

August 2015
Newsletter



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Thank you!

More than **5,500** participants consented to be part of the EPGP research effort, with an additional 250 healthcare providers and a study team of about **150** people. This newsletter is our way of reaching out once or twice a year to say **thank you** for your participation and keep you up to date with **new developments** in and related to EPGP.

Since our last newsletter, the EPGP investigative team has **continued their study of the genes** and information in the EPGP dataset.

- In the **Epi4K Project 1** for the epileptic encephalopathies, the EPGP cohort contributed to new gene discoveries: **two new genes** showed clear statistical evidence of association with epileptic encephalopathies (GABR3 and ALG13), and **many other genes** (CACNA1A, CHD2, FLNA, GABRA1, GRIN1, GRIN2B, HNRNPU, IQSEC2, MTOR and NEDD4L) also had de novo mutations (new changes in the genes that were not inherited from the participants' parents). The group has also shown that de novo mutations observed are enriched in specific gene sets, including genes regulated by the **fragile X** protein. This group is continuing to look for new gene discoveries in the families with infantile spasms, Lennox-Gastaut Syndrome, and polymicrogyria and periventricular heterotopia.
- Several of the investigators in the **Epi4K Project 2** are continuing to look very carefully at the families with generalized and focal epilepsies to look for **patterns in the genes and clinical features**.

In addition to these new discoveries, investigators have been making steps toward better understanding the **genes of epilepsy and the mechanisms of specific epilepsies**. For example, two scientific groups have been examining the **MRIs** and **brain tissue development** of participants with polymicrogyria and periventricular nodular heterotopia to better understand how these conditions develop, and which genes might be involved. These new findings have been presented at several meetings, including the American Epilepsy Society Meeting in Seattle, in December 2014.

The EPGP research group has also joined forces with many researchers from around the world to push forward the work toward **precision medicine** and an effort to focus on **patient-centered research**.

Precision Medicine

Precision medicine is developing treatments tailored to individual patients, based on their genetic, clinical, and risk factor profiles. The EPGP/Epi4K Consortium is working to obtain genetic findings that will translate into **"precision" medicine** for patients with many types of epilepsy. In this new paradigm, every patient can be compared against data and historical information from many other individuals with biomarkers like theirs, thus enabling their doctors to better predict how the patient will fare and to better **match treatments to the individual patient**.

In the field of epilepsy, **recent advances** in fields such as genetics, neuroimaging, stem cell biology and model systems are beginning to provide guidance when a doctor is choosing from existing therapies or wants to develop new therapies. These advances, combined with the

increased ease with which clinicians, scientists, and patients can work together collaboratively, have set the stage for a **new era in epilepsy care** in which some day more patients will benefit from having a highly accurate diagnosis of the cause of their epilepsy and, as an extension, an etiology-specific treatment plan.

On September 29-30, 2014, EPGP, Epi4K, and other investigators from around the world came together in a **Precision Medicine Conference** to map out a strategy for **accelerating the pace with which this goal can be achieved**. Scientists, clinicians, patients, and government officials discussed the key challenges to achieving precision medicine for epilepsy and mapped out strategies to address these challenges—including **new research collaborations**, protocols for **excellence in patient care**, and **immediate actions** that can improve many facets of genetic testing and information for patients, providers, and the health care system overall.



This group grew in size and met at the American Epilepsy Society Meeting in December 2014, and decided to form a **worldwide** collaboration of research projects. This new project will be known as **Epi25** and is comprised of more than **39,000 participants with epilepsy from 52 of the largest epilepsy research projects in the world**. Last month, the Epi25 Consortium supported an application by the Broad Institute (a large genetic sequencing center) to whole-genome-sequence 25,000 people with various diseases—a project that would be funded by the National Human Genome Research Institute (**NHGRI**) / National Institutes of Health (**NIH**). Many of those participants may come from the EPGP group! This new project will develop over the coming year, and we will keep you up to date with new information.

Patient-Centered Research

New treatments and better care for people with epilepsy are developed through research. **Successful research that leads to new discoveries comes from the contributions of the thousands of people, like you, who have volunteered in research projects.**

An important aspect of the EPGP team's ongoing work is striving toward **patient-centered research**. A team of research staff, scientists, and patients from EPGP and other research projects are working together to address a number of questions, such as:

- How can we make research projects more **patient-friendly**?
- How can we get **discoveries** to patients **faster**?
- How can we help research participants with similar diseases **connect with each other** to share information and improve their health care?
- How can we encourage **more doctors and hospitals to participate** in and offer research projects to their patients?
- How can we improve the ways that patients get information about research projects, so that they have a opportunity to participate in research that is **right for them**?
- What kinds of **benefits** can research projects provide to study participants?

Someday, we would like all research projects to have a patient advisory board, and that there is a well-designed research project that every family has a chance to consider participating in. We

will provide updates about these efforts, and in the meantime we have included a short resource list of information about epilepsy, as well as research and patient groups related to EPGP:

- [The Epilepsy Foundation's Epilepsy.com](#)
- [Citizens United for Research in Epilepsy \(CURE\)](#)
- [Finding a Cure for Epilepsy and Seizures \(FACES\)](#)
- [Rare Epilepsy Network \(for families with LGS and many other rare epilepsies\)](#)
- [Infantile Spasms Site by Child Neurology Foundation](#)
- [Lennox Gastaut Foundation](#)
- [Lennox-Gastaut Foundation Facebook Group](#)
- [Wishing for Elliott—an organization researching SCN8A](#)
- [The Charlie Foundation for Ketogenic Therapies](#)
- [Patient-Centered Outcomes Research Institute](#)
- [NIH Web Page about Clinical Research Trials](#)

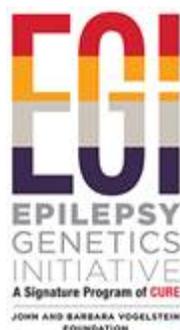
Continuing of our Research Network—Together We Can!

As **discoveries continue to emerge** from your contribution to the EPGP project, we wanted to **thank you** again for your commitment to epilepsy research and to improving the lives of people with epilepsy.

It is your partnership with ongoing research projects that creates information today—from which tomorrow's discoveries emerge! By continuing to work together, we can continue to build upon the already remarkable resource that we worked so hard to build—and continue to bring light to the questions that we all ask:

- [Why do I have epilepsy?](#)
- [Will my treatments work?](#)
- [Will I eventually no longer have epilepsy?](#)

Many new epilepsy studies and registries are active; some of the research projects highlighted below are projects by scientific groups who were part of EPGP; others are projects that are related to familial epilepsies like those studied by the EPGP Project.



[The Epilepsy Genetics Initiative \(EGI\)](#) is a new initiative created by the Citizens United for Research in Epilepsy ([CURE](#)), National Institute of Neurological Disorders and Stroke ([NINDS](#)), and Vogelstein Foundation to bridge the gap between people with epilepsy, clinicians, and researchers and advance [precision medicine](#) in epilepsy. EGI has created a centralized database to hold the [genetic data of people with epilepsy](#). The data (called exome data) will be analyzed and reanalyzed in an attempt to identify [the cause of the person's epilepsy](#). Findings will be reported back to the person's doctor. The data will also be made available to advance research. If you are having



genetic testing done, you can have your exome data contributed and studied at EGI. More information can be found [here](#). Contact the research team at Columbia for more information: (844) EGI-CURE or egi@CUREepilepsy.org

The [Human Epilepsy Project \(HEP\)](#) is a study about **biomarkers** in epilepsy (proteins in our blood or genes, or changes doctors can see on an MRI) and how people who were **newly diagnosed with epilepsy** are responding to their epilepsy **medications**. The research team, which includes many of the folks from EPGP, is enrolling 500 participants over 7 years. This new study has already yielded some interesting discoveries, particularly in brain MRIs and drug response. For more information: sabrina.cristofaro@nyumc.org



To expedite research into the rare epilepsies, ten rare epilepsy foundations have joined forces with the Epilepsy Foundation, Research Triangle Institute, Columbia University and New York University to create the first ever Rare Epilepsy Network (REN). The REN is building a patient registry to collect information about rare epilepsy patients to better understand these conditions, improve treatments, and improve the lives and quality of care of patients living with them. <http://www.epilepsy.com/ren>



[Ann Poduri, MD at the Epilepsy Genetics Program at Boston Children's Hospital](#) was one of the doctors who enrolled EPGP participants. Dr. Poduri continues to study **epilepsy genetic disorders**, particularly in infantile spasms, Ohtahara Syndrome, Dravet Syndrome, and malformations of cortical development. Contact the program for more information: (617) 355-8656



[Elliott Sherr, MD at the Brain Development Research Program](#) at the University of California, San Francisco helped develop the methods for studying the infantile spasms, Lennox-Gastaut Syndrome, and malformations participants in EPGP. His ongoing research is looking at the **epileptic encephalopathies** (infantile spasms and Lennox-Gastaut Syndrome), autism spectrum disorders, agenesis of the Corpus Callosum, and Aicardi Syndrome. Contact the Research Coordinator directly for more information: (415) 502-8039



Orrin Devinsky, MD at the New York University School of Medicine, has a [North American SUDEP Registry \(NASR\)](#). If any patient were to die from sudden unexplained death in epilepsy, the registry would like to talk to the family and include the patient's genetic sequence in the NASR Registry. Please contact the research group at (855) 432-8555 or [email](#) Dr. Devinsky directly.

New research studies continue to be developed. Please **stay in contact** with your clinical center, and look for opportunities to stay involved—through the central EPGP database or new research projects.

Together we can help improve the lives of people living with epilepsy!

Publications

Publications have been illuminating many sides of epilepsy—from migraine to Lennox-Gastaut phenotypes. Already published papers, talks, and presentations are listed on the EPGP website [here](#). **Highlights include** (click the link to see the paper):

The EPGP Collaborative. [The Epilepsy Phenome/Genome Project](#). Clin Trials. 2013 Aug;10(4):568-86. doi: 10.1177/1740774513484392. Epub 2013 Jul 1. PMID: 23818435

Epi4K Consortium; Epilepsy Phenome/Genome Project. [De novo mutation in epileptic Encephalopathies](#). Nature. 2013 Sep 12;501(7466):217-21. doi: 10.1038/nature12439. Epub 2013 Aug 11. PMID: 23934111

Pardoe, H., Mandelstam, S., Hiess, R., Kuzniecky, R., Jackson, G., Alzheimer's Disease Neuroimaging Initiative, The EPGP Project Investigators. [Quantitative assessment of corpus callosum morphology in periventricular nodular heterotopia](#). Epilepsy Research. 2015 109:40-47.

Dugan, P., Carlson, C., Bluvstein, J., Chong, D.J., Friedman, D., Kirsch, H.E., The EPGP Investigators. [Auras in Generalized Epilepsy](#). Neurology. 2014 Oct 14;83(16):1444-9.

Friedman D, Fahlstrom R; EPGP Investigators. [Racial and ethnic differences in epilepsy classification among probands in the Epilepsy Phenome/Genome Project \(EPGP\)](#). Epilepsy Res. 2013 Dec;107(3):306-10. doi: 10.1016/j.epilepsyres.2013.09.007. Epub 2013 Oct 1. PMID: 24139856

Widdess-Walsh P, Dlugos D, Fahlstrom R, Joshi S, Shellhaas R, Boro A, Sullivan J, Geller E; EPGP Investigators. [Lennox-Gastaut syndrome of unknown cause: phenotypic characteristics of patients in the Epilepsy Phenome/Genome Project](#). Epilepsia. 2013 Nov;54(11):1898-904.

Shain C, Ramgopal S, Fallil Z, Parulkar I, Alongi R, Knowlton R, Poduri A; EPGP Investigators. [Polymicrogyria-associated epilepsy: a multicenter phenotypic study from the Epilepsy Phenome/Genome Project](#). Epilepsia. 2013 Aug;54(8):1368-75. doi: 10.1111/epi.12238. Epub 2013 Jun 10.

Winawer MR, Connors R; EPGP Investigators. [Evidence for a shared genetic susceptibility to migraine and epilepsy](#). Epilepsia. 2013 Feb;54(2):288-95. doi: 10.1111/epi.12072. Epub 2013 Jan 7.

Nesbitt G, McKenna K, Mays V, Carpenter A, Miller K, Williams M; EPGP Investigators. [The Epilepsy Phenome/Genome Project \(EPGP\) informatics platform](#). Int J Med Inform. 2013 Apr;82(4):248-59. doi: 10.1016/j.ijmedinf.2012.03.004. Epub 2012 May 10.

