Role of SIRT1 in sepsis-induced encephalopathy: molecular targets for future therapies

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Abstract

Sepsis is a life-threatening organ dysfunction that results from dysregulated host response to infection. Multiple organ system dysfunction syndromes are prevalent among septic patients and are essential hallmarks of sepsis diagnosis. These syndromes involve failure of the pulmonary, hepatic, circulatory, renal, gastrointestinal and central nervous systems. Neurological dysfunction is part of this syndrome and has gained research attention recently [1]. Sepsis induces neuroinflammation, BBB disruption, cerebral hypoxia, neuronal mitochondrial dysfunction and cell death causing sepsis-associated encephalopathy (SAE). These pathological consequences lead to short- and long-term neurobehavioral deficits. Till now there is no specific treatment that directly improves SAE and its associated behavioral impairments. In this review, we discuss the underlying mechanisms of sepsis-induced brain injury with a focus on the latest progress regarding neuroprotective effects of SIRT1 (silent mating type information regulation-2 homologue-1). SIRT1 is an NAD+-dependent class III protein deacetylase. It is able to modulate multiple downstream signals (including NF-ϰB, HMGB, AMPK, PGC1α and FoxO) which are involved in the development of SAE by its deacetylation activity. There are multiple recent studies showing the neuroprotective effects of SIRT1 in neuroinflammation related diseases. The proposed neuroprotective action of SIRT1 is meant to bring a promising therapeutic strategy for managing SAE and ameliorating its related behavioural deficits.

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