Conclusions: These results suggested an impact of which may contribute to metoprolol GW25-e4228 apoptosis by inhibiting oxidative stress.

GW25-e4168 Dipeptidyl peptidase (DPP-4 inhibitor exhibits anti-apoptosis effects in isoproterenol-induced myocardial infarcted rats by inhibiting oxidative stress

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Objectives: Cardiac apoptosis plays an important role in the pathology of myocardial infarction. The protective effects of Dipeptidyl peptidase (DPP-4) inhibitor (vildagliptin) on cardiac apoptosis were evaluated in isoproterenol induced myocardial infarcted rats.

Methods: Male Wistar rats are treated intravenously with Vildagliptin (2 mg/kg/day) during a period of 21 days. After 21 days of pretreatment, isoproterenol (100 mg/kg) was injected subcutaneously to rats at an interval of 24 h for 2 days (on 22th and 23th day) to induce myocardial infarction. Cardiac diagnostic markers, heart lipid peroxidation, antioxidant system, histopathological changes of the heart and apoptosis were evaluated in isoproterenol induced myocardial infarcted rats.

Results: Isoproterenol induced myocardial infarcted rats showed a significant increase in the levels of serum cardiac diagnostic markers, heart lipid peroxidation products and a significant decrease in the activities/levels of heart antioxidants, compared with normal rats. Additionally, Histopathological findings of myocardial infarced rats revealed marked necrosis. Further, Polymerase Chain Reaction study revealed an increase in the myocardial expression of Bax, caspase-8, caspase-9 and Fas genes and a decrease in the myocardial expression of Bcl-2 and Bcl-xL genes. Vildagliptin (2 mg/kg/day) pretreatment decreased the levels of serum cardiac marker enzymes, reduced heart lipid peroxidation and minimized the alterations the activities/levels of heart antioxidants of isoproterenol-induced myocardial infarcted rats. Histopathological study evidenced that the pretreatment with Vildagliptin inhibited myocardial damage. Vildagliptin pretreatment also showed protective effects on apoptosis. In the in vitro study also revealed the free radical scavenging and anti-apoptosis activity of Vildagliptin.

Conclusions: Thus, Vildagliptin protected the myocardial infarcted rats’ heart against apoptosis by inhibiting oxidative stress.

GW25-e4228 Effect of metoprolol on expression and vasodilatation function of AT2R in SHR

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Objectives: The interactional relationship between the sympathetic nervous systems (SNS) and the renin-angiotensin-aldosterone system (RAAS) has been revealed but thoroughly understood. Here, the authors report for the first time the expression of AT2R in myocardial tissue among all rats groups in transcription and translation levels, Real-time RT-PCR, Immunohistochemistry and Western blot were used to assay the expression of AT1-AR gene.

Methods: (1) Construct pAAV-ZsGreen+ADRB1-shRNA plasmid; pAAV-ZsGreen+ADRB1-shRNA plasmid was constructed according to shRNA principle and AT1-AR coding sequence in Genebank. Confirmed by enzyme digestion and gene sequencing, showing that 100% identical to its accession number. The plasmid was then packaged to recombinant adeno-associated virus named AAV9- shRNA-ADRB1-ZsGreen and harvested (viral titer was 1.5x10^{+5}IU/ml). (2) Spontaneously Hypertensive Rats treatments; 36 SHRs were grouped into six randomly as follows: Group 1, AAV9-shRNA-ADRB1-ZsGreen + metropol + control; Group 2, AAV9-shRNA-ADRB1-ZsGreen + kitazol + control; Group 3, AAV9-CMV-ADRB1: ZsGreen + metropol (n=6); Group 4, AAV9-CMV-ADRB1:ZsGreen + saline (n=6); Group 5, sham + metropol (n=6); Group 6, sham + saline (n=6). Metropol were given by gavage in 50mg/kg/d dose. All of them were monitored their blood pressure weekly. Rats were killed and dissected the myocardial tissue after 4 weeks. (3) The research on the expression of AT1-AR in myocardial tissue among all rats groups in transcription and translation levels, Real-time RT-PCR, Immunohistochemistry and Western blot were used to assay the expression of β1-AR gene.

Results: (1) Comparison of the AT1-AR expression among each group: Real-time RT-PCR results showed that AAV9-shRNA-ADRB1-ZsGreen injection could significantly decrease β1-AR mRNA expression compared with the negative control group (P < 0.05). Immunohistochemistry results showed that it could significantly decrease the β1-AR protein expression compared with the negative control and sham group (P < 0.05). Western blot results showed that it also could significantly decrease the β1-AR protein expression compared with the negative control group (P < 0.05). (2) Comparison of the antihypertensive effects among each group: After 4 weeks of the intervention, systolic blood pressure in group 1, group 2, group 3, group 5 was significantly lower than group 4 and group 6 (P < 0.05); After 4 weeks of metropol intervention, the SBP drop pressure amplitude of AAV9-shRNA-ADRB1-ZsGreen injection group were significantly lower than the negative control group and the sham control group (22.84±1.72 vs. 78.28±2.72 vs. 30.16±5.71, P < 0.05).

Conclusions: (1) The AAV9-shRNA-ADRB1-ZsGreen is successfully constructed and it can significantly reduce the β1-AR expression in myocardial of SHRs. (2) Knockdown of β1-AR in myocardial tissue of Spontaneously Hypertensive Rats resulted in worse antihypertensive response to metropol; it may be one of the reasons for influencing individual antihypertensive response to metropol.

GW25-e4377 Expression of ZO-1 in iPS cells Mediated by Lentiviral Vector

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Objectives: The fundamental researches of cardiovascular disease verified that intercalated disc-related gene ZO-1 varies in different myocardial pathologic conditions, and it can interact with CsA. This research is about to construct recombinant lentivirus over-expressing vector of porcine ZO-1 gene, to infect iPS cells, to obtain iPS cells carrying this target gene.

Methods: The ZO-1 gene sequence published on Genbank was analyzed, and designed a couple of primer containing both BamHI and SalI. The porcine ZO-1 gene was amplified by PCR, and cloned into lentiviral expression vector, to construct the recombinant Lentivirus-EFla-EGFP-TRE/ZO1 vector; the vector was confirmed by DNA sequencing. The production of lentivirus was obtained by using pSVSG, delta 8.91and fuguene to transfect 293T cells. The titer of lentivirus was tested with fluorescent expression, to infect iPS cells.