MiR-125, which is a highly conserved miRNA throughout diverse species from nematode to humans, consists of three homologs hsa-miR-125a, hsa-miR-125b-1 and hsa-miR-125-2. Members of this family have been validated to be down-regulated, exhibiting its disease-suppressing properties in many different types of diseases, while they also have disease-promoting functions in certain contexts. MiR-125 targets a number of genes such as transcription factors, matrix-metalloprotease, members of Bcl-2 family and others, aberrance of which may lead to abnormal proliferation, metastasis and invasion of cells, even carcinomas. Furthermore, miR-125 plays a crucial role in immunological host defense, especially in response to bacterial or viral infections. In this review, we summarize the implication of miR-125 family in disease suppression and promotion, focusing on carcinoma and host immune responses.

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.