CONCLUSIONS Downregulation of XBP1 by transfection with XBP1 siRNA increased the TNF-α, PAI-1, MCP-1 and IL-6 at protein levels in 3T3-L1 adipocytes. In parallel, results from western blot analysis and ELISA further confirmed the reduction of TNF-α, PAI-1, MCP-1 and IL-6 protein levels induced by FFA in Ad-XBP1 treated 3T3-L1 adipocytes.

GW28-e0121

Preconditioning with endoplasmic reticulum stress mitigates FFA induced 3T3-L1 adipocyte Inflammation

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OBJECTIVES The endoplasmic reticulum (ER) is the principle cellular organelle responsible for proper folding and processing of transmembrane, secretory, or cell-surface proteins. ER stress protects cells against damage induced by inflammatory stress with unfolded protein response (UPR). Adipocyte inflammation is an important factor for insulin resistance and obesity. This study is to verify the hypothesis that preconditioning with ER stress has protective effect on FFA induced inflammatory response in cultured 3T3-L1 adipocytes.

METHODS ER stress preconditioning was achieved by pretreatment of 3T3-L1 adipocytes with tunicamycin (TM). To ascertain appropriate concentration of TM-induced ER stress, 3T3-L1 adipocytes were treated with different concentrations of TM (0, 0.1, 0.5,1 ng/ml) and different time course (0h, 1h, 2h, 4h, 6h, 8h) of TM. Then cells were pretreated with TM before exposed to FFA (0.5 mM) for 4 h. The pro-inflammatory cytokines tumor necrosis factor alpha (TNF-α), plasminogen activator inhibitor-1 (PAI-1), monocyte chemoattractant protein 1 (MCP-1) and interleukin 6 (IL-6) induced by FFA were determined at protein levels after FFA treatment. ELISA was used to measure protein secretion of MCP-1 and IL-6 in cell culture supernatants, and western blot analysis was used to examine TNF-α and PAI-1 protein expression in total cell protein.

RESULTS TM up-regulated XBP1 protein level in dose-dependent and time-dependent manners. Pretreated 3T3-L1 adipocytes with TM at the concentration of 0.5 ng/ml for 4h are an optimum condition to achieve ER stress conditioning without possibility to inflammation. ER stress conditioning suppressed FFA induced TNF-α, PAI-1 protein expression tested by western blot analysis and MCP-1 and IL-6 protein level tested by ELISA in cultured 3T3-L1 adipocytes.

CONCLUSIONS Preconditioning with endoplasmic reticulum stress inhibits FFA-induced adipocyte inflammation in 3T3-L1 adipocytes.

GW28-e0122

Ginsenoside Rb1 reverses FFA-induced inflammatory response in 3T3-L1 adipocytes

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OBJECTIVES Overweight and obesity have become a public health problem. In obese state, abundant fatty free acids (FFA) were released from hyperplastic adipose tissue and were release to adipocytes, skeletal muscle, liver, then leading to adipocytes inflammation and insulin resistance. Ginsenoside Rb1 was purified from Ginseng and was showed a protective effect on H_2O_2-induced premature senescence in our previous studies. However, the effect of Rb1 on FFA-induced inflammatory response has rarely been demonstrated. This study is to testify the effects of Rb1 on the expression of pro-inflammatory cytokines after induction by FFA in 3T3-L1 adipocytes.

METHODS In this study, 3T3-L1 adipocytes were exposed to 10 mM FFAs with or without Rb1 at concentrations of 10, 20, 40 μM. Tumor necrosis factor-α (TNF-α) expression and nuclear factor-κB (NF-κB) p65 phosphorylation were detected by western blotting. Monocyte chemotactic protein-1 (MCP-1) and interleukin-6 (IL-6) secretion were measured by enzyme-linked immunosorbent assays (ELISAs).

RESULTS FFA stimulated the expression of MCP-1 and IL-6 secretion as well as TNF-α expression which was blocked by Rb1 in a dose-dependent manner. Rb1 also suppressed FFA-induced NF-κB phosphorylation, suggesting that the protective effect of Rb1 from FFA induced inflammatory injuries was at least partially achieved by down-regulation of NF-κB phosphorylation, which leads to decreased expression of pro-inflammatory cytokines.

CONCLUSIONS Ginsenoside Rb1 suppresses productions of FFA-induced pro-inflammatory cytokines in 3T3-L1 adipocytes at least partially through down-regulation of NF-κB phosphorylation, which represents a new mechanism for the salutary effect of Ginsenoside Rb1 in anti-inflammation and anti-obesity studies in future.

GW28-e0124

An Experimental Model of Stanford Type A Aortic Dissection

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OBJECTIVES To create an experimental animal model of acute Stanford type A aortic dissection for researching its pathophysiological changes and offer a proper animal model for clinical therapy.

METHODS Eighteen adult beagle dogs (weight, 8-12 kg) were used. The ascending aorta was exposed by a standard full-length sternotomy. The entry of the aortic dissection was created surgically just distal to the origin of the ascending aorta. Normal saline solution was injected into the aortic wall (ie, media) create the dissection, the remaining media and intima was incised transversely and the incision of the adventitia and part of media were then sutured and the blood bleeding from the false lumen at the entry point .

RESULTS All of the 18 dogs, 3 died because of hemorrhagic shock .We created 15 models successfully, and all of the 15 surviving dogs had completely patent true and false lumina. The length of aortic dissection is 13.5 ~ 17.5cm (16.67±0.42cm). Microscopic examination showed that the dissection was created in the tunica media layer, making it identical to Stanford type A aortic dissection in humans.

CONCLUSIONS In this animal model of Stanford type A aortic dissection, the false lumen has excellent long-term patency and the dissection plane is histologically similar to that in human. This model may contribute to the development of researching its pathophysiologial changes of Stanford type A aortic dissection and offer a proper animal model for clinical therapy.

GW28-e0137

Exercise training modulated the autonomic nervous system imbalance without increasing the incidence of spontaneous arrhythmia in myocardial infarction mice

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OBJECTIVES Myocardial infarction (MI) is the leading course of sudden cardiac death, especially the accompanied arrhythmia induced by the autonomic nervous system (ANS) imbalance. Exercise can improve cardiac function after MI, however, the benefit of exercise still keeps controversial because of its proarrhythmic effect. In this study we investigated how exercise affects the incidence of arrhythmic events and the ANS in MI model mice.

METHODS Wild-type male mice which underwent sham-operation or MI-made operation were divided into one control group and two MI groups: sedentary group and exercise training group (MI-Ex). MI-Ex group underwent treadmill training from 7 days after MI for 7-8 weeks. Cardiac function and structural changes were assessed by echocardiography and histology. Based on telemetry recording, autonomic nervous function was evaluated by pharmacological blockades test and heart rate variability (HRV). The incidence of spontaneous ventricular arrhythmia was calculated through telemetry electrocardiography. Gene expressions in left ventricular tissues were investigated by real-time PCR and Western blotting.

RESULTS There were no significant differences in echocardiographic findings and survival rate between two MI groups. Also there was no obvious difference in the ratio of fibrotic area. Comparing with sedentary group, MI-Ex group showed lower incidence of spontaneous ventricular arrhythmia and increased parasympathetic tone index. The real-time PCR indicated changes in Ca2 + handling-related gene expressions (higher SERCA2a, lower phospholamban) in MI-Ex group.

CONCLUSIONS Chronic exercise training modulated the ANS imbalance without increasing the incidence of spontaneous arrhythmia in MI mice mainly through the normalization of Ca2 + dynamics.