GW25-e5201

The mechanism research of Compound Danshen dripping pills accruing myocardial infarction from the TLR4-NF-κB - PECA-M-I pathways

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Objectives: To observe the protection and its mechanism of Compound Danshen dripping pills on myocardial infarction.

Methods: 50 male Wistar rats were randomly divided into normal group, model control group, experimental model group, isosorbide dinitrate (ISD) group, Compound Danshen (FFDS) group, 10 rats in each group. The myocardial infarction models and the model of myocardial infarction with the Qi and blood stasis were established respectively, and the models rats were treated with isosorbide dinitrate and Compound Danshen dripping pills intervention. Cardiac ejection fraction, myocardial infarction, GMP-140 of blood serum and TRL4, TRAF-6, IL-1β, PECA-M, NF-κB protein and NF-κB protein expression of myocardial tissue were observed.

Results: After NBT staining, myocardial tissue in the normal group were stained purple; There were large grey infarcted region in myocardial tissue of each model group, the protein and NF-κB expression in the normal group was low, the model group were higher than normal group. The mechanism research of Compound Danshen dripping pills could decrease NF-κB, IL-1 protein and NF-κB pathway.

Conclusions: The effect of Compound Danshen dripping pills on myocardial protection may be relate to regulation of TLR4/TRAF-6/NF-κB pathway.

GW25-e5348

Effects of Simvastatin combined with ezetimibe on atherosclerosis in ApoE-/- mice

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Objectives: To investigate effects of Simvastatin combined with ezetimibe on atherosclerosis in ApoE-/- mice with high-fat diet.

Methods: 36 male apoE-/- mice (age, 8weeks) on a C57BL/6J background were randomly divided into three groups with 12 animals in each group. Animals were treated with intragastric administration as follows: Model group received PBS buffer 100nmol/L phorbol myristate acetate (PMA) for 48h, and treated with ox-LDL to induce foam cells. The mRNA and protein expression of SR-BI, ABCA1 were determined by RT-PCR and Western blot, the intracellular cholesterol efflux rate was detected by liquid scintillator.

Results: Compared with the control group, AngII decreased SR-BI and ABCA1 in both protein and mRNA, and inhibited the cholesterol efflux (P<0.05). Those effects could be attenuated by cotreated with Ang-(1-7) (P<0.05). However when incubated with A-779, an inhibitor of Ang-(1-7), the effects of Ang-(1-7) on promoting the expression of SR-BI, ABCA1 and the cholesterol efflux were significantly abolished (P<0.05).

Conclusions: Simvastatin + ezetimibe therapy inhibits atherosclerosis more obviously.

GW25-e5365

Bone Marrow stem cells: Immune property genes assay and effect of transplantation on the immune cells of heart failure patients

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Objectives: To investigate the effects of stem cells derived from bone marrow (BMSCs) are not immunogenic and have immunosuppressive.

Methods: To evaluate the related mechanisms and the effect of transplantation on body immunological, we examined immune property genes expression in BMSCs and levels of T-lymphocytes subgroups and immunoglobulins (Ig) in heart failure (HF) patients with and without BMSCs transplantation. BMSCs express immune tolerance genes HLA-E, HLA-A and HLA-F and immunomodulation genes VEGF, TGFB1, HGF, HMox1, IL-1b, IL-6, LIF, LGALS1-1/50, COX1/2 and PTGE, while they do not express immune response-related genes HLA-DR, HLA-DQ, HLA-DP, CD80, CD86, CD40 and CD40L.

Results: There were no significant differences in blood CD34+, CD4+, or CD8+ T-lymphocytes subgroups and the CD4+CD8+ ratio between patients who received cell infusion and those at the baseline and 3 days, 14 days and 1 month after transplantation. In addition, no significant differences among T-lymphocytes subgroups and CD4+/CD8+ ratio among different time points were found in the transplantation group or the control group. No obvious changes of plasma IgG/IgM were observed in HF patients with BMSCs transplantation.

Conclusions: The immune properties of BMSCs are due to the expression of immune avoidance and immunomodulation genes in the absence of immune response-related genes. BMSCs are secure in immunological aspects when used as seed cells for cardiac repair.

GW25-e5383

A RTK-based functional RNAi screen reveals determinants of PTX-3 expression

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Objectives: The aim of the present study was to explore the role of receptor tyrosine kinases (RTKs) in the regulation of expression of PTX-3, a protector in atherosclerosis.

Methods: Human monocyte U937 cells were infected with a shRNA lentivector library targeting human RTKs upon LPS stimuli and PTX-3 expression was determined by ELISA analysis. The involvement of downstream signaling in the regulation of PTX-3 expression was analyzed by both Western blotting and ELISA assay.

Results: We found that knocking down of ErbB2/3, EphA7, and FGFR3 and RET impaired PTX-3 expression without effects on cell growth or viability. Moreover, inhibition of AKT, the downstream effector of ErbB2/3, also reduced PTX-3 expression. Furthermore, we showed that FGFR3 inhibition by anti-cancer drugs attenuated p38 activity, in turn induced a reduction of PTX-3 expression.

Conclusions: Altogether, our study demonstrates the role of RTKs in the regulation of PTX-3 expression and uncovers a potential cardiotoxicity effect of RTK inhibitor treatment in cancer patients who have symptoms of atherosclerosis or are at the risk of atherosclerosis.

GW25-e5399

Effects of AngII and Ang-(1-7) on the Cholesterol Efflux in THP-1 Derived Foam Cells

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Objectives: To investigate the effects of angiotensin II (AngII) and angiotensin-(1-7) [Ang-(1-7)] on scavenger receptor class B type 1 (SR-BI), ATP-biding cassette transporter A1 (ABCA1) and cholesterol efflux in THP-1 derived foam cells.

Methods: Human monocytes cell line (THP-1) were induced into macrophages by 100nmol/L phorbol myristate acetate (PMA) for 48h, and treated with ox-LDL to construct the foam cells, then were randomly allocated into five groups: control group, AngII group, Ang-(1-7) group, Ang-(1-7) + AngII group and Ang-(1-7) + A-779 group. The mRNA and protein expression of SR-BI, ABCA1 were determined by RT-PCR and Western blot, the intracellular cholesterol efflux rate was detected by liquid scintillator.

Results: Compared with the control group, AngII decreased SR-BI and ABCA1 in both protein and mRNA, and inhibited the cholesterol efflux (P<0.05). Those effects could be attenuated by cotreated with Ang-(1-7) (P<0.05). However when incubated with A-779, an inhibitor of Ang-(1-7), the effects of Ang-(1-7) on promoting the expression of SR-BI, ABCA1 and the cholesterol efflux were significantly abolished (P<0.05).

Conclusions: In THP-1 derived foam cells, Ang-(1-7) via its specific receptor MAS attenuates the reduction of the expression of SR-BI and ABCA1 induced by AngII, and increases the cholesterol efflux.

GW25-e5426

Homocysteine impairs macrophage cholesterol efflux via LXR alpha hypermethylation

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Objectives: The mechanisms of homocysteine-mediated lipid disorder are poorly understood. Liver X receptors alpha, as a cholesterol-sensing nuclear receptors, are the key regulators of macrophage cholesterol efflux. This work aimed to explore the methylation modification mechanisms of LXR alpha in homocysteine impairing cholesterol efflux in THP-1 macrophage.

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