(3) The frequency and amplitude of the neural activity recorded from the SLGP, LSG and RSN were markedly increased by 1 hour intermittent hypoxia.

(4) EMF reversed all these changes induced by 1 hour intermittent hypoxia.

CONCLUSIONS EMF suppressed AF inducibility and the responses to SLGP and LSG stimulation induced by intermittent hypoxia. Inhibition of neural activities in the GP, LSG and RSN may be a mechanism underlying these results.

GW26-e2307
Acute arrhythmic effects of acetylcholine on sodium channel in primary rat atrial myocytes
Xinrong Fan,1,2 Chao Wang,2 Mengmeng Yang,3 Xiaorong Zeng,1 Hanxiong Liu,2 Lin Cai1
1The Institute of Cardiovascular Research, Luzhou Medical College, Luzhou, China; 2Department of Cardiology, Institute of Cardiovascular Disease of Chengdu, the Third People’s Hospital of Chengdu, Chengdu, China

OBJECTIVES Acetylcholine (previously named Guanfu base A), a novel diterpene alkaloid isolated from the root of aconitum coreanum (Levl.) raiapics which has been shown to effectively terminate AF and suppress arrhythmias in patients and animal models by blocking multi-ion channels, but its effects on cellular electro-physiological activities of sodium channels are largely unknown in atrial myocytes.

METHODS Primary atrial myocytes were isolated and cultured from neonatal Sprague-Dawley rats (born 1-2 days). A single-pipette whole-cell patch-clamp was used to investigate the acute effect of acetylcholine on sodium channels, and RT-PCR and western blot were used to quantify α and β-subunits mRNA and protein expression implied chronic effect on sodium channels.

RESULTS Atrial myocytes were cultured and plated into coverslips at 1-104/cm2, 48h later a single cell was ruptured and INa was recorded in absence and presence of acetylcholine. It inhibited INa in a positive rate-dependent and concentration-dependent manner, with IC50 value of 31.67±5.47μM/L. 50μM/L acetylcholine significantly shifted inactivation curves toward left and shifted activation curves to right, but did not modify the recovery kinetics from inactivation of sodium channels. In addition, incubation with 100μM/L acetylcholine for 3-24h caused significant decreases of α and β-subunits mRNAs in time-dependent manner (SCN1A decreased by 72.24±18.21%, SCNIB decreased by 52.81±19.77%, SCN3B decreased by 83.42±35.16% at 24h, p < 0.01 vs. untreated cells). Meanwhile, the quantification of protein levels was consistent with alteration of mRNA expression.

CONCLUSIONS These findings indicate that acetylcholine inhibits sodium channels by two modes, 1) inhibiting INa by binding to sodium channels and 2) downregulating α and β-subunits at mRNA and protein levels, which provides experimental evidence for anti-arrhythmia by acetylcholine.

GW26-e2401
Enhanced levels of miR-122-5p and let-7b-3p in aortas of spontaneously hypertensive rats associated with downregulated levels of Apelin, miR-1-3p, miR-376b-3p and miR-298-5p
Jiuchang Zhong,1,2 Ran Xu,1 Laijiang Chen,1,2 Zhenzhou Zhang,1,2 Yingle Xu,1 Qining Chang,1 Dingliang Zhu,1,2 Pingjin Gao1,2
1State Key Laboratory of Medical Genomics, Ruijin Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai Institute of Hypertension, China; 2Institute of Health Sciences, Shanghai Institute for Biological Sciences, Chinese Academy of Sciences, China

OBJECTIVES The deregulation of microRNAs (miRNAs), a class of short and small non-coding RNAs, has been shown to be involved in a wide range of cellular processes and cardiovascular pathologies. The Apelin/APl system has been implicated in the pathophysiology effects in cardiovascular system, which is a necessary process in the initiation and development of various cardiovascular diseases inclusive of hypertension. We hypothesized that Apelin is a negative regulator of hypertension-mediated pathological effects in spontaneously hypertensive rats (SHR) model.

METHODS The 3-month-old male SHR and Wistar-Kyoto (WKY) rats were obtained from Slac Laboratory Animal Co. Ltd. in China. Rats received daily administration of Apelin or saline for 4 weeks. Systolic blood pressure (SBP) of rat was measured by the tail-cuff method. Vascular morphological analysis was processed using the computer image analysis software for the quantification of the media thickness (MT), lumen diameter (LD), and the ratio of MT to LD, markers of vascular hypertrophy and remodeling.

RESULTS In the SHR model, the aortic expression of miR-122-5p and let-7b-3p were upregulated, while miR-1-3p, miR-376b-3p and miR-298-5p were downregulated and negative correlated with SBP levels. Compared with WKY rats, the MT and the MT/LD ratio of the thoracic aorta were significantly enhanced in SHR (MT: 0.72±0.5 um) vs. (8.18±3.9 um); MT/LD ratio: (7.3±1.1) vs. (6.8±3.1); P<0.01, respectively). These changes were linked with the reduction of Apelin expression and increased levels of ANF, and phosphorylated ERK1/2 and activated severe ultrastructural damage of the thoracic aorta. These effects were significantly blunted by Apelin treatment, in association with a lowering of phosphorylated ERK1/2 levels and improvement of ultrastructural injury. However, there were no changes in aortic expression of APJ receptor among groups.

CONCLUSIONS There are abnormal levels of miRNAs and Apelin in hypertensive status. In addition, Apelin is an important negative regulator of the hypertension-induced pathological hypertrophy and aortic remodeling and attenuates aortic ultrastructural injury in hypertonetic rats. These observations indicate that various miRNAs and Apelin signaling in vasculature may be linked with hypertension and provide novel pharmacologic implications for the prevention and treatment of hypertension.

This work was supported by Training Program of the National Major Research Plan (91339108), the National Basic Research Program of China (2014CB542300), and the National Natural Science Foundation of China (81370062 & 81170246).

GW26-e3880
The Reduced Expression of Ubc9 and the Intensity of SERCA2a-SUMOylation Were Reduced in Diet-induced Obese Rats and Partially Restored by Trimetazidine
Jing Yao,1 Tian-Chang Li,1 Xing-Hui Shao,1 Zheng-Ming Xu,1 Meng-Yue Yu,1 Si-Yong Teng,2 Yong-Jian Wu2
1Navy General Hospital, People’s Liberation Army; 2Fuwai Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College

OBJECTIVES Reduced expression of Sarcomplastic reticulum calcium-transporting ATPase isofom 2a (SERCA2a) has been shown to play a significant role in the cardiac dysfunction of obese animal models. It was reported recently that SUMOylation enhances the stability and activity of SERCA2a. We hypothesized that SERCA2a-SUMOylation might be involved in obesity-mediated reduction of SERCA2a.

METHODS Trimetazidine (TMZ), the drug that inhibits fatty acid oxidation, was used in diet-induced obesity (DIO) rats and palmitic acid (PA)-treated cardiomyocytes. The intensity of SERCA2a-SUMOylation in control cardiomyocytes. The variations of protein and intensity of SERCA2a-SUMOylation were observed in DIO rats and PA-treated cardiomyocytes. The reductions of SERCA2a protein and the intensity of SERCA2a-SUMOylation were observed in DIO rats and TMZ treated. Reductions of SERCA2a protein and the intensity of SERCA2a-SUMOylation were not changed by DIO and PA.

CONCLUSIONS TMZ alleviates the DIO-induced and PA-induced reductions of SERCA2a-SUMOylation. Ubc9 is involved in the reductions. Whereas the other proteins involved in SERCA2a-SUMOylation in control cardiomyocytes.
by inflammatory factors expression, and histological analysis of aortic blood vessel samples was performed.

RESULTS Hypertensive subjects with VC had higher serum OPN and OPG levels compared to these without VC, and their expressions were also increased in the calcific vessels (P < 0.05). Interestingly, the inflammatory factors from hypertensive patients with VC were significantly increased in cultured macrophages (P < 0.05), and were regulated by OPN and OPG.

CONCLUSIONS These findings provided a novel insight that OPN and OPG-mediated inflammatory factors expression in macrophages were involved in the processes of VC in hypertensive patients.

GW26-e0101 IFN21 Correlates with ARF and non-coding RNA ANRIL Expression and the Age of CAD Onset in Han Chinese

Yan Liu,1 Mingyu Zhang2
1University of North Carolina at Chapel Hill, 6th floor, Burnett-Womack Building, CB# 70757, Chapel Hill, NC 27599-7075; 2Department of Cardiology, The 4th Affiliated Hospital, Harbin Medical University, Harbin, China

OBJECTIVES Multiple unbiased genome-wide association studies have identified a strong link between ARF locus and atherosclerotic disease risk. However, the direct mechanism accounting for the 9p21.3 CAD (Coronary Artery Disease) risk still remains poorly understood and controversial. Previous work including ours demonstrated that altered expression INK4/ARF locus by non-coding RNA ANRIL might contribute to the 9p21.3 genetic atherosclerosis susceptibility. Studies from other groups also suggested possible physical interaction among 9p21.3, INK4/ARF locus and type I IFN gene cluster. However, recent study has showed that 9p21 locus does not affect risk of coronary artery disease through direct induction of type I IFNs.

METHODS To investigate whether type I IFN is co-regulated with INK4/ARF and contributes to clinical onset of CAD in Han Chinese, we first examined the relationship of IFN subtypes with 9p21.3 variants in 170 healthy individuals in US, followed by plasma IFN21 measurement in 300 Han Chinese with CAD of different severity.

RESULTS We found that mRNA expression of IFN21 correlated with the expression of ARF and cANRIL, as well as rs10757278 CAD risk allele. The expression of IFN21 did not correlate with CAD severity quantified by coronary angiography but was associated with the age of CAD onset in Han Chinese.

CONCLUSIONS These data suggest that type I IFNs does not contribute to CAD severity but may play a role in the age of onset of CAD, possibly through an ARF-mediated co-regulatory mechanism with INK4/ARF locus.

GW26-e2506 Genetic diagnosis of familial hypercholesterolemia by targeted exome sequencing

Wenfeng Wu,1 Lyva Wang2
1Beijing Anzhen Hospital Affiliated with Capital Medical University, Beijing, China; 2Department of Atherosclerosis, Beijing Institute of Heart Lung and Blood Vessel Diseases, Beijing, China

OBJECTIVES The aim of this study was to combine clinical criteria and next-generation sequencing (pyrosequencing) to establish a clinical diagnosis of familial hypercholesterolemia (FH).

METHODS A total of 39 subjects with a Dutch Lipid Clinic Network score of ≥8 (definite FH clinical diagnosis) were recruited from the Lipid Clinic at Anzhen Hospital, Beijing, China. Next-generation sequencing was performed in all subjects using a GenCap Custom Enrichment Kit (MyGenostics, Beijing, China), a kit that detects in 167 known FH-causing genes. Of these, 40 high frequency SNPs and top 10 genes were summarized. The fourth, a mutation in LDLR gene, has not previously been reported; it was found to segregate with high cholesterol levels in the family of the proband.

RESULTS A total of 24 mutations were detected in 39 subjects. Amongst these, 19 mutations were in the LDLR gene, three in the APOB gene and two in the PCSK9 gene. We also found 151 SNPs and 89 genes relevant with blood lipids. Of these, 40 high frequency SNPs and top 10 genes were summarized. The fourth, a mutation in LDLR, has not previously been reported; it was found to segregate with high cholesterol levels in the family of the proband.

CONCLUSIONS Using a combination of clinical criteria and targeted exome sequencing, we have achieved FH diagnosis with a high success rate. Furthermore, we identified a new mutation in the LDLR gene.