cytoskeleton reorganization and cell shape changes in terms of lamellipodia formation in KO VSMCs compared with WT VSMCs.

Conclusion: These findings suggest that CHF1/Hey2 is an important regulator of VSMC motility during vascular remodeling through control of PDGF and HB-EGF dependent signaling pathways.

Oxidized Low-Density Lipoprotein-Stimulated Smooth Cardiac Troponin Elevations in Marathon Runners: A Novel Mechanism Contributing to Atherosclerotic Lesion Formation

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Background: Oxidation of LDL has emerged as the initiating event in cardiovascular lesion formation. Little is known about the molecular mechanisms linking Ox-LDL and vascular smooth muscle cell accumulation, the harbinger of vascular lesion progression. The HLH transcription factor Id3 is a redox sensitive gene that is expressed in VSMC in response to mitogen stimulation and vascular injury. Id3 is a regulator of growth and differentiation in several other cell types. Accordingly we hypothesize that Id3 is an important mediator of Ox-LDL-induced VSMC growth.

Methods: Primary vascular smooth muscle cells were infected with AdId3 or AdGFP control and assayed for cell number, BrdU incorporation and p21cip1 expression by Western blot analysis. Parallel cultures were stimulated with Ox-LDL or nLDL or sera from hyperlipemic, atherosclerotic pigs or normolipemic pigs without vascular lesions.

Results: Results demonstrated that increasing Id3 expression in VSMC decreased pS21cip1 expression and increased BrdU incorporation and cell number. Co-transfection with pAdId3 and pS21cip1 promoter-luciferase reporter construct demonstrated that Id3 regulates pS21cip1 promoter activation in VSMC. Ox-LDL and hyperlipemic porcine sera induce Id3 protein expression and VSMC cell proliferation. Consistent with the role of Id3 as an inhibitor of pS21cip1 expression, infection with AdId3 increased BrdU incorporation and increased cell number. Stimulation with hyperlipemic sera increased cell number and S-phase entry. Furthermore, aortas of hyperlipemic pigs demonstrated significantly more Id3 positive normolipemic controls.

Conclusion: The HLH factor Id3 mediates the mitogenic effect of hyperlipemic sera and Ox-LDL in VSMC via inhibition of p21cip1 expression and inhibition of DNA synthesis. Moreover, hyperlipemic, atherosclerotic animals express greater amounts of Id3 protein in the vessel wall than normolipemic controls providing the first in vivo evidence implicating Id3 as an important mediator of atherogenesis.

Young Investigators Awards Competition: Clinical Investigations-Cardiology & Cardiovascular Surgery

Monday, March 08, 2004, 2:00 p.m.-3:15 p.m.
Morial Convention Center, Room 257

2:00 p.m.

Genetic Polyporphism G894T on Endothelial Nitric Oxide Synthase Gene as a Risk Factor for Premature, Nonfatal Myocardial Infarction in Young Male Smokers

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Background. Endothelial nitric oxide synthase (eNOS) gene polymorphism G894T has been associated with arterial hypertension and myocardial infarction (MI) in older ages. However, its role in the pathogenesis of premature MI remains unclear. We investigated whether this polymorphism is associated with premature non-fatal MI.

Methods. This case-control study enrolled 212 young patients with premature non-fatal MI (aged 46.5±5.2 years old) and 577 healthy age- matched controls (aged 48.1±13.5 years old), derived from ATTICA cohort. Polymerase chain reaction was done to detect homozygosity for the 894T allele. The frequency of T allele was 0.552 among cases and 0.518 among controls (p=0.126). In comparison to 894G homozygous patients, the odds ratio of 894T homozygotes was 3.367 (95%CI: 1.369 to 8.279, p=0.006) compared to GG, 2.935 (95%CI: 1.083 to 7.837, p=0.03) compared to GT and 1.359 (95%CI: 0.517-3.581, p=0.007) compared to GG/GT. However, no association between G894T polymorphism and premature MI was observed in male non-smokers and in female smokers or non-smokers.

Conclusion. These findings suggest that G894T polymorphism on eNOS gene may interact with smoking leading to premature, non-fatal myocardial infarction in young males.