LSU Health Sciences Center

Neuroscience Center of Excellence

FACULTY CANDIDATE

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Presenting

"Intracellular Fibroblast Growth Factors are Novel Regulators of Neuronal Excitability"

Although structurally related to the classical Fibroblast Growth Factors (FGF), the intracellular FGFs (FGF11-14) are not secreted proteins, do not operate via classical tyrosine kinase coupled FGF receptors, but rather interact directly with the pore-forming α subunits of voltage-gated Na^+ (Na_v) channels. Interestingly, a single missense mutation (*F145S*) in *FGF14* has been identified in individuals afflicted with spinocerebellar ataxia 27, a complex neurodegenerative disorder affecting motor and cognitive functioning, suggesting links between FGF14 and neuronal activity. During my talk, I will demonstrate that expression of the $FGF14^{F145S}$ mutation in hippocampal neurons disrupts the localization of Na_v channels at the axon initial segment, reduces Na_v current densities and impairs repetitive firing. In addition, I will demonstrate that the mutant $FGF14^{F145S}$ protein functions as a dominant negative, disrupting the interaction between wild type FGF14 and Na_v channel pore-forming α subunits. These findings provide the first molecular and cellular insights into the functional consequences of the $FGF14^{F145S}$ mutation and reveal pivotal roles for FGF14 in the regulation of neuronal excitability through direct interactions with neuronal Na_v channels. Potential roles for the intracellular FGFs in regulating trafficking of ion channels, synaptic transmission and plasticity and their implications in human neurological disorders will be discussed.

Monday April 14, 2008 11:30pm,
8th Floor Neuroscience Center Conference Room,
LSU Lion's Building, 2020 Gravier Street New Orleans