GW26-e4478
Effects of zinc status on high-fat diet-induced cardiac hypertrophy
Shudong Wang,1,2 Zhiguo Zhang,1 Zheng Xu,1 Yang Zheng1 1Cardiovascular Center of the First Hospital, the Jilin University

OBJECTIVES We investigated the effect of dietary zinc supplementation and deficiency in mice consuming a high-fat on cardiac inflammation, cardiac fibrosis, and left ventricular function and structure using an animal model of adolescent obesity.

METHODS Male C57BL/6J mice (3 weeks of age) were fed either high fat diet (HFD, 60% kcal fat) or normal diet (ND, 10% kcal fat) containing low zinc (L-Zn, 10 mg Zn per 4057 kcal), normal zinc (N-Zn, 30 mg Zn per 4057 kcal) or high zinc (H-Zn, 90 mg Zn per 4057 kcal) for 3 or 6 months. Left ventricular function and structure were measured by Echocardiography, TNN-alpha (TNF-α), nuclear factor kappa-B (NF-kB), B-cell CLL/Lymphoma 10 (BCL10), caspase recruitment domain (CARD9), and phosphorylated and total MAPK (p38, ERK1/2) were assessed by western blot. The mRNA expression of connective tissue growth factor (CTGF), transforming growth factor (TGF-b1), and atrial natriuretic peptide (ANP) in the heart were quantified by RT-PCR. The cardiac collagen was analyzed by Sirius red staining. For myocyte cross-sectional area, sections were stained for membranes with FITC-conjugated WGA (wheat germ agglutination).

RESULTS We found that HFD increased the expression of both phosphorylated and total p38 MAPK in the heart, along with the increased heart weight and hypertrophy in a time-dependent manner. Echocardiography demonstrated the cardiac hypertrophy in HFD mice, which were confirmed by WGA staining at cellular level. Although echocardiography and WGA revealed signs of cardiac hypertrophy in all obese mice, the increase in left ventricular (LV) mass and diameter was significantly more pronounced in Zn-defect HFD mice, and, the HFD with H-Zn attenuated the hypertrophy. Cardiac inflammatory levels and fibrosis were increased in obese animals compared to mice fed by ND. Cardiac hypertrophy increased level was positive correlation with inflammatory response and fibrosis change. The cardiac structural changes and cellular and molecular hypertrophy was significantly more pronounced in 6-month than 3 months. In 3-month time-point, Zn-defect HFD significantly increased the expression of TNF-α, BCL10, CARD9, ANP, CTGF, TGF-b1and NF-kB slightly increased. In contrast, at 6-month time-point, Zn-defect HFD significantly elevated levels of NF-kB, p38 MAPK, but only slightly increased. The secretion of NRG-1 was remarkable increased in the time of 4h/4h. Analysis of p38MAPK reduced the cardiac hypertrophy induced by HFD with Zn deficiency.

CONCLUSIONS Obesity with zinc deficiency caused no proarrhythmic activities. The apoplotosis of cardiomyocytes was detected by TUNEL method. The expression of secreted NRG-1 in CMECs culture medium, phosphorization of ErbB2 and ERK and the expression of COX-2 (P < 0.01 vs. Control) in cardiomyocytes were analyzed by Western blot. Measured caspase-3 activity reflected the apoplotosis of cardiomyocytes.

GW26-e4602
Role of NRG-1 released from cardiac microvascular endothelial cells in ischemia/reperfusion myocardium and its mechanism of action
Qimeng Hao, Wenyi Guo XiJing hospital

OBJECTIVES To explore the effects of NRG-1 that released from CMECs on cardiomyocytes during ischemia/reperfusion injury and discuss the possible mechanism.

METHODS Cardiac myocytes were isolated from the hearts of neonatal rats and CMECs from the adult rats. CMECs - cardiomyocytes coculture model was established. Then cells were treated for 4h/4h, collected CMECs culture medium during SI/R. CMECs were randomly divided into two groups: Control group, SI/R group, SI/R + Coculture group, SI/R + Coculture + anti-ErbB2 (ErbB2 inhibitor) group, SI/R + NRG-1 group, SI/R + NRG-1 + anti-ErbB2 group, SI/R + NRG-1 + PD group. The cell viability of cardiomyocytes was measured by MTT assay. The expression of secreted NRG-1 in CMECs culture medium, phosphorylation of ErbB2 and ERK and the expression of COX-2 in cardiomyocytes were analyzed by Western blot. Measured caspase-3 activity reflected the apoplotosis of cardiomyocytes.

RESULTS The cardiomyocytes viability was impaired in the SI/R (4h/4h) group (P < 0.01 vs. Control) while increased in the SI/R + Coculture group (P < 0.05 vs. SI/R). Within the groups of CMECs, the expression of ErbB2 was remarkable increased in the time of 4h/4h under SI/R (P < 0.01) when compared with the Control group. Within the groups of cardiomyocytes, the apoptosis index and Caspase-3 activity were increased after SI/R (27.97 ± 0.90 vs. 3.58 ± 0.23, P < 0.01; 375.93 ± 11.76 vs. 100.00 ± 0.00, P < 0.01). While treated with Coculture or NRG-1 during SI/R could prevent the apoptosis index and Caspase-3 activity (16.82 ± 1.03 vs. 27.97 ± 0.90, P < 0.01; 166.16 ± 15.15 vs. 375.93 ± 11.76, P < 0.01). Besides, they can significantly up-regulate the level of phosphorylation of ErbB2 and ERK and the expression of COX-2 (P < 0.01 vs. Control and SI/R). However, when cardiomyocytes were pretreated with ErbB2 or Erk1/2 inhibitor, the effect of Coculture and NRG-1 vanished (P > 0.01).

CONCLUSIONS In the process of I/R, the secretion of NRG-1 in CMECs protect cardiomyocytes against ischemic reperfusion injury through up-regulation of pErbB2 and activation of downstream ERK/COX-2 signal.
Cinnamomi. NXT has been used in the treatment of cardiovascular and cerebrovascular diseases like coronary artery disease in clinic. Due to the complex combination of herbs, the chemical analysis and mechanism are still not clear. In this research, based on UPLC/Q-TOF for ingredients investigation, we used the method of network pharmacology to explore the potential effect of NXT and the evidence of the rational combinations on herb combinations.

METHODS We used the five principles of drug absorption as a judgment rule to identify the chemical compositions that could be absorbed in blood form the all chemicals of NXT. Moreover, we predicted the main targets and related pathways of absorbable components by PharmMapper, Universal Protein and Molecule Annotation System. Finally, we constructed the networks including multiple components (from different source of herbal medicines) with multiple targets and pathways by Cytoscape.

RESULTS We got 83 chemical compositions from NXT, of which 52 predictions could be absorbed. By analyzing network pharmacological approach, there were 133 targets that could be regulated by these components. In addition, these targets were involved in 85 pathways (P < 0.01), including NFAT and Hypertrophy of the heart (Transcription in the broken heart), Nuclear Receptors in Lipid Metabolism and Toxicity, Aspirin Blocks Signaling Pathway Involved in Platelet Activated VEGF, Hypoxia, and Angiogenesis and Signaling Pathway from G-Protein Families, which were all closely associated with diseases of the cardiovascular and cerebrovascular system.

CONCLUSIONS The 52 main active components of NXT are included amino acids, senkyunolides, flavonoids, and organic acids. NXT plays a dramatic role in the treatment of cardiovascular and cerebrovascular diseases, especially in the pathway NFAT and Hypertrophy of the heart.

GW26-e0097 The relationship of the genetic polymorphism of ApoE and the stability of carotid plaque
Bo Zhang, Yongping Zhang
1Department of Cardiology, Xinqiao hospital, Third Military Medical University; 2Department of Neurology, Chongqing general hospital

OBJECTIVES The aim of the present study was to investigate the role of genetic polymorphisms of ApoE in carotid artery atherosclerosis and the instability of the plaque.

METHODS 238 subjects were divided into 3 groups: the instable plaque group, stable plaque group and control group according to the result of carotid ultrasound examination. The genotype of ApoE and serum ApoE concentration was measured. The relationship between the genetic polymorphism of ApoE and the instability of carotid plaque was studied with linear and logistic regression analysis.

RESULTS ①The frequency of ε4 allele in the CAS subjects was higher than the health people. It was higher in instable plaque group than the stable plaque, and this was statistically significant. ②The average of IMT of the subjects with ε4 allele was 1.22mm, which was significant thicker than the subjects without ε4 allele. ③The ApoE ε4 allele is an independent relative factor of the instable plaque when age, sex and blood fat were adjusted in logistic regression analysis. ④The level of Hs-CRP and MCP-1 in serum of the subjects with allele ε4 were higher than the subjects without it, which indicated that the inflammatory activity in subjects with ε4 allele was stronger than the subjects without ε4 allele.

CONCLUSIONS ApoE polymorphism was associated with carotid atherosclerosis and the instability of plaques. Patients with the ApoE4 isoform had a more severe CAS than the subjects without the ApoE4 allele. The genetic polymorphism of ApoE has influenced the atherosclerosis through adjusting the blood-fat or the chronic inflammation status.

GW26-e1073 Cellular repressor of EIA-stimulated gene overexpression in bone mesenchymal stem cells improves the treatment of myocardial infarction in rats
Jie Qin, Yuefei Guo, Xiuzhen Chen, Xuelian Liu
Department of Radiology, the Third Affiliated Hospital of Sun Yat-sen University

OBJECTIVES To study the effects of cellular repressor of EIA-stimulated genes (CREG) in bone mesenchymal stem cells (BMSCs) after transplantation into infarcted heart in rats.

METHODS 50ul PBS or 1.5×10^5 (Norm) BMSCs, (GFP) BMSCs or (CREG) BMSCs were implanted in myocardial infarction rat models. Cardiac function, fibrosis, apoptosis and angiogenesis were analyzed by echocardiography, masson, western blot and immunofluorescence staining, respectively. ELISA, western blot and matrigel assay were used in vitro to detect vascular endothelial growth factor (VEGF) secretion, signaling molecule expression, and angiogenic tube formation.

RESULTS Compared with group (Norm) BMSCs and group (GFP) BMSCs, prolonged cardiac function (14d LVEF: 51.84±1.14%; LVEF: 24.56±1.22%), decreased fibrosis (14d Fibrotic area: 28.32±1.12%) and apoptosis and increased angiogenesis were found in group (CREG) BMSCs. In vivo and in vitro, VEGF secretion from (CREG)BMSCs was markedly enhanced. In vitro, angiogenic tube formation in (CREG) BMSC supernatants significantly increased. CREG activated hypoxia-inducible factor-1α (HIF-1α), but not HIF-1β. Knockdown of HIF-1α with siRNA decreased VEGF secretion and angiogenic tube formation. Notably, CREG did not influence HIF-1α mRNA synthesis but inhibited the expression of Von Hippel-Lindau (VHL), a key protein that regulates HIF-1α degradation.

CONCLUSIONS Cellular repressor of EIA-stimulated gene overexpression in BMSCs could improve the treatment of myocardial infarction in rats.