These cule 1, 3-nitrotyrosine and 4-hydroxy-2-nonenal in the aorta. mediated diureis and natriuresis is impaired. However, the underlying mechanisms are not clear. G protein-coupled receptor kinase 4 (GRK4), whose gene locus 4p16.3 is linked to essential hypertension, cause sodium retention and increase blood pressure via impairment of renal dopamine receptor and enhancement of renin-angiotensin system functions. Due to the higher activity of GRK4 in kidney from spontaneously hypertensive rats (SHRs) and hypertensive patients, we hypothesize that GRK4 might be the cause of ETBR impairment in hypertension.

Methods: Experiments were carried out in male anaesthetised spontaneously hypertensive rats (SHR) and in normotensive Wistar-Kyoto (WKY) rats. The ETBR agonist, BQ-3020 (0.1,0.5,1.0μg/kg/min) were infused via supra-renal artery at a rate of 0.04ml/min for 40 minutes. The same experiments were conducted in GRK4 A142V and GRK4 Wild Type transgenic mice. The ETBR function were also checked in the wild-type and A142V transfected renal proximal tubule (RPT) cells from mice.

Results: We found that diuresis and natriuresis of ETBR agonist, BQ3020, in Wistar-Kyoto (WKY) rats, which was impaired in SHRs. The GRK4 expression was higher in renal cortex from SHRs as compared with WKY rats. In GRK4 A142V transgenic mice, it revealed that ETBR-mediated diuresis and natriuresis was impaired compared with Wild type. In wild-type transfected cells, activation of ETBR inhibited Na+-K+-ATPase activity; while in A142V transfected cells, the inhibitory effect was lost. There are co-localization and co-immunoprecipitation between ETBR and GRK4 in RPT cells. The linkage of ETBR/GRK4 was higher in wild-type cells than in A142V cells. Similar phenomenon was found in the kidney from WKY and SHRs, SHRs had higher ETBR/GRK4 linkage, accompanied with higher ETBR phosphorylation, which might account for the impaired ETBR function in hypertension.

Conclusions: This study provides a mechanism by which GRK4, via regulation of renal ETBR function, participates in the pathogenesis of hypertension.

GW25-e0055
Cardiac Electrical Activity Improved by Overexpression of the Sarcolemmal Reticulum Ca2+-ATPase in Rat Myocardial Failure After Myocardial Infarction Evaluated by Microelectrode Arrays Technology
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Objectives: To explore overexpression recombinant adenovirus (rAd) -mediated sarcoplasmic reticulum Ca2+-ATPase (SERCA2a) for cardiac rhythmicity and conductivity in rat heart failure after myocardial infarction and its possibly electrical mechanisms.

Methods: 26 adult male SD rats were randomly divided into three groups: sham group (n=10), rAd.β-gal group (n=8) and rAd.SERCA2a group (n=8). Sham operation consisted of thoracotomy and cardiac exposure but without coronary artery ligation. RAd.β-gal group and rAd.SERCA2a group were ligated the left anterior descending coronary artery for rat heart failure animal model after myocardial infarction, while the transfecting β-gal and SERCA2a gene into heart respectively. We used ultrasound electrocardiogram for evaluating cardiac diastolic and systolic function, ECG monitoring and microelectrode arrays (MEA) technology for myocardium electrical activity in vitro.

Results: rAd carrying SERCA2a and β-gal gene were successfully transfected in heart failure rats. rAd.SERCA2a group could improve failing heart function, the ventricular end diastolic volume, left ventricular end-systolic volume, left ventricular ejection fraction and fractional shortening. Compared with the SERCA2a group, ECG could be found that QT interval prolonged (94.75±1.55 ms vs.111.02±5.24 ms, n=6, P<0.05) and the incidence rate of premature ventricular contractions (PVC) was 71.5% in rAd.B-gal group, but in rAd.SERCA2a group QT interval shortened and the incidence rate of PVC was 14.3%. No significant difference in the heart rate of rAd.SERCA2a group by MEA records. However, compared with the rAd.β-gal group, the maximum field potential, the minimum field potential and field potential duration were prolonged (0.64 mV±0.13 ms vs. 0.82 mV±0.39 ms, 1.35 mV±0.57 ms vs. 1.88 mV±0.57 ms, 113.23 ms±12.02 ms vs. 124.17 ms±21.80 ms, respectively, n=6, P<0.05) in rAd.SERCA2a group. The field potential duration were statistically different between the infarct zone and the contralateral normal zone (60.36 ±2.08 ms vs. 103.24 ms±7.35 ms, n=5, P<0.05) in rAd.β-gal group, and field potential duration dispersion in infarct zone with 60 channels record was larger than rAd.SERCA2a group. The conduction time was simultaneous in rAd.SERCA2a group, and the cardiac electro-conduction activity could keep consistency and improve in myocardial infarction tissue.

Conclusions: Overexpression of SERCA2a may significantly improve left ventricular systolic and diastolic function, as well as it may be reduced incidence of arrhythmias in heart failure model after myocardial infarction and may improve uniform conduction of cardiac electrical activity. MEA technology is an ideal technology for observing rhythm, frequency and conduction activities in cardiovascular disease animal models.

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Anti-inflammatory Effects of Tanshimone IIA on Oxidative-injured Vascular Endothelial Cells Are Mediated by Estrogen Receptor Activation and Through ERK Signaling Pathway
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Objectives: To investigate the estrogen protective effect and mechanism of Tan- shimone IIA on oxidative-injured vascular endothelial cells.

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