**Objectives:** Orai3 is a store-operated Ca²⁺ channel specific for mammals. Previous studies found that 2-APB, an agonist of Orai3 channel, can either cause or prevent atrial fibrillation in animals. The aim of this study is to determine whether Orai3 mutation is a pathogenic factor of atrial fibrillation.

**Methods:** Genomic DNA was extracted from the peripheral blood of 124 patients with atrial fibrillation. The two exons of Orai3 gene were separately amplified from the genomic DNA and sequenced with corresponding primers. The coding regions were assembled and aligned with the reference sequence from GenBank. Mutation found in the alignment was confirmed by manual check on the original sequencing chromatograms.

**Results:** Two of the 124 patients were found to carry heterogenic mutation from C to T at position 711 of the nucleic acid sequence. However, this mutation does not lead to any change on translated amino acid sequence.

**Conclusions:** Due to the lack of non-synonymous mutation in Orai3 gene, we conclude that Orai3 channel is probably not directly involved in the cardiac action potential. The effect of 2-APB on atrial fibrillation is more likely related to other targets of this drug, such as IP₃ receptors.

**GW25-e3159**

**Screening of potassium channel mutations in patients with atrial fibrillation**

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**Objectives:** To identify gene mutations of potassium channels that contributed to the pathogenesis of atrial fibrillation.

**Methods:** Genomic DNA was extracted from the peripheral blood of 124 patients with atrial fibrillation. The coding regions of genes including KCNE1 (minK), KCNL1 (KCNE3), KCNE2 (MiRP1), KCNE4 (MiRP3), KCNJ2 (Kir2.1) and KCNJ5 (Kir2.5) were separately amplified from the genomic DNA and sequenced with corresponding primers. The obtained sequences were aligned with reference sequences from GenBank. Mutations found in the alignments were confirmed by manual check on the original sequencing chromatograms.

**Results:** Mutations leading to changes of amino acids and corresponding mutation rates were found: KCNE1, S37R (0.8%), S38R (92.7%), D85N (0.8%); KCNE2, Y13F (0.16%); KCNE3, none; KCNE4, M190Y (0.8%); D196E (91.1%); KCNE5, V393S (0.8%); KCNJ4, none.

**Conclusions:** Genetic mutations on potassium channels are important pathogenic factors of atrial fibrillation. Among the six genes screened KCNE1 and KCNE4 showed highest mutation rates. The electrophysiological functionality of these mutants needs to be examined in the future to understand their impacts to the cardiac action potential.

**GW25-e3168**

**Sodium tanshinol-Iia sulfonate improves tachycardia-induced electrical remodeling of canine**

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**Objectives:** To determine the effects of DS-201 on electrical remodeling of canine and cell membrane potassium ion channels.

**Methods:** Mongol canines were used for preparation of animal models with AF through rapid pacing left atrial appendage, and then the effect of DS-201 on AF was determined by frequency and duration of AF. And Kᵥ1.5 protein expression in atrial myocytes was detected with western blotting.

**Results:** It was showed that DS-201 significantly reduced both the frequency and duration of AF (P<0.05, n=5). The frequency of AF was reduced from 7.2±1.31 to 3.12±1.05, and the duration of AF was lowered from 5.2±2.13 to 0.89±1.23 s. It is interested that DS-201 did not inhibit Kᵥ1.5 protein expression but significantly increase its expression.

**Conclusions:** DS-201 improves tachycardia-induced electrical remodeling of canine by miorolating the low-level expression of Kᵥ1.5 in AF.

**GW25-e3173**

**Inhibition of TRPC channels by the cardioprotective drug sodium tanshinone IIA sulfonate**

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**Objectives:** Sodium tanshinone IIA sulfonate (STS) is a water-soluble derivative of tanshinone IIA, the major lipophilic component extracted from the root of Danshen (Salvia Miltiorrhiza). STS is clinically used in the treatment of myocardial infarction, coronary artery disease and other cardiovascular disorders. STS can protect the heart against pathological hypertrophy in laboratory animals. However, the direct molecular targets of STS on cardiomycocytes are still unclear. Here we aim to examine the effect of STS on the activity of TRPC channels, which have been suggested to be important mediators of pathological cardiac hypertrophy.

**Methods:** Intracellular Ca²⁺ measurement and patch clamp recordings were performed on HEK293 cells stably transfected with human TRPC1 and TRPC3 cDNA. STS was applied to the extracellular solution to test the drug effect.

**Results:** We found that STS at micromolar concentrations inhibited TRPC4 and TRPC5 channels. The potency of tanshinone IIA on the inhibition of these channels is much lower than that of STS, suggesting the sulfonation of this compound is important for its channel-inhibitory activity.

**Conclusions:** The inhibition of TRPC channels by STS found in this study is a novel aspect of the cardioprotective pharmacology of this drug. As STS has been used in patients by injection with safety approval, our results suggest that blockade of TRPC channels is a potentially safe strategy for clinical therapy.