Myocardial infarction accelerates the activation of systemic and local cellular immunity in STZ-induced type 1 diabetic rats

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Objectives: Clinically, diabetes is very common in patients hospitalized for acute myocardial infarction (AMI). It is a strong and independent co-morbidity of all-cause mortality and readmission for post-myocardial infarction chronic heart failure (CHF). The central role for monocyte subset accumulation in the heart following AMI and the role of the spleen as monocyte reservoir were all recently demonstrated. However, whether the associated cellular immunity mechanism was involved in AMI with diabetes was unknown.

Methods: We performed the comparison in four separate groups: 1) rats with sham surgery induced myocardial infarction (Ctr, n=10); 2) rats with surgically induced myocardial infarction (MI, n=10); 3) STZ-induced type 1 diabetic rats (DB, n=10); 4) STZ-induced type 1 diabetic rats with surgically induced myocardial infarction (DB+MI, n=10). The parameters of cellular immunity in the heart, spleen and blood were evaluated by flow cytometry and immunohistochemistry etc. In addition, cardiac remodeling and function was also evaluated.

Results: Twelve weeks after the operation, compared with DB or MI rats, DB+MI rats exhibited the following: 1) significantly increased cardiac enlargement, fibrosis and deteriorated cardiac function; 2) significantly increased infiltration of CD3+ T cells and the expression of IFN-gamma, IL-17 and IL-4 in heart. 3) significantly increased proportion of CD4+ T cells and producing-IFN-gamma, IL-17 and IL-4 in CD4+ T cells and a decreased Treg/TnTh17 ratio in spleen; 4) significantly increased the proportion of producing IFN-gamma, IL-17 and IL-4 CD4+ T cells and Treg in blood. However the circulating immune complexes (CIC) and IgG did not show the difference between them.

Conclusions: In this study, MI significantly accelerated cardiac infiltration of CD4+ T cell and the spleen and serum activation of CD4+ T cell especially its inflammation associated subgroups in STZ-induced type 1 diabetic rats. Systemic and local cellular immunity probably involved in the post-MI CHF progression in diabetes.

GW25-e5274

Lycopene protects endoplasmic reticulum stress-induced apoptosis against neonatal mouse cardiomyocytes hypoxia/reoxygenation injury

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Objectives: Endoplasmic reticulum (ER) stress induced apoptosis has been implicated as a critical cause in the pathogenesis of myocardial ischemia reperfusion (I/R) injury. Our previous studies demonstrated that lycopene exhibits great pharmacological potential in protecting against the I/R injury, but whether its effect is mediated through attenuation of ER stress-induced apoptosis remains unclear. The aim of this study was to investigate the effect of lycopene on hypoxia/reoxygenation (H/R) induced ER stress in primary cultured neonatal mouse cardiomyocytes.

Methods: Primary cardiomyocytes were isolated from neonatal C57BL/6 mice and divided into four groups: control, lycopene, H/R, lycopene + H/R. The cultured cardiomyocytes underwent 4h of hypoxia followed by 6h of reoxygenation to achieve H/R model. Cardiomyocytes were pretreated with lycopene (5 μM) prior to H/R treatment in lycopene + H/R. Cell viability was assessed using CCK-8 assay in each group. The Annexin-V-FITC/PI assay was used to evaluate cardiomyocytes apoptosis in the different treatment groups. The expression of GRP78, a widely used marker of endoplasmic reticulum stress, was measured via western blot. The expression of ER-related apoptotic maker of CHOP/GADD153 and caspase-12 was measured by real-time PCR.

Results: Our results demonstrate that the cell viability significantly decreased to 66.30±4.48% of the control levels following H/R, the cell viability markedly improved in lycopene + H/R (P<0.01). The results from flow cytometry with Annexin V and PI double-staining illustrated that after exposure to H/R, apoptotic percentage significantly increased to 26.42±2.71% (P<0.01), while that of control and lycopene group were 4.65±1.51% and 4.69±1.42%, respectively. In contrast, lycopene + H/R markedly prevented the H/R-induced apoptosis (16.38±2.12%, P<0.01). Compared to control and lycopene, the expression of GRP78 protein increased more than two-fold in H/R group (P<0.01), while the expression of GRP78 protein only increased by 1.46-fold in lycopene + H/R (P=0.01). In addition, H/R treatment evoked a significant increase in GADD153/CHOP mRNA expression compared to control groups (P<0.01). However, the GADD153/CHOP mRNA expression was markedly down-regulated to 1.68-fold of control levels with lycopene pretreatment (P<0.01). Furthermore, the caspase-12 mRNA expression was also significantly increased in H/R treatment (1.82 folds of control group, P<0.05). However, pretreatment with lycopene effi-

GW25-e5288

Non-antiplatelet effect of Clopidogrel: Improving endothelial function in Chinese healthy subjects with different CYP2C19 genotype

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Objectives: Clopidogrel is demonstrated to improve endothelial function in vitro and in patients with coronary artery disease (CAD). But it remains unclear whether this effect of clopidogrel is associated with CYP2C19 polymorphisms which determining antiplatelet effect of clopidogrel.

Methods: After genotyping, Chinese healthy subjects were enrolled in our study. Among them, 6 subjects were CYP2C19*1/*1 (extensive metabolisers, EMs) and the other 6 subjects were CYP2C19*2/*2 (poor metabolisers, PMs). All subjects received 300mg clopidogrel orally. Endothelial function was assessed by measurement of flow-mediated dilatation (FMD) of the brachial artery and ADP-induced platelet aggregation was determined using optical aggregometry before and 4h after administration of 300mg clopidogrel.

Results: FMD was significantly higher at 4h and 24h after a loading-dose administration of clopidogrel in both CYP2C19 EMs and PMs groups, which showed no significant difference between the two groups. ADP-induced platelet aggregation was greatly inhibited at 4h and 24h after administration of clopidogrel in CYP2C19 EM group. However, there was no statistical correlation between the change in FMD and ADP-induced platelet aggregation in the two CYP2C19 groups.

Conclusions: It is the first time to report that clopidogrel improves endothelial function in healthy Chinese subjects, which is unrelated with CYP2C19 genotype and independent of antiplatelet action.
GW25-e1659

Nicotine induce mast cells degranulation to promote the atherogenesis and reduce the atherosclerotic plaque stability

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Objectives: Nicotine has been identified to promote atherosclerosis. But the mechanism of nicotine induced atherogenesis has not been well elucidated. Mast cells play an important role in high-fat diet induced atherogenesis. This study focus on the role of mast cell in nicotine induced atherogenesis and plaque instability.

Methods: Peritoneal administration of 100mM disodium cromoglicate (DSCG) was introduced to inhibit mast cell degranulation. 45 ApoE de

Conclusions: Interaction between AT-I and IL-1β in the PVN contributes to deterioration of heart failure.

GW25-e1582

Impact of SOD mimetic and tempol training on NOS in spontaneously hypertensive rats

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Objectives: The exercise training (Ex) and superoxide dismutase (SOD) mimetic treatment have antihypertensive effects in spontaneous hypertensive rats (SHR). However, the effects of the combination with Ex and tempol on NOS expression in SHR remain to be elucidated. The present study tested the effects of the Ex and tempol on NOS expression in SHR.

Methods: A total of 180 Sprague-Dawley male rats were used. SHR were randomly divided into 3 groups: high-fat diet, high-fat diet + nicotine, and high-fat diet + nicotine + DSCG (n = 15 each). After 12 weeks of treatments, atherosclerotic lesion size of the aortas were quantified. Toluidine blue and tryptase staining identified mast cell count and distribution in the aorta lesion. Immunostaining of CD68, CD45 were used to evaluate the inflammatory filtration.SMA, Ki-67 and sinus red staining were used to study smooth muscle cell proliferation and collagen content in the lesion. In vitro, bone marrow-derived mast cells (BMMCs) were harvested and divided into 5 groups, with DMSO, tempol, tempol + 150ug/ml nicotine, 100ug/ml nicotine with 100mM DSCG pretreatment and nicotine 100ug/ml + 10ug/ml mecamylamine pretreatment. At 0.5hr, 1hr, 2hrs, supernatants were harvested to analyze the mast cell degranulation.

Results: Nicotine increases plaque size, and macrophage infiltration, decreases smooth muscle collagen content along with the increases in mast cells count and activation ratio at the lesion, which could be inhibited by DSCG. Nicotine induced mast cell degranulation at 2 hours comparing to PBS (43.60% vs 2.3%), which could be inhibited by mast cell stabilizer DSCG (23.7%) and meca-ylamine (20.35%). Macrophage migration ability in the compound 48/80 and nicotine conditioned medium group were significantly higher comparing to PBS, DSCG and mecamylamine group. Foam cell formation ratio in the compound 48/80 and nicotine conditioned group were significantly higher comparing to PBS, DSCG and meca-

Conclusions: Nicotine might induce mast cell degranulation through nACHR and then activate mast cell to release a range of proinflammatory mediators to increase the migration ability of macrophages and foam cell formation and promote the atherosclerotic plaque induced by the administration of nicotine. Administration of mast cell stabilizer revealed the potential of applying mast cell stabilizer in preventing nicotine induced atherogenesis.

GW25-e1589

Comparison of Transplantation of bone marrow-derived stem cells, adipose-derived stem cells and endometrium- derived stem cells in the Infarcted Heart

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Objectives: A variety of adult stem cells have been used to transplanta into the infarcted heart to cure myocardial infarction (MI), however, comparison studies are lacking to show more suitable source of cells for transplantation. Mesenchymal stem cells hold promise for myocardial regeneration therapy. Derivation of these cells from the endometrium tissue might be easier compared to bone marrow and adipose tissue. So, we tried to study the protective effect of the Ex, the present study tested the effects of the Ex and tempol on NOS expression in SHR.

Methods: The exercise training (Ex) and superoxide dismutase (SOD) mimetic tempol were also used to inhibit the macrophage migration and foam cell formation.

Results: In the present study, the effects of Ex and tempol on NOS expression in SHR remain to be elucidated. The present study tested the effects of the Ex and tempol on NOS expression in SHR.

Conclusions: These results indicate that tempol enhances the Ex-induced antihypertensive and renal-protective effects through the up-regulation of NOS expression and NO production in SHR. H2O2 may mediate these effects of the Ex and tempol in SHR.

GW25-e1654

Exhaustive Swimming Induces Cardiac Lesion in Rats

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Objectives: The purpose of present study was to investigate the heart injury caused by exhaustive swimming in detail in rats.

Methods: Adult male Sprague-Dawley rats randomly were divided into two groups: the control group and acute exhaustive group. The acute exhaustive group rats were exposed to exhaustive swimming. Refering to Thomas exhaustive standards, single exhaustive swimming in detail in rats.

Results: (1). The heart rate (HR) 258.47±19.54 beat/min vs 109.97±19.54 beat/min, P<0.05). The left ventricular end-systolic pressure

Conclusions: This is the first study comparing the in vivo results and vivo behavior of 3 types of MSCs in the infarcted heart. AdMSCs and BMMSCs do not tolerate well in the cardiac environment, resulting in more cell death and worse cardiac function than EnSCs groups.

GW25-e3339

Exhaustive Swimming Induces Cardiac Lesion in Rats

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Results: (1). The content of BNP, Trh, TnI in acute exhaustive rats in serum (86.80±4.33 ng/L, 90.40±19.26 pg/mL, 132.81±26.11 pg/mL) was markedly increased (P<0.05) compared with the values of control group (71.87±16.59 ng/mL, 58.82±21.65 pg/mL, 85.20±20.57 pg/mL) caused by exhaustive swimming. (2). Comparison with the values of E, NE in the control group (137.45±18.22 ng/L, 1005.95±19.90 ng/L), acute exhaustive group (158.74±23.69 ng/L, 330.35±14.90 ng/L) was obviously increased, and there were significantly differences (P<0.05). (3). After exhaustive swimming, stroke volume became larger while end-diastolic volume increased (143.54±25.43 μL vs 109.97±19.54 μL, 217.37±37.84 μL vs 165.80±33.58 μL, respectively, P<0.05). The left ventricular end-systolic pressure (LVESP) obviously decreased (P<0.05). The heart rate (HR) 258.47±52.69 bpm markedly decreased (P<0.05) compared with 399.94±67.34 bpm in Control group.

GW25-e1520

Exhaustive Swimming Induces Cardiac Lesion in Rats

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