watch television. I was so comfortable I fell asleep during a program I had intended to watch.

When I awoke from my nap, like Cinderella at a ball, it was gone. I had to make my way to the bedroom one step at a time. I lay down in bed, grabbed the side of the mattress with both hands and struggled to roll myself over in an attempt to get comfortable. It didn’t make me disgusted and angry like it usually did. I felt strangely calm and happy. It was a good feeling. Dave and I had been given a gift.

Thank you God.

Ten Common Symptoms of PD

If you recognize several of these warning signs in yourself or a loved one, the PROGENI staff recommends consulting a physician. Early diagnosis is an important step in getting appropriate care and support services.

1. Tremor
2. Rigidity
3. Bradykinesia (slow movement)
4. Postural instability
5. Shuffling Gait
6. Depression
7. Reduced facial expression
8. Change in handwriting
9. Speech changes
10. Personality change

As part of the PROGENI study visit, we asked all participants to tell us their first symptom of PD. In our sample, 52% of the subjects reported tremor as their first disease symptom. Another 6% said rigidity was the first symptom they noticed of PD. Nine percent of participants said their first symptom of PD was bradykinesia.



Thank You!

Thank you to all the families who have expressed interest in autopsy. At the time of our first newsletter, we had only planned eight autopsies. Since that time, we have completed, planned, or are in the active process of planning over 60 PROGENI autopsies! Your generous contribution towards Parkinson's research is greatly appreciated and respected.

For questions or additional information about the autopsy program, please contact Jessica Leatherland at 1-888-830-6299 or 317-278-8413.

PSG Coordinators

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shifted gears to try and obtain brain autopsies for those subjects who have died.

Deborah Fontaine

University of California-San Diego, San Diego, CA USA

How long have you and Dr. Shults been doing PD research?

Dr. Shults has been doing PD research for 21 years, 11 of them have been with me.

How many PD patients do you see in a day? a week?

We see subjects 2 days a week and the number we see varies. It all depends on the schedule of the study so some days are hectic and other days are very hectic.

How many PROGENI Study Visits have you done?

I believe we have seen 22 PROGENI subjects with several more in the works.

What is your favorite part of the Study Visit?

All PD visits are interesting because PD subjects have all been so warm and interesting. Their backgrounds are diverse and all have wonderful stories to tell. This is why I like the part where I go over all their occupations and where they all have lived. Some subjects have traveled the world and yet even some of the non-travelers have had interesting jobs.

What do you like most about your involvement with PROGENI? Why?

PROGENI and all PD research projects are interesting because they get us closer to better treatments and possibly a cure

Jo Belden

Indiana University
Indianapolis, IN USA

How long have you and Dr. Wojcieszek been doing PD research?

Approximately 8 years.

How many PD patients do you see in a day? a week?

About 10-12 per week (2 a day).

How many PROGENI Study Visits have you done?

63 visits.

What is your favorite part of the Study Visit?

I like the personal contact I have with the patients.

What do you like most about your involvement with PROGENI? Why?

I like the fact that we may be able to find answers to why patients get PD. I hope that we may be able to find a cure.

What can genetics tell us about PD?

By Tatiana Foroud, Ph.D. – Indiana University

A decade ago, many scientists and physicians thought that Parkinson disease was not a 'genetic disorder'. It appeared at that time that environmental factors, such as rural living, pesticide use, or head trauma, might be more important in determining whether an individual would or would not develop Parkinson disease. In the past few years, this thinking has changed dramatically.

A number of studies have carefully examined families with a member diagnosed with PD. They have found that the close relatives of an individual with PD, that is the person's parents, siblings and children, were at increased risk to also develop PD. Unfortunately, it has been difficult to estimate the exact increase in risk and the estimate provided by different studies has varied greatly. Some studies estimated the risk to close relatives of an affected person to be twice that of an individual from the general population while other studies have found the risk to be as much as 14 times higher. While it will require more research to better estimate how much the risk is increased, the most important lesson to be learned from these studies

The most important lesson to be learned from these studies is that genes are important in determining who will and will not develop PD.

is that genes are important in determining who will and will not develop PD.

The PROGENI study is striving to identify genes that determine an individual's risk to develop PD. It is only through the study of families having two or more living brothers and/or sisters diagnosed with PD that we will be able to identify the genes contributing to this disease.

Useful Sources for Genetic Information

There are many online resources that are available and provide more detailed information about human genetics. With the 50th anniversary of the discovery of the structure of DNA, there has been lots of information distributed about the human genome project and progress made in the field of genetics. The following web sites provide a glossary of genetic terms, information about the human genome project, more detailed descriptions of genetic concepts.

- <http://www.genome.gov/>
- <http://www.kumc.edu/gec/>
- http://www.ornl.gov/TechResources/Human_Genome/home.html



Spring into Exercise

By Jessica Leatherland – Indiana University

Spring weather seems to set the mood for getting fit and starting an exercise program. While you are doing some spring-cleaning around the house, dusting off the walking shoes would not be a bad idea! The physical and psychological benefits of exercise make it worthwhile for Parkinson's patients.

A regular exercise program will help keep joints flexible, muscles strong, and help maintain balance and mobility. Several PROGENI participants have commented on how exercise has improved their overall health and helped control some of their symptoms. Following are some suggestions for the PD patient interested in exercise:

- Consult your physician before starting an exercise program.
- If needed, consult a physical therapist for exercise suggestions that suit your needs.
- Ideally, one should exercise approximately three times per week.
- Before and after exercising, drink plenty of fluids and spend an adequate amount of time stretching and breathing.
- Never over exert yourself! Stop and rest when appropriate.
- Consider trying aerobic sports, such as walking or swimming (with your doctor's approval)
- We highly suggest trying water exercises because they are sensitive on the joints.

Questions from You

Is there a connection between spinal muscular atrophy and PD?

Idiopathic "garden variety" Parkinson disease is not associated with spinal muscular atrophy (SMA). However Parkinson disease is not an uncommon disease and may happen to patients with SMA. There is a rare condition seen in the island of Guam called Parkinsonism-dementia-ALS syndrome that may cause spinal muscular atrophy. The spinal muscular atrophy

seen in this condition tends to affect the distal portion of the extremities while the patient has significant dementia, stiffness and postural deformities. However, this syndrome is not a true SMA. In summary, there is not an increased risk of Parkinson disease in SMA patients or vice versa.

Xabier Beristain, MD
Assistant Professor in Neurology
Indiana University

Useful Sources for Information and Support

The American Parkinson Disease Association (APDA)

<http://www.apdaparkinson.com/>
Tel: 718-981-8001 or 800-223-2732

The Michael J. Fox Foundation for Parkinson's Research

<http://www.michaeljfox.com>
Tel: 800-708-7644

National Parkinson Foundation

<http://www.parkinson.org/>
Tel: 305-547-6666 or 800-327-4544

Parkinson's Disease Foundation (PDF)

<http://www.parkinsons-foundation.org>
Tel: 212-923-4700 or 800-457-6676

Parkinson Disease Information and Resources

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 66713111 (Italy)



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