Mutations of KCNE Gene Family in Inherited Arrhythmia Syndromes

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KCNE gene family consists of five different short genes encoding the regulatory proteins with a single transmembrane domain. The first member of the family (KCNE1) was cloned in 1988 (Takumi et al.) and was named as MinK because it reproduced slowly-activated voltage-gated K currents when expressed in Xenopus oocytes. Later in 1996, MinK (or KCNE1) has been shown to dramatically affect the expression of KCNQ1 channel, which is pore-forming subunit for human slow component of delayed rectifier K currents (I_{Ks}). Both are expressed in heart and inner ear. The reconstituted KCNE1/KCNQ1 channels display extremely slow activation and deactivation kinetics with enhanced current amplitude, which are much closer to those of human I_{Ks}. In contrast, another KCNE member (KCNE3) makes the channel constitutively open, and others reduce its amplitude or modulate gating. Interaction of KCNE family members with ion channels is very promiscuous. They drastically affect other pore-forming subunits of K channels such as KCNH2, KCNB1 (Kv2.1), KCND2 (Kv4.2) and KCND3 (Kv4.3). As they alter expression level, gating kinetics and second messenger regulation, their mutations may cause ion channelopathy through the malfunction of channels responsible for normal heart rhythm. In this symposium dedicated to Prof. Hiraoka, we would like to focus on these mutations in KCNE gene family and present several typical cases including our own experiences - KCNE1/KCNH2, KCNE2/KCND3, and KCNE3/KCNQ1.

Keywords: ion channel, mutation, arrhythmia