Kaiso

Transcriptional regulator Kaiso is a protein that in humans is encoded by the ZBTB33 gene.

This gene encodes a transcriptional regulator with bimodal DNA-binding specificity, which binds to methylated CGCG and also to the non-methylated consensus KAISO-binding site TCCTGCNA. The protein contains an N-terminal POZ/BTB domain and 3 C-terminal zinc finger motifs. It recruits the N-CoR repressor complex to promote histone deacetylation and the formation of repressive chromatin structures in target gene promoters. It may contribute to the repression of target genes of the Wnt signaling pathway, and may also activate transcription of a subset of target genes by the recruitment of catenin delta-2 (CTNND2). Its interaction with catenin delta-1 (CTNND1) inhibits binding to both methylated and non-methylated DNA. It also interacts directly with the nuclear import receptor Importin-α2 (also known as karyopherin alpha2 or RAG cohort 1), which may mediate nuclear import of this protein. Alternatively spliced transcript variants encoding the same protein have been identified.

Kaiso is highly expressed in TNBCs and correlates with a shorter metastasis-free survival. Notably, Kaiso expression is induced by the TGFβ pathway and silencing Kaiso expression in the highly invasive breast cancer cell lines, MDA-MB-231 (hereafter MDA-231) and Hs578T, attenuated the expression of several EMT-associated proteins (Vimentin, Slug and ZEB1), abrogated TGFβ signaling and TGFβ-dependent EMT. Moreover, Kaiso depletion attenuated the metastasis of TNBC cells (MDA-231 and Hs578T) in a mouse model. Although high Kaiso and high TGFβR1 expression is associated with poor overall survival in breast cancer patients, overexpression of a kinase-active TGFβR1 in the Kaiso-depleted cells was insufficient to restore the metastatic potential of these cells, suggesting that Kaiso is a key downstream component of TGFβ-mediated pro-metastatic responses. Collectively, these findings suggest a critical role for Kaiso in TGFβ signaling and the metastasis of TNBCs [1)].

Kaiso (ZBTB33) expression is closely associated with the progression of many cancers and microRNA (miRNA) processing. miR 181a plays critical roles in multiple cancers; however, its precise mechanisms in glioma have not been well clarified. The goal of a study of Wang et al., from the Harbin Medical University, Harbin, China, was to evaluate the interaction between Kaiso and miR-181a in glioma.

Quantitative real-time PCR (qRT-PCR) was performed to detect the levels of Kaiso and miR-181a in glioma tissues and cell lines. Cell proliferation, invasion, and the Epithelial-mesenchymal-transition (EMT) were evaluated to analyze the biological functions of miR-181a and Kaiso in glioma cells. The mRNA and protein levels of Kaiso were measured by qRT-PCR and western blotting, respectively. Meanwhile, luciferase assays were performed to validate Kaiso as a miR-181a target in glioma cells.

They found that the level of miR-181a was the lowest among miR-181a-d in glioma tissues and cell lines, and the low level of miR-181a was closely associated with the increased expression of Kaiso in glioma tissues. Moreover, transfection of miR-181a significantly inhibited the proliferation, invasion, and EMT of glioma cells, whereas knockdown of miR-181a had the opposite effect. Bioinformatics analysis predicted that Kaiso was a potential target gene of miR-181a, and the luciferase reporter assay demonstrated that miR-181a could directly target Kaiso. In addition, Kaiso silencing had similar

effects as miR-181a overexpression in glioma cells, whereas overexpression of Kaiso in glioma cells partially reversed the inhibitory effects of the miR-181a mimic.

miR-181a inhibited the proliferation, invasion, and EMT of glioma cells by directly targeting and downregulating Kaiso expression [2].

1)
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2)
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