COMMISSION ON GENETICS

Daniel Lowenstein

Chair
Dan Lowenstein (USA)

Members
Sam Berkovic (Australia)
Alica Goldman (USA)
Ingo Helbig (Germany)
Yuwu Jiang (China)
Mitsuhiro Kato (Japan)
Heather Mefford (USA)
Steve Petrou (Australia)
Parthasarathy Satishchandra (India)
Nigel Tan (Singapore)
MC Liaison
Helen Cross (UK)

Subcommission Members

Aims
- To organize the search for human epilepsy genes on a worldwide scale through broad participation by members of ILAE chapters.
- To prioritize complex epilepsies suitable for multicenter collaborative gene mapping studies.
- To make the results of genetic research on the epilepsies readily accessible to clinicians.
- To improve the public understanding of genetic factors in epilepsy.
- To work with related ILAE commissions to increase understanding of newly identified genes and their role in basic mechanisms of epileptogenesis and anti-epileptogenesis.
- Improving knowledge and application of genetics in epilepsy across the world.

Commission Activities June 2013 through June 2014

Initiative 1: Facilitate access to information regarding the identification and interpretation of gene mutations associated with epilepsy.

a. EpiGAD: The EpiGAD has been regularly maintained, updated and audited.
b. ILAE Genetics Commission Blog: To provide better outreach and communication to the professional community, the ILAE Genetics Commission has decided to run a blog on topics related to genes and seizures. We have adopted the "Beyond the Ion Channel" blog that was previously initiated by the European EuroEPINOMICS consortium. As of June 2014, this blog is now officially run by the ILAE Genetics Commission and we have usually posted 1-2 posts per week that are well received by the professional community. In June, we officially moved the blog to a self-hosted website and we are currently rebuilding the audience and online presence of the new website. Currently, the ILAE Genetics blog receives 2,000-5,000 views per month, largely from the US and Europe. Over the course of the last two years, this blog has had more than 60,000 visitors including epilepsy professionals, patient organizations and families. In addition to the blog, we issue "The Channelopathist," a weekly email newsletter for the epilepsy community.
c. Epilepsiome: As an extension of our current online strategy, we are in the process of developing a concept for a comprehensive database on epilepsy and genes that may allow professionals, patient organizations and families to quickly gather relevant information on epilepsy-related genes. For this effort, we have already enlisted the help of ~30 scientific volunteers who have indicated their willingness to coordinate this project. The Epilepsiome project is currently in an advanced planning stage, coordinating efforts with other initiatives such as ClinGen, ClinVar and EGI prior to presenting a full project proposal for the ILAE to approve. We are also exploring different options of supporting this project through patient organizations such as CURE (Citizens United for Research in Epilepsy) and intramural grants of the participating institutions.

Initiative 2: Assist in the creation of a centralized database of complete sequence data with variant calls paired with clinical information for as many patients as possible throughout the world that are sequenced for epilepsy of unknown cause. This concept, formally known as the "Epilepsy Genetics Initiative (EGI)" has now been launched as a result of planning between the NIH-sponsored "Epi4K Center Without Walls" and the Chicago-based "Citizens United for Research in Epilepsy," and with substantial assistance from members of the Genetics Commission. See: http://www.cureepilepsy.org/egi/index.asp. ILAE members are encouraged to track the growth of this project and become actively involved in helping patients learn about the benefits of participation.

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Initiative 3. Continue the important work of the ILAE Consortium on Complex Epilepsies, led by Sam Berkovic. The highlight of the Consortium's work this year was the publication in *Lancet Neurology* (Sept 2014; http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(14)70171-1/fulltext) of our first meta-analysis of GWAS data involving nearly 9,000 subjects. This 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 being planned to investigate epilepsy comorbidities, by combined analyses with consortia investigating migraine and neuropsychiatric disorders. Finally, the possibility of enlarging the data set of epilepsy patients is being explored.

Initiative 4: Improve genetic literacy among both patients and providers.

a. Educational Brochures: An English version of the educational brochure entitled "Epilepsy and Genetics: Things You Want to Know," designed by Alica Goldman and other Commission members for patients and family members, is now available through the ILAE Genetics Commission website. Positive public reception of the material has prompted Spanish translation aimed at the Spanish speaking Latin American population. This next version has been finalized and will be beta tested in a focus group and then submitted for review and approval by the ILAE by the end of 2014. At the same time, the Commission plans to pursue the same strategy for creating similar brochures in Chinese, Japanese and other languages considered to be high priority by the ILAE.

b. Genetic Literacy Series: Recognizing that clinicians are often uncertain about or uncomfortable with genetic testing in epilepsy and epilepsy genetics, the Genetics Commission, under the leadership of Nigel Tan, is starting a new series on Genetic Literacy in *Epilepsia*. This series of 12 papers aims to update and educate practicing clinicians about clinically relevant epilepsy genetics, using modern evidence-based educational methods to promote learning and knowledge retention. The series will start in 2015.

Recommendations for Future Work

Increased effort needs to be placed on helping clinicians stay up-to-date on the latest findings in epilepsy genetics, with an eye toward the emergence of individualized therapies based on the patient's genomic profile. We also need to encourage patients and family members living with epilepsy to understand the role that genetic testing may play in the evaluation of a seizure disorder, and the value of involvement in the Epilepsy Genetics Initiative.