Erastin

In a study, the A20-knockdown BV2 cell line (sh-A20 BV2) was constructed at first, and the oxygen-glucose deprivation/re-oxygenation (OGD/R) cell model was constructed. Both the BV2 and sh-A20 BV2 cells were treated with the Ferroptosis inducer erastin for 48 h, and the Ferroptosis-related indicators were detected by western blot. The mechanism of Ferroptosis was explored by western blot and immunofluorescence. Under OGD/R pressure, the oxidative stress level of sh-A20 BV2 cells was inhibited, but the secretion of the inflammatory factors TNF-α, IL-1β, and IL-6 was significantly upregulated. And sh-A20 BV2 cells had higher expression levels of GPX4 and NLRP3 proteins under OGD/R induction. Western blot further confirmed that sh-A20 BV2 cells inhibited OGD/R-induced Ferroptosis. Under the effect of erastin of the Ferroptosis inducer (0-1000 nM), sh-A20 BV2 cells had higher cell viability than wild-type BV2 cells and significantly inhibited the accumulation of ROS and the level of oxidative stress damage. It was confirmed that A20 could promote the activation of the IκBα/NFκB/iNOS pathway. It was confirmed by an iNOS inhibitor that iNOS inhibition could reverse the resistance effect of BV2 cells to OGD/R-induced Ferroptosis after A20 knockdown. In conclusion, this study demonstrated that inhibition of A20 mediates a stronger inflammatory response while enhancing microglial resistance by knocking down A20 in BV2 cells [1)].

In this study, glutathione (GSH) and reactive oxygen species (ROS) levels were found to be closely associated with the sensitivity of GBM cells to TMZ. We also found that TMZ markedly induced xCT, the subunit of glutamate/cystine transporter system xc- expression, which together with the GSH synthesis was increased while the TMZ-inducible ROS level was decreased in GBM cells. In addition, the cystathionine γ-lyase (CTH) acivity, a key enzyme in the transsulfuration pathway was enhanced by TMZ, which insured a cysteine supply and GSH synthesis in a compensatory manner when xCT was blocked. Thus, the individual inhibition of xCT by siRNA and a pharmacological inhibitor (sulfasalazine) only partially inhibited GSH synthesis and moderately enhanced the GBM cell sensitivity to TMZ. However, the TMZ-induced cytotoxicity was markedly increased along with a marked decrease in GSH levels as result of co-treatment with erastin, which inhibited cysteine uptake from xCT transporter and suppressed CTH activity, leading to impaired transformation from methionine to cysteine. In conclusion, to GBM therapy with a drug combination of TMZ and erastin may be beneficial [2)].

1)
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2)
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