C11orf95 and XIST, its related circRNAs were C2orf29_hsa_circ_000665, MYO9B_hsa_circ_001731 and SMAD2_hsa_circ_000030; GO, KEGG and PANTHER prediction found that MAPK, PI3K Akt, TGF beta, Oxidative stress response, Inflammation mediated by chemokine and cytokine and Apoptosis signaling pathway may relate to it; plasma has-miR-200b-3p expression was significantly lower than the control group ($P < 0.05$), and was negative correlation with FSTL1 (Pearson correlation coefficient is 0.66, $P < 0.05$). Luciferase analysis found that miR-200b-3p regulated FSTL1. AMI group rats plasma FSTL1 expression were increased significantly than the Sham group ($P<0.05$), the AUC is 1.000 ($P<0.05$); FSTL1 express both at the mRNA level and protein level were significantly lower in AMI rats ($P<0.05$) at postoperative 1d; plasma rno-miR-200b-3p expression were significantly decreased in AMI group ($P<0.05$), while heart tissue rno-miR-200b-3p expression were increased significantly in AMI rats ($P<0.05$).

CONCLUSIONS FSTL1 may be associated with AMI, and can be used as a biomarker of myocardial injury, and may involve in inflammation, oxidative stress and cell apoptosis in AMI by hsa-miR-200b-3p mediated regulation.

GW28-e0176

KCNJ2 M301K mutation in short QT syndrome results in ventricular proarrhythmia: insights from modelling study

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OBJECTIVES Short QT syndrome (SQTS) is a new congenital and heterozygous entity associated with familial atrial and/or ventricular fibrillation. Electrocardiographically, it is characterized by a shortened QT interval of less than 320 ms. However, to our knowledge, ionic mechanisms underlying cardiac arrhythmias of SQTS are incompletely understood. One form of the SQTS (SQT3) has been linked to a new gain-in-function mutation (KCNJ2 M301K), which results in larger outward currents than through Kir2.1 channels responsible for inward rectifier potassium current (I_{K1}). Therefore, this study used computational modelling to investigate mechanism by which the KCNJ2 M301K mutation facilitates and perpetuates ventricular arrhythmias.

METHODS The mathematical model developed by ten Tusscher et al. for human ventricular actin potentials (APs) was modified to incorporate the channel kinetics of M301K mutation to Kir2.1 function based on experimentally observed data: both wild-type (WT) and heterozygous (WT-M301K) scenarios were studied. Cell models were incorporated into one-dimensional (1D) and 2D models with transmural heterogeneities to compute the pseudo-ECG. Temporal and spatial vulnerability of ventricular tissue to re-entry was measured and dynamic behavior of re-entrant excitation waves was characterized.

RESULTS Incorporating the M301K mutation into 1D simulations reproduced defining feature of the SQTS: abbreviation of the QT interval (from 363 ms in the WT condition to 292 ms in the WT-M301K condition), and increases in T wave amplitude. In the single-cell model, the M301K mutant I_{K1} led to abbreviated ventricular cell AP duration at 90% repolarization (APD_{90}) (from 302 ms for ENDO cells in the WT condition to 250 ms in the WT-M301K condition). In the tissue simulation, the M301K mutant I_{K1} increased tissue temporal vulnerability of initiating re-entry, but reduced the minimum substrate size necessary to sustain re-entry. It also stabilized and accelerated re-entrant excitation waves, leading to sustained rapid re-entry.

CONCLUSIONS KCNJ2 M301K mutation in SQT3 abbreviated APD_{90} and increased vulnerable window for unidirectional conduction block, which generates an electrical substrate favorable to ventricular re-entrant arrhythmia.

GW28-e0198

CML/CD36 accelerating atherosclerotic progression via inhibiting foam cell migration

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OBJECTIVES To investigate the mechanism of CML/CD36 accelerating atherosclerotic progression via inhibiting foam cell migration.

METHODS In vivo investigation, male apoE−/−mice were rendered diabetic at six weeks of age by intraperitoneal injections of streptozotocin (STZ, 40 mg/kg) for five days in succession, the mice with blood glucose levels of ≥300 mg/dL were considered diabetic after the STZ administration for two weeks. Then the mice were divided into four groups: control group (normal diet, n=8), model group (high fat diet, n=8), CML group (high fat diet + the injection of CML 10 mg/kg/day, n=8), and anti-CD36 group (high fat diet + the injection of CML 10 mg/kg/day+ the injection of anti-CD36 antibody 100 μg/week, n=8). The mice were euthanized after four months and performed for serology analysis, morphological analysis, and molecular biology detection. In vitro investigation, foam cell model was formed by RAW264.7 cells loaded with 40μg/mL ox-LDL, the following studies were investigated based on the foam cell: the effect of CML on the foam cell CD36 expression and actin polymerization, the effect of CML on the foam cell migration, the role of CD36 in the foam cell migration induced by CML, and the related pathway of CML/CD36 in foam cell migration were investigated. The related analyses such as Oil red O staining, the enzyme method of cellular cholesterol contents,transwell migration assay and wound-healing assay, immunoprecipitation, immunofluorescence staining, DCF method of ROS generation, western blot assay and quantitative real time PCR were performed.

RESULTS In vivo investigation, CML can increase the atherosclerotic plaque areas, lipid accumulation and total cholesterol contents in atherosclerotic plaques of apoE−/− mice, while the areas of vascular plaque, lipid accumulation and total cholesterol contents in anti-CD36 group were significantly reduced. While in para-aorta lymph node, lipid accumulation and cholesterol contents increased in anti-CD36 group when compared with CML group. The CD68 protein expression of aortic plaque in anti-CD36 group was obviously lower than that of CML group, but the CD68 protein expression of para-aorta lymph nodes in anti-CD36 group was significantly higher than that of CML group. In vitro investigation, CML/CD36 inhibited the migration of RAW264.7-derived foam cells, and it was related with free cholesterol generation, ROS production, the activation of phosphorylated focal adhesion kinase (FAK), Arp2/3 and actin polymerization.

CONCLUSIONS CML/CD36 inhibited foam cells of plague migrating to para-aorta lymph nodes, accelerating atherosclerotic progression in apoE−/− mice, the corresponding mechanism may be via free cholesterol, ROS generation, p-FAK, Arp2/3, F-actin.

GW28-e0219

Chronic exercise training modulated the autonomic nervous system imbalance without increasing the incidence of spontaneous arrhythmia in myocardial infarction mice

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OBJECTIVES Myocardial infarction (MI) is the leading course of sudden cardiac death, especially the accompanied arrhythmia induced by the autonomic nervous system (ANS) imbalance. Exercise can improve cardiac function after MI, however, the benefit of exercise still keeps controversial because of its proarrhythmic effect. In this study we investigated how exercise affects the incidence of arrhythmic events and the ANS in MI model mice.

METHODS Wild-type male mice which underwent sham-operation or MI-made operation were divided into one control group and two MI groups: sedentary group and exercise training group (MI-Ex). MI-Ex group underwent treadmill training from 7 days after MI for 7-8 weeks. Cardiac function and structural changes were assessed by echocardiography and histology. Based on telemetry recording, autonomic nervous function was evaluated by pharmacological blockades test and heart rate variability (HRV). The incidence of spontaneous ventricular arrhythmia was calculated through telemetry electrocardiography. Gene expressions in left ventricular tissues were investigated by real-time PCR and Western blotting.

RESULTS There were no significant differences in echocardiographic findings and survival rate between two MI groups. Comparing with sedentary group, MI-Ex group showed lower incidence of spontaneous ventricular arrhythmia and increased parasympathetic tone index. The real-time PCR indicated changes in Ca2 + handling-related gene expressions (higher SERCA2a, lower phospholamban) in MI-Ex group.