

Cytochrome b558: NADPH oxidase of phagocytes - challenges and opportunities



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NADPH oxidase is a multicomponent enzyme responsible of the generation of reactive oxygen species (ROS). The catalytic core Nox2 of the NADPH oxidase has been first identified in phagocytes. In the last decade, several homologues (Nox1 to Nox5, Duox1 and Duox2) have been identified in various non-phagocytic cells with distinct features in tissue distribution, expression regulation, and physiological functions. Nox2 has been well-studied and remains the better basis for understanding Nox regulation overall. In the resting state, Nox2 is associated with p22phox to the membrane; both proteins constitute the cytochrome b558. Upon stimulation, the cytosolic components (p47phox, p67phox, p40phox and Rac1/2) of the NADPH oxidase are recruited to the membrane where they assemble with the cytochrome b558 to form the active enzyme.

Physiological concentrations of phagocyte NADPH oxidase-mediated ROS production are involved not only in the killing of invading microorganisms but are also used as a second messenger for signal transduction in the endothelium. However, an excessive ROS production can damage tissue and represents an important cause of injury in many chronic inflammatory disorders including rheumatoid arthritis, atherosclerosis, lung injury and inflammation-associated cancer.

Given the importance of the NADPH oxidase in the pathophysiology of inflammatory diseases, it appears that its activity needs to be firmly controlled by different mechanisms that ensure an appropriate physiological regulation.

This communication will summarize the distinct characteristics of Nox family proteins and especially focus on mechanisms underlining the phagocyte NADPH oxidase regulation. The role of Ca²⁺-binding S100A8/A9 proteins in the activation of NADPH oxidase and notably its interaction with cytochrome b558 will be discussed.

Where

Campus Limpertsberg - BS 0.15

When

Tuesday the 22nd November 2011 – from 1:45 pm to 3:00 pm

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