

Introduction

TRIM11 (tripartite motif-containing protein 11), a member of the TRIM/RBCC family of E3 ubiquitin ligases, is known to modulate neurogenesis and Alzheimer's disease-related neurotoxicity through ubiquitin-mediated protein degradation pathways (1-6). However, the effect of TRIM11 in brain tumors remains unknown. Here we investigated the gene expression levels of TRIM11 in multiple glioma specimens and demonstrated an important role for TRIM11 in tumorigenesis of glioma cells.

Methods

Gene expression levels of TRIM11 and CD133, a stem cell marker, were determined by quantitative RT-PCR in four glioblastoma cell lines, thirteen primary tumor cultures from glioma patients (Grade II to IV), and normal human neural stem/progenitor cell (NSPCs) cultures from three different patients. In addition, the oncogenic function of TRIM11 was studied in human glioblastoma cell lines by knocking down TRIM11 through RNA interference.

Fig.1. Glioma primary culture

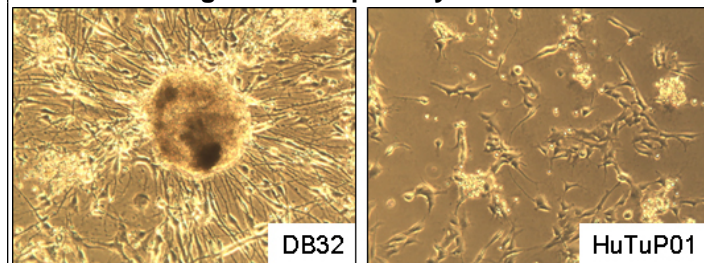


Table. The tumors used in the study.

Code	Tumor Type	Sex	Age
HuTuP01	Grade IV Glioblastoma	male	64
DB17	Grade IV Glioblastoma	female	32
DB26	Grade III Oligodendroglioma	male	71
DB29	Grade II Oligodendroglioma	male	73
DB30	Grade II Oligodendroglioma	female	52
DB32	Grade IV Glioblastoma	female	53
DB33	Grade III Oligodendroglioma	male	24
DB34	Grade IV Glioblastoma	female	61
DB37	Grade IV Glioblastoma	female	73
DB39	Grade II Oligodendroglioma	male	44
DB43	Grade II Oligodendroglioma	male	49
DB44	Grade II Oligodendroglioma	male	32
DB47	Grade III Oligoastrocytoma	male	30

Fig. 2. TRIM11 has higher levels in malignant glioma

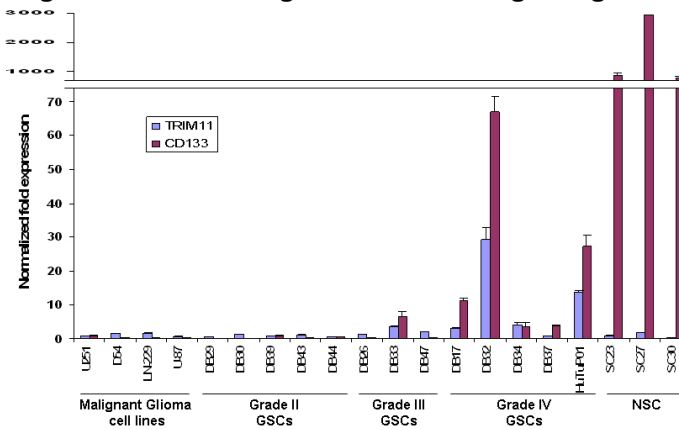


Fig. 3. Down-regulation of TRIM11 inhibits cell proliferation

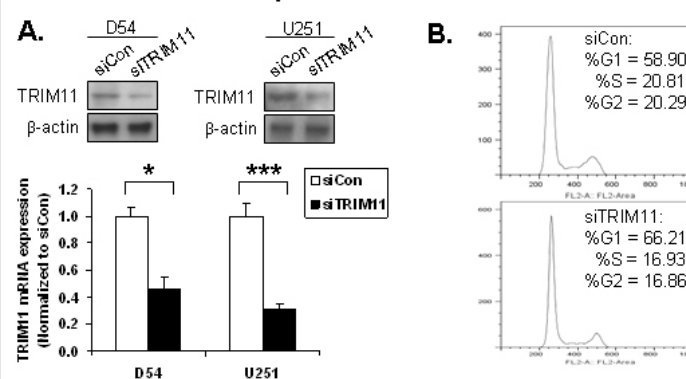


Fig. 4. TRIM11 downregulation inhibits cell migration

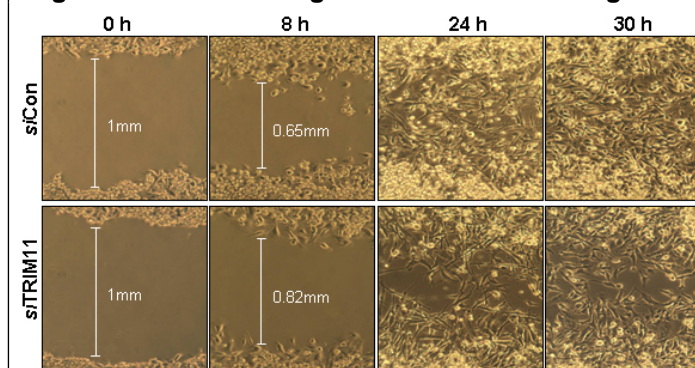
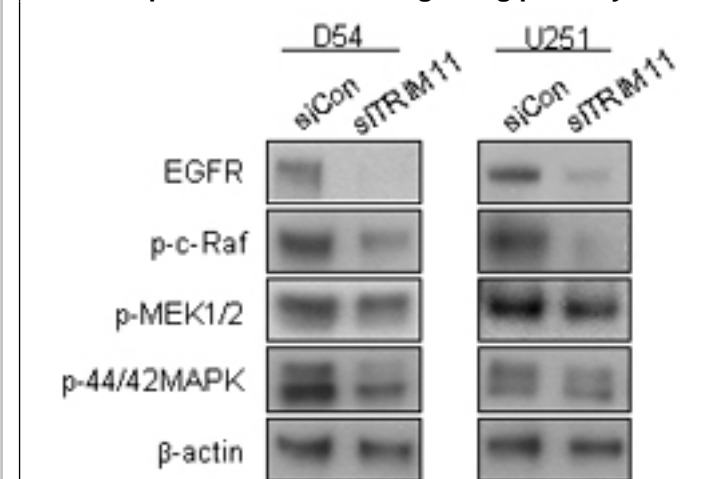


Fig. 5. TRIM11 downregulation inhibits EGFR expression & MAPKs signaling pathway



Conclusions

Our study has identified TRIM11 as a new cancer stem cell marker in gliomas. TRIM is up-regulated in high grade glioma stem-like cells and likely exerts its oncogenic function on glioma cell proliferation, migration and invasion, through EGFR and the MAPK signaling pathway.

Learning Objectives

Tripartite Motif-Containing Protein 11 (TRIM11) has been identified as cancer stem cell markers in glioma patients. We aim to educate the scientific community about this noble biomarker for cancer stem cells and how it involved in oncogenesis of glioma.

References

- Nisole S., Stoye J.P. and Saïbet A., 2005, Nature Reviews | Microbiology
- Niikura T., Hashimoto H., Tajima H., et al., 2003, European Journal of Neuroscience
- Ishikawa H., Tachikawa H., Miura Y., et al., 2006, FEBS Letters
- Tuoc T.C. and Stoykova A., 2008, Genes & Development
- Hong S.J., Chae H., Lardaro T., 2008, Biochem Biophys Res Commun
- Schwartz P.H., Bryant P.J., Fuja T.J., et al., 2003, Journal of Neuroscience Research