YIAB-5  KCNE5 Variants Are Novel Modulators of Brugada Syndrome and Idiopathic Ventricular Fibrillation

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Brugada syndrome (BrS) and idiopathic ventricular fibrillation (IVF) have a higher incidence among males. Among genes coding ion channels, KCNE5 is located in the X chromosome, encodes an auxiliary subunit for K channels and modifies the transient outward current (Ito). In 205 Japanese patients with BrS or IVF, who were negative for SCN5A mutation, we conducted a genetic screen for KCNE5 and identified two novel KCNE5 variants, Y81H in 1 male and 2 female, and D92E-E93X in one male from 4 unrelated families. All probands received ICD implantation. Functional consequences of the KCNE5 variants were determined through biophysical assay using co-transfection with KCND3 or KCNQ1. In the experiments with KCND3, Ito was significantly increased for both of the KCNE5 variants compared to WT. In contrast, there were no significant changes in KCNQ1 + KCNE5 WT and the two variants. With the simulation model, both variants demonstrated "notch and dome" or "loss of dome" patterns. In conclusion, novel KCNE5 variants increased Ito and appeared to cause ventricular fibrillation. Screening for KCNE5 is relevant for BrS or IVF.

Keywords: KCNE5, IVF, Brugada syndrome