STAT5B

Signal transducer and activator of transcription 5B is a protein that in humans is encoded by the STAT5B gene.

STAT5B orthologs have been identified in most placentals for which complete genome data are available.

The copy number and mRNA expression of STAT5b were assessed in samples from the TCGA repository of glioblastomas (Glioblastoma). The activation of this transcription factor was analyzed on tissue microarrays comprising 392 WHO 2016 Glioblastoma samples from our clinical practice. These data were correlated with patient survival using multivariable Cox analysis and, for a subset of 167 tumors, with signs of tumor invasiveness on the MRI. The effects of STAT5b knockdown by siRNA were assessed on the growth, therapeutic resistance, invasion, and migration of Glioblastoma cell lines U87, U87-EGFRVIII, and LN18 and primary cultures GM2 and GM3. The activation, but not the copy number or the mRNA expression of the nuclear transcription factor STAT5b expression correlated inversely with patient survival independently of IDH1R132H status, age, Karnofsky Performance Score, treatment, and tumor volume. STAT5b inhibition neither altered the cell proliferation nor reduced the clonogenic proliferative potency of Glioblastoma cells and did not sensitize them to the cytotoxic effect of ionizing radiation and temozolomide in vitro. STAT5b inhibition significantly increased Glioblastoma cell migration but decreased the invasion of some Glioblastoma cells in vitro. There was no correlation between the activation of STAT5b in clinical tumors and the extent of invasion on MRI OF patients. In conclusion, STAT5b is frequently activated in Glioblastoma and correlates inversely with patient survival. It does not contribute to the growth and resistance of these tumors and is thus rather a potential prognostic marker than a therapeutic target in these tumors [1)]

Function

The protein encoded by this gene is a member of the STAT family of transcription factors. In response to cytokines and growth factors, STAT family members are phosphorylated by the receptor-associated kinases, and then form homo- or heterodimers that translocate to the cell nucleus where they act as transcription activators. This protein mediates the signal transduction triggered by various cell ligands, such as IL2, IL4, CSF1, and different growth hormones. It has been shown to be involved in diverse biological processes, such as TCR signaling, apoptosis, adult mammary gland development, and sexual dimorphism of liver gene expression. This gene was found to fuse to the retinoic acid receptor-alpha (RARA) gene in a small subset of acute promyelocytic leukemias (APML). The dysregulation of the signaling pathways mediated by this protein may be the cause of the APML.

1)
Dubois N, Berendsen S, Tan K, Schoysmans L, Spliet W, Seute T, Bours V, Robe PA. STAT5b is a marker of poor prognosis, rather than a therapeutic target in glioblastomas. Int J Oncol. 2022 Oct;61(4):124. doi: 10.3892/ijo.2022.5414. Epub 2022 Sep 7. PMID: 36069226.