Objectives: As the most common sustained cardiac arrhythmia, atrial fibrillation (AF) is the most critical cardiac disease partially, mainly due to age-related oxidative injury in heterozygous mutations or single nucleotide polymorphisms (SNPs) in the exons coding regions. The relationship between AF occurrence and SNPs in nonprotein-coding micro-RNAs is still mysterious. Our study focused on this filed.

Methods: A total of 123 participants were enrolled from genetically unrelated ethnic Han Chinese living in Nantong city of Jiangsu Province. 66.5% patients were males (Male: 58.38%: Age: 69.75±13.44) confirmed with electrocardiogram or Holter. 58 normal individuals (Male: 48.28%; Age: 63.36±14.11) were assigned to control group. Genotypes of the pre-miRNA SNP rs11614913 in miR-196a2 were distinguished by the method of polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP) assay. The primers used for amplification were 5'-TCCA GATAGTGCACAGTGTAAGAA-3' (forward) and 5'-ATAGTGTGAGGAGCCGGA A-TA-3' (reverse). PCR products were digested by specific restriction enzyme Hha I (Enzyme Digestion) to yield 294 bp and 291 bp fragments. For hsa-miR-196a2 rs11614913 C/T, allele T is cuttable, yielding two fragments of 81 bp and 219 bp. Allele C is uncuttable and the fragment is still 300 bp. Hardy-Weinberg equilibriums were evaluated by chi-square test. Student’s t test for continuous variables and chi-square test for categorical variables were used. Odds ratio (OR) and 95% conﬁdence intervals (CI) were reported to estimate the associations between genotypes and AF risk using logistic regression analyses. Differences were considered statistically significant at P<0.05.

Results: The genotype frequencies were 15.4% (TT), 46.1% (TC), and 38.5% (CC) for the AF patients, while 39.7% (TT), 46.5% (TC), and 13.8% (CC) for the control participants. Significantly increased AF risk was found to be associated with C allele (P<0.0001; OR, 2.716; 95% CI, 1.602-4.553). Compared with miR-196a2 C allele carriers, those with TT genotype had significantly increased AF risk in carriers of variant homozygote CC (OR, 8.625; 95% CI, 2.939-25.316) and heterozygote TC (OR, 2.556; 95% CI, 1.032-6.326). After Adjusting for age and sex, participants with T/C/C genotypes still show high risk for AF statistically (OR, 3.614; 95% CI, 1.425-8.979).

Conclusions: Our study provides the first evidence that the SNP rs11614913 in miR-196a2 may be associated with increased risk of atrial fibrillation in Han Chinese population. It may be used as candidate biomarker for AF susceptibility.

GW25-e0432
Qiliangxin inhibits angiotensin II-induced transdifferentiation of rat cardiac firoblasts through suppressing interleukin-6
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Objectives: Qiliangxin (QL), a traditional Chinese medicine, had long been used to treat chronic heart failure. Recent studies revealed that differentiation of cardiac fibroblasts (CFs) into myofibroblasts played an important role in cardiac remodeling and development of heart failure, however little was known about whether QL-ameliorated myocardial remodeling via regulating CFs differentiation. The present study aimed to investigate the effects of QL on angiotensin II (AngII)-induced CFs transdifferentiation and the underlying mechanism.

Methods: Study was performed on in vitro cultured CFs from Sprague-Dawley rats. Cells were stimulated by AngII (100nM) for 24 h in the presence and absence of QL at 1 and 5 μg/ml. QL-treated cells were compared to vehicle controls. For the in vitro experiment, QL was added at the same time as AngII stimulation. For the in vivo experiment, keratin levels in the patients of acute heart failure was measured.

Results: QL inhibited the AngII-induced transdifferentiation of CFs, as indicated by decreased expression of α-SMA, IL-6, and TGF-β1. Lactate dehydrogenase activity was significantly decreased in QL-treated CFs compared to vehicle controls. The number of autophagosomes and autolysosomes was increased in QL-treated CFs compared to vehicle controls. The number of autophagosomes and autolysosomes was increased in QL-treated CFs compared to vehicle controls. The number of autophagosomes and autolysosomes was increased in QL-treated CFs compared to vehicle controls.

Conclusions: Our results suggest that QL inhibits AngII-induced CFs transdifferentiation by suppressing the expression of pro-inflammatory cytokines and IL-6, and stimulating autophagy.

GW25-e0557
Effects of Atorvastatin on Pregnancy Associated Plasma Protein-A Level in Vascular Smooth Muscle Cells Induced by Oxidized-low Density Lipoprotein
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Objectives: As pregnancy-associated plasma protein A (PAPP-A) and vascular smooth muscle cells (VSMCs) play roles in the development of atherosclerosis (AS). In this study, we investigated the effect of atorvastatin on PAPP-A level in VSMCs induced by oxidized-low density lipoprotein (ox-LDL) and its potential mechanism in AS.

Methods: Different concentrations of ox-LDL (75, 150, 300μg/ml) were added into the culture medium for different processing time (2, 12 and 24h) to induce rat VSMCs oxidative injury model. The level of PAPP-A mRNA and protein were evaluated by RT-PCR and Western Blotting. Then we observed the change in PAPP-A mRNA and protein expression after treatment with atorvastatin.

Results: Compared with control group, PAPP-A mRNA and protein levels increased in a dose and time-dependent manner when VSMCs were induced by ox-LDL. After exposure to ox-LDL (300 μg/ml) for 12 and 24h, PAPP-A mRNA and protein levels were dramatically increased (P<0.01). However, PAPP-A mRNA and protein levels were strongly decreased after atorvastatin treatment.

Conclusions: Atorvastatin can regulate the expression of PAPP-A mRNA and protein induced by ox-LDL, which demonstrate that PAPP-A is probably involved in the anti-inflammatory mechanism of atorvastatin.
Angiotensin II Type 2 Receptor Re-expression After the Collar-induced Adventitia Injury in the Rat Carotid Artery

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Objectives: The present study was undertaken to observe the effects of the chronic collar-induced adventitia injury on angiotensin II type 2 Receptor (AT2R) expression in the rat carotid artery.

Methods: Adventitia injury was induced by positioning a silicone collar around the right carotid artery for one week in 20 Wistar Kyoto rats. Both side of carotid was harvested for analysis of AT2R expression. The expression of AT2R mRNA and protein was upregulated in response to the collar placement. Collar-induced adventitia injury led to re-expression of AT2R in intima and adventitia of the rat carotid artery.

Results: The expression of AT2R mRNA and protein was upregulated in response to the collar placement. Collar-induced adventitia injury led to re-expression of AT2R in intima and adventitia of the rat carotid artery.

Conclusions: These data suggest that upregulation of UC2P may attenuate the development of salt-induced cardiovascular and renal damage.

GW25-e2215

Puerarin reduces inflammatory responses and apoptosis in LPS-stimulated cardiomyoblasts

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Objectives: To investigate the effect of puerarin, a kind of Chinese herbal medicine, on cardiomyoblast inflammatory response in a sepsis model using LPS.

Methods: H9c2 cardiomyoblasts were incubated with different concentrations of puerarin (1μM, 5μM, 10μM) or dimethyl sulfoxide (DMSO) (as the control). The mRNA expression of inflammatory cytokine including IL-1, IL-6 and TNFα was detected using real-time PCR. Immunofluorescence staining was used to evaluate NFκB p65 nuclear translocation. LPS-induced apoptosis was measured by TUNEL staining and immunochemistry of Bax and Bcl-2 expression. The activation state of NFκB signaling was investigated using Western Blotting.

Results: Puerarin blunted proinflammatory cytokine production in LPS-stimulated H9c2 cardiomyoblasts in a concentration dependent manner. In addition, treatment of H9c2 cardiomyoblasts with puerarin (40μM) inhibited LPS-induced apoptosis.

Conclusions: Puerarin may serve as a valuable protective agent in cardiovascular inflammatory diseases.

GW25-c3401

Exogenous Administration Of Adiponectin Could Effectively Alleviate Coronary No Reflow Injury In Type 2 Diabetic Rats

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Objectives: Coronary no reflow (NR) phenomenon of varying degrees widely exists in patients undergoing coronary revascularization therapy with type 2 diabetes mellitus (T2DM) significantly increasing the severity of it. Meanwhile, plasma adiponectin (APN) level is significantly reduced in patients with T2DM. To demonstrate whether hypoadiponectinemia could lead to aggravated coronary NR injury in T2DM patients, we evaluate the protective effect of APN on coronary microcirculation, we conducted the following experiments.

Methods: Healthy male SD rats of 6-week-old were fed with normal diet (10kcal %, ND) or high-fat and high-sugar diet (60kcal %, HD). All rats were fed continuously for 32 weeks. Body weight, fasting glucose, fasting insulin and serum APN levels were monitored regularly. 8 weeks later, intraperitoneal injection of glucose tolerance test (IPGTT) were performed every 4 weeks. And abnormal IPGTT was selected as a measurement for successful model of type 2 diabetes. Successfully fed type 2 diabetic rats and normal rats were divided into 4 groups: Sham group; normal control group (ND); diabetic rats group (DM); diabetic rats group (DM+gAd); gAd of 20μg/kg or 0.5ml of saline solution were injected into rats via tail vein at the 31st week. In each group, ischemia was induced via coronary artery slip-knot ligation for 1.5hours and then reperfusion for 12 hours. No reflow injury areas were measured using Evan’s Blue and Thioflavin S staining methods. The reperfusion areas of myocardial microcirculation were showed with fluorescent microscopes. Left ventricular pressure was measured to evaluate cardiac function of rats. Serum adiponectin (APN), endothelin-1 (ET-1), intercellular adhesion molecule-1 (ICAM-1) and vascular endothelial adhesion molecule-1 (VCAM-1) levels were measured simultaneously to assess vascular endothelial injury.

Results: Serum adiponectin levels of diabetic rats increased firstly and then continued to reduce in the process of HD feeding. ET-1, ICAM-1, VCAM-1 in both DM group and DM+gAd group were significantly increased in the 32th week. After administration of gAd, ET-1 was significantly reduced (108.63±8.428 vs.132.10±7.213, P<0.05). (2) NR injury in DM group was increased after IR (48.64±2.93% vs. 35.48±4.31%, P< 0.05). Cardiac function showed obviously impaired (+dp/dt: 2514.36±211.04 vs. 3714.73±221.04, P<0.01) and cardiac function after IR injury in DM+gAd group improved significantly (+dp/dt: 3280.18±192.84 vs.2514.36±188.93, P<0.05) with decreased serum ICAM-1 and VCAM-1 levels.

GW25-e3410

β3 adrenergic receptor selective agonist clenbuterol protects cardiac arrhythmia after reperfusion

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Objectives: Our Previous study has demonstrated that β3 adrenergic receptor (β3AR) activation reduces infarct size and myocardial apoptosis after myocardial ischemia/reperfusion. Cardiac arrhythmias are a major manifestation of reperfusion injury, which results in sudden death in acute myocardial infarction. The present study is designed to investigate whether β3AR agonist clenbuterol will protect cardiac arrhythmias induced by reperfusion.

Methods: Reperfusion arrhythmias were induced by 10 min ligation of the left anterior descending coronary artery, followed by a 30 min reperfusion in anesthetized rats. The expression of myocardial infarction size was monitored by the TTC staining. Cadmium damage was characterized by a higher incidence of reperfusion-induced ventricular tachycardia (VT) and ventricular fibrillation (VF).