Ferroptosis

Ferroptosis is a form of programmed cell death decided by iron dependent lipid peroxidation, which has unique biological effects on metabolism and redox biology.

This cell death mode featured by lipid peroxide accumulation can be attenuated by GPX4, yet whether and how MYCN regulates ferroptosis is not fully understood.

Zhang et al. aimed to investigate the regulatory role of Netrin-1 (NTN1) in ferroptosis after traumatic brain injury (TBI) in mice.

They assessed the expression pattern of NTN1 by RT-PCR, western blot, and immunofluorescence after establishing the TBI model in mice. After treatment with NTN1 shRNA or recombinant NTN1, we determined the biochemical and morphological changes associated with ferroptosis and netrin-1-related pathways. We used Nissl staining to assess lesion volume and the Morris water maze and beam-walking test to evaluate ethological manifestation.

The mRNA and protein levels of NTN1 were upregulated after TBI. The application of NTN1 shRNA increased the number of FJB-positive cells, malondialdehyde (MDA), and reactive oxygen species (ROSs) levels. However, the application of NTN1 recombinant had the opposite effect. Furthermore, knockdown or inhibition of GPX4, Nrf2, and UNC5B counteracted the effects of NTN1 recombinant. Intravenous injection of NTN1 recombinant reduced neuronal loss after CCI and improved motor and cognitive function.

NTN1 had a neuroprotective effect after TBI and inhibited ferroptosis via activating the UNC5B/Nrf2 pathway. These findings may provide potential therapeutic strategies for TBI [1].

Jiao et al. reported that primary cortical astrocytes (PA), microglia (PM), and neurons (PN) varied in their sensitivities to ferroptosis. Specifically, PM was the most sensitive to ferroptosis, while PN was relatively insensitive. In contrast, PN and PM were equally susceptible to apoptosis, with PA being less affected, whereas all three cell types were similarly susceptible to autophagic cell death. In the tri-culture system containing PA, PM, and PN, the cells were more resistant to ferroptosis than that in the monoculture. These results demonstrated that brain cells exhibit different sensitivities under ferroptosis stress and the difference may be explained by the differentially regulated iron metabolism and the ability to handle iron. Continued elucidation of the cell death patterns of neurons and glia will provide a theoretical basis for related strategies to inhibit the death of brain cells [2].

Ferroptosis in glioma

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Zhang Y, Lan J, Zhao D, Ruan C, Zhou J, Tan H, Bao Y. Netrin-1 upregulates GPX4 and prevents ferroptosis after traumatic brain injury via the UNC5B/Nrf2 signaling pathway. CNS Neurosci Ther. 2022 Dec 5. doi: 10.1111/cns.13997. Epub ahead of print. PMID: 36468399.
2)
Jiao L, Li X, Luo Y, Wei J, Ding X, Xiong H, Liu X, Lei P. Iron metabolism mediates microglia susceptibility in ferroptosis. Front Cell Neurosci. 2022 Aug 30;16:995084. doi: 10.3389/fncel.2022.995084. PMID: 36111246; PMCID: PMC9469838.