Inhibition of the NF-kB pathway by the R65 ribozyme gene via adeno-associated virus serotype 9 in human umbilical vein endothelial cells

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Objectives: NF-kB signaling plays a central role in the regulation of inflammatory responses in atherosclerosis. To our knowledge, it is less intensively studied whether R65 ribozyme gene can decrease the expression of NF-kB pathway by the R65 ribozyme gene via adeno-associated virus serotype 9 vector to deliver the R65 ribozyme gene (sAAV9-R65) into oxidized LDL (ox-LDL) induced human umbilical vein endothelial cells (HUVECs). We also assessed whether R65-mediated R65 ribozyme gene transfection can be expressed for a longterm and inhibit the activity of NF-kB.

Methods: sAAV9-R65 was transfected into HUVECs at different multiplicities of infection, which was measured by flow cytometry. The activity of NF-kB pathway was analyzed by Western blot and Immunofluorescence staining. NF-kB inflammatory factors and endothelial cell function markers were measured by ELISA. Cell apoptosis was detected by Flow cytometry.

Results: The effects of the sAAV9-R65 upon ox-LDL induced injury of the HUVECs were evaluated. First, sAAV9-R65 was transfected into HUVECs at different multiplicities of infection and it could be stably and efficiently expressed. Second, ox-LDL led to concurrent increased NF-kB expression in a dose- and time-dependent manner, and it increased inflammatory factors (TNF-a, IL-6) and cell apoptosis in HUVECs. Third, over-expression of sAAV9-R65 gene could inhibit the NF-kB pathway and protect HUVECs against ox-LDL induced cell apoptosis.

Conclusions: These results demonstrate that sAAV9-mediated R65 ribozyme gene transfection may inhibit the expression of NF-kB pathway. However, these effects were dose- and time-dependent.

Association of coronary artery disease and Metabolic Receptors C5aR and CS1L gene

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Objectives: Adipose tissue receptors C5aR and CS1L and their heterodimerization/ functionality and interaction with ligands C5a and acylation stimulating protein (ASP) have been evaluated in cell and rodent studies. Their contribution to coronary artery disease (CAD) factors in humans remains unclear. We hypothesized that C5a receptors, classically required for host defense, are also associated with CAD.

Methods: Anthropometry and fasting blood parameters were measured in 492 CAD patients and 577 control subjects. Results: CS1L gene Heterozygote carriers of the CT genotype were more frequent among CAD patients than among controls (7.3% versus 1.7%). The odds ratio (OR) for carriers of the CT genotype for CAD was 4.484 (95% confidence interval (CI) : 2.197-9.174). C5aR gene Heterozygote carriers of the CT genotype were more frequent among CAD patients than among controls (4.7% versus 1.6%). The odds ratio (OR) for carriers of the 969CT genotype for CAD was 4.484 (95% confidence interval (CI): 2.197-9.174). C5a gene Omental CS1L>C5aR carriers were increased with BMI (P<0.001) with correlations between CS1L>C5aR and waist circumference, HDL-C, and adiponectin.

Conclusions: Suggest relationship to The CT genotype of CS1L and C5aR gene may be a genetic maker of CAD and highlight adipose-immune interactions.

The Effects of Resveratrol on Cardioprotection of Ischemic Postconditioning in Diabetic and non-diabetic Rat Hearts

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Objectives: This study aimed to investigate whether acute or chronic administration of the Resveratrol (3, 5, 4'-trihydroxystilbene) affect the cardioprotective effects of ischemic postconditioning (Ipost) in diabetic and non-diabetic rat hearts.

Methods: Isolated rat hearts were subjected to 30 min of global ischemia, followed by 120 min of reperfusion. The hearts were subjected to the following treatments: non-chronic treatment (Ipost, six cycles of 10-s reperfusion-ischemia after ischemia), acute Resveratrol (10 µmol/L Resveratrol during reperfusion), acute Resveratrol with Ipost, chronic Resveratrol (10 mg/kg/day Resveratrol for 2 weeks), and chronic Resveratrol with Ipost. Infarct size, haemodynamics and expression of Akt and eNOS were measured.

Results: Our results show that Ipost did not limit infarct size and recover contractile dysfunction in the hearts of diabetic rats (infarct size: 58.1% and 59.2%, P<0.05). Acute Resveratrol treatment with Ipost resulted in infarct size-limiting and contractile dysfunction-recovering effects in both diabetic and non-diabetic hearts (infarct size: 38.8% and 59.2% in diabetic ones and 24.3% and 43.7% in non-diabetic ones, P<0.05, respectively), and produced a further activation of Akt and eNOS signaling pathways to

Distributional characteristics of β-adrenergic receptors gene polymorphisms and association with serum lipidin Han and Uighurpopulations in Xinjiang

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Objectives: To investigate the distributional characteristics of β1-adrenergic receptors gene polymorphisms (rs2289423 and rs6966132) and association with serum lipid in Han and Uighur populations in Xinjiang.

Methods: The genotypes of the ADRB3 gene were detected in 362 Uighur and 653 Han healthy individuals by real-time PCR (TaqMan).

Results: (1) The frequencies of TT, GT and GG genotypes of the rs2289423 locus were 28.1%,55.9% and 16.0% in Han, 74.7%,23.3% and 2.0% in the Uighurs. There was no significant difference in distribution of genotypes between the two populations (P=0.065); (2) The frequencies of GG:AG and AA genotypes of the rs6966132 locus were 81.5%,16.6% and 1.9% in Uighurs, and 59.6%,33.7% and 6.7% in Hans. There was significant difference in distribution of genotypes between the two populations (P=0.001); (3) Total cholesterol and low density lipoprotein cholesterol level were significantly higher in GG or GT genotype than in TT genotype carrier of rs2289423 in Uighur individuals, but not in Han populations. The serum lipid level which include TC, LDL-C, TG, HDL-C did not have significant difference, P<0.05.

Conclusions: However, the protein expression of NADPH oxidase inhibitor, can reduce the up-regulation of NADPH oxidase/MAPK/MMP 9 signal pathway and suppress the abnormal proliferation of atrial fibrobast and the combined stimulus has more remarkable effects. Similarly to the mechanism of H2O2, glucose enhances the expression of fibrosis-related protein MMP 9 through up-regulating the function of NADPH oxidase and the expression and phosphorylation level of JNK 1 and p38. Apocynin, a NADPH oxidase inhibitor, can reduce the up-regulation of NADPH oxidase/MAPK/MMP 9 signal pathway and suppress the abnormal proliferation of atrial fibrobast.