**Objectives:** Cardiac fibrosis is associated with the emergence of fibroblasts originating from endothelial cells through endothelial-mesenchymal transition (EndMT). The aim of the study was to explore the effect of UII on EndMT and its possible mechanisms.

**Methods:** Growth-arrested cardiac microvascular endothelial cells from neonatal rats were incubated in serum-free medium with UII (10⁻⁹ mol/l) and/or its receptor antagonist SB710411 (10⁻⁸ mol/l). To investigate the roles of Smad2, Smad3 in EndMT induced by UII, a small interfering RNA (smad2 siRNA or smad3 siRNA) was transfected into the cells. The phosphorylated Smad2/3 protein levels, 2-smooth muscle-actin (2-SMA) and VE-cadherin induced by UII were evaluated by western blot. The CD31 were evaluated by flow cytometry.

**Results:** UII induced 2-SMA expression in a dose-dependent manner, with maximal effect at a concentration of 10⁻⁸ mol/l (23.4%), it decreased VE-cadherin expression in a dose-dependent manner, with maximal effect at a concentration of 10⁻⁹ mol/l (91.3%). UII significantly reduced expression of CD31. In addition, UII promoted Smad2/3 phosphorylation in a time-dependent manner, with maximal effect at 24h (81.6%). The effect was significantly inhibited by treatment with the UT inhibitor SB710411 (10⁻⁹ mol/l). Furthermore, Knockdown of Smad2 and Smad3 expression with siRNA significantly reversed the effect of UII.

**Conclusions:** Our data show for the first time that UII stimulates endothelial-mesenchymal transition, which is mediated partly by the activation of the Smad2/3 signal pathways.

GW25-e3329

**Geniposide Protects against Pressure Overload-Induced Cardiac Remodeling via 5′-Adenosine Monophosphate-Activated Protein Kinase-2**

Ma Zhenguo1, Qizhu Tang1,2

1Department of Cardiology, Second Affiliated Hospital of Wunan University, 2Cardiovascular Research Institute of Wunan University

**Objectives:** Cardiac remodeling featured as left ventricular dilatation, impaired systolic function predisposes the affected individuals to heart failure. Genetic and environmental factors contribute to the development of cardiac remodeling. Increased arterial pressure, increased cardiac mass and left ventricular hypertrophy have been reported in patients with arterial hypertension. Moreover, 50mg/kg GE abolished increased atriopeptin, brain natriuretic peptide, and decreased left ventricular diastolic diameter, restored ejection fraction and hypertrophied protein expressions of proteins. TUNEL was used to assay apoptosis.

**Methods:** GW25-e3239 endotoxemia-induced heart failure model was established by cecal ligation and puncture (CLP). The rats were administered two groups: the control group (C) and the GE administration group (G). After 7 days, the ventricles were excised. The hearts were weighed and perfused with phosphate-buffered saline (PBS). The hearts were cut, washed with PBS, and then weighed. The heart weight to body weight ratio was calculated. The left ventricular septum thickness and left ventricular posterior wall thickness were measured. The histology of the left ventricle was observed under the optical microscope. The left ventricle was taken out and sliced into thin slices. The slices were fixed in 10% formaldehyde solution and dehydration was performed. After dehydration, the slices were embedded in paraffin, cut into 5 μm sections, stained with hematoxylin and eosin (HE), and observed under the optical microscope.

**Results:** The left ventricular weight (LVW), heart weight (HW), and tibia length (TL) were examined. HE and WGA staining were performed to evaluate the chambers 8 weeks after TAC. The indices, namely body weight (BW), heart weight (HW), and tibia length (TL) were significantly increased in the TAC group compared to the control group. The control group had a lower body weight (91.3%). UII also significantly reversed the effect of UII.

**Conclusions:** Our data show for the first time that UII stimulates endothelial-mesenchymal transition, which is mediated partly by the activation of the Smad2/3 signal pathways.

GW25-e3328

**Adenosine Monophosphate-Activated Protein Kinase-2**

Kun Min, 1Xiao Long, 1Jia Li, 1Ji Xing, 1Qin Chen, 1Wen Li, 2Jun Wang, 3Qin Li

1Department of Cardiology, Second Affiliated Hospital of Nanchang University, 2Cardiovascular Research Center/Thrombosis Research Center, Department of Pharmacology, Temple University School of Medicine, Philadelphia, PA 19140

**Objectives:** Abundant epidemiological and clinical studies have revealed the close relationship between hyperhomocysteinemia (HHcy) and CVD. Daily life habits and others have demonstrated that HHcy can inhibit the endothelial cell growth and postischemic reendothelialization, accelerate neointimal formation. However, the fundamental basis of endothelial progenitor cell in HHcy impaired angiogenesis remains unknown.

**Methods:** (1) Angiogenesis of HHcy mice under myocardial infarction. Cardiac function was measured with echocardiography (VisualSonics Vevo 770). Hearts were viewed in the short-axis and analyzed in M-mode. Changes in cardiac morphology and function were quantified as fractional shortening (FS, %) and fractional area (A, %). Hearts were moved at 2 weeks/6 weeks after myocardial infarction and kept at -80°C. Frozen heart tissues were cut into 5 μm thick slices. Adjacent sections were stained with rabbit polyclonal antibodies against CD31. Capillary density was expressed as CD31⁺ endothelial cells per high-power field (HPF). (2) Flow cytometry analysis. A total of 100 000 events were performed by LSR II flow cytometer. Heart samples were stained dark with monoclonal antibodies against mouse vascular endothelial growth factor receptor 2 (VEGFR2) followed by PE-conjugated secondary antibody, with the APC-labeled monoclonal antibodies against mouse Stem cell antigen 1 (Sca-1). Each analysis included 100 000 events. The data were analyzed by LSR II flow cytometer.

**Results:** (1) HHcy impairs mouse cardiac function. Ejection fraction (EF) and fractional shortening (FS) were lower in HHcy mice group than control group, as well as heart capillary density. HHcy mice hearts have depressed function and less capillary density. (2) Hypochondriacal remodeling and increased atriopeptin, brain natriuretic peptide, and decreased left ventricular diastolic diameter, restored ejection fraction and hypertrophied protein expressions of proteins. TUNEL was used to assay apoptosis.

**Conclusions:** Our data show for the first time that UII stimulates endothelial-mesenchymal transition, which is mediated partly by the activation of the Smad2/3 signal pathways.