Collagen III, connective tissue growth factor (CTGF) in neonatal rat cardiac fibroblasts induced by TGF-β1. DIM attenuated the increased phosphorylation of AKT and GSK-3β induced by TGF-β1.

**CONCLUSIONS** Our results showed that DIM was a potential drug to attenuate myofibroblast differentiation and modulate the excessive ECM production induced by TGF-β1, through down-regulated AKT/GSK-3β signaling pathways.

**GW26-e4573**

**Anti-inflammatory effect of 3,3’-Diindolylmethane on LPS-induced inflammatory injury in neonatal rat cardiac myocytes via suppressing TLR-4/MAPKs signaling pathways**

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**OBJECTIVES** 3,3’-Diindolylmethane (DIM), extracted from cruciferous plants, has been shown to possess anti-inflammatory properties in various models of inflammatory diseases. However, whether DIM has an anti-inflammatory effect on lipopolysaccharide (LPS)-induced neonatal rat cardiac myocytes injury is poorly understood. Therefore, this study aimed to investigate the protective effect of DIM on LPS-induced inflammatory injury in neonatal rat cardiomycocytes and explore the anti-inflammatory molecular mechanisms.

**METHODS** The cultured neonatal rat cardiomycocytes in vitro were stimulated with LPS (10 mg/L) for 12 or 24 h to induce inflammatory injury, and DIM was incubated with these cells in the presence and absence of LPS. Cell viability was measured by MTT assay, whereas the productions of IL-6, TNF-α and HMGB1 were measured with Real-time PCR and Western Blotting analysis.

**RESULTS** Our data showed that DIM could obviously attenuate the increased mRNA expression levels of pro-inflammatory cytokines including interleukin (IL)-6, tumor necrosis factor (TNF)-α and high mobility group box 1 (HMGB1) induced by LPS. Moreover, DIM could also remarkably inhibit the elevated protein expression levels of Toll-like receptor-4 (TLR-4), phosphorylated extracellular signal-regulated kinases 1/2 (ERK1/2), phosphorylated P38 and phosphorylated c-Jun NH2-terminal kinase (JNK) induced by LPS.

**CONCLUSIONS** Our results suggested that DIM had a protective effect on LPS-induced inflammatory injury in neonatal rat cardiomycocytes, and modulated the excessive production of pro-inflammatory cytokines IL-6, TNF-α and HMGB1 via suppressing the TLR-4/MAPKs signaling pathways.

**GW26-e4587**

**IL-24 gene protects against H2O2-mediated injury of human umbilical vein endothelial cells and may be useful as a treatment for cardiovascular disease**

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**OBJECTIVES** To investigate the protective effect of IL-24 on H2O2-induced vascular endothelial injury and to examine the association between IL-24 and cardiovascular disease.

**METHODS** Human umbilical vein endothelial cells (HUVECs) were treated with increasing concentrations of H2O2 in the presence or absence of IL-24, which was introduced via Lipofectamine 2000-mediated transfection. Successful uptake of IL-24 plasmid was confirmed by RT-PCR 24 hours post-transfection. The effect of H2O2 and IL-24 on HUVEC proliferation and migration was determined by migration assays. Cell viability was determined by CCK-8. Apoptosis and measurement of intracellular ROS levels were determined by flow cytometry. Real-time PCR and Western blot were used to detect levels of multiple cardiovascular disease-associated factors. Experiments were also performed in a rat hypertension model. RNA and protein levels of IL-24 were measured in both control and hypertensive rats; the effects of enalapril and nifedipine treatments on IL-24 levels were also examined.

**RESULTS** IL-24 protects against H2O2-mediated injury of human umbilical vein endothelial cells and might provide new benefits for the treatment of cardiovascular disease.

**GW26-e4589**

**Ctg/Tumor Necrosis Factor-Related Protein-9, a Novel Adipocyte-Derived Cytokine, suppresses high glucose-induced proliferation and collagen synthesis in rat cardiac fibroblasts**

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**OBJECTIVES** Ctg/TNF-related protein (CTRP 9) is an adipocytokine that is downregulated in obese mice. The objectives of the present study were to determine the effects of CTRP9 on high glucose (HG)-induced proliferation and collagen production in rat cardiac fibroblasts (GFs) and to investigate the molecular mechanism involved.

**METHODS** Rat CFs were cultured in Dulbecco’s modified Eagle’s medium, supplemented with 5.0 or 25 mmol/L D-glucose or 5.0 mmol/L D-glucose + 19.5 mmol/L mannose, in the presence of absence of CTRP 9. Proliferation was measured by the MTT assay, whereas the productions of IL-6, TNF-α and HMGB1 were measured with real-time PCR and the protein expression levels were examined with Western Blotting analysis.

**RESULTS** Our data showed that DIM could obviously attenuate the increased expression of cardiovascular disease-related factors. In vivo animal experiments showed that IL-24 expression was lower in hypertensive rats compared to healthy controls. Additionally, IL-24 levels increased following anti-hypertension therapy.

**CONCLUSIONS** IL-24 protects against H2O2-mediated injury, cell damage and might provide new benefits for the treatment of cardiovascular disease.

**GW26-e4642**

**The effects of AGES and RAGE on the accelerated progression of age-related intrarenal small arterial stiffness in hypertensive rats**

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**OBJECTIVES** To dynamically investigate the morphological change of age-related intrarenal small arterial stiffens (IRSA) in Spontaneously hypertensive rat (SHR) and Wistar-Kyoto (WKY) rats respectively and to explore the effects of Advanced glycation end-products (AGEs) and Receptor for AGES (RAGE) on the progression of age-related IRSA stiffness accelerated by hypertension.

**METHODS** SHR and WKY rats were respectively randomized into 4, 12, 24, 48 and 72-week-old group (n=16). Minimal renal vascular resistance (minRVR) was detected at each group. Renal arcuate arteries (RAA) and interlobular arteries (RILA) were analyzed by EVG, H&E, Sirius-red staining, z-smooth muscle actin (z-SMA) immunofluorescent technique and proliferating cell nuclear antigen (PCNA). AGES, RAGE immunohistochemical staining, and various morphological indexes and medial cell proliferation index (MIPI) were measured. The concentration of serum AGES was assessed by ELISA.

**RESULTS** The minRVR and the morphological indexes of medial nuclear area, medial collagen area and medial thickness of RAA and RILA had shown an age-dependent increase since 24w in SHR and 72w in WKY respectively, accompanied by the increased expression of RAGE in media. The expressions of AGES in serum and both IRSA media were also significantly elevated at 72w WKY consistently, while the levels of AGES began to increase from 48w in SHR. Interestingly, the collagen area and the expression of RAGE in RILA media at 12w SHR had begun to be much higher than that in 4w SHR group (p <0.05).

**CONCLUSIONS** Hypertension accelerates the progression of age-related intrarenal small arterial stiffness and the hypertension to