The role of STIM1/Orai1 in mediating Ca^{2+} entry in vascular smooth muscle cell contractions

G.Y. Rychkov, School of Medical Sciences, University of Adelaide, Adelaide, SA 5005, Australia.

Vascular Smooth Muscle Cells (VSMCs) form a major structural and functional layer in the blood vessel wall. The contractile state of these cells determines vascular tone and consequently tissue perfusion. Vascular contraction is initiated by the Ca^{2+}/Calmodulin-dependent activation of myosin light chain kinase resulting in the interaction of actin and myosin and consequent cross bridge cycling. Cytosolic free Ca^{2+} ($[Ca^{2+}]_{cyt}$) is therefore the key second messenger activating vascular contraction and its regulation is vital in the control of vascular tone.

Elevations of $[Ca^{2+}]_{cyt}$ in VSMCs are chiefly mediated by voltage-gated L- and T-type Ca^{2+} channels and receptor-operated Ca^{2+} permeable channels. Receptor-operated channels include second messenger-activated non-selective cation channels on the plasma membrane and membranes of intracellular organelles and store-operated Ca^{2+} channels. Recent evidence suggests that VSMCs express stromal interacting molecule 1 (STIM1) and Orai1 proteins, which form a certain type of store-operated channels on the plasma membrane, called Ca^{2+} release activated Ca^{2+} (CRAC) channels (Potier, *et al.*, 2009; Hoth & Penner, 1992). Although initially characterised exclusively in non-excitable cells, CRAC channels have been recently shown to be present in skeletal and smooth muscle cells and other excitable tissues, where they interact with L-type voltage-gated Ca^{2+} channels and Transient Receptor Potential channels and contribute to specific cellular functions and regulation of intracellular Ca^{2+} signals (Wang, *et al.*, 2010; Dirksen, 2009).It has been suggested that CRAC channels are required for VSMCs proliferation and migration following vascular injury, and may contribute to the development of hypertension (Potier, *et al.*, 2009; Giachini, *et al.*, 2010). However, the exact contribution of CRAC channels to the regulation of vascular tone and receptor-mediated VSMCs contractions is not well understood.

Dirksen RT. (2009) *Journal of Physiology* **587:** 3139-47.
Giachini FR, Webb RC, Tostes RC. (2010) *Clinical Science* **118:** 391-396.
Hoth M, Penner R. (1992) *Nature* **355:** 353-356.
Potier M, Gonzalez JC, Motiani RK, Abdullaev IF, Bisaillon JM, Singer HA, Trebak M. (2009) *FASEB Journal* **23:** 2425-37.
Wang Y, Deng X, Mancarella S, Hendron E, Eguchi S, Soboloff J, Tang XD, Gill DL. (2010) *Science* **330:** 105-9.