In search of therapeutic targets for neurodegeneration

\textit{Neuroinflammation is a key process associated with neurodegenerative diseases. Understanding the underlying mechanism is central for the identification of novel therapeutic targets.}

NADPH oxidases (NOX) are transmembrane enzymes that utilise NADPH and oxygen as substrates to catalyse the formation of superoxide and hydrogen peroxide. Under physiological conditions, NOX are essential mediators of host defence, and mutations cause an immunodeficiency known as chronic granulomatous disease.

Excessive reactive oxygen species (ROS) production has pathological consequences and leads to tissue oxidative damage such as in the case of microglia-mediated neuroinflammation seen in amyotrophic lateral sclerosis (ALS). At the same time, the absence of ROS enhances the severity of autoimmune-mediated neuroinflammation, such as in the case of multiple sclerosis (MS).

The EU-funded NEURINOX (NOX enzymes as mediators of inflammation-triggered neurodegeneration: modulating NOX enzymes as novel therapies) project wished to delineate the link between neuroinflammation, NOX enzyme activity and neurodegenerative diseases. Researchers worked to clarify NOX localisation in the central nervous system to identify novel molecular pathways and oxidative biomarkers involved in NOX-dependent neuroinflammation. The aim was to develop specific therapies based on NOX modulation.

To aid their research, partners developed various in vitro and in vivo models of neuroinflammation that further allowed them to identify redox-dependent pathways regulated by NOX. Results showed a strong association between NOX2 and progression of neurodegenerative diseases. However, despite the correlation of NOX2 activity and neuroinflammation, inhibition of NOX provided limited beneficial effects in neurodegenerative disorders.

Researchers concluded that NOX2 up-regulation is indeed a common feature of neurodegenerative disease, but NOX2 inhibition is not disease-modifying. Nonetheless, NOX2 could be measured in the blood, rendering it a promising biomarker for future evaluation of therapies for neurodegeneration. Additional oxidative biomarkers were identified for ALS and MS patients.

Collectively, the concerted efforts of the NEURINOX study significantly advance existing knowledge on brain dysfunction, neuroinflammation and its association with neurodegenerative disorders. The discovery of therapeutic targets alongside the development of small molecule inhibitors will help slow down the clinical progression of neurodegenerative disorders.

\textit{Related information}
Final Report Summary - NEURINOX (NOX enzymes as mediators of inflammation-triggered neurodegeneration: modulating NOX enzymes as novel therapies)

Subjects
Life Sciences

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