FUNCTIONAL ANALYSIS showed a significant molecular function and cellular structure. Significant gene transcripts have been proved to relate to biological processes. Transcripts were down-regulated in HUVECs treated with TXL. These associated with apoptosis, cell cycle pathway, enzyme, immunity protein, microtubular dynamic, nucleic acid binding, signal transduction. 3499 gene transcripts were up-regulated while 121 gene transcripts were down-regulated in HUVEC treated with TXL. These gene transcripts have been proved to relate to biological processes, molecular function and cellular structure. Significant changes were observed in genes involved in apoptosis, cellular proliferation, cell signal transduction and oxidative stress, including vascular endothelial growth factor (VEGF), IGF receptors, p42/44 mitogen activated protein (MAP) kinase, endothelial nitric oxide synthase (eNOS), chemokine (C-C motif) ligand 2 (CCL2), chemokine (C-C motif) ligand 5 (CCL5), chemokine (C-X-C motif) ligand 10 (CXCL10), and toll like receptor 3 (TLR3).

CONCLUSIONS TXL may protect endothelial function via the regulation of gene expression which involved in apoptosis, cellular proliferation, cell signal transduction and oxidative stress.

GW26-e4023 Prenatal Lipopolysaccharide Exposure Causes Mesenteric Vascular Dysfunction Through the NO-cGMP Pathway in Offspring

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OBJECTIVES Cardiovascular diseases, such as hypertension, could be programmed in fetal life. Prenatal lipopolysaccharide (LPS) exposure in utero results in increased blood pressure in offspring, but the vascular mechanisms involved are unclear. METHODS Pregnant Sprague-Dawley (SD) rats were intraperitoneally injected with LPS (0.79 mg/kg) or saline (0.5 ml) on gestation day 8, 10, and 12, and the vascular function was tested after treatment with vehicle or TEMPO in offspring at 15 weeks.

RESULTS The offspring of LPS-treated dams had higher blood pressure and decreased acetylcholine (ACh)-induced relaxation and increased phenylephrine (PE)-induced contraction in endothelium-intact mesenteric arteries. Endothelium removal significantly enhanced the PE-induced contraction in offspring of control but not LPS-treated dams. The arteries pretreated with L-NAME to inhibit nitric oxide synthase (eNOS) in the endothelium or ODQ to inhibit cGMP production in the vascular smooth muscle, had attained ACh-induced relaxation but augmented PE-induced contraction to a larger extent in arteries from offspring of control than those from LPS-treated dams. In addition, the endothelium-independent relaxation caused by sodium nitroprusside (SNP) was also decreased in arteries from LPS-treated dams. The function of vessels was accompanied by a reduction in the expression of eNOS and soluble guanylate cyclase (sGC) and production of NO and cGMP in arteries from offspring of LPS-treated dams. Furthermore, LPS-treated dam’s offspring arteries had increased oxidative stress and decreased anti-oxidative capacity. Three-week treatment with TEMPO, a reactive oxygen species (ROS) scavenger, normalized the alterations in the levels of ROS, eNOS, and sGC, as well as in the production of NO and cGMP and vascular function in the arteries of the offspring of LPS-treated dams.

CONCLUSIONS Prenatal LPS exposure programs vascular dysfunction of mesenteric arteries through increased oxidative stress and impaired NO-cGMP signaling pathway.

GW26-e4401 miR-195-3p/-5p decrease cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts

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OBJECTIVES MicroRNAs (miRNAs, miRs) contribute to many essential physiological and pathological processes including fibrosis. This study aims at investigating the role of miR-195-3p/-5p in cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts. METHODS Neonatal cardiac fibroblasts (NRCFs) were isolated and miR-195-3p/-5p was forced expressed with agomirRs. Proliferation as determined by EdU and Ki67 staining, α-SMA (a marker of myofibroblast transdifferentiation) was determined by quantitative reverse transcription polymerase chain reactions (RT-PCRs) and western blotting (WB). Target genes of miR-195-3p/-5p were detected by WB.

RESULTS In isolated primary neonatal cardiac fibroblasts (NRCFs), forced expression of miR-195-3p/-5p with agomirRs could attenuate fibroblast proliferation as determined by EdU and Ki67 staining while inhibition of miR-195-3p/-5p with antagonomirRs could increase fibroblast proliferation. By quantitative reverse transcription polymerase chain reactions (RT-PCRs) and western blotting (WB), α-SMA (a marker of myofibroblast transdifferentiation) was found to be suppressed in the miR-195-3p/-5p agomiR-treated NRCFs at both mRNA and protein levels, while was increased in the miR-195-3p/-5p antagonomir-treated NRCFs. Moreover, Chek-1 was identified as a target gene of miR-195-3p/-5p responsible for cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts by RT-PCR and WB and immunofluorescent staining. Silencing of Chek-1 attenuates cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts as detected by α-SMA/EDU staining. In addition, Chek-1 mediated the effects of miR-195-3p/-5p in cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts.

CONCLUSIONS miR-195-3p/-5p decrease cardiac fibroblast proliferation and the transdifferentiation into myofibroblasts. Therefore, miR-195-3p/-5p might be promising therapeutic targets for cardiac fibrosis.

GW26-e4425 Effect of Extract of Leaves of Ginkgo biloba pretreatment on rat Cardiomyocytes with hypoxia / reoxygenation injury

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OBJECTIVES To study the effect and mechanism of Extract Leaves of Ginkgo biloba (EGb) pretreatment on rat Cardiomyocytes with hypoxia/reoxygenation (H/R) injury. METHODS Cardiomyocytes were pre-incubated with extract leaves of Ginkgo biloba, hypoxia reoxygenation model on myocardial ischemia reperfusion injury after 2 h, and then detected the cell viability, MDA content, SOD activity and GSH / GSSG ratio. The effects of EGb on Keap1, Nrf2, GCLC and GSTP1 mRNA expression were determined by RT-PCR method.

RESULTS The cell viability, SOD activity and GSH/GSSG ratio of EGb pretreatment group increased significantly compared with H/R group, whereas the MDA content reduced significantly; Keap1 mRNA expression reduced significantly, while Nrf2, GCLC and GSTP1 mRNA expression increased significantly, and the difference among the three concentrations were conspicuous; these changes were reversed after ATRA added.

CONCLUSIONS EGb plays a protection role in cardiomyocytes H/R injury, and its mechanism was associated with Keap1 / Nrf2 / ARE signaling pathway.

GW26-e4505 Type 2 Ryanoide Receptor Hyperphosphorylation Plays a Role in the Development of Hypertensive Heart Failure

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OBJECTIVES Type 2 ryanodin receptor (RYR2) hyperphosphorylation plays an important role in the development of myocardial infarction caused heart failure (HF). However, it remains unclear whether there is similar process in the development of hypertensive left ventricular hypertrophy (LVH) and heart failure (HF). We tested the hypothesis that RYR2 hyperphosphorylation also plays an important role in the development of hypertensive LVH and HF.

METHODS Hypertensive LVH (70% diameter stenosis, n=16) and HF (90% diameter stenosis, n=12) rabbit models were prepared through