Results 1. In addition to expressing characteristic hHCN4 protein, mHCN4-transfected hMSCs also express an anticipated high level of hHCN4 gene by RT-PCR and Western blot analysis. And immunofluorescence image is shown for GFP. Control MSCs were negative. 2. With the use of the whole cell configuration of the patch-clamp technique, I_f was elicited using hyperpolarizing steps in 10-mV increments from -40 mV to -140 mV from a holding potential of -40 mV and was voltage-dependent. The threshold of voltage for activation of I_f is around -80 mV. Remarkably, all hHCN4 positive cells exhibit a large caesium-sensitive I_f and it was significantly inhibited by 4 mM caesium chloride.

Conclusions The pacemaker current of I_f can be elicited from the mesenchymal stem cells transfected with HCN4 genes by LentiV. The genetically engineered MSC expressing hHCN4 is a demonstration of feasibility of preparing MSC-based biological pacemaker cells.

e0032 ROLE OF ATRIAL SUBSTRATE REMODELLING IN INDUCIBILITY OF ATRIAL FIBRILLATION AFTER EPICARDIAL GANGLIONIC PLEXI ABLATION

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Objective Investigating the long-term effect of ganglionated plexi (GP) ablation on atrial fibrillation (AF) after GP ablation.

Methods 13 dogs were randomly divided into sham-operated group and GP ablation group. All animals underwent a right thoracotomy at the 4th intercostal space. Induced AF and atrial effective refractory period (AERP) were measured by burst rapid pacing at right atrium. After anterior right GP and inferior right GP ablation, AF and AERP were measured again in the GP ablation group. The animals were allowed to recover for 8 weeks, after which, AF and AERP was measured again. The levels of atrial natriuretic peptide (ANP), TNF- α and interleukin (IL)-6 in blood and atrial tissues were examined. Immunocytochemical staining of cardiac nerves was performed in tissues from the dogs.

Results AF was easily induced in the GP ablation group after 8 weeks while AF was not observed in the sham-operated group, and immediately after GP ablation. AERP and dispersion of AERP (dAERP) were increased after GP ablation, while AERP recovered after 8 weeks. Compared with sham-operated group, the levels of ANP, TNF- α and IL-6 in the right atrium increased significantly 8 weeks after GP ablation (204.6 ± 31.2 vs 299.1 ± 32.5 ; 1.3 ± 0.5 vs 4.7 ± 0.7 ; 0.9 ± 0.3 vs 1.8 ± 0.5 ; $p < 0.05$). In GP ablation group, the density of GAP43-positive, TH-positive and ChAT-positive nerves in the right atrium was 821 ± 752 , 481 ± 627 and 629 ± 644 per mm^2 , respectively, which was significantly ($p < 0.01$) lower than the nerve density in sham-operated tissues (2590 ± 841 , 1752 ± 605 and 3147 ± 886 per mm^2 , respectively).

Conclusion Atrial substrate remodelling after GP ablation may be the mechanism of induced AF.

e0033 MECHANISMS OF LOSARTAN ATTENUATES VENTRICULAR REMODELLING AND CARDIAC FUNCTION IN AORTIC BANDED RATS WITH CHRONIC HEART FAILURE

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Objective To investigate the regulation of Losartan (Los) on ventricular remodelling and cardiac functioning chronic heart failure rats induced by aortic banded.

Methods Sprague-Dawley (SD) rats underwent abdominal aorta coarctation to induce CHF, confirmed by ultrasound cardiograph and Catheterisation, or sham operation, followed by 8 weeks treatment with Losartan (20 mg/kg per day, orally) or vehicle (drinking water). Plasma norepinephrine (NE) was measured by ELISA, and plasma and tissue angiotensin II (Ang II) levels were measured using RIA. Cardiomyocyte apoptosis was examined by agarose gel electrophoresis and TUNEL's method. The mRNA levels of Bax and Bcl-2 were determined by RT-PCR and the protein expression of phosphorylated and total Akt (t-Akt and p-Akt) were assessed by Western blot.

Results Losartan-treated CHF rats had lower left ventricular end-diastolic pressure (LVEDP) [COA+Los: (11.47 ± 5.06) mm Hg vs COA+Vehicle: (21.18 ± 6.56) mm Hg, $p < 0.01$], higher left ventricular ejection fraction (LVEF) [COA+Los: (63.28 ± 4.32)% vs COA+Vehicle: (43.27 ± 4.25)%, $p < 0.05$] and lower left ventricle/body weight ratios [COA+Los: (2.41 ± 0.15) mg/g vs COA+Vehicle: (3.12 ± 0.18) mg/g, $p < 0.05$], lower plasma NE [COA+Los: (682.24 ± 64.66) pg/ml vs COA+Vehicle: (908.24 ± 75.10) pg/ml, $p < 0.05$] and myocardium Ang II [COA+Los: (60.15 ± 6.22) pg/mgprot vs COA+Vehicle: (92.31 ± 8.31) pg/mgprot, $p < 0.05$], but higher plasma Ang II [COA+Los: (629.68 ± 85.71) pg/ml vs COA+Vehicle: (475.67 ± 51.12) pg/ml, $p < 0.05$] than vehicle-treated CHF rats. Losartan-treated HF rats had no obviously "DNA ladder" which was the character of apoptosis, and the apoptosis index was also reduced [COA+Los: (5.49 ± 0.45)% vs COA+Vehicle: (9.62 ± 0.51)%, $p < 0.05$] with a lower express of Bax/Bcl-2 gene [COA+Los: (109.58 ± 7.53)% vs COA+Vehicle: (136.76 ± 8.82)%, $p < 0.05$] and a higher protein expression of p-Akt [COA+Los: (70.80 ± 6.40)% vs COA+Vehicle: (50.30 ± 4.80)%, $p < 0.05$].

Conclusion Losartan might inhibit cardiomyocyte apoptosis and improve cardiac function in aortic banded rats by blocking Ang II to bind AT₁-R and promoting the activation of Akt.

Conclusion Los attenuated ventricular remodelling and improve cardiac function in aortic banded rats by blocking angiotensin II to bind AT₁-R and reducing angiotensin II, aldosterone and inflammatory cytokine in myocardium.

e0034 INHIBITION OF ATORVASTATIN ON THE AUTOPHAGY OF VASCULAR ENDOTHELIAL CELLS

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Objective To explore the mechanism of atorvastatin's protection on vascular endothelial cells, we conducted the research of impact of atorvastatin on vascular endothelial cells autophagy in different times.

Methods We used the Hank's to replace the normal medium to induce autophagy of vascular endothelial cells. In pre-inducement and induction procedure, the cells were incubated with normal medium which includes atorvastatin or not and Hank's, respectively. Experimental cells were randomly divided into four groups: control group (Group I), the group of pre-inducement with atorvastatin (Group II), the group of inducement with atorvastatin (Group III) and the group of pre-inducement and inducement both with atorvastatin (Group IV). Transmission electron microscope (TEM) was used to detect autophagy. The RT-PCR was employed to detect the autophagy-specific markers' (Beclin 1 and Map1lc3) expression in each group of cells.

Results Compared with the group I, target genes (Beclin 1 and Map1lc3) of the group III and the group IV had a significant decreased expression ($p < 0.01$). The expression of the group II were all lower than the group I ($p > 0.05$). The group IV was better than the group III ($p > 0.05$). Via TEM detection, the cells showed typical