Idiopathic Generalized Epilepsy Ictogenesis and Epileptogenesis: a Cross-disciplinary Discussion from Molecule to Human Brain

American Epilepsy Society Annual Meeting 2008
Investigators’ Workshop
Seattle, WA
December 6, 2008

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  - Provide feedback on the workshop
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- American Epilepsy Society home page and link to annual meeting

Investigators’ Workshop Abstract

This session is designed to be a participatory workshop focused on addressing questions of ictogenesis and epileptogenesis in idiopathic generalized epilepsy (IGE) via a cross-disciplinary approach. Four investigators from the fields of molecular neuroscience, thalamocortical network physiology, transgenic animal physiology/behavior, and human/animal neuroimaging will serve as workshop speakers. To provide a basis for discussion, the speakers will use the first half of their presentation time to describe the relevant work from their respective laboratories. In the second half of their allotted presentation time, the speakers and workshop attendees will discuss how the results obtained in the speaker’s experimental system address questions of IGE ictogenesis and epileptogenesis and complement the work done in other experimental systems. Participants will also use this time to “workshop” new experiments that could be performed within the speaker’s area of scientific expertise that would answer questions deemed important to IGE investigators from all disciplines.

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<th>speaker</th>
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<tr>
<td>Martin J. Gallagher MD, PhD</td>
<td>workshop coordinator</td>
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<td>Robert L. Macdonald MD, PhD</td>
<td>GABA\textsubscript{A} Receptor Mutations and IGEs</td>
<td>Kang, J. and Macdonald, RL, (2004). The GABA\textsubscript{A} receptor $\gamma 2$ subunit R43Q mutation linked to childhood absence epilepsy and febrile seizures causes retention of $\alpha 1\beta 2\gamma 2S$ receptors in the endoplasmic reticulum, <em>J Neurosci</em>, 8672-7</td>
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<td>Feng H-J, Kang J-Q, Song L and Macdonald RL, (2006). The $\delta$ subunit susceptibility variants E177A and R220H associated with complex epilepsy alter channel gating and cause endoplasmic reticulum retention of $\alpha 4\beta 2\delta$ GABA\textsubscript{A} receptors, <em>J Neurosci</em>, 1499-1506</td>
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<td>Gallagher, MJ, Ding, L, Maheshwari, A, and Macdonald, RL, (2007), The GABA\textsubscript{A} receptor $\alpha 1$ subunit epilepsy mutation A322D inhibits transmembrane helix formation and causes proteosomal degradation, <em>Proc Natl Acad Sci USA</em>, 12999-13004</td>
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Summary of Workshop Discussion

I would really like to thank all the speakers for their efforts. I was really pleased with the content of the talks and with the discussion. It is very difficult to have a true workshop in such a large meeting room. Nonetheless, I think it worked out pretty well. As would be expected, there were many specific questions that pertained directly to the individual talks. However there were several workshop-like ideas that developed and I’ll list a few of them here. So I don’t overburden our web guru, Dr. John Fang, with endless updates to this page (thanks for your help, John!) I’ll defer most of the commentary to the Comments and Discussion page.

- Utilizing molecular neuroscience techniques to probe one of the surprising results observed in the knock-in mice.
  - How do missense mutations in epilepsy genes alter targeting of the affected protein to the axon initial segment? Would this occur in neuronal culture? Perhaps we can overexpress recombinant and appropriately tagged or chimeric wild type or mutant protein in neurons and determine the domains/binding partners of the wild type and mutant proteins.

- Testing the effect of augmented AMPAergic signaling in stargazin and Gria4 mice using behavioral and EEG data
  - What would be the effect of administering AMPAergic drugs? Would they augment cognition? Would they be pro-convulsant?

- Using fMRI/DTI to explore connectivity in monogenic epilepsy
  - It is of interest. DTI has been done in mice. fMRI is a little more difficult due to mouse anesthesia.

- Utilizing molecular techniques with thalamocortical recordings to determine distribution of AMPA receptor compensation.
  - EM is definitely of interest. Molecular studies are also planned to determine the mechanism of compensation.