METHODS The case-control study including a Han population (410 EH patients and 410 control subjects) and a Uygur population (371 EH patients and 463 control subjects). Individuals was conducted to identify the association of three SNPs in CYP19 with EH by using χ^2 test or fisher exact test. Differences in lipids and the parameters of echocardiography among individuals with different genotypes were assessed by using one way analysis of variance(ANOVA).

RESULTS For women in Han, the distribution of rs2289105 in CYP19 gene showed a significant difference between EH and controls(P=0.049) and the dominant model (CC vsCT+TT) has a significant lower risk than the homozygous wild-type CC((p=0.014), the dominant model of rs12050772 (GG vsGT+TT) has a significant lower risk in EH patients(p=0.021). For men in Uygur, the recessive model of rs4774585 (AA vsAG+GG) has a significant higher risk in EH patients (p=0.021). ANOVA indicated the left ventricular end-diastolic dimension is significant higher in the homozygous wild-type (respectively p=0.001 and P=0.015).

CONCLUSIONS The T allele of rs2289105 in CYP19 gene might be a protective genetic marker of EH for women in Han population. The T allele of rs12050772 in Han population and the A allele of rs4774585 in Uygur population could be a protective genetic marker, but further study is needed.

GW26-e2201

Recombinant adeno-associated virus serotype 9 transfection of atherosclerosis mice: determination of the optimal expression time in vivo

Jia Xie, Yining Yang, Xiaomei Li, Bangdang Chen, Fen Liu, Qingjie Chen, Hui Zhai, Yiyong Ma
Department of Cardiology, First Affiliated Hospital of Xinjiang Medical University, Urumqi, China

OBJECTIVES To explore the optimal time point of recombinant adeno-associated virus serotype 9-enhanced green fluorescent protein (rAAV9-eGFP) expression in the aorta of atherosclerosis mice.

METHODS Atherosclerosis model was established with high-fat diet in 30 $ApoE^{-/-}$ mice for 16 weeks. Among them, 25 mice were injected with 5.0×10^{11} vg (virus genomes) rAAV9-eGFP through the tail vein, while the remaining 5 mice were injected with saline, serving as the control group. The virus-transfected mice were killed at 14, 21, 28, 35 and 60 days after transfection, and aortic tissue was harvested. The expression of enhanced green fluorescent protein was detected with laser scanning confocal microscope. Western blot assays were used to detect the expression of enhanced green fluorescent protein in aorta. The expression of enhanced green fluorescent protein in vivo was observed and the optimal expression time point was determined.

RESULTS rAAV9-eGFP effectively transfected the aorta of atherosclerosis mice, enhanced green fluorescent protein was expressed in aortic tissue, and the expression intensity increased gradually with the increasing transfection time. The highest expression level was found at 35 days after transfection and then maintained stable at 60 days. There were significant differences at different time points after transfection ($P < 0.05$).

CONCLUSIONS rAAV9-eGFP can be effectively expressed in the aorta of atherosclerosis $ApoE^{-/-}$ mice and rAAV9-eGFP can be regarded as the optimal vector in the treatment of atherosclerosis.

GW26-e4640

A critical role of miR-195 in pressure overload-induced cardiac remodeling

Shijun Wang, Lei Xu, Jian Wu, Feng Zhang, Hui Gong, Aijun Sun, Junbo Ge, Yunzeng Zou
Shanghai Institute of Cardiovascular Diseases, Zhongshan Hospital, Fudan University

OBJECTIVES Cardiac angiogenesis plays a crucial role in adaptive hypertrophy in response to pressure overload. We previously showed that impaired angiogenesis in HSF1 knockout (KO) mice under increased workload manifested maladaptive hypertrophy and heart failure. However, the potential mechanism is still incompletely understood. Here we investigated the function of microRNAs involved in HSF1-dependent angiogenesis and cardiac hypertrophy to pressure overload.

METHODS Ten weeks old HSF1 KO mice and wild-type (WT) C57BL/6J mice as control were subjected to transverse aorta constriction (TAC) for four weeks. Next heart samples from both groups were performed with microRNAs array analyses based on the microRNA database release 20. In vitro cultured endothelial cells were transfected with AMP-activated protein kinase (AMPK)α1 or AMPKα2 plasmids, and then protein levels were determined by Western blot after mechanical stretch for 24 h. Capillary formation was analyzed by calculating the numbers of tube-like structures in whole wells.

RESULTS MicroRNAs array analyses from heart samples revealed that miR-29, miR-195 and miR-451 were significantly upregulated in HSF1 KO hearts compared with those in WT hearts. We further confirmed that HSF1 deficiency caused a pronounced increase of miR-195 in endothelial cells. Induction of miR-195 significantly inhibited AMPKα2 but not affected AMPKα1. Overexpression of AMPKα2 but not AMPKα1 in endothelial cells, suppressed p53 activity and enhanced HIF-1α expression in response to mechanical stretch. AMPKα2 overexpression also significantly increased the level of VEGF and promoted endothelial angiogenesis. Importantly, AMPKα2-mediated p53 suppression and HIF-1α-dependent angiogenesis were abolished by mimic transfection of miR-195. Furthermore, we confirmed that HSF1 induction could suppress the enhanced miR-195 level in endothelial cells with mechanical stress, which strengthened the AMPKα2 expression and attenuated the nuclear accumulation of p53. In addition, we demonstrated that transfection of Ad-AMPKα2 in HSF1 KO mice effectively improved cardiac angiogenesis, reduced cell apoptosis and alleviated myocardial remodeling in response to TAC.

CONCLUSIONS Our findings indicate that miR-195 is critically involved in cardiac remodeling via impairment of HIF-1α-dependent angiogenesis. Induction of HSF1 might be a novel and effective target to pressure overload-induced heart failure through regulating the miR-195/AMPKα2 pathway therapeutically.

GW26-e4649

The role of augmented late sodium current in atrial fibrillation

Qiaomei Yang, Lu Ren, Wei Yang, Sihui Huang, Xiaohong Wei, Lin Wu
Peking University First Hospital

OBJECTIVES To determine the role of increased late sodium current in atrial fibrillation (AF) by investigating the effect of sea anemone toxin-II (ATX-II) on atrial action potential duration (APD) and effective refractory period (ERP) and the incidence of AF.

METHODS Female New-Zealand rabbit hearts were isolated and perfused in Langendorff method. Hearts were paced at right appendage at fixed rate and left atrial and ventricular endo- and epicardial APDs were recorded. Hearts were treated with ATX-II (3 nM) and paced at right atrium in a programmable mode of S1S2 to create AF. Ranolazine and TTX at different concentrations were administered to hearts with AF in order to observe their effectiveness on suppressing AF.

RESULTS When hearts were paced at 350 ms, ATX-II (3-15 nM) significantly prolonged atrial $MAPD_{90}$ by 46 ± 5 ms (n=6, P <0.001). In the presence of ATX-II (10-15 nM), spontaneous AF were investigated in 64.3% (n =14) of hearts, but TTX (1μM) and ranolazine (10 μM) terminated AF. When hearts were paced at 440 ms, ranolazine alone prolonged atrial and ventricular endo- and epi-cardial $MAPD_{90}$ by 17 ± 4 ms, 28 ± 5 ms and 23 ± 6 ms (n=6, p <0.01). However, in the presence of ATX-II (3 nM), ranolazine shortened atrial $MAPD_{90}$ by 33 ± 4 ms (n =6, P <0.001). ATX-II (1-3 nM) increased AF window, AF burden in concentration dependent manners by 31 ± 11 s and 103 ± 8 ms (n =6, P <0.05), respectively. In the presence of ATX-II (3 nM), ranolazine (3-10 μM) and TTX (0.1-1 μM) significantly reduced AF window and AF burden in concentration dependent manners.

CONCLUSIONS When late sodium current was increased, AF was induced by prolonging atrial MAPD and ERP, which was the new mechanism of AF. Both ranolazine and TTX shortened atrial MAPD and exerted the ability of reducing AF window and AF burden and preventing AF.