Evidence for the regulation of ion channels in the heart by reactive oxygen species – mechanism for mediating pathology

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Oxygen is a substrate for reactive species that can be deleterious to cell function. An increase in reactive oxygen species (ROS) is commonly associated with cellular necrosis or apoptosis and therefore presumed irreversible. However, it is now recognised that ROS may mediate cardiac pathology as cellular signals in sublethal concentrations by way of modification of key thiol groups on proteins. One of these, hydrogen peroxide is a feature of various cardiovascular diseases including ischemic heart disease, hypertension, cardiomyopathies, cardiac hypertrophy and congestive heart failure. Cations, in particular Ca^{2+} ions are also important regulators of cardiac cell function and cell signalling pathways. The dominant route by which Ca^{2+} enters cardiac myocytes is through voltage-dependent L-type Ca^{2+} channels. The channels play an integral role in cardiac excitation and contraction. L-type Ca^{2+} channel function is regulated by hydrogen peroxide and thiol-specific reducing agents. The evidence suggests the redox state of ion channels may be an important determinant of pathology under conditions of altered production of ROS such as hypoxia or oxidative stress.