surgery without LAD ligation; b). Sham-H-PHC group. The rats were administrated with high dose of penehyclidine hydrochloride (H-PHC; 1 mg/kg bodyweight) by i.v. 30 min before sham surgery; c). Ischemia reperfusion (I/R) group: The rats were subjected to a 30 min LAD coronary artery ligation followed by 3 h reperfusion; d). I/R-H-PHC group: The rats were administrated with the low dose of PHC (0.3 mg/kg bodyweight) 30 min before I/R; e). I/R-M-PHC group: The rats were administrated with moderate dose of PHC (M-PHC; 0.3 mg/kg bodyweight) 30 min before I/R; f). I/R-H-PHC group: The rats were injected with H-PHC (1 mg/kg bodyweight) 30 min before I/R. Cardiac function was measured by echocardiography 30 min before I/R. Cardiomyocyte apoptosis was evaluated by TUNEL assay. The release of inflammatory cytokines and platelet spreading on immobilized fibrinogen were detected to detect the phosphorylation levels of signaling molecules by Western blotting. For platelet spreading on immobilized fibrinogen, the average size of the platelets that spread on Fg were 1950.8 ± 950.09 pixels for ATII, 9508.76 ± 2107.95 pixels for the platelets in the presence of DMSO. In the FeCl3-induced carotid artery thrombosis model, the average time to first occlusion was 12.19 min for the ATII, and 9.67 min for ATIII mice. In contrast to 6.76min in control mice. The average ratio of clot retraction of ATII with platelets was 0.1659 ± 0.0115, ATII with platelets was 0.2892 ± 0.0118 versus DMSO with platelets 0.7183 ± 0.0359.

**RESULTS** We found that PHC improved cardiac function by elevating ejection fraction (EF), fractional shortening (FS) and left ventricular end systolic pressure (LVESP), and downregulating left ventricular end-diastolic pressure (LVEDP). PHC treatment remarkably decreased the activities of creatine kinase (CK), aspartate aminotransferase (AST), lactate dehydrogenase (LDH) and malondialdehyde (MDA) content, suppressed superoxide dismutation (SOD) activity. Additionally, PHC reduced the infarct size and the apoptotic rate of cardiomyocytes in a dose dependent manner. Administration of PHC significantly decreased serum IL-1β, TNF-α, PEG-2 and IL-6 levels and myocardium COX-2 level. Meanwhile, the expression levels of p-α and p-β were downregulated, leading to the effective expression of NF-κB was upregulated. These results suggest that PHC exert dose-dependent effects on I/R-induced myocardial injury by inhibiting oxidative stress, apoptosis and inflammation, and reduce the levels of nuclear NF-κB and p-α and p-β.

**CONCLUSIONS** PHC presented significantly dose dependent effects on myocardial IRI by inhibiting inflammation, oxidative stress and apoptosis, and reducing the levels of nuclear NF-κB and p-α and p-β.

**GW26-e1245**

**Atractylenolide II and Atractylenolide III Inhibit Platelets Activities and Thrombus Formation**

Yizhu Chen,1 Xiaolin Wu,2 Junling Liu,2 Junfeng Zhang1

**OBJECTIVES** Antiplatelet treatment has been proved to be an effective strategy for the prevention of cardiovascular disease (CVD). However, a major disadvantage of this strategy is the increasing risk of hemorrhages. Developing new platelet inhibitors with minimal adverse effects is important for clinical treatment of CVD. AtractylenolideII(ATII) and III(ATIII) are the major active components in Atractylodes macrocephala. The effects of the components including anti-inflammatory and anti-cancer have been demonstrated. However, their effects on platelet activation are unknown. Therefore, we explored the effects of ATII and ATIII on platelet activities such as platelet aggregation, platelet spreading, thrombus formation and so on. We also investigated the effects of ATII and ATIII on essential signaling mediator in platelet activation.

**METHODS** Human platelets were adjusted to 3 × 10⁶ platelets/ml for platelet aggregation. ATII, ATIII and Acetylsalicylic acid were incubated with the platelets for 3 min prior to stimulation, respectively. When the platelet aggregation was terminated, the target proteins were detected to detect the phosphorylation levels of signaling molecules by Western blotting. For platelet spreading on immobilized fibrinogen, platelets were incubated with ATII and ATIII respectively for 3 min and allowed to spread on immobilized fibrinogen. The cell reaction was done as following, human platelet-depleted plasma was mixed with washed human platelets to a concentration of 4 × 10⁹/ml and was incubated with ATII and ATIII for 3 min respectively. Plasma was induced to coagulate with 0.4U/ml thrombin. We examined thrombus formation by FeCl3-induced carotid artery injury murine thrombosis model. After mice were treated with ATII(ATIII) at 60mg/kg dose by oral administration, carotid artery blood flow was monitored.

**RESULTS** Compared to Acetylsalicylic acid, ATII(ATIII) inhibited platelet aggregation with lower concentration(10μM) in response to thrombin and collagen. Akt and other signaling molecules such as p-38, Erk have been proved to play critical roles in platelet activation. Akt Ser473phosphorylation levels were significantly diminished for ATII(ATIII) treatment in response to thrombin, but no changes were found in the phosphorylation levels of p-38 and Erk. The average size of the platelets that spread on Fg were 1904.0±1059.86 pixels for ATII(0.1mM) versus 9508.76±2107.95 pixels for the platelets in the presence of DMSO. In the FeCl3-induced carotid artery thrombosis model, the average time to first occlusion was 12.19 min for the ATII, and 9.67 min for ATIII mice. In contrast to 6.76min in control mice. The average ratio of clot retraction of ATII with platelets was 0.1659±0.0115, ATII with platelets was 0.2892±0.0118 versus DMSO with platelets 0.7183±0.0359.

**CONCLUSIONS** The work demonstrates that ATII and AT III inhibit platelets aggregation, spreading, clot retraction and arterial thrombosis formation in vivo. The results suggest that ATII and ATIII have the potential to be an efficient platelet inhibitors.

**GW26-e1464**

**PHA665752, Hepatocyte Growth Factor/c-Met Inhibitor, Reduces the Ventricular Fibrillation Threshold in Myocardial Infarction Rats Treated with Cardiac Stem Cells Transplantation**

Shaoxin Zheng, Fei Wang, Huihong Long, Jingying Hou, Tong Wang1, The Sun Yat-sen Memorial Hospital of Sun Yat-sen University, Guangzhou, China

**OBJECTIVES** Our previous studies found that cardiac stem cells (CSCs) transplantation improved the ventricular fibrillation threshold (VFT) in myocardial infarction (MI) rats. However, the mechanisms remain unclear. Therefore, we sought to explore the therapeutic mechanisms.

**METHODS** MI was induced in 30 male Sprague-Dawley rats. 2 weeks later, animals were randomized to receive 5 × 10⁶ CSCs labeled with PKH26 in phosphate buffer solution (PBS) (20 rats) or PBS (10 rats) via tail vein injection every day for 2 weeks. After that, 10 rats with CSCs transplantation received PHA665752 (Hepatocyte Growth Factor/c-Met Inhibitor, 15mg/kg) in PBS and DMSO (PHA665752 group), 10 rats with CSCs transplantation received PBS and DMSO (CSC group) and 10 rats with PBS injection received PBS and DMSO (PBS group) via tail vein injection every day for 2 weeks. Then the VFTs were measured. Labeled CSCs were observed in 5μm cryostat sections from each heart to detect the myocardiab fibrosis.

**RESULTS** Comparisons of CSC group, the VFTs were deteriorative in PHA665752 group (PHA665752 group vs. CSC group vs. PBS group: infarct zone: 3.9±1.7mA vs. 10.3±1.9mA vs. 3.4±0.7mA p < 0.05 infarct marginal zone: 4.2±1.4mA vs. 9.7±1.4mA vs. 2.9±0.7mA p < 0.05 non infarct zone: 2.9±0.9mA vs. 9.1±1.1mA vs. 2.6±0.7mA p < 0.05). Masson detection showed that the myocardial fibrosis in PHA665752 group was obviously more severity than that in CSCs group.

**CONCLUSIONS** PHA665752, hepatocyte growth factor/c-Met inhibitor, reduces the VFT and enhances the myocardial fibrosis in MI rats treated with CSCs transplantation, which indicates that CSCs paracing hepatocyte growth factor ameliorate myocardial fibrosis leading to VFT improvement.

**GW26-e1492**

**Changes of Small-conductance calcium-activated K⁺ channels 3 (SK3) in Patients with Persistent Atrial Fibrillation**

Qiang Xu,1 Miaoling Li,2 Tangting Chen,2 Huan Lan2

1Department of Histology and Embryology, Luzhou Medical College; 2Department of Biochemistry and Molecular Cell Biology of Shanghai Jiao Tong University School of Medicine

**OBJECTIVES** We had reported that the current density of apamin-sensitive SK channels was significantly increased in AF group with persistent atrial fibrillation than SR group. The purpose of this study was to investigate whether the current density increase of SK channels in patients with persistent atrial fibrillation was because of its differential expression between the sinus rhythm (SR) and persistent atrial fibrillation patients and whether SK3 channel is involved in electrical remodeling of human persistent atrial fibrillation.

**METHODS** The right atrial appendage myocytes were obtained from 16 sinus rhythm (SR) and 14 persistent atrial fibrillation patients
underwent surgical valve replacement. KCNN3 expression were associated with mitral valve quantitative PCR analysis.

RESULTS The mRNA expression levels of KCNN3 were obviously increased in persistent atrial fibrillation patients compared with SR patients (p < 0.05). This was consistent with the change of current density of apamin-sensitive SK channels.

CONCLUSIONS Our results demonstrated that SK3 are involved in electrical remodeling of persistent atrial fibrillation. The SK3 showed increased expression in persistent atrial fibrillation. These findings provide a new insight into mechanisms of electrical remodeling of human persistent atrial fibrillation.

GW26-e1796 Effect of Ruanmailing containing serum on twinnfil-in-1 in PDGF-activated vascular smooth muscle cells Ruonian Gao,1 Guili Lian,2,∗ Liangdi Xie1,2,∗ Fujian Hypertension Research Institute; 3First Affiliated Hospital of Fujian Medical University; 4Fujian Medical University Union Hospital

OBJECTIVES It was confirmed previously by our group that Ruanmailing, one of traditional Chinese Medicine, may inhibit migration of vascular smooth muscle cells (VSMCs) induced by PDGF. In this study, we tested the effect of Ruanmailing containing serum on twinnfil-in-1 in PDGF-activated VSMCs to further illuminate the possible mechanism of Ruanmailing in anti-vascular remodeling.

METHODS Ruanmailing containing serum was prepared from rats after drug gavage every 12 hours for 5 days. VSMCs were isolated from thoracic aortas of Sprague-Dawley rats. Cells at 90% confluences were passaged by trypsinization and cells between 3-5 passage were used for experiment. Twinnfil-in-1 in cells was detected by confocal microscopy with Alexa647 staining. Structure of actin filament was detected by FITC-phalloidine labeling under confocal microscope.

RESULTS In quiescent cells without any stimulants in medium, twinnfil-in-1 was localized in cytoplasm prominently around the nucleus with no apparent stress fibers in cells. Compared with the control, after PDGF (10ng/ml) stimulation, twinnfil-in-1 was upregulated and redistributed mainly from peri-nucleus to the whole cytoplasm, especially lamellipodia and actin rich filopodias. Actin cytoskeleton was rearranged with a cluster of stress fibers intensely distributed in cytoplasm. Interestingly however, after treatment with 10% Ruanmailing containing serum, both expression and redistribution of twinnfil-in-1 induced by PDGF were suppressed. Twinnfil-in-1 scarcely localized to the lamellipodia and filopodias. The stress fiber was markedly reduced and loosely arranged simultaneously. Treatment of 5mol/l LY294002 led to the same change of twinnfil-in-1 and cytoskeleton to that of 10% Ruanmailing containing serum.

CONCLUSIONS PDGF induces expression and redistribution of twinnfil-in-1 together with the rearrangement of cytoskeleton in VSMCs. Ruanmailing containing serum may suppress twinnfil-in-1 in VSMCs and inhibit the rearrangement of actin cytoskeleton induced by PDGF.

GW26-e2200 Association of a SNP in the CYP19 gene with risk of coronary heart disease Bei Wang, Zhen Y. Fu, Ding Huang, Fen Liu, Chun L. Dong, Ting Wang, Ya J. Meng, Yitong Ma Department of Cardiology, First Affiliated Hospital of Xijing Medical University, Urumqi, 830054 P.R., China

OBJECTIVES There is a positive relationship between the imbalance of sex hormone ratio and coronary heart disease(CHD). Aromatase is the enzyme in the conversion of androgen to estrogen, and play an important role in the balance of the sex hormone levels. There is little related research. The goal of this study was to investigate the interaction between the SNPs in CYP19 gene and coronary heart disease.

METHODS We collect 1706 blood samples and use propensity score matching techniques to match the confounding factors between the case and control. Finally, the case-control study including 596 individuals was conducted to identify the association of three SNPs in CYP19 with CHD by using $\chi^2$ test or Fisher exact test and binary Logistic regression analysis. Differences in lipids and the parameters of echocardiography among individuals with different genotypes were assessed by using one way analysis of variance(ANOVA).

RESULTS The distribution of rs2289105 in CYP19 gene showed a significant difference between CHD and controls(P=0.014) and the heterozygote GT has a significant lower risk than the homozygous GG(P=0.006) and OR=0.575. ANOVA indicated the blood lipids and the parameters of echocardiography among individuals with different genotypes did not differ from case and control, at the same time, although we find out the distribution of rs4774585 may be associated with CHD in Uygur population, after adjustment for potential confounders, the associations are not statistically significant.

CONCLUSIONS The GT genotype of rs2289105 in CYP19 gene is associated with CHD and might be a protective genetic marker of CHD.

GW26-e2462 Effects of Rosuvastatin on Aortic Artery and Expression of IL-6 as well as hs-CRP in ApoE−/− Mice Zhiyun Wang Affiliated Hospital of Shangdong Academy of medical Sciences

OBJECTIVES To aim the effects of Rosuvastatin on articular atrophy and expressionof IL-6 as well as hs-CRP in ApoE−/− mice.

METHODS 30 male ApoE−/− mice were randomly divided into model group, interventional group and control group. Model group and interventional group were fed with high-fat diet, while control group was fed with normal diet and mice in interventional group were administered orally with Rosuvastatin, once a day for 13 weeks. All mice were sacrificed when the mice were 19 weeks old, blood was collected and plasma triglyceride (TG), total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C) were measured, and expression level of interleukin-6 (IL-6) and high sensitive C reaction protein (hs-CRP) was measured by double antibody clip art in ELISA detection. Aortic sections were stained with hematoxylin and eosin (HE) to observe the aortic pathological changes in mice.