Sirtuin 1

Sirtuin 1, also known as NAD-dependent deacetylase sirtuin-1, is a protein that in humans is encoded by the SIRT1 gene.

SIRT1 stands for sirtuin (silent mating type information regulation 2 homolog) 1 (S. cerevisiae), referring to the fact that its sirtuin homolog (biological equivalent across species) in yeast (S. cerevisiae) is Sir2. SIRT1 is an enzyme that deacetylates proteins that contribute to cellular regulation (reaction to stressors, longevity).

A gene screening analysis of aging associated markers in brain microvessels isolated from “aged” mice (C56Bl6, 18-20 months) and human brain samples showed a significant decline in sirtuin-1 expression (Sirt1; ~2.8-fold) confirmed at mRNA and protein levels and by activation assay. Experiments in Sirt1 transgenic mice and brain endothelial cell-specific Sirt1 knockout mice indicated that Sirt1 affects BBB integrity, with loss increasing permeability. Similarly, in vitro, overexpressing Sirt1 or increasing Sirt1 activity with an agonist (Sirt1720) protected against senescence-induced brain endothelial barrier hyperpermeability, stabilized claudin-5/ZO-1 interactions and rescued claudin-5 expression. These findings reveal a novel role of Sirt1 in modulating aging-associated BBB persistent leakage [1)].

The aim of a study was to investigate the neuroprotective effect of resveratrol and elucidate the underlying mechanisms of resveratrol associated regulation of the NLRP3 inflammasome in TBI. The results demonstrated that the activation of NLRP3, caspase-1 and sirtuin 1 (SIRT1), enhanced the production of inflammatory cytokines and reactive oxygen species (ROS) following TBI. Administration of resveratrol alleviated the degree of TBI, as evidenced by the reduced neuron-specific enolase (NSE) and brain water content (WBC). Resveratrol pretreatment also inhibited the activation of NLRP3 and caspase-1, and reduced the production of inflammatory cytokines and ROS. In addition, resveratrol further promoted SIRT1 activation. Furthermore, the suppressing effect of resveratrol on the NLRP3 inflammasome and ROS was blocked by the SIRT1 inhibitor, sirtinol. The results revealed that the activation of the NLRP3 inflammasome and the subsequent inflammatory responses in the cerebral cortex were involved in the process of TBI. Resveratrol may attenuate the inflammatory response and relieve TBI by reducing ROS production and inhibiting NLRP3 activation. The effect of resveratrol on NLRP3 inflammasome and ROS may also be SIRT1 dependent [2)].

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Stamatovic SM, Martinez GR, Hu A, Choi J, Keep RF, Andjelkovic AV. Decline in Sirtuin-1 expression and activity plays a critical role in blood-brain barrier permeability in aging. Neurobiol Dis. 2018 Sep 6. pii: S0969-9961(18)30555-2. doi: 10.1016/j.nbd.2018.09.006. [Epub ahead of print] Review. PubMed PMID: 30196051.

2)
Zou P, Liu X, Li G, Wang Y. Resveratrol pretreatment attenuates traumatic brain injury in rats by suppressing NLRP3 inflammasome activation via SIRT1. Mol Med Rep. 2017 Dec 11. doi: 10.3892/mmr.2017.8241. [Epub ahead of print] PubMed PMID: 29257276.