International Doctoral School
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The *WWOX* gene as a modulator of the structure and function of the cytoskeleton and intercellular communication in glioblastoma

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Introduction

WWOX encodes a protein whose deficiency severely impacts brain development. The task of determining the nature of *WWOX* in glioblastoma (GBM) is still considered to be at the initial stage; however, the influence of this gene on the GBM malignant phenotype has already been reported. Because most of the available *in vitro* research does not consider several cellular GBM models, the present study aimed to determine the main processes by which *WWOX* exhibits anticancer properties in GBM, while taking into account the phenotypic heterogeneity between cell lines. Ectopic *WWOX* overexpression was studied in T98G, DBTRG-05MG, U251MG, and U87MG cell lines that were compared with the use of assays investigating cell viability, proliferation, apoptosis, and invasiveness.

Methodology

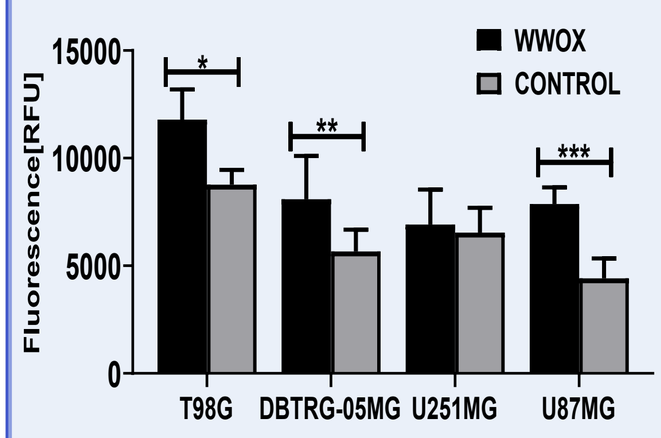
***In vitro* assays were performed on the DBTRG-05MG, T98G, U251MG, and U87MG cell lines**

1. Apoptosis
2. Proliferation
3. Cell viability
4. Alpha and Beta Integrins
5. Invasion
6. Gelatin degradation

Results

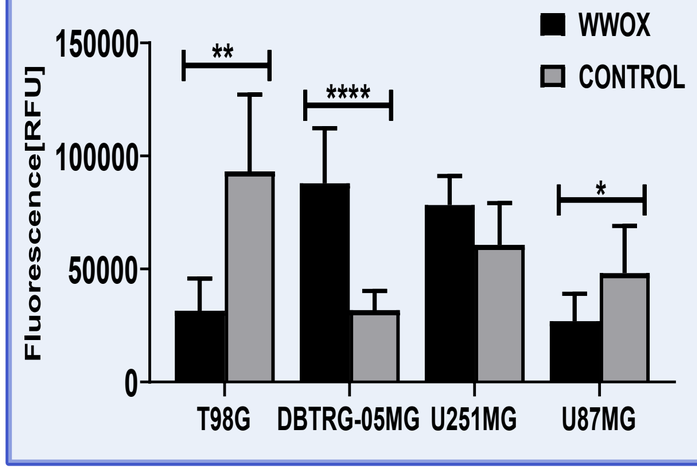
1

Overexpression of *WWOX* significantly intensified the programmed cell death of T98G, DBTRG-05MG, and U87MG cells.



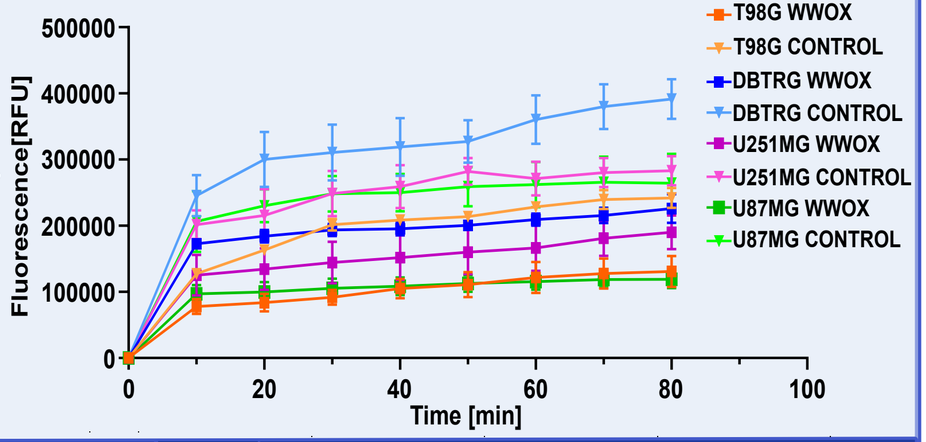
2

In terms of proliferation, the "WWOX" variant significantly reduced this biological process in T98G and U87MG cells, whereas it increased in DBTRG.



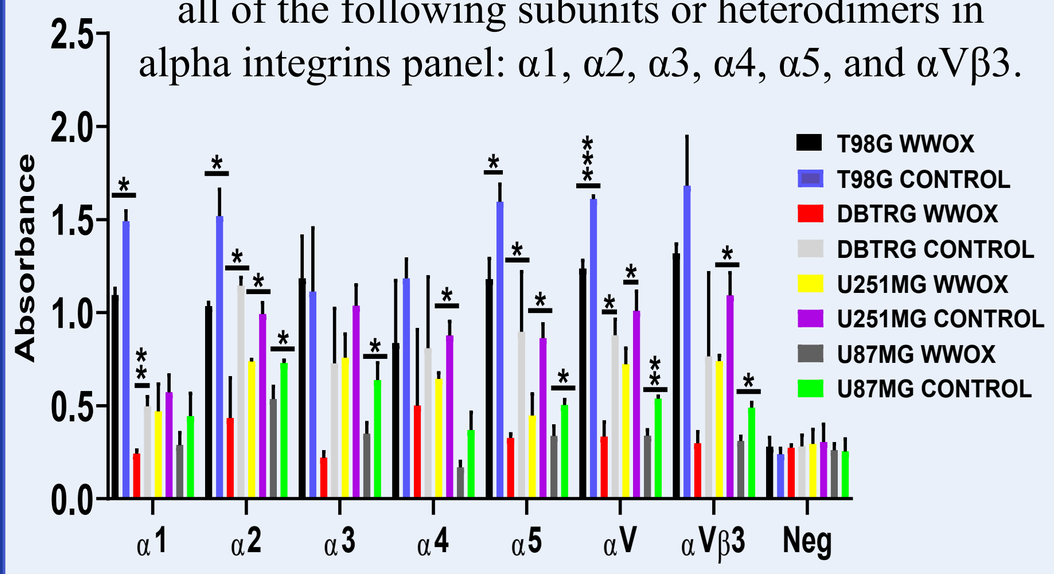
3

In each analyzed cell line, *WWOX*-overexpressing cells significantly diminished the mitochondrial redox potential, except for the 10-min measurements for the T98G and DBTRG-05MG cells.
The most statistically significant decrease in cell viability was observed for the U87MG cell line compared with the others.

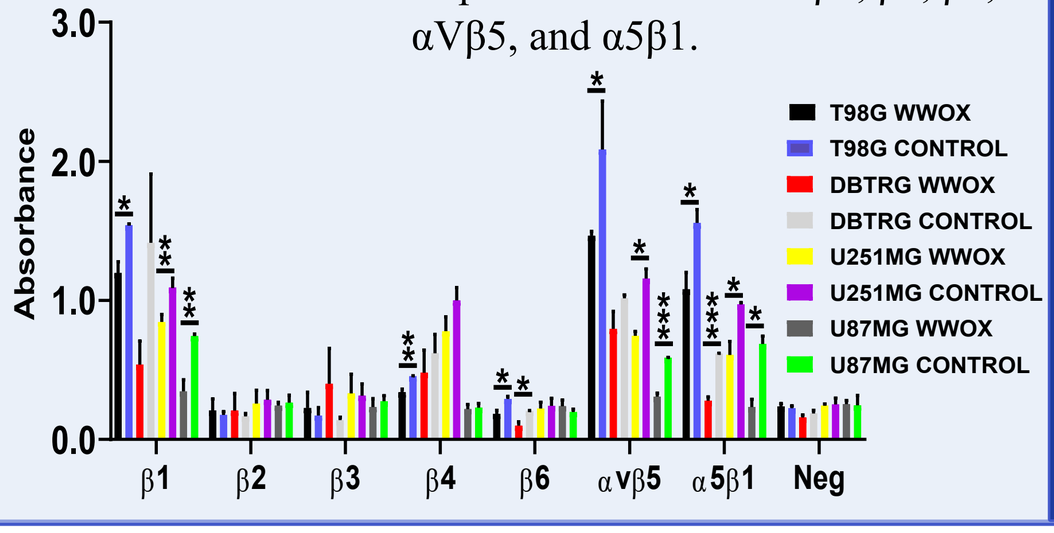


4

The "WWOX" variant significantly decreased all of the following subunits or heterodimers in alpha integrins panel: α1, α2, α3, α4, α5, and αVβ3.

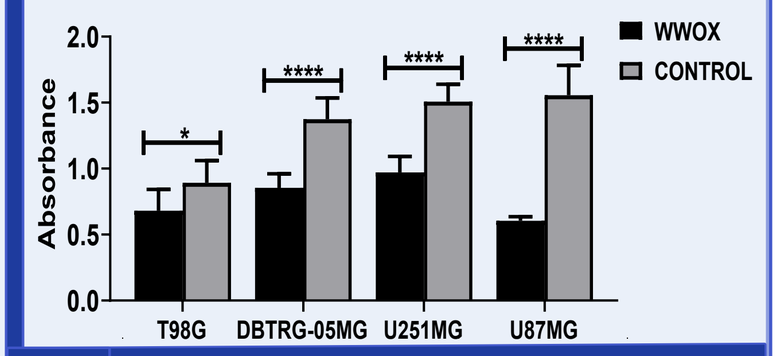


Considering the beta integrins panel, the variant with WWOX overexpression diminished β1, β4, β6, αVβ5, and α5β1.



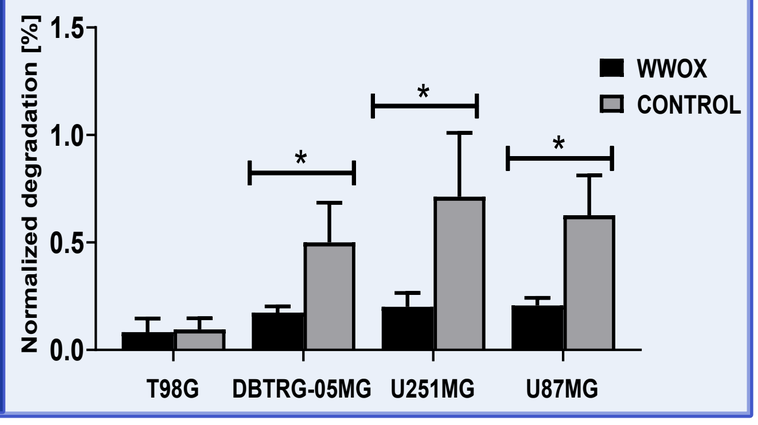
5

Observations of the *WWOX* overexpression effect were consistent in all cases, indicating a reduction of invasiveness in the tested cell lines.



6

The results of gelatin degradation assay are corresponding and indicate that *WWOX*-overexpressing cells significantly diminished the invasion.



Conclusions

Our study indicates that WWOX intensifies apoptosis, suppresses proliferation, diminished viability, and reduces the invasiveness of GBM. These findings apply to the T98G, U251MG, and U87MG cell lines, whereas particular attention should be given to DBTRG-05MG cells that presented discrepancies in tumor proliferation. Independently of the cause, we presume that DBTRG-05MG cells are successfully opposed by increased apoptosis and viability, as well as by reduced invasion, the extensiveness of which affects the recurrences and short survival that entail the inferior outcomes of patients. To conclude, this research demonstrates that, even in various cell line-specific circumstances, WWOX exhibits its anti-GBM nature mainly via reductions in cell viability and in the invasiveness of glioblastoma.