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**JB Strosznajder***Mossakowski Medical Research Centre-Polish Academy of Sciences, Poland***PARP-1 inhibition modulates gene expression of mitochondria sirtuins and APP secretases: The role of PARP and sirts interaction in amyloid beta toxicity**

Poly(ADP-ribose) polymerase-1 (PARP-1) is responsible for 90% of protein poly(ADP-ribosylation) in the brain and is a key cellular NAD<sup>+</sup> consumer involved in DNA repair. However, its over activation leads to cells death. Intracellular NAD<sup>+</sup> level also regulates the activity of type III histone deacetylases sirtuins (Sirts). The interplay between PARPs and sirts is crucial in genomic stability and energy metabolism. Our recent study is focused on the effect of amyloid beta on signaling pathways and the role of PARP-1 in regulation of gene expression for enzymes involved in processing of AB precursor protein (APP) and mitochondrial sirts. PC12 cells transfected with human genes for wild type APP and bearing double Swedish mutation (APP<sup>wt</sup> and APP<sup>sw</sup>) were used in this study. Additionally the effects of extracellular AB on PC12 cells were examined. Our data showed that AB<sub>42</sub> decreases gene expression of secretase alpha (ADAM10), the main enzyme in non amyloidogenic metabolism of APP, and enhances expression for secretase beta (BACE-1) and subunits of secretase gamma which are responsible for the liberation of AB. Endogenous AB peptides liberated in APP<sup>wt</sup> and APP<sup>sw</sup> cells activate gene expression for BACE1 and secretase gamma subunits. AB also activates mitochondria sirt(s) and DNA bound PARPs expression. Pharmacological inhibition of PARP-1 leads to down regulation of gene expression for BACE1 and activates of mitochondrial sirts transcription. It seems that specific activators of Sirt1 and Sirt3 and also PARP-1 inhibitors will be promising for cytoprotection against AB and other amyloidogenic proteins in neurodegenerative diseases.

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**Biography**

JB Strosznajder obtained MD and Specialization in Neurology at Medical University of Warsaw and PhD in Biochemistry at Polish Academy of Sciences (PAS). After PhD, she spent 2 years as Alexander von Humboldt Fellow in Department of Biochemistry, University of Cologne. She is internationally recognized Neuro Scientist in the field of brain lipids, oxidative stress and signaling pathways in relation to cancer, brain ischemia, aging and neurodegeneration. She was the Head of Dept. of Cellular Signaling and the President of Scientific Council in Medical Research Centre, PAS. She trained large number of graduates. She organized many meetings and published close to 200 articles. She was awarded many times.

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