can lead to end-stage cardiac failure. MicroRNAs (miRNAs, miRs) participate in many essential biological processes and their dysfunction has been implicated in a variety of cardiovascular diseases including fibrosis. miR-433 has recently been implicated in renal fibrosis, however, its role in cardiac fibrosis is unclear.

METHODS Cardiac fibrosis were induced by TGF-β (10ng/ml, 24h) and AngII (100nmol, 48h) on neonatal cardiac fibroblasts. Quantitative reverse transcription polymerase chain reactions (RT-PCRs), immunoﬂuorescence and western blotting were used to determine the expression levels of cardiac fibrosis, including-z-SMA and collagen. EdU and Ki-67 staining were used to evaluate cell proliferation.

RESULTS miR-433 was increased in heart samples from dilated cardiomyopathy patients. In addition, miR-433 was also consistently upregulated in mice model of cardiac fibrosis after myocardial infarction or heart failure. Additionally, miR-433 was found to be enriched in fibroblasts compared to cardiomyocytes. In neonatal cardiac fibroblasts, forced expression of miR-433 promoted cell proliferation as indicated by EdU and Ki-67 staining. Moreover, miR-433 overexpression promoted the transdifferentiation of fibroblasts into myofibroblasts as determined by z-SMA and collagen whether in the presence of TGF-β, AngII or not, indicating that miR-433 is sufficient to induce fibrosis. In addition, knockdown of miR-433 will partially attenuate the transdifferentiation into myofibroblasts, indicating that miR-433 is required for cardiac fibrosis. Interestingly, miR-433 did not affect the migration of cardiac fibroblast. Importantly, miR-433 antagonism could partially attenuate cardiac fibrosis induced by myocardial infarction in mice.

CONCLUSIONS miR-433 controls cardiac fibrosis both in vitro and in vivo. Inhibition of miR-433 represents a novel therapeutic strategy for cardiac fibrosis.

GW26-e3832 Rosuvastatin Improves Atherosclerotic Plaques Stability: An Intravascular Ultrasound Elastography Study
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OBJECTIVES The present study aimed to investigate the association between potent rosuvastatin therapy and plaque mechanical stabilization imaged by IVUSE.

METHODS 14 purebred New Zealand rabbits underwent a high-cholesterol diet, then balloon-induced abdominal aorta endothelium injury after 2 weeks. Seven rabbits received potent rosuvastatin treatment for 8 weeks since the 13th week, while the seven other rabbits took in saline. Intravascular ultrasound (IVUS) images of abdominal aortas were acquired before and after the administration. Each rabbit were chosen 2 obvious atherosclerotic plaques and 2 consecutive frames near the end-diastole images in situ were used to construct an IVUS elastogram.

RESULTS Plaques in the rosuvastatin group demonstrated a stable magnitude of shear strain (SS) and area strain (AS) in the total plaque (2.23±2.62% vs. 1.58±1.67%, p = NS; 3.84±4.63% vs. 2.93±2.36%, p = NS, respectively), but the untreated rabbits displayed a signiﬁcantly reduced SS and AS index (1.91±1.05% vs. 3.54±1.73%, p < 0.005; 3.46±2.10% vs. 5.95±2.59%, p = 0.008; respectively). Differences of the changes in SS and AS between the rosuvastatin and control groups on serial follow-up were signiﬁcant (-0.99±2.83% vs. 1.15±1.96%, p = 0.013; -1.67±5.05% vs. 1.25±2.29%, p = 0.022; respectively). SS and AS were negatively correlated with collagen (r2 = 0.341, p = 0.001 and r2 = 0.222, p = 0.002, respectively) and smooth muscle cell content (r2 = 0.308, p = 0.002 and r2 = 0.277, p = 0.004, respectively) and positively with macrophage (r2 = 0.266, p = 0.005 and r2 = 0.198, p = 0.018, respectively), lipid content(r2 = 0.288, p < 0.001 and r2 = 0.357, p = 0.001, respectively) and vulnerability index (r2 = 0.557, p < 0.001 and r2 = 0.483, p < 0.001, respectively).

CONCLUSIONS These findings prove rosuvastatin therapy is associated with less vulnerable plaque features. IVUSE provides a technique that may develop into a clinically available tool for detecting vulnerable plaques and monitoring treatments.

GW26-e3859 Atorvastatin Calcium Inhibits Phenotypic Modulation of PDGF-BB-Induced VSMCs Via Down-Regulation the Akt Signaling Pathway
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OBJECTIVES Plasticity of vascular smooth muscle cells (VSMCs) plays a central role in the onset and progression of proliferative vascular diseases. In adult tissue, VSMCs exist in a physiological contractile phenotype, which is defined by lack of the capacity of proliferation and migration, while high expression of contractile marker proteins. After injury to the vessel, VSMC shifts from a contractile phenotype to a pathological synthetic phenotype, associated with increased proliferation, migration and matrix secretion. It has been demonstrated that PDGF-BB is a critical mediator of VSMCs phenotypic switch. Atorvastatin calcium, a selective inhibitor of 3-hydroxy-3-methyl-glutaryl 1 coenzyme A (HMG-CoA) reductase, exhibits various protective effects against VSMCs. In this study, we investigated the effects of atorvastatin calcium on phenotype modulation of PDGF-BB-induced VSMCs and the related intracellular signal transduction pathways.

METHODS VSMCs were grown to 70-80% confluence and pre-cultured in serum-free medium for 24h before treatment. Atorvastatin calcium dissolved in ethanol for a stock solution of 100mM and then diluted to desired concentrations with media prior to cell treatment. Cells were treated with various concentrations of atorvastatin calcium from 1 to 50M in cell proliferation assay, 10M in cell morphology and western blotting on quiescent cells with or without 20ng/ml PDGF-BB for designated times.

RESULTS Treatment of VSMCs with atorvastatin calcium showed dose-dependent inhibition of PDGF-BB-induced proliferation. Atorvastatin calcium co-treatment inhibited the phenotype modulation and cytoskeleton rearrangements and improved the expression of contractile phenotype marker proteins such as -SMA actin, SM22a and calponin in comparison with PDGF-BB alone stimulated VSMCs. Although Akt phosphorylation was strongly elicited by PDGF-BB, Akt activation was attenuated when PDGF-BB was co-administrated with atorvastatin calcium.

CONCLUSIONS In conclusion, atorvastatin calcium inhibits phenotype modulation of PDGF-BB-induced VSMCs and activation of the Akt signaling pathway, indicating that Akt might play a vital role in the modulation of phenotype.

GW26-e4374 Tanshinone IIA Protects H9c2 Cells From Oxidative Stress-Induced Cell Death Via Up-Regulation of MicroRNA-133 and Akt Activation
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OBJECTIVES In this study the cardioprotective effect and molecular mechanisms of tanshinone IIA were investigated.

METHODS Cardiac H9c2 cells were cultured in Dulbecco’s modiﬁed Eagle’s medium supplemented with 10% fetal bovine serum. For transfection experiments, cells were transfected with 50 nM miR-133 mimic or inhibitor; 8 hours later transfected cells were treated for 24 hours with various combination of H2O2 and tanshinone IIA as indicated in ﬁgure legends. For inhibitor experiments, cells were pre-incubated with selective Pi3K inhibitor for 30 min, then treated with H2O2 and/or tanshinone IIA. Cell viability was determined by CCK-8. Data were presented as percentage of control. MiR-133 expression levels were relatively quantiﬁed by Bulge-Loop™ miRNA qRT-PCR Primer Set in conjunction with real-time PCR with SYBR. The relative expression of miR-133 was calculated and normalized to U6 using the comparative Ct method. Relative expression values were calculated as 2-ΔΔCt. After treatment H9c2 cells were harvested and lysed in RIPA lysis buffer (Applygen Technologies Inc. Beijing, China). Then the whole cell lysates were resolved by 12% sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and transferred onto a 0.4 um PVDF membrane. After blocking in 5% nonfat milk for 2 h at room temperature, the PVDF membranes were probed with primary antibody overnight. Following a 30 minute wash, the membranes were incubated with secondary antibody conjugated to HRP for 1 hour at room temperature. The membranes were then washed for 30 minutes and