Mucin 1

Based on CRISPR-Cas9 library screening, Tong et al. found that mucin 1 (MUC1) is essential for EGFRvIII glioma cell survival and temozolomide (TMZ) resistance. They revealed that MUC1-C was upregulated in EGFRvIII-positive cells, where it enhanced the stability of EGFRvIII. Knockdown of MUC1-C increased the colocalization of EGFRvIII and lysosomes. Upregulation of MUC1 occurred in an NF-κB dependent manner, and inhibition of the NF-κB pathway could interrupt the EGFRvIII-MUC1 feedback loop by inhibiting MUC1-C. In a previous report, we identified AC1Q3QWB (AQB), a small molecule that could inhibit the phosphorylation of NF-κB. By screening the structural analogs of AQB, we obtained EPIC-1027, which could inhibit the NF-κB pathway more effectively. EPIC-1027 disrupted the EGFRvIII-MUC1-C positive feedback loop in vitro and in vivo, inhibited glioma progression, and promoted sensitization to TMZ. In conclusion, we revealed the pivotal role of MUC1-C in stabilizing EGFRvIII in glioblastoma (GBM) and identified a small molecule, EPIC-1027, with great potential in GBM treatment [1].

1)
Tong F, Zhao JX, Fang ZY, Cui XT, Su DY, Liu X, Zhou JH, Wang GX, Qiu ZJ, Liu SZ, Fu JQ, Kang CS, Wang JC, Wang QX. MUC1 promotes glioblastoma progression and TMZ resistance by stabilizing EGFRvIII. Pharmacol Res. 2022 Dec 11;187:106606. doi: 10.1016/j.phrs.2022.106606. Epub ahead of print. PMID: 36516884.