CONCLUSIONS The TT genotype and T allele of rs2617849 in g78 gene could be a risk genetic marker of T2DM in Han population in China. In contrast, the CC genotype and C allele of rs2617849 in g78 gene could be a protective genetic marker of T2DM in Han population in China.

GW26-e4586 Endothelin-1 Upregulates CTRP9 Gene Expression in Cardiomyocytes
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OBJECTIVES CTRP9/TNF-related protein (CTR9) 9, as an adipocytokine, is a potential therapeutic target for cardiovascular and metabolic disorders. This study aims to investigate the effects of Endothelin-1 (ET-1) on CTRP9 gene expression and the underlying mechanisms in hypoxic cardiomyocytes.

RESULTS ET-1 was found to cause a significant time- and dose-dependent increase in CTRP9 gene expression, and this effect was inhibited by the ET type A receptor (ETAR) antagonist BQ-610 but not by the ETBR antagonist BQ-788. To explore the underlying mechanism, we examined the involvement of the cAMP-dependent protein kinase A, phospholipase A2, protein kinase C, and MAPK mediated pathways using inhibitors and found that only PD98059, an inhibitor of MAPK/ERK kinase activity, could activate the ERKs, prevented ET-1-induced up-regulation of CTRP9.

CONCLUSIONS These data suggest a mechanism whereby ET-1 upregulates CTRP9 gene expression in NRVMs via the ET type A receptor/ MAPK/ERK signaling pathway.

GW26-e4778 Constitutive Expression of IGF-1 in BMSCs Improves Migration, Attenuates Cardiomyocyte Apoptosis and Promotes Cardiac Function After Acute Myocardial Infarction in Rats
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OBJECTIVES In this study, we explored the potential role of intramyocardial BMSCs-IGF-1 transplantation in reducing cardiomyocyte apoptosis, mediating cell migration and restoring myocardial function.

METHODS BMSCs were lentivirally transduced to express stable IGF-1 transgene. On the other hand, MI and U0126, inhibitors that blocked MAPK/ERK kinase mediated pathways using inhibitors and found that only PD98059, an inhibitor of MAPK/ERK kinase activity, could activate the ERKs, prevented ET-1-induced up-regulation of CTRP9.

RESULTS ET-1 was found to cause a significant time- and dose-dependent increase in CTRP9 gene expression, and this effect was inhibited by the ET type A receptor (ETAR) antagonist BQ-610 but not by the ETBR antagonist BQ-788. To explore the underlying mechanism, we examined the involvement of the cAMP-dependent protein kinase A, phospholipase A2, protein kinase C, and MAPK mediated pathways using inhibitors and found that only PD98059, an inhibitor of MAPK/ERK kinase activity, could activate the ERKs, prevented ET-1-induced up-regulation of CTRP9.

CONCLUSIONS These data suggest a mechanism whereby ET-1 upregulates CTRP9 gene expression in NRVMs via the ET type A receptor/MAPK/ERK signaling pathway.

GW26-e5332 Downregulation of MicroRNA-17 Improves Cardiac Function After Myocardial Infarction Via Attenuation of Apoptosis in Endothelial Cells
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OBJECTIVES Impairment of microcirculation is one of the major reasons for the aggravation of cardiac function after myocardial infarction (MI). Studies have indicated that microRNA - 17 (miR-17) has the ability to inhibit angiopoiesis in tumors. Here we hypothesized that downregulation of miR-17 might enhance cardiac function after MI though improving endothelial function and increasing the density of new blood vessels after MI.

METHODS Human umbilical vein endothelial cells (HUVECs) were infected with adenovirus containing pre-miR-17,antagonmir-17 or control adenovirus (Ad(N)) for miR-17 over expression (Ad-Pre-miR-17) or miR-17 silencing (Ad-Antagon-mir-17). Apoptosis was induced and determined by Annexin V-7AAD/PI. Real time RTPCR was used to evaluate levels of miR-17 and ERK. Protein levels of ERK and apoptosis proteins including bcl-2,bax,caspas3 and casp9 were determined by western blot In vivo, MI model was established in SD male rats. Adenoviruses (5109/100ml) mentioned above were injected in left apex of heart. Cardiac function was evaluated by echocardiography before models were built, and reevaluated at 7 days or 28 days after MI. Followed with echocardiography cardiac tissue of infarction border area was removed for histological examination, real time RT-PCR and western blot, as described above.

RESULTS MiR-17 level was down regulated by 23% in Ad-Antagomir-17 group, but up regulated 2.7-fold in Ad-Pre-miR-17 group (p <0.05). ERK pathway could be stimulated by miR-17 silencing, which demonstrated increased levels of phosphorylated ERK(ERK) and anti-apoptosis protein bcl-2 and 1.4-fold and 1.40-fold. However, apoptosis proteins, including bax,caspas3, casp9 were decreased by 23.1%,29.2%,33%, respectively (p <0.05). ERK pathway could be stimulated by miR-17 silencing, which demonstrated increased levels of phosphorylated ERK(ERK) and anti-apoptosis protein bcl-2 and 1.4-fold and 1.40-fold. However, apoptosis proteins, including bax,caspas3, casp9 were decreased by 23.1%,29.2%,33%, respectively (p <0.05).

CONCLUSIONS Apoptosis in ECs could be inhibited by down regulation of miR-17 could enhance the heart ejection fraction (EF) by 2.18-fold at 7 days, and 2.24-fold at 28 days (p <0.05). After 7day MI or 28day MI, histological examination showed that infarction areas and collagen fiber were decreased by 43.7% and 73.2%,53.3% and 61.1%, respectively in AD-Antagon-mir-17 group (p <0.05). Tunel staining showed that down regulation of miR-17 could attenuate apoptosis of cardiac tissue compared to Ad(N) group (0.23 ±0.101 vs. 0.61±0.056,0.20±0.0108 vs. 0.41±0.038, p <0.05). CD31 staining also indicated that miR-17 silencing could promote endothelial growth after MI(0.814±0.047 vs.0.360±0.166,0.736±0.069 vs.0.432±0.181,p <0.05).

CONCLUSIONS Apoptosis in ECs could be inhibited by down regulation of miR-17, though ERK pathway. Down regulation of miRNA17 could improve cardiac function after myocardial infarction via attenuation of apoptosis in endothelial cells.

GW26-e0112 Curcumin Modulates Macrophage Polarization Through the Inhibition of the Toll-Like Receptor 4-Mitogen Activated Protein Kinase/Nuclear Factor-κB Pathways
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OBJECTIVES Curcumin, the active ingredient in curcuma rhizomes, has a wide range of therapeutic effects. However, its anti-inflammatory activity in human acute monocyctic leukemia THP-1 cells remains unclear. We investigated the activity and molecular mechanism of action of curcumin in polarized macrophages.

METHODS Phorbol myristate acetate (PMA)-treated THP-1 cells were differentiated to macrophages, which were further polarized to M1 cells by lipopolysaccharide (LPS; 1 ng/mL) and interferon (IFN)-γ (20 ng/mL) and treated with varying curcumin concentrations. [H] thymidine ([H]-Tdr) incorporation assays were utilized to measure curcumin-induced growth inhibition. The expression of tumor necrosis factor-α (TNF-α), interleukin (IL)-6, and IL-12 were measured.