Results: Our results demonstrate that the cell viability significantly decreased to 66.39 ± 4.84% of the control levels following H/R, the cell viability markedly improved in lycopene + H/R (P < 0.01). The results from flow cytometer with Annexin V and PI double-staining illustrated that after exposure to H/R, apoptotic percentage significantly increased to 26.42 ± 2.71% (P < 0.01), while that of control and lycopene group were 4.96 ± 1.51% and 4.69 ± 1.42%, respectively. In contrast, lycopene + H/R markedly prevented the H/R-induced apoptosis (16.38 ± 2.12%, P < 0.01). Compared to control and lycopene, the expression of GRP78 protein increased more than two-fold in H/R treatment (P < 0.01), while the expression of GRP78 protein only increased to 1.68-fold in lycopene + H/R (P < 0.01). In addition, H/R treatment evoked a significant increase in GADD153/CHOP mRNA compared to control groups (P < 0.01). However, the GADD153/CHOP mRNA expression was markedly down-regulated to 1.68-fold of control levels with lycopene pretreatment (P < 0.01). Furthermore, the caspase-12 mRNA expression was also significantly increased in H/R-treatment (1.82 folds of control group, P < 0.05). However, pretreatment with lycopene efficiently reduced caspase-12 mRNA expression caused by H/R treatment.

Conclusions: These findings reveal that lycopene protects against H/R injury by attenuation of ER stress and ER stress-induced apoptosis in primary cultured cardiac mouse cardiomyocytes; the protective effect of lycopene on cardiomyocytes-highlights the therapeutic potential of plant-derived antioxidants against ER-injury.

GW25-e5413
Elevated circulating BMP7 reflects dysfunction of pulmonary vasculature in PAH patients
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Objectives: This study aimed to show whether circulating BMPs levels are associated with phenotype and increased risk of mortality in PAH patients.

Methods: Circulating BMPs were measured by ELISA in plasma samples from 10 patients with PAH and 16 corresponding unaffected relatives with BMP2 mutations. We also explored the role of BMPs in PAH in n=43, unrelated PAH (n=113) and normal controls (n=51).

Results: Circulating BMP7 concentrations but BMP2 and BMP4 were greatly increased in the 10 PAH patients compared with their unaffected relatives. Receiver operating characteristic (ROC) curves indicated that BMP7 concentration of 13.9 pg/ml could discriminate unaffected mutation carriers from affected mutation carriers with 70.0% sensitivity and 93.8% specificity. PAH patients had significantly higher BMP7 concentrations than PAH patients and controls (20.1 (2.8-95.5) vs. 6.5 (0.6-41.3) and 2.5 (0.1-31.8) pg/ml respectively, P < 0.001). Elevated plasma BMP7 concentrations were associated with a higher risk of mortality after adjustment for age, sex, 6-minute walk distance, mean pulmonary arterial pressure, pulmonary vascular resistance, and cardiac output (HR = 2.674, 95% CI 1.152-6.211; P = 0.022).

Conclusions: Elevated circulating BMP7 reflects dysfunction of pulmonary vasculature and serve as a specific biomarker of disease progress in patients with PAH.

GW25-e0523
Interaction of HSF1 and Smad3 inhibits cardiac fibrosis and maladaptive hypertrophy induced by pressure overload
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Objectives: Heart failure was induced by chronic rapid right ventricular pacing at 200 beats/min respectively for 3 weeks and 6 weeks in dogs. Sham-operation was performed in another 6 dogs as control. Pan-microvessel density (MVD) was assessed by CD31 and neovascularization was increased by CD105.

Results: Three-week tachycardia pacing induced mild/moderate heart failure and 6-week pressure could induce severe heart failure. Mean CD31-MVD and CD105-MVD were signiﬁcantly increased after 3-week pacing. However, CD31-MVD was significantly decreased by 80% in 6-week pacing group compared with 3-week pacing group, whereas CD31-MVD was only decreased slightly (10%; P < 0.05). Myocardial proangiogenic factors stromal cell-derived factor 1 (SDF-1), hypoxia-inducible factors 1α (HIF-1α, a transcription factor which could regulate SDF-1 expression), serum SDF-1 levels and circulating EPCs mobilization greatly elevated after 3 weeks pacing but returned to baseline after 6 weeks pacing. Our results showed that there were changes of the neovascularization levels assessed by CD105. Angiogenesis and migrating ability of EPCs were enhanced after stimulation of SDF-1, which could be abolished by pretreatment with SDF-1 receptor antagonist AMD3100. In addition, angiogenesis and migrating functions of EPCs were significantly enhanced by the serum from 3-week pacing dogs, but had much weaker response to the serum from 6-week pacing dogs.

Conclusions: Tachycardia pacing induced non-ischemic heart failure, promoted myocardial neovascularization and mobilized circulating EPCs, which might be mediated partly through SDF-1 pathway.

GW25-e5314
BS-KS treatment improves LPA-stimulated endothelial hyperpermeability via RhoA/ROCK pathway
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Objectives: Endothelial hyperpermeability is a signiﬁcant problem in many cardio-vascular disorders, including vascular inﬂammation, ischemia-reperfusion injury, thrombosis and atherosclerosis. BS-KS, total traditional Chinese medicines, has been used for many years in China to treat cardiovascular disease. Our previous experiments have revealed that BS-KS could anti-lipid peroxidation injury, protect endothelial cell function, stabilize Atherosclerotic plaque, and prevent the development of Atherosclerotic. While the mechanisms remain elusive. This study examined whether BS-KS exerted anti-hyperpermeability effect in EA.hy926 cells through the RhoA/ROCK pathway.

Methods: Transwell chamber model was used to study the permeability changes of endothelial cells and it was quantiﬁed by assessing leakage of FITC-dextran. FITC-Phalloidin immunofluorescence staining was employed to observe the enhanced changes in the distribution of F-actin. And the determination of expression of proteins associated RhoA/ROCK pathway was dependent on Western Blot and Q-PCR methods.

Results: The level of endothelial cell (EA.hy926) permeability was increased in LPA treatment group. Western Blot with the model group, BS-KS treated group signiﬁcantly attenuated effects of LPA on cells’ hyperpermeability responses (P < 0.05). Immunofluorescence showed that treatment of cells reduced stress ﬁber formation. At the same time, RhoA activity was inhibited, and P-MLC and ROCK2 expression was signiﬁcantly downregulated, while GAPDH mRNA and protein levels (P < 0.05 or P < 0.01).

Conclusions: BS-KS has a role in protecting endothelial cells and inhibiting LPA-induced endothelial hyperpermeability response. Which may be achieved by...