S50-4 Beta adrenergic regulation of cardiac repolarization via a macromolecular complex of the cardiac IKs channel

◯Junko KUROKAWA[1], Tetsushi FURUKAWA[1]

[1]Tokyo Med. & Dent. Univ., MRI

Cardiac K^+ channels are important in maintaining the cardiac electrical activity because they control cellular resting potential and action potential duration. The I_{Ks} channel comprised of KCNQ1 and KCNE1 is a determinant of cardiac repolarization. β-adrenergic receptor (β-AR) activation increases current (I_{Ks}), carried by KCNQ1/KCNE1 channels, and contributes to sympathetic nervous system (SNS)-mediated action potential shortening in human heart.β-AR mediated I_{Ks} stimulation is a consequence of PKA phosphorylation of Ser^{27} in the KCNQ1 amino-terminus. A leucine zipper motif in the KCNQ1 carboxy (C-) terminus binds the targeting protein yotiao which coordinates the assembly of a macromolecular complex required for Ser^{27} phosphorylation. Actually, carriers of mutations in either KCNQ1 (LQT-1) or KCNE1 (LQT-5) are at risk of sudden cardiac death during increased SNS activity, which is explained at least in part by the macromolecular complex. Moreover, transgenic mice revealed co-localization between the macromolecular complex and β2-AR. Recently, we identified the region of C-terminus of KCNE1, which is required for the functional regulation. Here, we introduce our recent progress to understand molecular mechanisms of cAMP regulation of the I_{Ks} channel via the macromolecular complex including KCNE1.