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Poster Presentation

NADPH Oxidase Type 4 Inhibits Immune Cell Trafficking into The Central Nervous System During Neuroinflammation

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Abstract

Transendothelial trafficking of immune cells into the central nervous system (CNS) and disruption of the blood brain barrier (BBB) are pathophysiological hallmarks of neuroinflammatory disorders like multiple sclerosis (MS). Accumulating evidence suggest that oxidative stress plays a major role in the pathogenesis of MS, whereas a specific influence of oxidative stress on BBB dysfunction in MS was unclear so far. Here, we identify NADPH oxidase type 4 (NOX4) as a specific and direct modulator of BBB integrity. Deficiency of NOX4, but not NOX1 or NOX2, rendered mice more susceptible to experimental autoimmune encephalomyelitis (an animal model of MS) and was accompanied by a remarkable enhancement of BBB disruption and CNS inflammation. Murine and human in vitro analysis revealed that lack of NOX4 amplifies leukocyte trafficking by modified endothelial cells. Further, reduced endothelial NOX4 expression was found in CNS tissue of individuals suffering from MS indicating an important role of NOX4 also in humans. Our study demonstrates, for the first time, that NOX4 is an important and direct regulator of BBB integrity. NOX4 activation can decrease BBB damage and cell invasion during neuroinflammation and may offer a novelstrategy for the treatment of MS.

Keywords: NADPH Oxidase, Immune Cells, Neuroinflammation

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