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Review

NADPH oxidase-derived reactive oxygen species in the regulation of endothelial phenotype

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Abstract:
Endothelial dysfunction comprising impairment of endothelium-dependent vasodilator function and increased endothelial activation contributes to the pathophysiology of cardiovascular diseases such as atherosclerosis, diabetic vasculopathy, heart failure and hypertension. The changes in endothelial phenotype in these conditions occur in response to diverse stimuli including inflammatory cytokines, activation of renin-angiotensin-aldosterone system, hyperlipidaemia, hyperglycemia, ischemia-reperfusion and mechanical forces. An increased production of reactive oxygen species (ROS), such as superoxide and H_2O_2, is involved in the genesis of these alterations in endothelial phenotype. The NADPH oxidases, Nox2 and Nox4, are major sources of ROS in endothelial cells and are implicated both in vasodilator dysfunction and in the modulation of redox-sensitive signalling pathways that influence endothelial cytoskeletal organisation, adhesion molecule expression, permeability, growth, migration and other functions. NADPH oxidases appear to be especially important in redox signalling in that they are specifically activated by diverse agonists and regulate the activation of downstream protein kinases, transcription factors and other biological molecules. This review provides an overview of NADPH oxidase structure and regulation in endothelial cells and their role in pathophysiology, focussing particularly on endothelial activation.

Key words:
endothelial dysfunction, activation, ROS, NADPH oxidase, redox signalling