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Carotid Extra-Media Thickness: A Novel Measure of Vascular Structure That Is Associated with Cardiovascular Risk Factors

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Angiotensin II Reduces Abundance of PPAR γ in Aortic Smooth Muscle Cells via the TGF β1 Activated p38 MAP Kinase in a Smad-2 Independent Manner

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Objective: Infusion of angiotensin II (AngII) increases the incidence of abdominal aortic aneurysms (AAA) in hyperlipidemic mice that is associated with the downregulation of PPAR gamma. Since defects in smooth muscle cells (SMCs) may be responsible for AAA initiation, the purpose of this study was to determine the mechanism of AngII-mediated regulation of PPAR gamma in this cell type. ***Methods and Results:*** Aortic SMCs were isolated and cultured from male C57BL/6 mice and incubated with either AngII (1 uM) or saline for 24 hr. Incubation with AngII reduced the abundance of PPAR gamma mRNA ($p<0.05$) and protein ($p<0.05$) in cultured SMCs. The reductions were mediated by AT1 receptors as demonstrated by the attenuation in the presence of losartan (10 uM). AngII is known to promote synthesis and activation of TGF beta1. A neutralizing antibody was used to determine the role of this cytokine. The co-incubation of SMCs with a TGF beta1 neutralizing antibody prevented the AngII-induced reduction of PPAR gamma protein abundance. The AngII-TGF beta1 axis activates many intracellular signaling pathways. To determine the specific pathway mediating the AngII-induced reduction of PPAR gamma, SMCs were incubated with inhibitors of p38 MAPK (SB203580), ERK (PD38059), JNK (SP600125), or PKC (GF109230X). Only the p38 MAPK inhibitor significantly prevented the AngII-induced reduction in PPAR gamma protein abundance ($P < 0.05$). The p38 MAPK inhibitor also prevented reductions in PPAR gamma abundance with incubation of recombinant TGF beta1. TGF beta1 promoted the phosphorylation of Smad-2 in the presence of the p38 MAPK inhibitor, and therefore, this pathway was not involved in AngII-induced reduction of PPAR gamma. ***Conclusion:*** These findings suggest that AngII decreases abundance of PPAR gamma in cultured aortic SMCs via an AT1 receptor dependent manner. AT1 receptor stimulation leads to TGF beta1 elaboration and reduction of PPAR gamma via activation of p38 MAPK in a Smad-2 independent manner.

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Transforming Growth Factor-β Activity in Macrophages Protects from Angiotensin II-Induced Aortic Aneurysm in Mice

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The TNFα-Induced Gene Sister of Mammalian Grainyhead (SOM) Importantly Contributes to Endothelial Cell Migration and Sprout Formation: Crucial Role in Atherosclerosis?

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Scavenger Receptors Participate in the Effects of Carbamylated LDL Toward Endothelial Cells

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