

by quantitative real-time polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA). Macrophage polarization and its mechanism were evaluated by flow cytometry and western blot. Additionally, toll-like receptor 4 (TLR4) small interfering RNA and mitogen-activated protein kinase (MAPK) inhibitors were used to further confirm the molecular mechanism of curcumin on macrophage polarization.

RESULTS Curcumin dose-dependently inhibited M1 macrophage polarization and the production of TNF- α , IL-6, and IL-12. It also decreased TLR4 expression, which regulates M1 macrophage polarization. Furthermore, curcumin significantly inhibited the phosphorylation of ERK, JNK, p38, and nuclear factor (NF)- κ B. In contrast, siTLR4 in combination with p-JNK, p-ERK, and p-p38 inhibition reduced the effect of curcumin on polarization.

CONCLUSIONS Curcumin can modulate macrophage polarization through TLR4-MAPK/NF- κ B pathway inhibition, indicating that its effect on macrophage polarization is related to its anti-inflammatory and atheroprotective effects. Our data suggest that curcumin could be used as a therapeutic agent in atherosclerosis.

GW26-e0196

Effects of Niacin on ApoE^{-/-} Mice' Adipose Tissue, Serum Lipid and Atherosclerosis

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OBJECTIVES To investigate the effects of Niacin on ApoE^{-/-} mice' adipose tissue, serum lipid and atherosclerosis, and furthermore to explore the potential relation among them.

METHODS Total 28 male ApoE^{-/-} mice were randomly divided into 3 groups: control group (n=8), model group (n=10), Niacin treatment group (n=10), respectively fed with normal diet, high cholesterol diet, high cholesterol diet +1%(w/w) Niacin. After 14 weeks, serum lipid level (total triglyceride, total cholesterol, HDL cholesterol, LDL cholesterol and apoA-I) was measured by enzymatic method and by immunoturbidimetry. Lesions of aortic arteries were stained with hematoxylin eosin. The content of cholesterol in arterial wall and subcutaneous adipose tissue in groin was quantitated by high performance liquid chromatography. The expression of LXR α , ABCA1 and ABCG1 mRNA in subcutaneous adipose tissue was determined by RT-PCR.

RESULTS The content of cholesterol in subcutaneous adipose tissue in control group, model group, Niacin treatment group was (3.13 \pm 0.19), (20.81 \pm 1.97) and (4.00 \pm 0.81) mg/g, respectively. Compared with model group, Niacin treatment could increase the expression of LXR α , ABCA1 and ABCG1 mRNA 144%, 47.3% and 73.8%, respectively. And furthermore, it could also downregulate the level of serum total triglyceride, total cholesterol and LDL cholesterol, upregulate the level of serum HDL cholesterol, apoA-I. Pearson correlation analysis showed that there was a positive relation between the content of cholesterol in arterial wall and the ratio of intima/media thickness ($r=0.58$, $P<0.05$). In addition to those above, Niacin treatment could thin the intima thickness, decrease the ratio of intima/media thickness and downregulate the sub-endothelium lipid-accumulation, especially cholesterol -accumulation.

CONCLUSIONS Niacin treatment may promote the reverse cholesterol transport of peri-adipose tissue, bring the changes of serum lipid profile, and furthermore influence the sub-endothelium lipid-accumulation, especially cholesterol -accumulation, and subsequently reverse the aortic atherosclerosis.

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Renalase Protects the Cardiomyocytes of Sprague-Dawley Rats Against Ischemia and Reperfusion Injury by Reducing Myocardial Cell Necrosis and Apoptosis

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OBJECTIVES Renalase, a novel flavoprotein expressed in the kidney and heart, reduces renal tubular necrosis and apoptosis, which suggests that it might protect against myocardial ischemia reperfusion injury (MIRI) in the same manner. This experiment sought to explore the effects of renalase on Sprague-Dawley (SD) rats subjected to MIRI.

METHODS We used Lentivirus-mediated RNA interference (RNAi) to inhibit the renalase gene expression in the heart tissue via pericardial

cavity injection. The MIRI animal model was established by blocking the left anterior descending artery for 45mins followed by 4h of reperfusion. Real-time PCR and western blotting were used to detect renalase expression in the heart tissue. Double staining and TUNEL were used to detect the necrosis and apoptosis in the myocardial cells, respectively.

RESULTS All rats subjected to MIRI exhibited lower levels of renalase in the heart tissue than did the sham-operated group ($P<0.05$, $n=6$). The (RNAi) group rats exhibited lower renalase levels than did the controls and also exhibited more serious necrosis (7.12 \pm 0.56% vs. 3.32 \pm 0.93%, $P<0.05$, $n=6$) and apoptosis (151.8 \pm 8.2 vs. 66.8 \pm 6.5, $P<0.05$, $n=6$); however, pretreatment with the recombinant renalase significantly reduced myocardial cell necrosis (1.51 \pm 0.12% vs. 4.13 \pm 0.02%, $P<0.05$, $n=6$) and apoptosis (21.3 \pm 5.0 vs. 52.6 \pm 10.4, $P<0.05$, $n=6$) relative to the control rats.

CONCLUSIONS Exogenous recombinant renalase protein reduced myocardial cell necrosis and apoptosis. Recombinant renalase protein might be a new cardiovascular drug for ischemia/IR injury.

GW26-e0734

Roles of (p)rr Gene Activation in the Heart in Hypertensive Rats

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OBJECTIVES Discovery of (pro)renin receptor (P)RR uncovered a novel function of (pro)renin as receptor ligand in addition to enzyme and its precursor, but the roles and mechanisms of (P)RR on the end-organ damage remains unclear so far. Recently, some findings support the (pro)renin-(P)RR interaction at exceptionally high (pro)renin levels *in vitro*. However, the conflicting results obtained with handle region peptide (HRP) *in vivo* and *in vitro* argue against the idea that this drug truly blocks the (pro)renin-(P)RR interaction in the intact animals. In this study, we investigated the roles of cardiac (P)RR and its downward signals on cardiac hypertrophy in hypertensive rats with abdominal aortic constriction, following treatment of HRP and PLC-b3 inhibitor, U73122.

METHODS Seventy-five SD rats were divided into 5 groups ($n=15$ each group) as following: sham operated (SO), rats with the aortic ligation (AL), AL rats were given HRP (4 μ g kg⁻¹ d⁻¹, SC), AL rats given U73122 (40 μ g kg⁻¹ d⁻¹, SC) and AL rats given HRP+U73122. MAP was recorded using a tail-cuff method. After 4 weeks of treatment, levels of (P)RR, PLC-b3, PKC-a and ERK1/2 in the heart were examined by RT-PCR and western blot. The surface area of cardiomyocytes was measured.

RESULTS The levels of (P)RR and PLC-b3 significantly increased in the left ventricle in hypertensive rats ($P<0.01$, respectively). The surface area of cardiomyocytes and MAP rose markedly ($P<0.01$). HRP significantly decreased the level of (P)RR and U73122 suppressed PLC-b3 expression. Treatment of both HRP and U73122 significantly decreased levels of PKC-a, ERK1/2 and Raf-1 in the heart ($P<0.001$). Meanwhile, the surface area of cardiomyocytes and MAP were decreased after treatment ($P<0.01$).

CONCLUSIONS This study demonstrates that (P)RR inhibitor, HRP and PLC-b3 inhibitor, U73122 decreased levels of (P)RR, PLC-b3, PKC-a, ERK1/2 and Raf-1 in the heart, respectively. Meanwhile, administration of both reagents lowered the surface area of cardiomyocytes and MAP. These findings indicate that cardiac (P)RR may activate PLC-b3, PKC, ERK1/2 and Raf-1 signals and lead to hypertension and cardiac hypertrophy.

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Protective Effects and Mechanism of Penethylidine Hydrochloride on Myocardial Ischemia Reperfusion Injury in rats

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OBJECTIVES To investigate the effects and mechanisms of penethylidine hydrochloride (PHC) on myocardial ischemia reperfusion injury (IRI).

METHODS A rat model of myocardial IRI was established by the ligation of left anterior descending coronary artery for 30 min followed by 3 h perfusion. The rats were randomly divided into 6 groups ($n=18$ in each group): a). Sham group: The rats underwent sham