rCTRP9

Neuroinflammation is a crucial factor contributing to neurological injuries after intracerebral hemorrhage (ICH). C1qtnf9, an agonist of adiponectin receptor 1 (AdipoR1), has recently been shown to reduce inflammatory responses in systemic diseases. The objective of this study was to investigate the protective role of CTRP9 against neuroinflammation after ICH in a mouse model and to explore the contribution of adenosine monophosphate-activated protein kinase (AMPK)/nuclear factor kappa B (NFκB) pathway in AdipoR1-mediated protection.

Adult male CD1 mice (n = 218) were randomly assigned to different groups for the study. ICH was induced via intrastriatal injection of bacterial collagenase. Recombinant CTRP9 (rCTRP9) was administered intranasally at 1 h after ICH. To elucidate the underlying mechanism, AdipoR1 small interfering ribonucleic acid (siRNA) and selective phosphorylated AMPK inhibitor Dorsomorphin were administered prior to rCTRP9 treatment. Brain edema, short- and long-term neurobehavior evaluation, blood glucose level, western blot, and immunofluorescence staining were performed.

Endogenous CTRP9 and AdipoR1 expression was increased and peaked at 24 h after ICH. AdipoR1 was expressed by microglia, neurons, and astrocytes. Administration of rCTRP9 reduced brain edema, improved short- and long-term neurological function, enhanced the expression of AdipoR1 and p-AMPK, and decreased the expression of phosphorylated NFκB and inflammatory cytokines after ICH. The protective effects of rCTRP9 were abolished by administration of AdipoR1 siRNA and Dorsomorphin.

The findings demonstrated that administration of rCTRP9 attenuated neuroinflammation through AdipoR1/AMPK/NFκB signaling pathway after ICH in mice, thereby reducing brain edema and improving neurological function after experimental ICH in mice. Therefore, CTRP9 may provide a potential therapeutic strategy to alleviate neuroinflammation in ICH patients [1)].

1)
Zhao L, Chen S, Sherchan P, Ding Y, Zhao W, Guo Z, Yu J, Tang J, Zhang JH. Recombinant CTRP9 administration attenuates neuroinflammation via activating adiponectin receptor 1 after intracerebral hemorrhage in mice. J Neuroinflammation. 2018 Jul 30;15(1):215. doi: 10.1186/s12974-018-1256-8. PubMed PMID: 30060752; PubMed Central PMCID: PMC6066941.