

ILAE/AES Translational Task Force of the Neurobiology Commission: An Update on the Translational Initiatives

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The newly assembled ILAE / AES Translational Task Force of the Neurobiology Commission of the ILAE has been tasked to continue the work of the ILAE working group for preclinical epilepsy drug discovery and pursue the next steps that were set as priorities following the 1st Joint ILAE/AES Translational Workshop in London (2012). The Co-Chairs of the new Translational Task Force (Jacqueline French, Aristea Galanopoulou, Terence O'Brien, and Michele Simonato) along with the elected members (Amy Brooks-Kayal, Marco de Curtis, Akio Ikeda, Frances Jensen, Solomon (Nico) Moshé, Asla Pitkanen, Helen Scharfman) are currently in the process of selecting working group members that will address the following next steps.



Aristea Galanopoulou



Jackie French



Michele Simonato



Terrence O'Brien

Infrastructure to harmonize video-EEG interpretation and analysis in rodents

At present, there is significant heterogeneity in the recording, interpretation, and analysis of electrophysiological recordings of neuronal activity in vivo and in vitro animal models of seizures. This heterogeneity in interpretation of animal EEG has created significant hurdles in the comparison of studies describing epilepsy development in animal models and is a major obstacle in the evaluation of anti-epileptogenesis treatments. The co-leaders of this Step (Aristea Galanopoulou, Marco de Curtis, Akio Ikeda) have been tasked with four goals:

- (1) Develop standards for recordings and interpretation of rodent EEGs (cortical and depth) across the life span.
- (2) Develop standards for the interpretation of in vitro seizure models.
- (3) Enhance and optimize depositories of annotated video-EEG data and analysis software to permit the analysis and interpretation of studies from different laboratories using the same tools and standards.
- (4) Generate publications that will disseminate the products of our working groups.

We hope that the products of our working groups will provide working definitions, classification systems, and analysis methods that will facilitate the translation and comparison of studies from different laboratories, and will set the foundations for the generation of common data elements for electrophysiological studies and multi-center anti-epilepsy therapy multi-center trials (below).

Review of animal model data for particular clinical syndromes, including treatments, biomarkers, and comorbidities

In basic and preclinical research, reviews are always descriptive and never systematic, meta-analysis of the data is difficult, because of varying approaches, models and tech-

niques. Organizing and coordinating databases and systematic reviews on regarding animal research in epilepsy is needed. The goal of this Step is to establish means to generate, publish and periodically update (in journals and / or websites) these databases and reviews. Creating a Cochrane-like collaboration will facilitate identification of what is strong and what is weak, what is promising for clinical application and what would benefit from in-depth analysis. Systematic reviews could pave the way for large, multi-center studies with appropriate characteristics and statistical power; in addition, the reviews will provide material for common data elements (see other Steps below). The co-leaders of this Step are Michele Simonato, Amy Brooks-Kayal and Frances Jensen.

Common data elements (CDEs) in preclinical research

CDEs standardize the collection of investigational data and facilitate comparison of results across studies. They allow more effective aggregation of information into significant metadata results. The NINDS has spearheaded an effort to create a group of CDEs for > 10 neurologic diseases (<http://www.commondataelements.ninds.nih.gov/default.aspx#page=Default>). Epilepsy has been one of the areas for which CDEs have been created, and they are now in common use. Preclinical CDEs for epilepsy ensure that important data elements (e.g., experimental conditions, collection of EEG or behavioral data) are obtained in all studies in a similar fashion. CDEs will provide a tool that can be applied in multiple ways in preclinical research. They will serve the needs of individual laboratories as well as the large scale research consortia to standardize the study protocols. Implementation of preclinical CDEs may influence design of studies for grant applications and the preparation of scientific articles. The co-leaders of this Step include Jackie French, Asla Pitkanen, and Helen Scharfman.

Develop infrastructure for multi-center preclinical studies

Because preclinical studies can be resource intensive partnerships among government-related funding organizations (NIH, European Community), industry, philanthropic foundations and academia is necessary. These studies will represent a "Phase II" of preclinical studies, similar to clinical Phase II/III multicenter, randomized, double-blinded studies, and the goal is to generate more rigorous pre-clinical data for efficacy than is currently generated from single laboratory "Phase I" studies. These single lab studies are usually underpowered, are often unrepliated and suffer from significant experimental limitations. The ultimate goal is to improve the evidence from pre-clinical studies for investigational new drugs that show strong promise in initial "Phase I" studies and thus to increasing the chances that clinical studies will be successful. More predictive preclinical results may encourage industry and government to invest in a prospective therapy's clinical development. The co-leaders of this Step include Terry O'Brien, Nico Moshé, and Akio Ikeda.

Dissemination

Finally, the Translational Task Force has undertaken an intense dissemination activity to inform epileptologists as well as the broader scientific and medical community about its mission while at the same time seeking feedback and suggestions. The summaries and recommendations of the proceedings of the "Joint AES / ILAE Translational Workshop to Optimize Preclinical Epilepsy Research", held in London in 2012, have been published in a special supplement in *Epilepsia* (Volume 54, Supplement s4, 2013), and a brief critical summary of the work performed to date is in press as a "Personal view" in *Lancet Neurology*. Moreover, a workshop has been proposed and accepted at the 17th World Congress of Basic and Clinical Pharmacology (Cape Town, South Africa, July 2014). In this workshop, entitled "Optimizing anti-epilepsy drug discovery", Michele Simonato, Terrence O'Brien, Aristea Galanopoulou, Asla Pitkanen and Jerome (Pete) Engel will present and discuss the ongoing work of the Task Force to an audience of pharmacologists.