Genetics Commission

2022 Annual Report

MEMBERS

Piero Perucca (Australia), chair
Holger Lerche (Germany)
Alina Esterhuizen (South Africa)
Iscia Tereznha Lopes Cendes (Brazil)
Meng Han Tsai (Taiwan)
J. Helen Cross (UK), MC liason

GENETIC LITERACY

TASK FORCE

Daniel H. Lowenstein (USA), co-chair
Nigel Tan (Singapore), co-chair
Norman Delanty (Ireland)
Alina Esterhuizen (South Africa)
Faiza Fakhfakh (Tunisia)
Ingo Helbig (Germany)
Amy McTague (UK)
Emma Palmer (Australia)

The Task Force has continued to organise the Genetic Literacy series as part of the education mission of the ILAE, with contributions from authors all over the world. One paper was accepted for publication in Epileptic Disorders, and 3 more are in preparation.

EPILEPSIOME

TASK FORCE

Ingo Helbig (USA), co-chair
Heather Mefford (USA), co-chair
Ahmad Abou Tayoun (USA)
Ganna Balagura (Italy)
Gordon Jing (China)
Lakshminarayanan Kannan (India)
Roland Krause (Luxembourg)
David Lewis-Smith (USA)
Nigel Tan (Singapore)

The Task Force has undertaken 3 main activities: a) the Epilepsiome blog, which remains a widely read resource on epilepsy genetics; b) the curation of genes and variants associated with epilepsy, in collaboration with ClinGen; c) the use of the recently revised epilepsy-related Human Phenotype Ontology (HFO) terms in genetics research endeavours.

SEQUENCING DATA SHARING (ILAE GENOMICS)

TASK FORCE

Holger Lerche (Germany), chair
Samuel F. Berkovic (Australia)
Roland Krause (Luxembourg)
Daniel H. Lowenstein (USA)

Gianpiero Cavalleri (Ireland)
Ingo Helbig (Germany)
Sanjay Sisodiya (UK)

The Task Force has been able to accrue sequenced data from >38,000 cases with epilepsy. These data have been collected from different sources, including EpiPGX, CENet, Epi4K, Epi25, the Italian EMA study group, and CoGIE. Appropriate control data have been obtained from the UK Biobank and other sources.

CLINICAL GENETIC TESTING

TASK FORCE

Andreas Brunklaus (UK), co-chair
Gaetan Lesca (France), co-chair
Alina Esterhuizen (South Africa)
Katherine Helbig (USA)
Michael Hildebrand (Australia)
Gagandeep Singh (India)
Iscia Tereznha Lopes Cendes (Brazil)
Chahnez Charfi Triki (Tunisia)
Sarah Weckhuysen (USA)

The Task Force's work has been focused on the development of a survey to assess genetic testing practices around the world. The survey was formatted into an electronic version using SurveyMonkey and then piloted across 9 international centers. The survey has been translated into French and Spanish and will be distributed across ILAE chapters internationally in 2023.

ILAE CONSORTIUM ON COMPLEX EPILEPSIES

The Consortium has had a successful year completing its third GWAS analysis (ILAE 3) with almost 30,000 cases with epilepsy and >52,000 controls. The paper reporting on ILAE 3 is currently under review.

ACCOMPLISHMENTS

- A major accomplishment has been the completion of 'ILAE 3', the third GWAS of the ILAE Consortium on Complex Epilepsies, which included 29,944 cases with epilepsy and 52,538 controls. This analysis identified 26 genome-wide significant loci, 19 of which specific to the genetic generalized epilepsies (GGEs). These findings substantially advance our understanding of the genetic architecture of common epilepsies, particularly the GGEs. The paper is currently under review and also available as a preprint on MedRxiv (doi: https://doi.org/10.1101/2022.06.08.22276120). The summary statistics are available for use on EpiGAD (https://www.epigad.org/).
- In work with ClinGen, members of the Epilepsiome Task Force have contributed to the curation of 93 genes that have been associated with epilepsy (https://search.clinicalgenome.org/kb/affiliate/10005?page=1&size=25&search=&sort=classification&order=asc)

- The recently formed Task Force on Sequencing Data Sharing (ILAE Genomics) has been able to collect >38,000 exomes from cases with epilepsy (sequenced as part of various studies) which will be interrogated in 2023.

HIGHLIGHTS

- The ILAE Consortium on Complex Epilepsies has completed its third GWAS (ILAE 3) including almost 30000 cases with epilepsy and >50000 controls. This analysis identified many significant 'hits' among common epilepsies, particularly among the genetic generalised epilepsies.
- There is a new addition to the ILAE Genetic Literacy Series, with a paper on 'Self-limited familial epilepsy syndromes with onset in neonatal age and infancy' by Charissa Millevert and Sarah Weckhuysen having recently been accepted for publication in Epileptic Disorders.
- The new Task Force on Clinical Genetic Testing has devised a survey which will be distributed internationally to investigate practices in genetic testing in people with epilepsy around the world.

RESEARCH AND PUBLISHED ARTICLES

- Krey I, Platzer K, Esterhuizen A, Berkovic SF, Helbig I, Hildebrand MS, Lerche H, Lowenstein D, Møller RS, Poduri A, Sadleir L, Sisodiya SM, Weckhuysen S, Wilmshurst JM, Weber Y, Lemke JR, on behalf of the ILAE Genetics Commission and the Task Force on Clinical Genetic Testing in the Epilepsies Current practice in diagnostic genetic testing of the epilepsies. *Epileptic Disord* 2022;24(5):765-786.
- Millevert C, Weckhuysen S for the ILAE Genetics Commission. Genetic literacy series: Self-limited familial epilepsy syndromes with onset in neonatal age and infancy. *Epileptic Disord* (accepted for publication)

MEETINGS

In 2022, we had three Zoom meetings (7 March, 20 June, and 6 October) and one 'hybrid' meeting (3 December, at the American Epilepsy Society Meeting in Nashville, USA) involving the members of the Genetics Commission and chairs of the associated Task Forces. These meetings have provided the opportunity to coordinate the activities of the different Task Forces through discussions between the Genetics Commission members and the Task Force chairs.

Report submitted by Piero Perucca