GSTO2

“GSTO2” typically refers to Glutathione S-transferase omega-2, which is a gene that encodes a protein involved in the cellular detoxification process. Glutathione S-transferases are enzymes that play a role in the detoxification of various substances, including xenobiotics and products of oxidative stress.

Previous research has found that an adaptive response to ferroptosis involving glutathione peroxidase 4 (GPX4) is triggered after intracerebral hemorrhage. However, little is known about the mechanisms underlying adaptive responses to ferroptosis. To explore the mechanisms underlying adaptive responses to ferroptosis after intracerebral hemorrhage, Lin et al. used hemin-treated HT22 cells to mimic brain injury after hemorrhagic stroke in vitro to evaluate the antioxidant enzymes and performed bioinformatics analysis based on the mRNA sequencing data. Further, they determined the expression of GSTO2 in hemin-treated hippocampal neurons and a mouse model of hippocampus-intracerebral hemorrhage (h-ICH) by using Western blot. After hemin treatment, the antioxidant enzymes GPX4, Nrf2, and glutathione (GSH) were upregulated, suggesting that an adaptive response to ferroptosis was triggered. Furthermore, they performed mRNA sequencing to explore the underlying mechanism, and the results showed that 2234 genes were differentially expressed. Among these, ten genes related to ferroptosis (Acsl1, Ftl1, Gclc, Gclm, Hmox1, Map1lc3b, Slc7a11, Slc40a1, Tfrc, and Slc39a14) were altered after hemin treatment. In addition, analysis of the data retrieved from the GO database for the ten targeted genes showed that 20 items on biological processes, 17 items on cellular components, and 19 items on molecular functions were significantly enriched. Based on the GO data, we performed GSEA and found that the glutathione metabolic process was significantly enriched in the hemin phenotype. Notably, the expression of glutathione S-transferase omega (GSTO2), which is involved in glutathione metabolism, was decreased after hemin treatment, and overexpression of Gsto2 decreased lipid reactive oxygen species level in hemin-exposed HT22 cells. In addition, the expression of GSTO2 was also decreased in a mouse model of hippocampus-intracerebral hemorrhage (h-ICH). The decreased expression of GSTO2 in the glutathione metabolic process may be involved in ferroptotic neuronal injury following hemorrhagic stroke [1)].

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Lin L, Li XN, Xie ZY, Hu YZ, Long QS, Wen YQ, Wei XB, Zhang LY, Li XS. Pivotal Role of GSTO2 in Ferroptotic Neuronal Injury After Intracerebral Hemorrhage. J Mol Neurosci. 2024 Feb 22;74(1):24. doi: 10.1007/s12031-023-02187-y. PMID: 38386166.