

stimulator, to create the tachycardia cardiomyopathy animal model, and then to pace the right ventricle.

RESULTS After one week of right ventricular pacing, cardiac ultrasound examination confirmed the left ventricular end diastolic diameter enlargement, reduction of left ventricular ejection fraction, increased serum BNP and MMP-9, and decreased TIMP-1. Pathology of HE staining showed myocardial structural derangement and interstitial inflammatory cell infiltration. Electron microscopy revealed mitochondrial swelling, dislocation, or even lysis and destruction, fuzzy Z line and unclear intercalated discs. Three weeks later, the heart color, serum BNP, MMP-9, TIMP-1, EF, FS in the rabbits recovered to former levels.

CONCLUSIONS Conclusions It is a simple and practical method to establish an animal model of tachycardiomyopathy by stimulating animal's right ventricle with mapping electrode line to create non-sustained ventricular tachycardia under minimally invasive, venous technique without X-ray radiation.

GW26-e2451

Correlation Between the BDNF Val66Met Polymorphisms and Metabolic Risks in Long-Lived Zhuang Population

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OBJECTIVES We aim to evaluate the possible association between BDNF Val66Met polymorphism and common metabolic risks including BMI, fasting blood glucose (FBG) and lipid levels in a longevous population dwelling in Guangxi Hongshui River basin.

METHODS BDNF Val66Met was genotyped by ARMS-PCR technique for 487 Zhuang long-lived inhabitants (aged ≥ 90 , long-lived group, LG), 593 offspring (age 60-77, offspring group, OG) and 582 matched healthy controls (aged 60-75, control group, CG) in Hongshui River Basin. Impacts of genotypes on metabolic risks were then evaluated.

RESULTS No significant difference was noted on the distribution of genotypic and allelic frequencies of BDNF Val66Met among the three groups (all $P > 0.05$), regardless of sex; however, AA genotype was dramatically higher in females than in males in the CG. The HDL-C level of A genotype (GA/AA) carriers was significantly lower than was non-A genotype (GG) carriers in the overall population and the CG ($P = 0.009$ and 0.006 , respectively), which remained in females, hyperglycemic subgroup and normolipidemic subgroup of CG through stratification of sex, BMI, glucose and lipid status. In addition, A genotype carriers, with a higher systolic blood pressure, have 1.63 folds higher risk than non-A carriers to become overweight in CG (95% CI: 1.05~2.55). Multiple regression analysis showed that the TC level of LG was negatively correlated with BDNF Val66Met genotype.

CONCLUSIONS BDNF 66Met may lower the serum HDL-C level and lead to overweight in the general population in Hongshui River area but has less impact on the long-lived population and their offspring.

GW26-e2453

Beneficial Effect of Lycopene on Hypoxia/Reoxygenation-Induced Endoplasmic Reticulum Stress in Neonatal Mouse Cardiomyocytes

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OBJECTIVES Endoplasmic reticulum (ER) stress has become an important therapeutic target for myocardial ischemia reperfusion (I/R) injury. It has been reported that lycopene exhibits great pharmacological effect in alleviating myocardial I/R-injury, but whether it attenuates ER stress remains to be elucidated. The purpose of this study was to explore the potential protective benefits of lycopene against ER stress induced by hypoxia/reoxygenation in cultured neonatal mouse cardiomyocytes.

METHODS Primary cultured neonatal C57BL/6 cardiomyocytes were used to establish H/R model and divided to control, lycopene, H/R(4 h hypoxia followed by 6 h reoxygenation) and lycopene+H/R group (the cardiomyocytes were pretreatment with $5\mu\text{mol/L}$ lycopene for 4 h before H/R treatment). TUNEL assay was used to assess cardiomyocytes apoptosis. Western blotting was used to evaluate the expression of cleaved caspase-3, the level of phosphorylated eIF2 α , a downstream target of the PERK pathway and the expression of CHOP, an ER stress-related apoptotic maker. The expression of GRP78 mRNA

and level of the sliced Xbp-1 mRNA, a downstream target of the IRE1 pathway, were determined by Real-time PCR.

RESULTS The rate of TUNEL-positive cells significantly increased to $25.62\pm 2.61\%$ and that of control and lycopene group were respectively $4.87\pm 1.54\%$ and $4.91\pm 1.63\%$ ($P < 0.01$). After pretreatment with lycopene, the rate decreased to $18.18\pm 2.18\%$ ($P < 0.05$). Representative western blotting analysis and Quantitation of the Western blotting by densitometric scanning showed approximately a 1.89-fold increase in cleaved caspase-3 level ($P < 0.01$), 1.84-fold increase in p-eIF2 α ($P < 0.05$) and 1.98-fold increase in CHOP expression ($P < 0.01$) compared with the control group after H/R treatment. The cleaved caspase-3 level decreased to 1.36-fold of normal levels ($P < 0.05$), the level of phosphorylated eIF2 α reduced to 1.47-fold of normal levels ($P < 0.05$) and the CHOP expression decreased to 1.54-fold of control levels ($P < 0.05$) with lycopene pretreatment. Data from real-time PCR displayed that H/R treatment induced a more than 4-fold increase in the expression of GRP78 mRNA ($P < 0.01$). Conversely, the mRNA expression of GRP78 was significantly attenuated to approximately 2-fold of normal levels with $5\mu\text{M}$ lycopene pretreatment ($P < 0.01$), but not completely come back the control levels. The level of the sliced Xbp-1 mRNA had a 2.23-fold increase in H/R-treated cardiomyocytes compared to control groups ($P < 0.01$), in contrast, the level of the sliced Xbp-1 mRNA was markedly downregulated to 1.20-fold of control levels with $5\mu\text{M}$ lycopene pretreatment ($P < 0.01$), but not completely come back the normal levels.

CONCLUSIONS The present study demonstrated that lycopene protects primary cultured neonatal mouse cardiomyocytes against H/R injury by inhibiting the activation of the PERK and the IRE1 pathway of the ER stress, the protective effect of lycopene on cardiomyocytes highlights the therapeutic potential of plant-derived antioxidants against I/R-injury.

GW26-e2455

Vagal Nerve Stimulation Reverses Cardiac Dysfunction and Subcellular Calcium Handling in Heart Failure Rats After Myocardial Infarction

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OBJECTIVES Vagal nerve stimulation (VNS) as a non-pharmacological approach to retrieve the autonomic balance, has showed beneficial therapeutic effects for chronic heart failure (CHF). Moreover, calcium cycling is critical in cardiac excitation-contraction coupling (ECC) and participates in the antiarrhythmic effects of VNS. Taken together, we hypothesized that VNS could improve the calcium handling properties which might be underlying mechanisms of VNS for heart failure treatment.

METHODS In this study, 32 SD rats were divided into three groups as Control (sham operated), CHF-SS (CHF rats with sham stimulation) and CHF-VNS (CHF rats with VNS). Cardiac function was evaluated by echocardiography while the structural remodeling was assessed by HE and Masson staining. ELISA was used to detect the plasma BNP, norepinephrine and angiotensin II concentrations. The proteins and mRNAs expression of sarcoplasmic reticulum Ca²⁺ ATPase (SERCA2a), phospholamban (PLB), ryanodine receptor 2 (RyR2), Na⁺-Ca²⁺ exchanger 1 (NCX1) were analyzed by Western blot and RT-PCR.

RESULTS Compared with CHF-SS rats, rats from CHF-VNS group received 8 weeks of VNS showed significantly improved left ventricular ejection fraction (LVEF, $P=0.001$) and less myocardial interstitial collagen. The elevated plasma concentrations of BNP, norepinephrine and Ang II in CHF rats were partially restored by VNS. After VNS, the rats in CHF-VNS group exhibited statistically significant higher cardiac SERCA2a protein and mRNA contents than CHF-SS group. RyR2 and depressed PLB expressions were unaffected between rats with or without VNS, whereas NCX1 expression was significant lower in CHF-VNS group.

CONCLUSIONS The results suggest that the improvement of cardiac performance by VNS is accompanied with reversal of changes in calcium handling properties including SERCA2a, PLB and NCX1 which may be underlying mechanisms of VNS for heart failure therapy.

GW26-e3532

miR-433 Controls Cardiac Fibrosis

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OBJECTIVES Cardiac fibrosis, a result of multiple injurious insults in heart, is a final common manifestation of chronic heart diseases and