Twist1

Twist-related protein 1 (TWIST1) also known as class A basic helix-loop-helix protein 38 (bHLHa38) is a basic helix-loop-helix transcription factor that in humans is encoded by the TWIST1 gene.

Twist1 is A master regulator of the epithelial to mesenchymal transition (EMT).

The Glioblastoma cells were isolated and cultured in vitro, and then transfected with miR-489 inhibitor, miR-489 mimics and miR-negative control (NC) or TWIST1-small interfering RNA (siRNA) and TWIST1-NC. The expression levels of miR-489 and TWIST1 gene in the cells were measured via quantitative reverse transcription-polymerase chain reaction (qRT-PCR), and the proliferative capacity of cells in each group was detected by cell counting kit-8 (CCK-8) assay. Besides, the target gene TWIST1 of miR-489 was predicted to construct the luciferase reporter gene vectors of TWIST1 containing miR-489 target sites.

Results: The expression level of miR-489 in Glioblastoma tissues and Glioblastoma cells isolated and cultured in vitro was remarkably lower than that in normal tissues and cells ($p<0.01$). The proliferative capacity of Glioblastoma cells was enhanced notably after inhibiting the expression of miR-489 ($p<0.01$), while it was obviously weakened by overexpressed miR-489 or TWIST1-siRNA ($p<0.01$). Moreover, the apoptosis rate was increased from 2.3±0.4% to 19.6±1.2% following miR-489 overexpression. TWIST1-siRNA could markedly down-regulate the expression level of TWIST1 ($p<0.01$) but evidently up-regulate the protein expression levels of Caspase-3 and Caspase-8 ($p<0.01$). The results of luciferase reporter assay manifested that miR-489 mimics significantly repressed TWIST1 ($p<0.01$).

MiR-489 can repress the proliferation and promote the apoptosis of glioma cells by targeting TWIST1 [1)].

In vitro, promotes mesenchymal change, invasion and self-renewal in glioblastoma (Glioblastoma) cells. However the potential therapeutic relevance of TW has not been established through loss of function studies in human Glioblastoma cell xenograft models. The effects of TW loss of function (gene editing and knock down) on inhibition of tumorigenicity of U87MG and Glioblastoma4 glioma stem cells were tested in orthotopic xenograft models and conditional knockdown in established flank xenograft tumors. RNAseq and the analysis of tumors investigated putative TW associated mechanisms. Multiple bioinformatics tools revealed significant alteration of ECM, membrane receptors, signaling transduction kinases and cytoskeleton dynamics leading to identification of PI3K/AKT signaling. We experimentally show alteration of AKT activity and periostin (POSTN) expression in vivo and/or in vitro. For the first time we show that effect of TW knockout inhibits AKT activity in U87MG cells in vivo independent of PTEN mutation. The clinical relevance of TW and candidate mechanisms was established by analysis of the TCGA and ENCODE databases. TW expression was associated with decreased patient survival and LASSO regression analysis identified POSTN as one of top targets of TW in human Glioblastoma. While we previously demonstrated the role of TW in promoting EMT and invasion of glioma cells, these studies provide direct experimental evidence supporting pro-tumorigenic role of TW independent of invasion in vivo and the therapeutic relevance of targeting TW in human Glioblastoma. Further, the role of TW driving POSTN expression and AKT signaling suggests actionable targets, which could be leveraged to mitigate the oncogenic

effects of TW in Glioblastoma [2].

Acromegaly had minimal effects on tested mRNAs specific for osteoblast or osteoclast function except for downregulated ALP expression. The expressions of miR known to be involved in mesenchymal stem cell commitment and downregulated TWIST1 expression indicate negative effect of acromegaly on osteoblastogenesis [3].

Kahn et al. identified a mechanism in which NOTCH1 activates BMI1 through the activation of TWIST1. NOTCH1 expression and activity are directly related to medulloblastoma metastasis and decreased survival rate of tumor-bearing mice [4].

1)
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