GW25-e3479

Distribution of genetic polymorphisms of EGR3 gene in healthy Uygur and Chinese Han population in Xinjiang

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Objectives: To investigate the genetic polymorphisms of rs1008949 and rs1996147 of EGR3 gene in healthy Chinese Han and Uygur population of Xinjiang.
Methods: The genotypes of the EGR3 gene were detected in 303 Uygur and 351 Han healthy individuals using the TaqMan SNP genotyping assay.
Results: The genotype distributions of both populations were in the Hardy-Weinberg equilibrium (P>0.05). The frequencies of CC,CT and TT genotypes of the rs1008949 locus were 34.3%,50.2%,and 15.5% in the Uygurs, and 28.2%,49.3%and 22.5% in the Han participants. There was significant difference in distribution of genotypes between the two populations (P<0.001). The frequencies of AA, AG and GG genotypes of the rs1996147 locus were 24.7%, 51.5%, and 23.8% in Uygur participants, and 14.0%, 44.4%and 41.6%in Han participants. There was also significant difference in distribution of genotypes between the two populations (P<0.001).
Conclusions: The mutational frequencies of the tagging SNPs in rs1008949 and rs1996147 loci of the EGR3 gene were significantly different between Uygur and Han populations.

GW25-e3489

Evaluation anti-atrial fibrillation drug model of multi-ion channels as a target with micro-electrode chip technology

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Objectives: To screen and evaluate effection of anti-atrial fibrillation drug on rapid atrial pacin rabbit model with microelectrode arrays (MEA).
Methods: 32 rabbits were randomely divided into 4 groups: TEA group (n=8), $BaCl_2$ group (n =8), $CdCl_2$ group (n =8), Amiodarone group (n=8). The electrode was inserted into right atrium via internal jugular vein with rapid right atrial pacing (600 beat/min). effection of anti-atrial fibrillation drug on ion channels were observed after giving drugs (TEA, $BaCl_2$, $CdCl_2$ and Amiodarone).
Results: field action potential (fAPD) prolonged in TEA group and $BaCl_2$ group (control vs blocker: 176.67±8.66 ms vs 196.11±10.76 ms, 182.22±12.87 ms vs 191.11±13.09 ms, respectively, P<0.05). fAPD prolonged in $CdCl_2$ group (control vs blocker: 176.67±8.66ms vs 196.11±10.76ms) (P<0.05). fAPD obviously extended in Amiodarone group (control vs Amiodarone: 167.38±13.67ms 185±15.14ms, P<0.01).
Conclusions: Atrial fibrillation induced by rapid atrial pacing is a stable and reliable Anti-arrhythmic drug therapy for atrial fibrillation screening model on rabbit, It can be used for anti-atrial fibrillation drug development at early the rapid screening combines with microelectrode chip technology.

GW25-e3491

Association of Intercellular Adhesion Molecule-1 Gene Polymorphism with Coronary Heart Disease in Han population in Xinjiang, China

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Objectives: Intercellular adhesion molecule-1 is an important adhesion molecule that plays a crucial role in lymphocyte migration and in atherosclerosis pathogenesis activation. The aim of the present study was to explore the association between the rs5498 polymorphism of the *ICAM-1* Gene and coronary heart disease (CHD) in Han population in Xinjiang, China.
Methods: rs5498 polymorphism of *ICAM-1* gene was detected with method of polymerase chain reaction-restricted fragments length polymorphism in 674 CHD patients and 779 control subjects.
Results: For total, the frequency of G allele was significantly higher in CHD patients than that in controls (29.2% vs. 23.3%, P<0.001). The frequency of AG+GG genotypes was higher in patients with CHD than that in controls (49.7% vs. 40.8%, P=0.001). Multiple logistic regression analysis showed AG+GG was an independent risk factor for CHD (OR=1.919, 95%CI: 1.471-2.503, P<0.001). For men, the frequencies of G allele and AG+GG genotype were also higher in CHD patients than those in control subjects (29.9% vs. 22.7%, P<0.001 for frequency of G allele; 50.6% vs. 40.3%, P=0.001 for AG+GG genotype). For women, we didn't observe any significant difference in genotype or allele distribution between the two groups.
Conclusions: In the present study, rs5498 polymorphism of *ICAM-1* gene was associated with CHD in men of Chinese Han population. Men with G allele (AG and GG genotype) might have higher risk for CHD than those with AA genotype.

GW25-e3503

OSM induced cardiomyocyte dedifferentiation regulates the progression of diabetic cardiomyopathy through B-Raf/MeK/Erk signaling pathway

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Objectives: It has been reported that oncostatin M (OSM) could initiate cardiomyocyte dedifferentiation both in vivo and in vitro. OSM-induced cardiomyocyte dedifferentiation might be a new target for the treatment of diabetic cardiomyopathy (DCM). This study was designed to determine the role of OSM in cardiomyocyte dedifferentiation and the progression of DCM.
Methods: Mouse DCM model were established to evaluate the effects of OSM in vivo by injection of STZ for 5 consecutive days and random blood glucose value of ≥ 16.7mmol/L was considered as a cutoff point for diabetes. Transthoracic echocardiography was applied to determine cardiac function. Immunofluorescence staining was used to detected dedifferentiation markers such as Runx1 and ANP. Sirus red staining was used to detect fibrosis area and Transmission electron microscopy (TEM) was used to evaluate mitochondria impairment. Real Time PCR and Western blot were performed to detect relative mRNA expression and the expressions of cardiomyocytes dedifferentiation related proteins such as c-kit, scal-1, a-SM-actin, Runx1 and ANP.
Results: DCM mice exhibited multiple functional and structural changes in cardiomyocytes and OSM treatment induced similar biological changes as those detected in DCM mice. LVEF (49.25±3.75% vs. 70.07±4.37%, P<0.05) and FS (28.20 ±3.30% vs. 38.02±5.66%, P<0.05) were decreased, while LVEDV (87.18±7.47μL vs. 75.50±8.23μL, P<0.05) and LVESV (40.09±2.99μL vs. 22.15±4.32μL, P<0.05) were increased by OSM treatment as compared with the saline treated group. OSM administration increased cardiac fibrosis area (4.03±0.53% vs. 1.11±0.44%, P<0.05) and aggravated mitochondria impairment as compared with control mice. Immunofluorescence staining showed OSM administration also significantly up-regulated the expressions of dedifferentiation makers Runx1 and ANP. Real-time PCR detected the mRNA expression of OSM, Oβ, c-kit, Runx1 and ANP were increased in OSM treated mice compared with control mice and Western blot revealed the protein expression of dedifferentiation makers (Runx1, a-SM-actin and ANP), typical fetal genes (c-kit, scal-1) were increased in OSM treated mice compared with control mice. OSM recepror Oβ KO mice were used and B-Raf, Mek, P-Erk and total-Erk expressions were detected by Western blot, indicating the mechanism of OSM induced cardiomyocyte dedifferentiation was associated with B-Raf/Mek/Erk signaling pathway through Oβ receptor.
Conclusions: We provided direct evidence that OSM played a crucial role in the progression of diabetic cardiomyopathy through inducing cardiomyocyte dedifferentiation. The mechanism of OSM induced cardiomyocyte dedifferentiation was associated, at least in part, with B-Raf/Mek/Erk signaling pathway. The findings of the present study might provide a new therapeutic molecular target for the further treatment of diabetic cardiomyopathy.

GW25-e3514

Resveratrol Alleviates Diabetic Cardiomyopathy through Improvement of Mitochondrial Biogenesis and Function in a SIRT1-dependent Manner

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Objectives: Diabetic cardiomyopath (DCM) is associated with impaired mitochondrial biogenesis and function. Resveratrol, an activator of SIRT1, has been reported to increase mitochondrial mass. Our study was designed to investigate whether resveratrol is capable of protecting against DCM via mitochondrial regulation.
Methods: Cardiac-specific SIRT1 KO mice ($SIRT1^{CKO}$) were generated with $SIRT1\text{-}floxp^{+/+}$ and Myh6-Cre transgenic mice. Mice model were divided into six groups: control group, DCM group, DCM+ Resveratrol group (DCM+ RES), $SIRT1^{CKO}$ group, $SIRT1^{CKO}$+ DCM group ($SIRT1^{CKO}$+ DCM) and $SIRT1^{CKO}$+ DCM+ Resveratrol group ($SIRT1^{CKO}$+ DCM +R). DCM mice were injected with streptozotoin. Resveratrol was added at the dose of 25 mg/kg/day for two months. Echocardiography, HE, Masson trichrome, Sirus red staining and transmission electron microscope were applied to reveal heart function, remodeling and mitochondrial morphology. Cardiomyocyte apoptosis was assessed with TUNEL. In vitro H9c2 cell study included six groups: control group, high glucose treated group (HG), HG+ Resveratrol group (HG+ RES), sh-SIRT1 group, sh-SIRT1+ HG group (sh-SIRT1+ HG) and sh-SIRT1+ HG+ Resveratrol group (sh-SIRT1+ HG+ R). Mitochondrial function was evaluated by ATP generation, membrane potential (TFRM fluorescence) and citrate synthase activity. Mitochondrial biogenesis was analyzed with mtDNA copy number. Immunoprecipitation was done to reveal the acetylation of SIRT1 targeted PGC-1α. mRNA and protein expression of PGC-1α downstream genes (NRF-1, NRF-2, ERR-α and TFAM) were analyzed with Real-time PCR and Western blot.
Results: SIRT1 expression was nearly undetectable in heart tissue of $SIRT1^{CKO}$. As compared with WT mice, DCM mice showed reduced cardiac function, damaged cardiac ultrastructure and remodeling, accompanied with increased cardiomyocyte apoptosis, decreased ATP generation and mtDNA amount (P<0.05), indicating impaired mitochondrial function and biogenesis. DCM mice showed reduced SIRT1 expression in heart tissue. Resveratrol reversed these changes in DCM mice, but not in DCM+ $SIRT1^{CKO}$ mice. In vitro results revealed that HG increased cell apoptosis as compared with control group (P<0.05). Moreover, HG reduced mitochondrial biogenesis and function in cardiomyocytes, evidenced by decreased ATP generation,