

Second International Calcium Channel Conference - Placencia, Belize  
March 28 – April 2, 2010

## **Cav3 calcium channels link to the Kv4 channel complex to control neuronal output**

D Anderson, W H Mehaffey, M Iftinca, R Rehak, JDT Engbers, S Hameed, GW Zamponi and RW Turner

*Hotchkiss Brain Institute, University of Calgary, Calgary AB Canada*

The Kv4 family of low voltage-activated A-type potassium channels are widely expressed in excitable cells where they control action potential firing and synaptic integration. Kv4 channels exist as a complex that includes K<sup>+</sup> channel interacting proteins (KChIPs), a member of the calcium sensor family that confers the potential for calcium dependent modulation of the Kv4 channel. However, neither a physiological source of calcium that can modulate Kv4 function nor the end result on A-type function had been identified. A unique aspect of the Kv4 complex is the ability to activate and inactivate at membrane potentials subthreshold to action potential generation. One of the few voltage-gated calcium channels that operate within this range are members of the Cav3 family of T-type channels. Cerebellar stellate cells express both the Cav3.2 and Cav3.3 channel isoforms, and a prominent Kv4-mediated  $I_A$  that operate over the same voltage range to influence firing properties. Here we show that Cav3 and Kv4 channels form a novel signaling complex that allows T-type calcium channels to provide a physiological source of calcium to modulate  $I_A$  function. A link in the region of the Cav3 C-terminus allows calcium entry to interact with the KChIP3 protein to selectively shift the  $I_A$  inactivation curve rightward into the physiological range to control stellate cell firing. The widespread expression of these channels suggests that this novel signaling complex will control a diverse range of output properties of central neurons.