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5-Lipoxygenase and ADP-Ribose transferase-1 in Alzheimer's disease: The novel targets for neuroregeneration

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Antiinflammatory (AI) drugs are considered for the treatment of Alzheimer's disease (AD). AI drugs could slow the progression or could delay the onset of AD. Our data using AD models showed that inhibition of cyclooxygenases (COXs) and lipoxygenases (LOXs) protects against amyloid beta ($A\beta_{1-42}$) evoked cognition impairment. Our data indicated that systemic inflammatory response (SIR) significantly modulates $A\beta_{1-42}$ toxicity in animal model of AD. SIR induces expression of several prooxidant genes in hippocampus and activates genes for enzymes regulating arachidonic acid release (PLA_2) and its metabolism, including 5-LOX and 12/15-LOX. The enhancement of genes expression for members of ADP-ribose tranferases (ART1,3,9,12,14; formerly PARP) family and the stimulation of ART-1 activity was also found. More recent study presented that family of COXs and LOXs, and ART-1, the important regulator of transcription, could be involved in functioning of AD brain via mechanisms different from classical inflammation. These mechanisms include the bioactive molecules generated by activity of these enzymes and by their specific interaction. The last studies presented that these enzymes interact with gamma secretase complexes and regulate Aβ concentration, and/or interact with specific kinases engaged in tau hyperphosphorylation observed in AD. The inhibitors of ART-1 modulate the phosphatidylinositol 3-kinase and glycogen synthase kinase-3-activity. Our data indicated that 5-LOX and ART-1 inhibitors protect hippocampal neurons against death evoked by several molecular and metabolic events occurring in AD (oxidative/nitrosative stress, glucose deprivation, inflammation). We propose that inhibition of 5-LOX and ART-1 could be considered as the novel strategy for neuroregeneration in AD therapy

Biography

1963 MD Diploma Academy of Medicine Warsaw, 1970 PhD in biochemistry, 1968-1971 specialization in neurology 1971-1973 Alexander von Humboldt Fellowship Cologne Germany, 1991 full Professor at Medical Research Centre Polish Academy of Science. Head of Dep. of Cellular Signalling. Visiting Professor in: Baylor College Houston, German Cancer Research Centre, Heidelberg; Weizman Institute Rehovot; Universities of Catania, Perugia, Kyoto. Authors of more as 600 scientific contributions including original papers, abstracts, books. All together over 50 scientific awards and grants. Achievements include original findings in the study of carcinogenesis, pathomechanism of brain aging, ischemia neurodegenerative disorders as Alzheimer's and Parkinson's diseases

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