Mitochondrial Enzyme Monoamine Oxidase : Oxidative Stress & its Impact on Neurological & Cardiovascular Regulation

S.H.Parvez; C. Collin; F. Gulshan & S.Parvez

Neuroendocrine Unit, French National Research Center (CNRS), TIT Graduate School, Bat 5, 91190 Gif Sur Yvette, France

Monoamine oxidase is localized on the outer membrane of mitochondria and plays an important role in oxidative stress for the control of health and disease. Two, isoforms, MAO-A & B are the most intensively investigated amine oxidases due to their role in metabolism of neurotransmitters such as serotonin, dopamine & other biogenic amines. Altered activity of both MAO-A & B has been found in numerous neuro-psychiatric and cardiovascular diseases and MAO inhibitors are widely used in clinical practice. MAO-A inhibitors are effective antidepressants & MAO-B inhibitors are employed to treat Parkinson's disease. This explains the high popularity of MAOs as target for development of numerous drugs.

The present conference summarizes the essential role of this oxidative enzyme and also describes its molecular structure, affinity sites for drug action, schematic mechanisms of action and its regulatory factors that bring nervous/immune systems very close. The presence of MAO in peripheral and brain tissues is of particular interest since it regulates both cardiovascular and nervous activities. The presence of MAO in human platelets provides a direct index of brain diseases and counts for a very valuable tool of investigation for the processes of neurodegeneration. Platelet MAO as marker of different pathologies or substance addiction such as smoking and schizophrenic patients has been shown. The studies presented in this seminar show molecular information along with high resolution NMR imaging of the normal and pathological as well as criminal brain. The therapeutic impliment of MAO inhibitors in Parkinson's disease and their possible role as neuroprotectors from early stages of PD to late stages is reviewed. A wide classification of MAO inhibitors as well as their role as suicide modulators is illustrated.

In response to NGF & Cytokines, MAO produces superoxide which is metabolized to hydrogen peroxide & both these ROS serve as 2nd messengers & activate multiple intracellular signaling pathways. The vascular NAD(P)H oxidases are essentiel for physiological response of vascular cells, including growth factors, migration & modification of the extra-cellular matrix. They have been linked to hypertension & to pathological states associated with uncontrolled growth & inflammation such as atherosclerosis.

Renalase is a novel, soluble monoamine oxidase that regulates cardiac function and blood pressure. In humans, Renalase gene expression is highest in the kidney but also detectable in heart, skeletal muscle & small intestine. Plasma concentration of Renalse is markedly reduced in patients with end stage renal disease. Renalase infusion causes decrease in cardiac contractility, heart rate & blood pressure & prevents compensatory increase in peripheral vascular tone.

Brain Derived Neurotropic Factor (BDNF) & enhancement of its gene expression by I-MAO and augmentation of BDNF content after I-MAO has been illustrated both by immunohistochemical studies as well as molecular assays.

Finally, MAO modulation during iron deficiency anaemia along with different metallic anions and cations in cerebrospinal fluid caused by neurodegenerative pathologies is discussed. Iron-MAO interactions carry a great physiological impact for the survival of the neurone as both MAO metabolic products as well as high iron concentrations lead to neuronal apoptosis.

Immune-MAO dependence during perinatal development as well as adult life due to its feed back regulation by pituitary-adrenal axis through glucocorticoids demonstrates a true link between the origin of synaptic transmission and oxidative stress via development of immune sensitivity.

References: of Books on MAO published by Parvez et al

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