



World Congress on

# Neuroscience and Epilepsy

November 16-17, 2018 Tokyo, Japan

## Workshop Day 1

World Congress on

## NEUROSCIENCE AND EPILEPSY

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**Attitudes and experience of cannabinoid-based therapies for epilepsy in the Australian community****Carol Ireland and Lisa Todd**

Epilepsy Action Australia, Australia

**Purpose:** Epilepsy Action Australia (EAA) sought to understand the attitudes toward and lived experiences of adults and parents of children living with epilepsy of cannabinoid-based therapies in an ever-changing climate of public opinion, government legislation and clinical trials in Australia.

**Method:** Two studies were undertaken with the first informing the second study. A nationwide online survey was conducted assessing demographics, clinical factors, including diagnosis and seizure types and experiences with and opinions towards cannabis use in epilepsy. The second study (PELICAN) focused on experiences of 61 families of children with epilepsy under the age of 16 years who desired, were currently or had previously administered cannabinoid-based therapies to their children to manage seizures. Semi-structured interviews were conducted; samples collected with subsequent laboratory analysis.

**Results:** 976 responses met the inclusion criteria of the initial survey. 15% of adults with epilepsy and 13% of parents/guardians of children with epilepsy were currently using, or had previously used, cannabinoid-based products to treat epilepsy. Of those with a history of cannabis product use, 90% of adults and 71% of parents reported success in reducing seizure frequency. 41 of the 65 families participating in the second study (PELICAN) were currently or had previously administered cannabinoid-based therapies to their children. Analysis of the products highlighted a wide variability of cannabinoid content and low concentration of Cannabidiol (CBD) while  $\Delta 9$ -tetrahydrocannabinol (THCA9) was present in nearly every sample.

**Conclusion:** The survey provides insight into the use of cannabis products for epilepsy, in particular some of the likely factors influencing use, as well as novel insights into the experiences of and attitudes towards medicinal cannabis in people with epilepsy in the Australian community while the PELICAN study highlighted the profound variation in the illicit cannabis extracts being utilized as therapies in epilepsy in Australia warranting further investigation.

**Biography: Carol Ireland & Lisa Todd**

Carol Ireland, CEO and Managing Director of Epilepsy Action Australia (EAA), Carol has an extensive background spanning 35 years in the not-for-profit human services sector, holding a variety of executive positions. She has been at the forefront of the medical cannabis movement in Australia. In her role at Epilepsy Action Australia she has had significant contact with many individuals and families faced with managing very challenging forms of medication resistant epilepsy, with few or no options left in the conventional treatment bucket. Carol has heard and seen the changes in people's lives, including reduction in the severity and frequency of seizures, resulting from use of medicinal cannabis. Carol serves on the Australian Advisory Council for the Use of Medicinal Cannabis, Advisory Board of The Lambert Initiative for Cannabinoid Therapeutics, Steering Committee for the NSW government's Pediatric Epilepsy Trials (MC Research), and is a founding Director of the Medicinal Cannabis Council. She is a strong and active advocate for people living with epilepsy.

Lisa Todd is a Clinical Nurse Consultant in Epilepsy and Clinical Governance Manager for Epilepsy Action Australia. She is a Registered Nurse with a Post Graduate Certificate in Neuroscience Nursing and Masters of Education. Lisa is a trained cannabis nurse, having attended numerous educational seminars, conferences and master classes for health care professionals in the United States and Australia. She was the lead investigator and co-author on 'An Australian nationwide survey on medicinal cannabis use for epilepsy: History of antiepileptic drug treatment predicts medicinal cannabis use' published in *Epilepsy & Behaviour* (2017) and Co-investigator in the PELICAN study (Pediatric Epilepsy Lambert Initiative Cannabinoid Analysis) with the University of Sydney. Prior to her work in the field of Medicinal Cannabis Lisa was seconded to the George Research Institute for Global Health for several years as Research Fellow for the SEMISIC study (Sydney Epilepsy Incidence Study to Measure Illness Consequences).

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## Scientific Tracks & Abstracts

### Day 1

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## Iqsec2 knockout mice recapitulate the intellectual disability and epilepsy phenotype of patients with loss-of-function mutations

Cheryl Shoubridge, Matilda R Jackson and Karagh E Loring  
University of Adelaide, Australia

The IQ motif and SEC7 domain-containing protein 2 (IQSEC2) is an X-chromosome gene mutated in both males and females leading to Intellectual Disability (ID) and severe early-onset seizures. The pathogenesis underpinning these mutations remains unknown. Utilizing CRISPR/Cas9 targeted editing, we have generated an Iqsec2 KO mouse model to investigate the molecular and cellular deficits in this gene resulting in disease outcomes; a fundamental step towards the design and implementation of potential treatment options. We confirmed the loss of Iqsec2 mRNA expression and the lack of Iqsec2 protein detected within the brain of founder and progeny mice. Recapitulating the human setting, both male (48%) and female (45%) Iqsec2 KO mice present with frequent and recurrent seizures. There was an increased occurrence of seizures, reabsorption and unsuccessful nurturing of live young in breeding females. Developmentally, the KO mice exhibit significantly increased hyperactivity, altered anxiety and fear responses, decreased social interactions, delayed learning capacity and decreased memory retention/novel recognition; recapitulating the psychiatric issues, autistic-like features and cognitive deficits present in patients with loss-of-function IQSEC2 mutations. Interestingly, the loss of Iqsec2 function not only causes severe ID and seizures in KO male mice, but in agreement with the patient setting, similar severity is also noted in females despite being in a heterozygous state for this X-chromosome gene. We contend this newly generated mouse model provides a highly relevant biological tool required to interrogate IQSEC2/Iqsec2 function in the brain.

### Biography

Cheryl Shoubridge is an Associate Professor of Human Genetics with a research focus on investigating the molecular pathogenesis underpinning genetic causes of intellectual disability and seizures. Her research utilizes numerous experimental models relevant to the associated clinical phenotypes, including rodent models, primary neurons in culture through to clinical specimens. Currently, she is working in the pre-clinical setting on identifying and validating treatments to improve disease outcomes. Her expertise in genetics, neuroscience and molecular biology underpin her more recent focus on investigating the pathogenic mechanisms contributing to disease outcomes of intellectual disability and seizures due to deficits in synaptic plasticity.

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## The development of ErbB2-targeted therapy for Alzheimer's disease

Yung-Feng Liao, Bo-Jeng Wang, Yun-Wen Chen and Pei-Yi Wu

Institute of Cellular and Organismic Biology-Academia Sinica, Taiwan

$\gamma$  Secretase catalyzed production of Amyloid- $\beta$  ( $A\beta$ ) underlies the pathogenesis of Alzheimer's Disease (AD). The aim is to identify genetic modifiers that can selectively affect  $\gamma$ -secretase cleavage of Alzheimer's disease amyloid protein precursor i while sparing Notch cleavage, we generated cell-based assays employing Bioluminescence Resonance Energy Transfer (BRET) technology to monitor the protein-protein interactions between PS1 and two  $\gamma$ -secretase substrates, Alzheimer's disease amyloid protein precursor i C-terminal fragment (C99) and extracellular domain truncated Notch (N $\Delta$ E). An RNAi screen identified 14 candidate genes whose downregulation resulted in a selective decrease in the interaction between PS1 and C99. Among those 14 candidate genes, an ErbB2-centered interaction network was found to preferentially govern the proteostasis of APP-C99. We further demonstrated that overexpression of ErbB2 upregulates the levels of C99 and AICD effectively. The knockdown of ErbB2 selectively decreased the protein levels of C99, AICD, and secreted  $A\beta$ 40 but not those of N $\Delta$ E and NICD. Selective suppression of ErbB2 expression by CL-387,785, an ErbB1/2-selective irreversible tyrosine kinase inhibitor can preferentially attenuate the levels of C99 and AICD, resulting in a significant reduction in  $A\beta$  production. Down-regulation of ErbB2 by CL-387,785 also resulted in a significant decrease in the levels of C99 and secreted  $A\beta$  in both zebrafish and mouse models of AD, through the activation of autophagy. Oral administration of CL-387,785 for 3 weeks significantly improves the cognitive functions of APP/presenilin-1 (PS1) transgenic mice. These findings unveil a noncanonical function of ErbB2 in modulating autophagy and established ErbB2 as a novel therapeutic target for AD.

### Biography

Yung-Feng Liao has completed his PhD in Biochemistry and Molecular Biology from University of Georgia and Postdoctoral studies from Harvard Medical School/Massachusetts General Hospital/Brigham and Women's Hospital. He is the Principal Investigator of the Laboratory of Molecular Neurobiology in the Institute of Cellular and Organismic Biology, Academia Sinica, Taiwan. He has published more than 50 papers in reputed journals and has been serving as an Editorial Board Member and as a Peer Reviewer of prestigious journals.

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## A study to assess the noise stress-induced changes on cognition in Wistar albino rats

**Archana A**

University of Madras, India

**Background:** In our modern lifestyle exposure to noise stress/pollution not only affects the auditory system but rather extend to the central nervous system.

**Objective:** The aim of the study is to investigate the effect of acute noise stress on cognitive functions in male Wistar albino rats.

**Methods:** Adult albino rats were randomly divided into two groups. Each group contains six animals. Rats exposed to acute noise stress (100 dB/4 hour) were compared with control animal and assessed for cognition by using T-maze, hole board test, open field test, marble burying test and social interaction behavior.

**Results:** The rats exposed to acute noise stress shown the significance ( $p < 0.05$ ) of behavioral alterations such as impaired learning and memory, memory retention, increased fear and anxiety, obsessive-compulsive behavior, social avoidance and decreased social interaction.

**Conclusion:** The results report that acute noise stress affects the cognition and it became chronic may confer the increased risk of neurodegenerative disorders.

### Biography

Archana A is currently pursuing her PhD in Stress Physiology in Department of Physiology, University of Madras, Tamil Nadu. She has published two papers in sleep deprivation and unpredictable acute and chronic stress. She is currently researching noise stress on hippocampus and Alzheimer's disease.

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