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Role of Potassium Ion in Oxidative Stress at the Heart

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Summary

We have demonstrated that progesterone (P_4) or testosterone (DHT) suppress a cAMP-stimulated L-type Ca^{2+} currents ($I_{Ca,L}$) cGMP-dependently, whereas P_4 or DHT enhance I_{Ks} channel currents (I_{Ks}) cGMP-independently without cAMP-stimulation. Upon the enhancement of I_{Ks}, cysteine at 445 in the C-terminus of KCNQ1 (α subunit of the I_{Ks} channel) is *S*-nitrosylated by NO production stimulated by P_4 or DHT. Here, we found that oxidative stress by H_2O_2 suppressed I_{Ks}. Mutagenesis analysis (Cys-scanning) revealed that the suppression of I_{Ks} is controlled by Cys 642 in the C-terminus of KCNQ1. Actually, patch-clamp assay in native cardiomyocyte suggested that the suppression involves cAMP/NO signaling crosstalk. Therefore, we investigated substantial fraction of sex hormonal signaling molecules and cAMP signaling molecules clustered in the caveolae (lipid/raft) fraction where KCNQ1 exists. These results suggest that KCNQ1 localizes around PDE2 in caveolae. The impact on the function would be a future study.