

論 文 要 旨

Mechanisms underlying the modulation of L-type Ca^{2+} channel by hydrogen peroxide in guinea pig ventricular myocytes

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Although Cav1.2 Ca^{2+} channels are modulated by reactive oxygen species (ROS), the underlying mechanisms are not fully understood. In this study, we investigated effects of hydrogen peroxide (H_2O_2) on the Ca^{2+} channel using a patch-clamp technique in guinea-pig ventricular myocytes. Externally applied H_2O_2 (1 mM) increased Ca^{2+} channel activity in the cell-attached mode. A specific inhibitor of Ca^{2+} /calmodulin-dependent protein kinase II, (CaMKII) KN-93 (10 mM), partially attenuated the H_2O_2 -mediated facilitation of the channel, suggesting both CaMKII-dependent and independent pathways. However, in the inside-out mode, 1 mM H_2O_2 increased channel activity in a KN-93-resistant manner. Since H_2O_2 -pretreated calmodulin did not reproduce the H_2O_2 effect, the H_2O_2 target was presumably assigned to the Ca^{2+} channel itself. A thiol-specific oxidizing agent mimicked and occluded the H_2O_2 effect. These results suggest that H_2O_2 facilitates the Ca^{2+} channel through oxidation of cysteine residue(s) in the channel as well as via the CaMKII-dependent pathway.