Sirtuin

Sirtuins are a class of proteins that possess either mono-ADP-ribosyltransferase, or deacylase activity, including deacetylase, desuccinylase, demalonylase, demyristoylase and depalmitoylase activity.

Sirtuins regulate important biological pathways in bacteria, archaea and eukaryotes. The name Sir2 comes from the yeast gene 'silent mating-type information regulation 2', the gene responsible for cellular regulation in yeast.

Sirtuins have been implicated in influencing a wide range of cellular processes like aging, transcription, apoptosis, inflammation and stress resistance, as well as energy efficiency and alertness during low-calorie situations.

Sirtuins can also control circadian clocks and mitochondrial biogenesis.

Yeast Sir2 and some, but not all, sirtuins are protein deacetylases. Unlike other known protein deacetylases, which simply hydrolyze acetyl-lysine residues, the sirtuin-mediated deacetylation reaction couples lysine deacetylation to NAD hydrolysis. This hydrolysis yields O-acetyl-ADP-ribose, the deacetylated substrate and nicotinamide, itself an inhibitor of sirtuin activity. The dependence of sirtuins on NAD links their enzymatic activity directly to the energy status of the cell via the cellular NAD:NADH ratio, the absolute levels of NAD, NADH or nicotinamide or a combination of these variables.

Sirtuins (SIRT1-SIRT7) are unique histone deacetylases (HDACs) whose activity depends on NAD+ levels and thus on the cellular metabolic status. SIRTs regulate energy metabolism and mitochondrial function. They orchestrate the stress response and damage repair. Through these functions sirtuins modulate the course of aging and affect neurodegenerative diseases. SIRTSs interact with multiple signaling proteins, transcription factors (TFs) and poly(ADP-ribose) polymerases (PARPs) another class of NAD+-dependent post-translational protein modifiers. The cross-talk between SIRTs TFs and PARPs is a highly promising research target in a number of brain pathologies. This review describes updated results on sirtuins in brain aging/neurodegeneration. It focuses on SIRT1 but also on the roles of mitochondrial SIRTs (SIRT3, 4, 5) and on SIRT6 and SIRT2 localized in the nucleus and in cytosol, respectively. The involvement of SIRTs in regulation of insulin-like growth factor signaling in the brain during aging and in Alzheimer's disease was also focused. Moreover, we analyze the mechanism(s) and potential significance of interactions between SIRTs and several TFs in the regulation of cell survival and death. A critical view is given on the application of SIRT activators/modulators in therapy of neurodegenerative diseases [1)].

SIRT6

see SIRT6.

1)
Jęśko H, Wencel P, Strosznajder RP, Strosznajder JB. Sirtuins and Their Roles in Brain Aging and Neurodegenerative Disorders. Neurochem Res. 2017 Mar;42(3):876-890. doi: 10.1007/s11064-016-2110-y. Epub 2016 Nov 24. Review. PubMed PMID: 27882448; PubMed Central

PMCID: PMC5357501.