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p22phox-Dependent Reactive Oxygen Species Modulate the Phenotype of Vascular Smooth Muscle Cells

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Recent work has shown reactive oxygen species are involved in fundamental biological processes such as growth, apoptsis, migration and differentiation. Emerging evidence indicates that reactive oxygen species, especially superoxide and hydrogen peroxide, are important signaling molecules in smooth muscle cells. A major source of hydrogen peroxide is a membrane-bound NADH/NADPH oxidase, the activity of which is regulated by hormones, growth factor, and mechanical stress. P22phox is a component of the vascular smooth muscle O2--generating NADPH/NADH oxidase. However, its role in signal transduction is only partially understood and the role in cell differentation should be elucidated.
In this study, we report that the complete inhibition of p22phox mRNA expression by stable transfection of antisense p22phox cDNA into VSMCs results in a significant inhibition of PDGFAA induced NADH/NADPH-dependent superoxide production, furthermore, which prevented PDGDFAA-induced p38MAPK but not ERK activation. P22phox-deficiency cells express lower SMC differentiation marker protein. In a word, the present data shows that (1) P22phox is a critical component of superoxide-generating vascular NADH/NADPH oxidase. (2) P38MAPK is a critical component of the oxidant stress (H2O2)-sensitive signaling pathways activated by PDGFAA. (3) Antisense against p22phox solely inhibited PDGFAA-induced p38MAPK activation but did not affect ERK. (4) P22phox generation reactive oxygen species regulate smooth muscle cells phenotype. (5) P38MAPK plays an important role in redox regulation of VSMC differentiation.
Taken together, basic ROS could maintain differentiation phenotype in VSMCs, over-suppressed physiological ROS may lead to cell apotosis. That could be explained the negative results of the various antioxidant trials.