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NADPH oxidases in endothelial function and dysfunction

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The family of NADPH oxidases (Nox) consists of 7 members whose sole function is the production of reactive oxygen species (ROS). Of the Nox family the homologues Nox1, Nox2, Nox4 and Nox5 are expressed in the vascular system. The specific function of each family member is dependent on its expression site, its mode of activation and the type of ROS produced. In endothelial cells, most data cover the enzymes Nox1, Nox2 and Nox4.

Nox1 and Nox2 are activated by cytosolic subunits and produce $O2^{-}$. $O2^{-}$ on one hand can be detrimental as it scavenges NO to form $ONOO^{-}$ which limits the positive effects of NO for endothelial function. On the other hand an acute locally and timely controlled increase in $O2^{-}$-formation is involved in endothelial signalling. This for example facilitates the transient inhibition of protein tyrosine phosphatases such as Shp2, to allow a prolonged phosphorylation of downstream signal molecules of the EPO-receptor. Alternatively, ROS maintain the activity of cofactors involved in Notch signalling such as the alpha secretase ADAM17. This than influences fundamental cellular characteristics of endothelial cells, such as tip or stalk cell phenotype.

The NADPH Oxidases Nox4 in contrast is constitutively active and produces H2O2. Therefore, the ROS production of this enzyme is controlled by its expression level and mainly contributes to constitutive and long lasting signalling. Nox4 maintains endothelial

cells stable and in a quiescence state and limits macrophage adhesion. Therefore, Nox4 is involved in the prevention of atherosclerosis. Further Nox4 is involved in differentiation and survival of endothelial cells.

The talk will cover those aspects of the differential functions of the NADPH oxidases.

Short Biography

Prof. Katrin Schröder

Katrin Schröder received her PhD in 1999 at the University of Rostock and habilitated in 2011 at the University of Frankfurt. Since 1016 she is associate professor for physiology at the institute of cardiovascular physiology at the medical faculty of the University of Frankfurt. The focus of her work is the identification of physiological functions of the family of NADPH oxidases. She found that the transient formation of reactive oxygen species by acutely inducible NADPH oxidases is involved in phosphatase inhibition or modulation of enzyme activity. The main focus of her work is Nox4. She identified this constitutive active NADPH oxidase to be an essential component of cellular differentiation and to play protective roles against vascular inflammation and atherosclerosis.

Literature:

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