ELSC Seminar: Nathan Dascal

November 12, 2015

On the topic of "Regulation of GIRK channel by G proteins and lithium: a link between neuronal excitability and bipolar disorder?"

ELSC cordially invite you
to the lecture given by:

Nathan Dascal
Department of Physiology and Pharmacology, Sackler School of Medicine, Tel Aviv University

On the topic of

"Regulation of GIRK channel by G proteins and lithium: a link between neuronal excitability and bipolar disorder?"

The lecture will be held on Thursday, November 12, 2015
at 17:00, at ELSC: Silverman Bldg., 3rd Wing, 6th Floor, Edmond J. Safra Campus

Light refreshments at 16:45

Abstract:

G protein-gated K+ channels (GIRK) are important regulators of neuronal excitability and are involved in a number of neuronal disorders, pain, and drug and alcohol effects. GIRKs are activated by G?? subunits derived from Gi/o proteins following activation of GPCRs (G protein-coupled receptors) and also possess basal activity. We discovered that GIRK channels are dually regulated by lithium (Li+), a drug widely used to treat bipolar disorder (BPD). In hippocampal neurons, therapeutic doses of Li+, 1-2 mM, increased GIRK basal current (Ibasal) but attenuated neurotransmitter-evoked GIRK currents (Ievoked) mediated by GABAB and adenosine receptors. We investigated the underlying mechanisms in biochemical and cellular models (Xenopus oocytes and HEK293 cells) and in neurons. Quantitative characterization and mathematical modeling of the signaling cascade reveal a complex mechanism in which Ibasal and Ievoked are reciprocally regulated by G?? and G? subunits of G proteins. The regulation deviates significantly from the classical G protein schemes and offers novel insights into mechanisms of GIRK function and GPRC-G protein-effector coupling. We further demonstrate that the two opposing Li+ actions on GIRK are G protein-dependent, and elucidate the underlying mechanism. We propose that the dual effect of Li+ on GIRK may profoundly regulate neuronal excitability, reducing the span of inhibitory regulations mediated by GIRK channels. Our findings possibly shed light on a long-sought link between Li+, neuronal excitability, and the
known cellular and genetic targets of BPD: GPCRs, G proteins and ion channels.

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