Hexokinase 2

Recent studies revealed that Hexokinase 2 (HK2)-mediated glycolysis is one of the sources, as the association of chemoresistance and the expression of HK2 was confirmed in multiple cancers. However, there has been little knowledge of the functional contribution of HK2 to TMZ resistance in GBM. Zhang et al. found that HK2 expression is crucial for GBM proliferation and chemoresistance. In contrast to the healthy brain, HK2 expression is much higher in human GBM, especially in those patients with recurrent glioblastoma. High HK2 expression is negatively related to the overall survival in GBM patients. HK2 depletion in GBM cells suppressed the GBM cell proliferation and increased sensitivity to TMZ-induced apoptosis. Both HK2-mediated glycolysis and mitochondria permeability transition pore opening (MPTP) were associated with its function in chemoresistance. Furthermore, they also revealed that the abnormal expression of HK2 was modulated by the expression of HOTAIR, a long non-coding RNA (lncRNA). The absence of HOTAIR in GBM cells suppressed the HK2 expression in protein and mRNA level and, therefore, inhibited the cell proliferation and enhanced the cytotoxicity of TMZ both in vivo and in vitro. HOTAIR promoted the expression of HK2 by targeting mir 125, which suppressed the GBM cell proliferation and increased the TMZ-induced apoptosis. These findings shed light on a new therapeutic strategy in modulating HOTAIR/miR 125, which may interfere with the expression of HK2, and enhance the therapeutic sensitivity of GBM to TMZ [1].

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Zhang J, Chen G, Gao Y, Liang H. HOTAIR/miR-125 axis-mediated Hexokinase 2 expression promotes chemoresistance in human glioblastoma. J Cell Mol Med. 2020 Apr 12. doi: 10.1111/jcmm.15233. [Epub ahead of print] PubMed PMID: 32279420.