



PROGRESS IN NEUROSCIENCE PINS



Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&

The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 3/20/14, 4 PM, coffee at 3:45 PM
Weill Auditorium

Elementary Calcium Signals Through Endothelial TRPV4 Channels Regulate Vascular Function: Disruption in Hypertension

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Abstract:

Major features of the transcellular signaling mechanism responsible for endothelium-dependent regulation of vascular smooth muscle tone are unresolved. We identified local calcium (Ca^{2+}) signals (“sparklets”) in the vascular endothelium of resistance arteries that represent Ca^{2+} influx through single TRPV4 cation channels. Gating of individual TRPV4 channels within a four-channel cluster was cooperative, with activation of as few as three channels per cell causing maximal dilation through activation of endothelial cell intermediate (IK)- and small (SK)-conductance, Ca^{2+} -sensitive potassium (K^+) channels. Endothelial-dependent muscarinic receptor signaling also acted largely through TRPV4 sparklet-mediated stimulation of IK and SK channels to promote vasodilation. These results support the concept that Ca^{2+} influx through single TRPV4 channels is leveraged by the amplifier effect of cooperative channel gating and the high Ca^{2+} sensitivity of IK and SK channels to cause vasodilation.

Recent relevant publications:

1. Sonkusare SK, Bonev AD, Ledoux J, Liedtke W, Kotlikoff MI, Heppner TJ, Hill-Eubanks DC, & **Nelson MT**. Elementary Ca^{2+} signals through endothelial TRPV4 channels regulate vascular function. *Science*, 2012 May 4; 336(6081): 597-601. PMID 22556255.
2. Nausch LW, Bonev AD, Heppner TJ, Tallini YN, Kotlikoff MI, & **Nelson MT**. Sympathetic nerve stimulation induces local endothelial calcium signals to oppose vasoconstriction of mouse mesenteric arteries. *Am J Physiol Heart Circ Physiol*, 2012 Feb 1; 302(3): H594-602. doi: 10.1152/ajpheart.0073.2011. PMID 22140050



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