ILAE Commission on Genetics

Daniel Lowenstein, Chair

Daniel Lowenstein

The ILAE Commission on Genetics (Daniel Lowenstein, Chair) was created with several goals. Its first goal is to organize the search for human epilepsy genes on a worldwide scale, including the complex epilepsies that require for multicenter collaboration. Secondly, it will make the results of genetic research on the epilepsies readily accessible to clinicians, and improve the public understanding of genetic factors in epilepsy. Finally, the Commission will work with other ILAE commissions to increase understanding of how these genes cause epilepsy.

In the last several years, the Commission has worked on several initiatives. The first is to facilitate access to information about the identification and interpretation of gene mutations associated with epilepsy. The Epilepsy Genetic Association Database (EpiGAD) is growing and is being used regularly. However, to simplify an investigator's search, it will be merged with Epilepsiome, which is a more comprehensive database on epilepsy and genes that will allow professionals, patient organizations and families to gather relevant information on epilepsy-related genes. Epilepsiome will integrate with other available online resources (ClinGen, GeneReviews), but will have "trusted expert opinion" and regular updates as distinguishing features. Forty scientific volunteers are fully engaged in the gene curation efforts of this project. The Epilepsiome project is currently in a beta phase and the commission is coordinating efforts with other initiatives to provide a new visually oriented web.

The Commission also posts new messages weekly on the ILAE Genetics Commission Blog on topics related to genes and seizures. These posts are well received by the professional community, as the blog receives 5,000-7,500 views per month and has had more than 60,000 visitors since it started. In addition to the blog, we issue "The Channelopathist," a weekly email newsletter for the epilepsy community. For the Genetics Commission, the blog has been proven extremely valuable as an outreach tool for the community.

The second initiative is to assist in the creation of a centralized database of complete sequence data with variants that are paired with clinical information for as many patients as possible throughout the world. Formally known as the "Epilepsy Genetics Initiative (EGI)," it has been launched through a collaboration of the NIH-sponsored "Epi4K Center Without Walls" and the Chicago-based "Citizens United for Research in Epilepsy." The website http://www.cureepilepsy.org/egi/index.asp allows people to track this project and to help patients learn about the benefits of participation.

The third initiative continues the work of the ILAE Consortium on Complex Epilepsies. Lancet Neurology (Sept 2014; http://www.ncbi.nlm.nih.gov/pubmed/?term=lancet+neurology+++consortium+on+complex+epilepsies) published the consortium's first meta-analysis of GWAS data from nearly 9,000 subjects, which demonstrated risk alleles for the combined epilepsy cohort and for genetic generalized epilepsy. The Consortium is now undertaking sub-analyses of more specific phenotypes and of the relationship of loci influencing brain structure to those raising risk for epilepsies. Further collaborations are planned on epilepsy comorbidities by combined analyses investigating migraine and neuropsychiatric disorders.

Finally, the commission is working to increase genetics literacy among patients and clinicians. There are two primary efforts: the creation of educational brochures and the development of a Genetics Literacy Series for clinicians. The educational brochures include "Epilepsy and Genetics: Things You Want to Know," and were designed by Alica Goldman and other Commission members for patients and family members. It is available through the ILAE Genetics Commission website. Culturally sensitive Spanish and Arabic translations (http://www.ilae.org/Commission/genetics/) are on the ILAE website. A Japanese translation is under the review of the Japanese Epilepsy Society and the approval is planned for early 2016. Similar brochures in Chinese and other languages are a high priority by the ILAE. The Genetic Literacy Series targets clinicians who are often uncertain about or uncomfortable with genetic testing in epilepsy. The Genetics Commission, under the leadership of Nigel Tan, has a new series on Genetic Literacy in *Epilepsia*. These 12 papers aim to update and educate practicing clinicians about clinically relevant epilepsy genetics. The first paper was published in November 2015, and we anticipate this series will run to mid-2017.

Looking forward, there needs to be further effort in helping clinicians stay up-to-date on the latest findings in epilepsy genetics, given that we are now beginning to see the emergence of individualized therapies based on the patient's genomic profile. We will encourage patients and family members to understand the role that genetic testing may play in epilepsy evaluation and the value of involvement in the Epilepsy Genetics Initiative. Finally, we intend to explore the potential value of a global registry of patients with defined epilepsy gene mutations, with the goal of expediting observational studies and treatment trials.