USP20

Ischemic stroke is a leading cause of death worldwide. The lack of effective pharmacotherapies for ischemic stroke is mainly attributed to the incomplete understanding of its pathogenesis. Deubiquitinase ubiquitin-specific protease 20 (USP20) plays an important role in regulating multiple cellular processes. However, its effects on cerebral ischemic stroke still remain unknown. Pan et al. found that USP20 expression was markedly increased in the early phase of ischemic stroke in mice with middle cerebral artery occlusion (MCAO) operation, and were then considerably decreased in mice with ischemia-reperfusion (I/R) injury. Double immunofluorescence staining showed USP20 abundance in both microglial cells and neurons. We then found that promoting USP20 expression remarkably ameliorated MCAO-induced ischemic brain injury, along with significantly reduced infarct volume, neurological scores, and brain water contents. In addition, cognitive impairments in MCAO-operated mice were considerably alleviated by USP20 over-expression. Furthermore, USP20 over-expression dramatically restrained microglial activation, inflammatory response and neuronal death in mice with ischemic stroke. Moreover, our results indicated that phosphatase and tensin homolog (PTEN) expression was highly decreased in the infarct areas of MCAO-treated mice while being greatly rescued by USP20 over-expression. All these effects mediated by USP20 during cerebral I/R injury were confirmed in the cultured primary microglial cells and cortical neurons stimulated by oxygen-glucose deprivation and reoxygenation (OGD/R). Mechanistically, we found that USP20 directly interacted with PTEN. Notably, suppressing PTEN with its specific inhibitor dramatically abolished the function of USP20 to ameliorate neuroinflammation and neuron death induced by OGD/R. Collectively, our results illustrated that USP20 could effectively mitigate the severity of the cerebral ischemic stroke and improve behavioral deficits in MCAO-operated mice, and identified the USP20/PTEN axis as a promising therapeutic target for ischemic stroke treatment [1].

1)

Pan R, Xie Y, Fang W, Liu Y, Zhang Y. USP20 mitigates ischemic stroke in mice by suppressing neuroinflammation and neuron death via regulating PTEN signal. Int Immunopharmacol. 2021 Dec 22;103:107840. doi: 10.1016/j.intimp.2021.107840. Epub ahead of print. PMID: 34953448.