Title

TRIM11 IS A NOVEL AND SPECIFIC GLIOMA STEM-LIKE CELL MARKER THAT ALSO PLAYS A ROLE IN GLIOMA BIOLOGY THROUGH THE EGFR PATHWAY

Authors

Di, Kaijun
Linskey, Mark
Bota, Daniela A

Publication Date

2011

NO-73. TRIM11 IS A NOVEL AND SPECIFIC GLIOMA STEM-LIKE CELL MARKER THAT ALSO PLAYS A ROLE IN GLIOMA BIOLOGY THROUGH THE EGFR PATHWAY

Kaijun Di, Mark Linskey, and Daniela A. Bota; UC Irvine, Orange, CA

SUMMARY: Expression of tripartite motif-containing protein 11 (TRIM11), a member of the TRIM/RBCC family of E3 ubiquitin ligases, is upregulated in high grade glioma-derived tumor stem-like cells (GSCs) while remaining low in glioblastoma multiforme (GBM) cell lines, low-grade glioma-derived GSCs, and normal neural stem/progenitor cells (NSCs) studied *in vitro*. The expression pattern of *TRIM11* strongly correlated with that of the stem cell markers *CD133* and *nestin* in GSCs. Knockdown of TRIM11 inhibited proliferation, migration, and invasion of glioma cells and caused decreased EGFR levels and MAPK activity. These findings suggest that TRIM11 can be used to specifically identify and potentially target GBM-derived GSCs while selectively sparing normal NSCs and that TRIM11 also functions as an oncogene that promotes tumor growth and invasion. SIGNIFICANCE: GSCs are important for tumor initiation, resistance to conventional therapies, and tumor recurrence after therapy. Unfortunately, all reported markers for identifying and potentially targeting these cells are shared in common with normal NSCs. Damage to normal NSCs resulting from glioma therapies can produce profound cognitive side effects. The potential to selectively identify and target GSCs while sparing NSCs is an important advance. In addition, identifying TRIM11 as a novel new oncogene for malignant glioma with linkage into the EGFR signaling pathway expands our knowledge of TRIM11 biology and opens the door to exploring a potential new translational target for malignant glioma therapy. HIGHLIGHTS: 1) *TRIM11* is up-regulated in high-grade glioma GSCs, but not in low grade GSCs and NSCs studied in appropriate *in vitro* conditions relative to their cell type. 2) The expression pattern of *TRIM11* strongly correlates with that of *CD133* and *nestin* in GSCs. 3) TRIM11 promotes the proliferation, migration, and invasion of malignant glioma cells. 4) TRIM11 modulates EGFR expression, possibly through regulating the transcription of HB-EGF