NFAT2

Deregulation of the nuclear factor of activated T cell (NFAT) pathway has been reported in several human cancers. Particularly, NFAT2 is involved in the malignant transformation of tumor cells and is identified as an oncogene. However, the role of NFAT2 in glioblastoma (GBM) is largely unknown.

METHODS: The expression and prognostic value of NFAT2 were examined in REMBRANDT and TCGA databases and clinical samples. The functional effects of silencing or overexpression of NFAT2 were evaluated in glioma stem cell (GSC) viability, invasion and self-renewal in vitro and in tumorigenicity in vivo. The downstream target of NFAT2 was investigated.

RESULTS: High NFAT2 expression was significantly associated with mesenchymal (MES) subtype and recurrent GBM and predicted poor survival. NFAT2 silencing inhibited the invasion and clonogenicity of MES GSC-enriched spheres in vitro and in vivo. NFAT2 overexpression promoted tumor growth and MES differentiation of GSCs. A TCGA database search showed that histone deacetylase 1 (HDAC1) expression was significantly correlated with that of NFAT2. NFAT2 regulates the transcriptional activity of HDAC1. Rescue of HDAC1 in NFAT2-knockdown GSCs partially restored tumor growth and MES phenotype. Loss of NFAT2 and HDAC1 expression resulted in hyperacetylation of NF-κB, which inhibits NF-κB-dependent transcriptional activity.

CONCLUSION: Our findings suggest that the NFAT2-HDAC1 pathway might play an important role in the maintenance of the malignant phenotype and promote MES transition in GSCs, which provide potential molecular targets for the treatment of GBMs [1].

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Song Y, Jiang Y, Tao D, Wang Z, Wang R, Wang M, Han S. NFAT2-HDAC1 signaling contributes to the malignant phenotype of glioblastoma. Neuro Oncol. 2019 Aug 11. pii: noz136. doi: 10.1093/neuonc/noz136. [Epub ahead of print] PubMed PMID: 31400279.