Ca²⁺ entry mechanisms in redox physiology

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Ca²⁺-permeable cation channels encoded by the transient receptor potential (trp) gene superfamily are characterized by a wide variety of activation triggers that act from outside and inside the cell. Reactive species such as reactive oxygen species (ROS), reactive nitrogen species (RNS) and other electrophiles are known to exert stress on organisms, but are also emerging as molecules that mediate cell signaling responses. Understanding the physiological significance and activation mechanisms of TRP channel regulation by reactive species has lead us to consider TRP channels as viable pharmacological targets; modulators of these channels may offer therapeutic options for previously untreatable diseases. Recent studies have revealed that multiple TRP channels sense reactive species and induce diverse physiological and pathological responses, such as cell death, chemokine production, and pain transduction. TRP channels sense reactive species either indirectly through second messengers or directly via oxidative modification of cysteine residues. I describe the activation mechanisms and biological roles of redox-sensitive TRP channels. Especially, I will focus on TRPA1 channels and discuss its unique and high sensitivity to molecular oxygen. Also, I will extend my discussion toward new insights in redox biology.