What's where and why at a vascular myoendothelial signaling complex?

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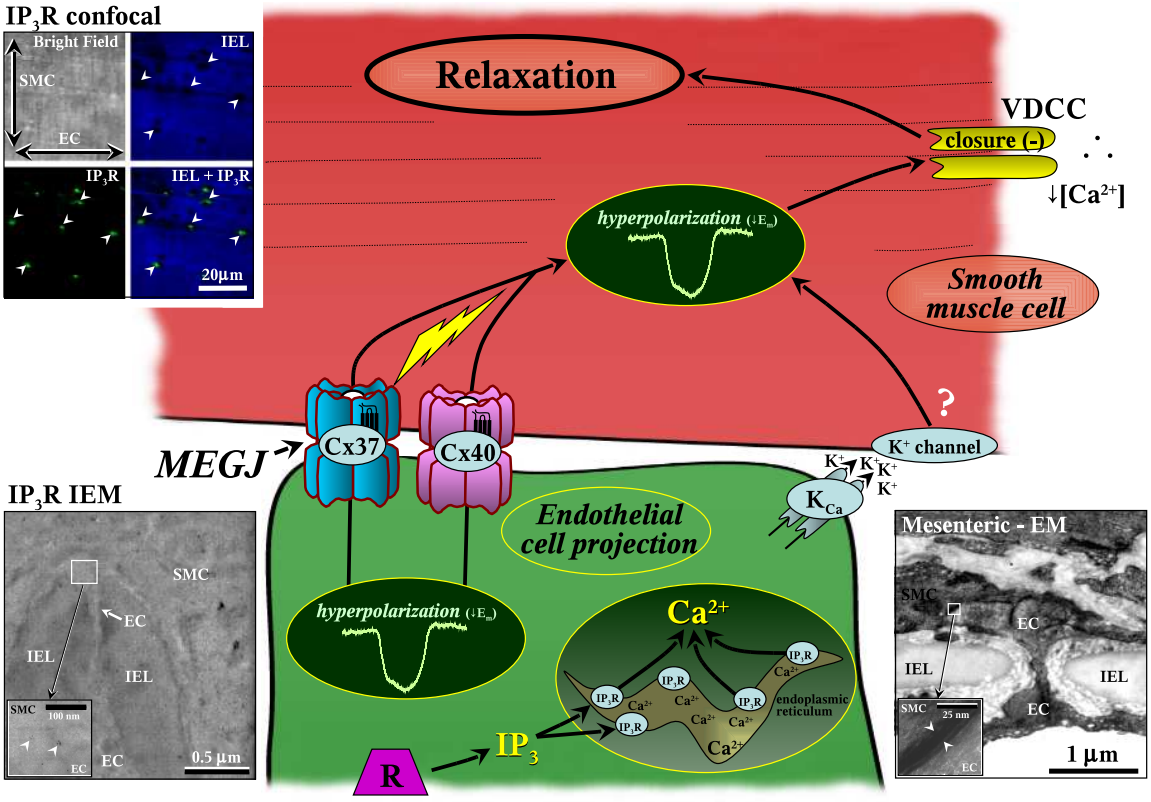
Localized vasodilator function due to endothelium-derived hyperpolarization (EDH), and conduction of vasodilator and vasoconstrictor responses over distance, are associated with heterocellular endothelial-smooth muscle myoendothelial gap junctions. Such junctions are critical for current and small molecule transfer to coordinate arterial function. In addition, the spatial and temporal modulation of calcium dynamics is critical for vascular function, and recent anatomical and functional studies suggest an association between gap junction connexins and sites of calcium release and action. In rat mesenteric arteries, adjacent endothelial cells are coupled by the gap junction connexins (Cxs)37, 40 and 43, which are associated with densities of small conductance calcium-activated potassium channels (SK_{Ca}); whilst myoendothelial gap junction Cxs37 and 40 are associated with densities of intermediate (I) K_{Ca}; corresponding to different facets of the functional EDH response. The aim of this study was to further examine the high resolution spatial association of Cxs and sites of calcium modulation. Segments of rat and mouse mesenteric arteries were high pressure frozen, freeze-substituted and low temperature embedded. Serial consecutive sections were incubated with multiple Abs to Cxs37, 40 and 43 and pan-IP_3R and secondary 5 and 10 nm Au conjugate. Confocal labeling of the same and other fixed flat tissue segments was also carried out using the same Abs and secondary Alexa conjugates. Confocal staining was overlayed with internal elastic lamina (IEL) autofluorescence to show the relationship between Cxs, IP_3R and IEL holes (as potential myoendothelial gap junction sites between endothelial and smooth muscle cells). In the mouse, in contrast to rat mesenteric artery, SK_{Ca} was localized to myoendothelial gap junctions. Intense IP_3R labeling was present at the intimal myoendothelial gap junction site in both rat and mouse mesenteric arteries (Figure). At the confocal level, the apparent K_{Ca} and gap junction relationship differed between species and vascular beds. The differential spatial localization of sites of calcium modulation and vascular Cxs suggests the potential for a causal relationship of their functional activation, in that these sites of current transfer and calcium modulation interact. Such interactions may represent a selective target for the control of vascular tone.



Rat and mouse mesenteric artery myoendothelial Cx, K_{Ca} and IP_3R relationship