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Poly(ADP-ribose)polymerases and sirtuins the promising targets for novel natural compounds against amyloidogenic proteins toxicity

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Poly(ADP-ribose) polymerases (PARPs) and Sirtuins (Sirts) are NAD⁺ dependent enzymes involved in regulation of energy homeostasis, genomic stability. The interplay between PARPs and Sirts is crucial in brain ischemia, Alzheimer's Disease (AD) and other neurodegenerative disorders. Our recent study focused on the role of these enzymes in toxicity of amyloidogenic protein: amyloid beta (AB) and alpha synuclein (ASN) the key players in pathomechanism of AD. Our data indicated that inhibition of PARP-1 leads to activation of gene expression for Sirt1 and mitochondria Sirts (3,4,5) in PC12 cells. The inhibition of PARP-1 downregulated expression of beta secretase (BACE-1) the crucial enzyme in amyloidogenic metabolism of AB precursor protein (APP). This amyloidogenic pathway is activated by extracellular AB42 and ASN which upregulated expression of BACE-1 and also the subunits of secretase gamma. AB and ASN oligomers decreased the signaling pathways regulated by sphingosine kinase-1 and Akt kinase leading to apoptosis. Concomitantly, inhibition of Sirt1 and activation of genes for mitochondria Sirts and DNA bound PARPs occurred. Resveratrol and quercetin protect small population of cells against AB toxicity therefore it is a big request for the novel phytochemicals. We hope that PARPs and Sirts are very promising targets for novel therapeutic strategy of neurodegenerative disease.

Biography

Joanna B Strosznajder obtained her MD and specialization in Neurology from Medical University of Warsaw and PhD in Biochemistry from Polish Academy of Sciences (PAS). After PhD, she spent 2 years as Alexander von Humboldt fellow at the Department of Biochemistry, University of Cologne. She is an 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 Signalling and the President of Scientific Council in Medical Research Centre PAS. She is training a large number of students and graduates. She organized many meetings and published 200 articles. She has received many awards.

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