

## **Heterogeneity in vascular endothelial $K_{Ca}$ expression: relationship to function?**

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Activation of endothelial cell (EC) small (S) and intermediate (I) conductance calcium-activated potassium channels ( $K_{Ca}$ ) and current or molecular transfer *via* myoendothelial gap junctions underlies endothelium-derived hyperpolarization (EDH) leading to vasodilation. The mechanism underlying the  $K_{Ca}$  component of vasodilator activity and the characteristics of gap junctions are targets for the selective control of vascular function. In rat mesenteric artery, S/ $IK_{Ca}$  are critical for the hyperpolarization and repolarization phases of EDH, respectively, and are spatially associated with EC-EC and myoendothelial gap junctions, respectively. This differential functional S/ $IK_{Ca}$  activation and spatial localization suggests a causal relationship between channel activity and distribution; with such localizations representing a potentially selective target for control of vasodilator function and vascular tone. The present study addressed the question of whether the spatial separation of S/ $IK_{Ca}$  occurs in other selected model vascular beds commonly used to examine mechanisms of vascular function in rat and mouse. Tissues were obtained from anaesthetized (3g/kg urethane, i.p.) animals and SK $_{Ca}$  and IK $_{Ca}$  distribution examined using three different SK3 (SK $_{Ca}$ ) and three different IK1 (SK4; IK $_{Ca}$ ) antibodies, with conventional confocal immunohistochemistry. IK1 was diffusely expressed in the endothelium of rat and mouse cremaster and rat middle-cerebral artery. As in rat mesenteric artery, IK1 was also expressed in a punctate manner at myoendothelial gap junction sites in the mouse, but not in rat cremaster or middle-cerebral artery. SK3 was diffusely expressed in the endothelium of all three vessels and, as in the rat mesenteric artery, was also associated with adjacent EC-EC gap junctions in the rat and mouse cremaster. Marked heterogeneity exists within and between vascular EC S/ $IK_{Ca}$  expression, and may reflect different underlying functional mechanisms within and between these beds; thus representing potentially selective therapeutic targets for control of vascular tone.