IW.28
ION CHANNEL TRAFFIC JAMS IN EPILEPTOGENESIS

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Summary: Excitability of neurons and neuronal compartments (e.g., dendrites) is governed by several ion channels, and it is likely that the ratios among different currents, rather than their absolute expression levels, determine the nature of neuronal electrical responses. An eloquent example is the interaction between I_h and IA, that sets the rate of post-inhibitory rebound. Activity dependent trafficking and dendritic expression of IA (Kv4.2 channels) and Ih (Hyperpolarization activated cyclic nucleotide gated, or HCN channels) have been described recently. In the context of seizures and epileptogenesis, these modulations of channel distribution may contribute to circuit hyperexcitability. Here we aim to synthesize these recent data, provide the molecular foundation of the ion channel redistribution, and attempt to integrate their combined effect on neuronal and circuit excitability.

The session will include Dax Hoffman, who will discuss the regulation of dendritic excitability by activity-dependent trafficking of the A-type K+ channel subunit Kv4.2 in hippocampal neurons. Dane Chetkovich will share his work on activity-dependent regulation of HCN channel distribution in hippocampal CA1 pyramidal neurons, and its relevance to epileptogenesis. Tallie Z. Baram will discuss the multiple mechanisms of activity-dependent HCN channel trafficking. Finally, Christophe Bernard will discuss dendritic channelopathies in epilepsy, and synthesize the available information on this topic.

Taken together, the presentations in the session will highlight coordinated and homeostatic mechanisms used by neurons to regulate their activity in response to varying input and/ or to alterations in abundance or distribution of a given ion channel. The disruption or corruption of these processes might contribute to abnormal neuronal and network properties characteristic of epilepsy.

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