Role of reactive oxygen species in cardiac signaling – from mitochondria to plasma membrane ion channels

L.C. Hool, Physiology, University of Western Australia, Crawley, Perth, WA, Australia

Reactive oxygen species (ROS) are well recognised as important mediators of cardiovascular pathology including hypertrophy, hypertension, atherosclerosis and heart failure. The one electron-reduction of oxygen leads to the formation of superoxide anion that readily dismutates to hydrogen peroxide, a stable and diffusible signalling molecule. Although it is well recognised that re-oxygenation with reperfusion after ischemia leads to an increase in ROS, there is still controversy regarding the generation and site of ROS production during the hypoxic/ischemic event. The mitochondrial electron transport chain participates directly in the reduction of oxygen and has been implicated as an oxygen sensor. We have examined the effects of hypoxia on the cardiac L-type Ca^{2+}channel and the role of the mitochondria in the response of the channel to hypoxia. The L-type Ca^{2+} channel plays an integral role in cardiac excitation and contraction. Therefore understanding how the cell detects changes in oxygen tension and translates this into functional ion channel responses is important in determining the mechanisms that lead to cardiac arrhythmia during acute events. In addition, alterations in intracellular ROS and Ca^{2+} are important in regulating cell growth. In vascular tissue chronic increases in cellular ROS lead to smooth muscle cell hypertrophy and hypertension. The role of ROS in acute hypoxic events in cardiac myocytes and in the pathophysiology associated with hypertrophic growth abnormalities will be discussed.