exposure to high glucose, as evidenced by decreases in the expression of Runx2, activity of ALP (alkaline phosphatase) as well as calcium nodules.

CONCLUSIONS These results suggest that high glucose induces the ER stress response and apoptosis, leading to high glucose-elevated vascular calcification.

GW26-e5405 Establishment of Swine End-Stage Dilated Cardiomyopathy Model by Percutaneous Venous Intervention
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OBJECTIVES To establish a model of swine end-stage dilated cardiomyopathy (DCM) model by percutaneous venous intervention.

METHODS Ten male pigs were randomly divided into 2 groups, namely DCM group and control group. The DCM group underwent rapid right ventricular pacing by a modified Medtronic unipolar pacemaker connected to an apical pacing lead via percutaneous venous intervention, which at the rate of 230 beats per minute for 4 weeks, and 190 beats per minute for another 4 weeks, while the control group received sham operation. The clinical symptoms and hemodynamic parameters were used to evaluate the severity of heart failure.

RESULTS Cardiac output in the DCM group (3.1 +/- 1.1 L.min-1) was significantly less (P less than 0.01) than in control group (5.4 +/- 0.8 L.min-1). Compared with control group (0.67 +/- 0.19 cm), thickness of left ventricular posterior wall was significantly less (P less than 0.01) than in control group (0.51 +/- 0.18 cm).

CONCLUSIONS We established a model of swine end-stage dilated cardiomyopathy model by percutaneous venous intervention, which demonstrates that 4 weeks of rapid ventricular pacing at 230 beats/min and another 4 weeks of 190 beats per minute produces a realistic model of end-stage dilated cardiomyopathy in the pig.

GW26-e1009 Protective effect of astaxanthin on contrast-induced acute kidney injury in experimental rats
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OBJECTIVES To explore the protective effect and mechanism of astaxanthin (AST) on the acute kidney injury induced by iohexol in rats.

METHODS Thirty rats were randomly divided into five groups: control group (CON), iohexol group (CM), astaxanthin group (AST, 100mg/kg), low astaxanthin dose group (LAST, 50mg/kg) and high astaxanthin dose group (HAST-CM, 100mg/kg). The rats in AST, LAST-CM, HAST-CM groups were administrated with AST by oral gavage using an intubation needle for 10 consecutive days. The other rats in CON, CM groups were given with dissoviant instead in equal volume. Except for the CON and AST groups, on day 8, rats were given indomethacin, L-NAME and iohexol in their femoral vein under chloral hydrate anesthetics to build a contrast-induced nephropathy (CIN) model. At the end of the experiment (72h after CIN induction), the rats were sacrificed. The serum creatinine (SCR) level, blood urea nitrogen (BUN) level, renal histology, renal tissue activities in superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), Gluthathione (GSH) and level of malondialdehyde (MDA) were performed. Apoptosis of renal cells was detected by Bcl-2, Bax and Caspase 3 with Western blot.

RESULTS ① Compared with CON group, renal function of SCR, BUN levels were significantly increased in CM group (P < 0.01), while compared with CM group, the indicators were decreased in treatment groups (P < 0.01). Renal tubular structure damage, medulla congestion, loss of brush border, vacuolar degeneration, apoptosis and proteinaceous casts were observed the CM group, and the renal injury scores were higher compared with CON group (P < 0.05), however, administrated with AST could significantly improve the changes (P < 0.01). ② The oxidative stress indicators show that MDA level were increased while SOD, GPx, GSH activities were significantly decreased at CM group (all P < 0.05) and the indicators above were ameliorated in treatment groups (P < 0.05). ③ Western blot showed that the expression of Bcl-2 was down-regulated while the Bax, caspase 3 p17 was up-regulated respectively at CM group (P < 0.05), while the HAST-CM group could prevent the changes.

CONCLUSIONS Iohexol can results in oxidative stress increased in kidney, which activate caspase-3 p17 signal path, down-regulated Bcl-2 expression, up-regulated Bax expression respectively, and lead to cell apoptosis. AST can ameliorate the changes, especially with high AST dose, which suggest that the possible protection mechanism is by ameliorating oxidative stress and inhibiting apoptosis pathways.

GW26-e1242 Sodium tanishononel-A sulfonate Relaxes Human Mesenteric Artery Via large-conductance Ca2+-activated potassium channels
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OBJECTIVES Danshen as a traditional Chinese medicine is widely used to remedy cardiovascular and cerebrovascular diseases partly by its effects of vasodilatation, and sodium tanishononel-A sulfonate (DS-201) a water-soluble derivative of its active ingredient. We aimed to explore the vasodilatation mechanism of DS-201 at the molecular level by observing the effect of DS-201 on large-conductance Ca2+-activated potassium channels (BKca) in human mesenteric artery smooth muscle cells.

METHODS Rings of human mesenteric artery were contracted with 60 mM KCl, and changes in isometric tension were recorded. Then we observe the effect of DS-201 on BKca, by using patch clamp technique.

RESULTS DS-201 (20 to 120 μM) induced a concentration-dependent relaxation with a maximum of 64 ± 3% in human mesenteric artery without endothelium (n=6, P<0.05). These relaxations were inhibited by 300mM iberiotoxin. In cell-attached patch (Vm=-40 mV), 80μM DS-201 stimulates BKca activity, DS-201 enhanced open probability (NOP) of BKca from 0.012±0.001 to 0.039±0.009, the mean open time (To) of BKca is markedly increased from 7.3±1.1 ms to 15.3±1.3 ms and the mean close time (TC) of BKca is decreased from 1829.3±408.2 ms to 267.3±82.3 ms(n=6, P<0.05), but there were no significant changes in amplitude of current. In inside-out patch (Vm=-40 mV), 80μM DS-201 stimulates BKca activity significantly: DS-201 enhanced NOP of BKca from 0.027±0.008 to 0.175±0.084, To is markedly increased from 19.8±3.1 ms to 41.3±3.3 ms and TC is decreased from 708.1±408.2 ms to 85.67±32.3 ms(n=6, P<0.05). In the amphotericin-perforated whole-cell patch-clamp configuration, the current density of BKca at the voltage of -60 to +30 mV had no significant change before and after adding 80 μM DS-201, but the current density of BKca at the voltage of +40 mV, +50 mV and +60 mV was increased significantly after adding 80 μM DS-201, from 12.4 ± 3.6 pA/pF, 17.5 ± 3.8 pA/pF and 24.1 ± 4.6 pA/pF to 18.2 ± 3.6 pA/pF, 25.8 ± 5.2 pA/pF and 34.5 ± 3.8 pA/pF (P<0.05).

CONCLUSIONS DS-201 relaxes human mesenteric artery via stimulation of BKca.

GW26-e1386 Mechanism of hERG potassium channel block by tolterodine
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OBJECTIVES The goal of this study was to determine whether two aromatic residues in the S6 region (Y652 and F656) are important for the open state of the channel. In addition, it was found that the mutants of Y652A and F656A significantly increased in IC50, and produced about 345-fold and 124-fold increases in IC50.

RESULTS The data collected from wild type channels indicated that the mutants of Y652A and F656A significantly increased in IC50.

METHODS hERG cRNA solution (wild type, Y652A and F656A) were injected and expressed in Stages IV and V Xenopus laevis oocytes. And the oocytes were incubated at 17° C in ND96 solution. The currents were recorded using standard two-microelectrode voltage-clamp technique.

RESULTS The goal of this study was to determine whether two aromatic residues in the S6 region (Y652 and F656) are important for the inhibition effect of tolterodine on hERG channel.

METHODS hERG cRNA solution (wild type, Y652A and F656A) were injected and expressed in Stages IV and V Xenopus laevis oocytes. And the oocytes were incubated at 17° C in ND96 solution. The currents were recorded using standard two-microelectrode voltage-clamp technique.
CONCLUSIONS Tolterodine inhibited hERG channel in open channel state-dependent and concentration-dependent manner, and was a potent inhibitor of hERG channel expressed in Xenopus oocytes. Two aromatic residues: Y652 and F656, on the inner (S6) helix, seemed to be critical for high-affinity of tolterodine binding to hERG channel.

GW26-e0246 Metformin Activate AMPK, Inhibit GRP78 in liver and improve Insulin Sensitivity in Polycystic Ovarian Syndrome Rats

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OBJECTIVES To investigate the effects of metformin on insulin sensitivity and possible mechanism in rats with polycystic ovarian syndrome (PCOS).

METHODS PCOS rat model was induced by subcutaneous injecting dehydroepiandrosterone (0.6mg/kg-day) up to 20 days and then divided randomly into PCOS and metformin group (metformin 140mg/kg-day for 15 days). Blood were collected to test free glucose and insulin levels before and after metformin intervention. Liver tissues were collected to test triglyceride (TG) content and protein expression.

RESULTS PCOS rats exhibit insulin resistance and metformin treatment improve insulin sensitivity in PCOS rats. TG levels, glucose regulated protein 78 (GRP78) and sterol regulatory element-binding protein -1c (SREBP-1c) protein expression in the liver of PCOS rats were higher than those of the controls, whereas phosphorylation adenine monophosphate-activated protein kinase (AMPK) protein expression was lower than that of the normal controls (p<0.05). After metformin treatment, TG levels, GRP78 and SREBP-1c protein expression in the liver of PCOS rats were significantly decreased (p<0.05) and AMPK protein expression was increased to the level similar with that of normal controls.

CONCLUSIONS Metformin protect PCOS rats from insulin resistant and hepatocytic fat deposition largely through the effects on activating AMPK pathway and on inhibiting endoplasmic reticulum stress in liver.

GW26-e1050 Effect of Jiashen prescription on left ventricular remodeling and inflammatory response at the early stage of myocardial infarction

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OBJECTIVES This study was designed to determine the effects of Jiashen prescription (JSP) on left ventricular remodeling and inflammatory response at the early stage of MI in rats.

METHODS MI was induced by the ligation of left anterior descending coronary artery in Sprague-Dawley rats. The rats were divided into five groups after 24 hours: sham-operated group; MI-vehicle group; JSP-3g (3g/kg/day) group; JSP-6g (6g/kg/day) group and losartan (10mg/kg/day) group. The left ventricular structure and function were measured by echocardiography at week 4 after MI. The infiltration of monocyte/macrophage in the myocardial tissue was evaluated by the use of immunohistochemical stain. The expression of intercellular adhesion molecule-I (ICAM-1) and vascular cell adhesion molecule-1 (VCAM-1) was determined using Western blot.

RESULTS Compared to MI-vehicle rats, JSP at the dose of 6 g/kg/day attenuated the increases in left ventricular end-diastolic diameter (8.8±0.5 vs. 7.1±0.3 mm, P<0.05) and left ventricular end-systolic dimension (7.1±0.6 vs. 4.4±0.2 mm, P<0.05), and the decreases in ejection fraction (42.6% vs. 74.1%, P<0.05) and fractional shortening (19.3% vs. 39.1%, P<0.05) at week 4 after MI. In addition, treatment with JSP at the dose of 6 g/kg/day inhibited the number of monocyte/macrophages (14.3±1.8 vs. 9.3±0.3, P<0.05) and expression of ICAM-1 and VCAM-1 compared to MI-vehicle rats at week 4 after MI (ICAM-1: 0.23±0.05 vs. 0.58±0.02%GAPDH arbitrary units, P<0.05). Losartan treatment has a similar results with JSP at the dose of 6 g/kg/day.

CONCLUSIONS Our studies showed that JSP administered after MI improved cardiac function, and inhibited left ventricular dilatation. The results were associated with the inhibition of monocyte/macrophage infiltration and the decreased production of inflammatory mediators. Our data suggest that JSP improves left ventricular remodeling possibly via inhibiting inflammatory response at the early stage of MI. [This work was supported by a grant from the National Natural Science Foundation of China (No. 81173410) to M.J.Z.].

GW26-e1063 Effects of Danqi Pill on altered global gene expression pattern induced by myocardial ischemia

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OBJECTIVES To systematically characterize altered gene expression pattern induced by myocardial ischemia (MI) in rat model and to investigate the effects of Danqi Pill(DQP) on global gene expression in the treatment of myocardial ischemia.

METHODS Myocardial ischemia rat model was induced by left anterior descending coronary artery ligation. Nine rats were randomly divided into sham-operated group, model group and DQP-treated group. At 28 days after treatment, cardiac function was evaluated by echocardiography. Heart tissues in infarct border zone were homogenized and total mRNA was extracted. Global mRNA expression was measured using Illumina's digital gene expression profiling method. Differentially expressed genes between model group and sham operated group were investigated and differentially expressed genes between DQP group and ischemia model group were also analyzed. The gene ontology (GO) enrichment analysis and pathway analysis of all differentially expressed genes were carried out using DAVID Functional Annotation Tool.

RESULTS Ejection Fraction (EF) and fractional shortening (FS) of rats in model group were significantly lower than those of sham-operated group, indicating that MI model was successfully induced. In DQP group, EF and FS increased compared with those in model group. We detected and quantified 539 differentially expressed genes in these three groups. Compared with sham-operated group, expressions of 360 genes were up-regulated and 179 genes were down-regulated in model group. GO and pathway analysis showed that up-regulated genes were enriched in extracellular matrix organization, response to wounding and defense response pathways, indicating changes in cardiac hypertrophy and remodeling. Down-regulated genes were enriched in fatty acid metabolism, pyruvate metabolism, PPAR signaling pathways, etc. This indicated that energy metabolism disorders occurred in MI. In DQP group, expressions of genes in the altered pathways were regulated back towards normal levels. DQP reversed expression of 90% of the 539 differentially expressed genes in model group. For example, genes involved in remodeling process, such as collagen I and III, connective tissue growth factor and MMP2, were down-regulated by DQP. Genes involved in energy metabolisms, such as acetyl-coenzyme A dehydrogenase, mitofusin and sirtuins, were up-regulated by DQP. DQP also regulated the expressions of 12 deregulated transcription factors, including adipocyte enhancer binding protein delta, which plays roles in lipid metabolism and nuclear factor of activated T-cell 4, which regulates mitochondrial function and promotes cardiac fibrosis.

CONCLUSIONS Danqi pill exerts cardio-protective effect by regulating global gene expression pattern in ischemic heart tissue. It could inhibit remodeling global gene expression pattern in MI tissue and improve cardiac metabolism by up-regulating genes involved in lipid metabolism and energy production pathways.

GW26-e1309 Effects of rosiglitazone on the levels of high mobility group protein box1 from cultured human umbilical vein endothelial cells induced by LPS

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OBJECTIVES To investigate the expression of HMGB1 on LPS-induced HUVECs in vitro and the effect of rosiglitazone on the expression of HMGB1.

METHODS Cultured HUVECs in vitro at passage 3 to 7 were used for experiment. There were three groups: (1) control group; (2) LPS groups; HUVECs were incubated with 1mg/L LPS for different periods to measure cytoactive of HUVECs by MTT colorimetric assay and HMGB1 expression (by ELISA) at 6h, 12h, 24h, Then observe the effect of different concentration rosiglitazone (RSG ) on the cell proliferating vitality and HMGB1 expression compared with control group and LPS groups by ELISA.