OSMR

OSMR is a member of the type I cytokine receptor family. This protein heterodimerizes with interleukin 6 signal transducer to form the type II oncostatin M receptor and with interleukin 31 receptor A to form the interleukin 31 receptor, and thus transduces oncostatin M and interleukin 31 induced signaling events.

EGFRvIII-STAT3 signaling is important in glioblastoma pathogenesis. Jahani-Asl et al., identified the cytokine receptor OSMR as a direct target gene of the transcription factor STAT3 in mouse astrocytes and human brain tumor stem cells (BTSCs). They found that OSMR functioned as an essential co-receptor for EGFRvIII. OSMR formed a physical complex with EGFRvIII, and depletion of OSMR impaired EGFRvIII-STAT3 signaling. Conversely, pharmacological inhibition of EGFRvIII phosphorylation inhibited the EGFRvIII-OSMR interaction and activation of STAT3. EGFRvIII-OSMR signaling in tumors operated constitutively, whereas EGFR-OSMR signaling in nontumor cells was synergistically activated by the ligands EGF and OSM. Finally, knockdown of OSMR strongly suppressed cell proliferation and tumor growth of mouse glioblastoma cells and human BTSC xenografts in mice, and prolonged the lifespan of these mice. Our findings identify OSMR as a critical regulator of glioblastoma tumor growth that orchestrates a feed-forward signaling mechanism with EGFRvIII and STAT3 to drive tumorigenesis [1].

In total, the authors' work establishes a link between OSMR and EGFRvIII-STAT3 signaling as it relates to tumor growth. More important, they demonstrate that depletion of OSMR retards tumor growth and highlight a potential therapeutic target for the treatment of glioblastoma [2].

1)
Jahani-Asl A, Yin H, Soleimani VD, Haque T, Luchman HA, Chang NC, Sincennes MC, Puram SV, Scott AM, Lorimer IA, Perkins TJ, Ligon KL, Weiss S, Rudnicki MA, Bonni A. Control of glioblastoma tumorigenesis by feed-forward cytokine signaling. Nat Neurosci. 2016 Jun;19(6):798-806. doi: 10.1038/nn.4295. Epub 2016 Apr 25. PubMed PMID: 27110918; PubMed Central PMCID: PMC4984527.
2)
Newman WC, Amankulor NA. Control of Glioblastoma Tumorigenesis by Feed-Forward Cytokine Signaling. Neurosurgery. 2016 Oct;79(4):N9-N10. doi: 10.1227/NEU.0000000000001381. PubMed PMID: 27635977.