Experimental Study

GW25-0555

4-O-methylhyconol prevent cardiac hypertrophy via suppression of lipid accumulation, oxidative stress and inflammation in obesity mice induced by high fat diet

Zhiqiu Zhang1,2, Shadong Wang1,2, Shanshan Zhou1,2, Xiaoxing Yan1, Yang Zheng1, Yi Tan1, Lu Cal1, Young Hei Kim3

1Cardiovascular Center, the First Hospital of Jinlin University, Changchun, China, 2KCHRI at the Department of Pediatrics, University of Louisville, KY, USA, 3Bioland R&D Center, Cheonan, Changnam, South Korea

Objectives: Obesity is associated with cardiac inflammation, oxidative stress, apoptotic cell death, resulting in cardiac hypertrophy cardiac dysfunction. Magnolia associated insulin resistance, lipid accumulation and in hypertrophy in high-fat diet (HFD)-induced obese mice. However, the extract

Methods:

Cardiac blood glucose, glucose tolerance, plasma triglyceride and cardiac function were normal (10 kcal% fat) fat diet or HFD (60 kcal% fat) feeding. At the endpoint (5mg/kg), MH (0.5mg/kg) or MH (1.0mg/kg) by gavage daily, during 24-weeks of

Results:

In each group, the Western blotting results showed that berberine can up-regulate the expression of PPAR-gamma in N2a-APP695 cells. 10

Conclusions:

We used different concentrations of berberine treated with N2a-APP695 and PPAR-gamma expression after the treatment of N2a-APP695 cells with Swedish mutant (APPsw) cells (N2a-APP695), a widely used AD model in

GW25-2285

S-Propargyl-cysteine (SPRC) diminishes mitochondrial dysfunctions in heart failure

Wu Dan, Qingsuan Hu, Yi Zhun Zhu

Department of Pharmacology and School of Pharmacy, Fudan University

Objectives: One of the important factors of heart failure (HF) is mitochondrial dysfunction. Growing evidences indicate that damage of mitochondria causes mitochon-
drdial pathway apoptosis and the loss of cardiomyocytes, which are significant in the process of HF. At the meantime, the injury of mitochondria respiratory chain results in a decrease of cellular ATP level in HF. Hydrogen sulfide (H2S) is the third gasotransmitter, which presents a wide range of cell function in the body. S-Propargyl-cysteine (SPRC) is water-soluble H2S endogenous donor which has protective effect on acute myocardial infarction in rats. The aim of this study was to investigate how SPRC diminishes mitochondrial dysfunctions in HF.

Methods: HF in C57BL/6 mice (male, 6-8 weeks old) was induced by Isoproterenol (7.5 mg/kg), which was administrated for 3 weeks, once a day by subcutaneous in. Hydrogen peroxide (H2O2) 200 μM was used to induce Myocardial oxidative damage in H9c2 cells. H&E stain and masson trichrome stain were used to determine the histopathological change. Cell viability assay was used to determine the protective effect of SPRC in vitro. Caspase activity assay was used to determine the apoptosis level. Lipid peroxidation, antioxidant enzymes, ATP level, mitochondrial ΔΨm, AMPK, PGC1α, and mitochondrial dysfunction were used to determine the mitochondrial function. Western blot was used to deter-

Results: H2O2 and masson trichrome stain showed a significant loss of mitochondrial and increased fibrosis in isoprotene group compared with the vehicle group. After SPRC (10, 25 mg/kg) treatment, the level of myocardial fibrosis was significantly reduced. SPRC (10 - 50 μM) were found to increase cell viability significantly, which reduced by H2O2 in H9c2 cells. SPRC (10, 25 mg/kg) significa-
tly reduced ROS induced by H2O2 in mouse cardiac in vivo. The same result was observed in SPRC (10 - 50 μM) treated H9c2 cells. The level of myocardial glutathione (GSH) and superoxide dismutase (SOD) was recovered by SPRC treatment and the content of mitochondrial lipid peroxidation (LPO) was decreased compared with H2O2 group. The content of ATP and the activity of mitochondrial respiratory chain complexes were significantly increased in SPRC treated group which were severely reduced in H2O2 group. The mitochondrial membrane potential was significantly reduced and the calcium swelling was markedly decreased in the SPRC groups. SPRC induced translocation of PGC1α to mitochondria, which reduced by H2O2.

Conclusions: This study suggests the therapeutic ability of SPRC in HF through the protective effect of mitochondrial dysfunction.

GW25-2341

Growth hormone releasing hormone agonist enhances cell survival and anti-apoptosis of bone marrow derived mesenchymal stem cells via activating STAT3 signaling pathway to promote angiogenesis of hindlimb ischemia

Xia xiangyan, Hong Yu

Cardiovascular Key Lab of Zhejiang Province, the Second Affiliated Hospital, School of Medicine, Zhejiang University

Objectives: growth hormone releasing hormone (GHRH) is an endocrine hormone produced by pituitary gland and stored and released to the circulating system by hypothalamus and GHRH receptor has been confirmed to exist on bone-marrow mesenchymal stem cells to adjust the functions of these cells. The effectiveness of MSC transplantation has been limited to a relative low level mainly by the restricted survival rate after injection. As to an artificially synthesized polypeptide compound, the GHRH analogue JI-34 is better at the stability and stimulating efficiency through by less degradation compared with physiological GHRH. Therefore, to testify a newly use of GHRH agonist JI-34 whether it can enhance the survival of MSC will be attractive.

Methods: the survival, viability, migration angiogenesis ability and anti-apoptosis rate of MSC is compared between two groups of mice MSC pretreated with JI-34 or not. CCK-8, transwell assay, Western blot, quantitative RT-PCR, tube formation assay and TUNEL staining kit were used in this paper. In vivo study we revealed the angiogenesis ability of pretreated MSC by cell injection into ischemic hindlimb of 6 weeks old C57BL/6 mice.

Results: After JI-34 pretreatment for 24hours, MSC’s viability had increased by 23%±0.5% compared with controls in normoxia condition and 26%±1% in hypoxia conditions (0.5% O2). Cell migration capacity can also be raised after pretreatment of JI-34 in transwell chamber with a relatively increased 27%±2% migration rate in a 24-hour’s assay with 10% gradient of Fetal Bovine Serum (FBS). Similarly, the supernatants of MSC pretreated with JI-34 co-cultured with Human Umbilical Vein Endothelial Cells (HUVEC) depicted a higher possibility of tube formation with longer tube length (754mm±37mm) than control cells (580mm±40mm) in each visual field on the matrigel. RT-PCR and Western Blot showed that a highly augment of pro-angiogenic factors of VEGF-A and SDF-1 with 8 fold and 7.5 fold increase relating to control respectively. All these effects can be blocked by adding the specific antagonist of JI-34. The JI-34 to shut down the benefits of JI-34, western blot showed that STAT3 and other signaling pathway molecules acted as the switch could be activated in 10minutes and picked at 30minutes, stayed for about 2 hours then gradually turned down to the normal level. By adding specific inhibitor of
STATIC, these results could not be observed. In vivo results demonstrated that a single injection of hindlimb ischemia, mice (n=12) treated with Ji-34 pretreated MSC, MSC and PBS revealed a significantly different incidence of limb recovery and reformation of newly formed vessels. Ultrasound Doppler displayed that mice injected with treated cells gained a better recovery of blood perfusion in day 3 after surgery and sustained to day 4 and MSC and PBS group. Intramuscular administration of MSC, TUNEL and immunohistochemistry also suggested that the results that treated with Ji-34, MSC increased vasularization and angiogenesis of mice hindlimb ischemia.

Conclusions: the agonist of GHRH can activate the receptor of MSC to enhance its viability and paracrine effect through STAT3 signaling pathway to promote the angiogenesis of ischemic hindlimb of mice.

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Targeted Delivery of Hydrogen Sulfide Using Ultrasound and Intravenous Microbubbles Attenuates Myocardial Ischemia-Reperfusion Injury
Gangbin Chen, Jiapeng Bin, Shengcan Guo, Chaunzi Zhang, Yongkang Lu, Yan Wang, Shuxin Shen, Xinzhong Li, Juewei Su
Cardiovascular Division, Nanfang Hospital, Southern Medical University, Guangzhou, People’s Republic of China

Objectives: Myocardial ischemia-reperfusion injury is a major cause of cardiac damage following revascularization in acute myocardial infarction. Hydrogen Sulfide (H\textsubscript{2}S) has emerged as a critical signaling molecule with a profound cardioprotective effect. However, the delivery of H\textsubscript{2}S remains limited by its instability. We hypothesized that intravenous administration of microbubbles encapsulating H\textsubscript{2}S gas combined with ultrasound exposure may enable effective myocardial ischemia-reperfusion injury.