FOXM1

Forkhead Box M1 (FOXM1), is a FOX protein, well demonstrated to be critical for proliferation, apoptosis, migration and invasion of human cancer [1].

It is encoded by the FOXM1 gene.

FOXM1 has been awarded the Molecule of the Year 2010 for its growing potential as a target for cancer diagnosis and therapies.

Temozolomide resistance is considered to be one of the major reasons responsible for glioblastoma treatment failure. CXCL12/CXCR4 has been demonstrated to be involved in cell proliferation, cell migration, cell invasion, angiogenesis, and radioresistance in glioblastoma (Glioblastoma). However, its role in TMZ resistance in Glioblastoma is unknown. Wang et al. aimed to evaluate the role of CXCL12/CXCR4 in mediating the TMZ resistance to Glioblastoma cells and explore the underlying mechanisms. They found that the CXCL12/CXCR4 axis enhanced TMZ resistance in Glioblastoma cells. Further study showed that CXCL12/CXCR4 conferred TMZ resistance and promoted the migration and invasion of Glioblastoma cells by up-regulating FOXM1. This resistance was partially reversed by suppressing CXCL12/CXCR4 and FOXM1 silencing. This study revealed the vital role of CXCL12/CXCR4 in mediating the resistance of Glioblastoma cells to TMZ, and suggested that targeting CXCL12/CXCR4 axis may attenuate the resistance to TMZ in Glioblastoma [2].

Silencing of FoxM1 could reverse TGF-β1-induced invasion and epithelial-mesenchymal transition (EMT) of endometriotic epithelial cells (EECs) [3].

FoxM1 is overexpressed in human glioblastomas and contributes to glioma tumorigenicity [4] , by enhancing MMP-2 gene transcription and thus tumor-cell invasion [5] , enhancing VEGF gene transcription and thus tumor angiogenesis [6] , in cooperation with p53 and pRB inhibition in NHA cells, promotes astrocyte transformation and Glioblastoma formation through multiple mechanisms [7].

FoxM1-beta-catenin interaction controls Wnt target gene expression, is required for glioma formation, and represents a mechanism for canonical Wnt signaling during tumorigenesis [8].

Results indicate that FoxM1 is regulated by HSF1 and is critical for HSF1-mediated heat shock response. Dai et al. demonstrated a novel mechanism of stress resistance controlled by HSF1 and a new HSF-FoxM1 connection that mediates cellular thermotolerance [9].

Findings provide both clinical and mechanistic evidences that FoxM1 contributes to glioma development by directly up-regulating Anxa1 expression [10].

Results fadd a new FoxM1-Sirt1 connection that mediates cell proliferation in glioma [11].

Liu et al. found that the oncogenic transcription factor FOXM1 was also downregulated in PHDGH-silenced glioma cells. Using LC/LC MS analysis, we identified PHGDH as a novel binding partner of FOXM1. PHGDH interacted with and stabilized FOXM1 at the protein level, promoting the proliferation, invasion and tumorigenicity of glioma cells. Our data identified PHGDH as a potential prognostic marker of glial brain tumors and identified a non-metabolic role for PHGDH in glioma tumorigenesis, providing a novel angle of targeting the PHGDH-FOXM1 axis in future brain tumor therapy [12].

CXCL12 promotes Glioblastoma cell invasion in part by increasing the expression of FOXM1, which is mediated in part by a PI3K/AKT-dependent mechanism in vitro [13].

Targeting the FoxM1-Rad51 axis may be an effective method to reverse TMZ resistance in recurrent Glioblastoma [14].

Data suggest that targeting FOXM1 with small-molecule inhibitors results in potent antitumor activity and chemosensitizing effects in human medulloblastoma cells [15].

Overexpression of miR-216b inhibited the expression of FoxM1 in glioma cells. Rescue experiments demonstrated that co-transfection of FoxM1 lacking the 3'-untranslated region partially prevented miR-216b-induced inhibition of glioma cell growth and invasion. In vivo studies indicated that ectopic expression of miR-216b impeded the proliferation of glioma xenograft tumours in nude mice, coupled with a decreased in FoxM1 protein expression and the percentage of Ki-67-positive tumour cells. Taken together, our results provide evidence of the suppressive activity of miR-216b in glioma, which is largely ascribed to downregulation of FoxM1. Restoration of miR-216b may provide a novel potential therapeutic agent for glioma [16].

Elevated FOXM1 expression is associated with poor survival in most solid tumors. FOXM1 is a potential biomarker for prognosis prediction and a promising therapeutic target in human solid tumors [17].

FOXM1 in meningioma

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