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Nrf2 inhibits NLRP3 inflammasome activation through regulating Trx1/TXNIP complex in cerebral ischemia reperfusion injury

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The Nod-like receptor protein 3 (NLRP3) inflammasome has a critical role in inflammation damage during ischemic injury, and the activation of the inflammasome is closely related to the interaction with thioredoxin interacting protein (TXNIP), which dissociates from the thioredoxin 1 (Trx1)/TXNIP complex under oxidative stress. However, the negative regulator of NLRP3 inflammasome activation has not been fully investigated. Nuclear factor erythroid 2-related factor 2 (Nrf2) takes on a critical part in the antioxidant stress system, which controls the driven genes of antioxidant response element (ARE). Activated Nrf2 can inhibit the activation of NLRP3 inflammasome in acute liver injury and severe lupus nephritis. We aimed at exploring the protective effect of Nrf2 in inhibiting the NLRP3 inflammasome formulation through the Trx1/TXNIP complex in cerebral ischemia reperfusion (cerebral I/R) injury. Middle cerebral artery occlusion/reperfusion (MCAO/R) model was used to imitate ischemic insult. Tert-Butylhydroquinone (tBHQ) was intraperitoneally (i.p.) injected before the MCAO model to overexpress Nrf2. After upregulating Nrf2, the expression of TXNIP in cytoplasm, NLRP3 inflammasome, and downstream factors caspase-1, IL-18, and IL-1 β were significantly reduced. Nrf2 siRNAs were injected into the rats' brains 24 h prior to establishing the Nrf2 knockdown MCAO model, which yielded the opposite results. Trx1 knockdown produced the same effect of Nrf2 inhibition and the protective effect of Nrf2 was mostly abolished by Trx1 knockdown. In conclusion, these results suggested that Nrf2 acted as a protective regulator against NLRP3 inflammasome activation by regulating the Trx1/TXNIP complex, which could possibly represent an innovative insight into the treatment of ischemia and reperfusion injury.

Biography

Jing Zhao is working in Department of Pathophysiology, Chongqing Medical University, Chongqing, People's Republic of China. She has also published many research papers in international journals.

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