



Intrinsic PD-1 Expression in Glioblastoma and Its Role in Temozolomide Resistance

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BACKGROUND

Temozolomide (TMZ) resistance significantly contributes to treatment failure in glioblastoma (GBM). Programmed death 1 (PD-1) was traditionally thought to be only expressed on immune cells, but a recent study revealed its expression on human GBM brain specimens and its role in promoting the proliferation and self-renewal of brain tumor-initiating cells through nuclear factor κ B without involving PD-L1 ligation, suggesting potential therapeutic targets through inhibiting the PD-1 pathway. This study investigates whether PD-1 is also expressed in differentiated human GBM cell lines and whether it plays a role in contributing to TMZ resistance in GBM.

POTENTIAL MECHANISM

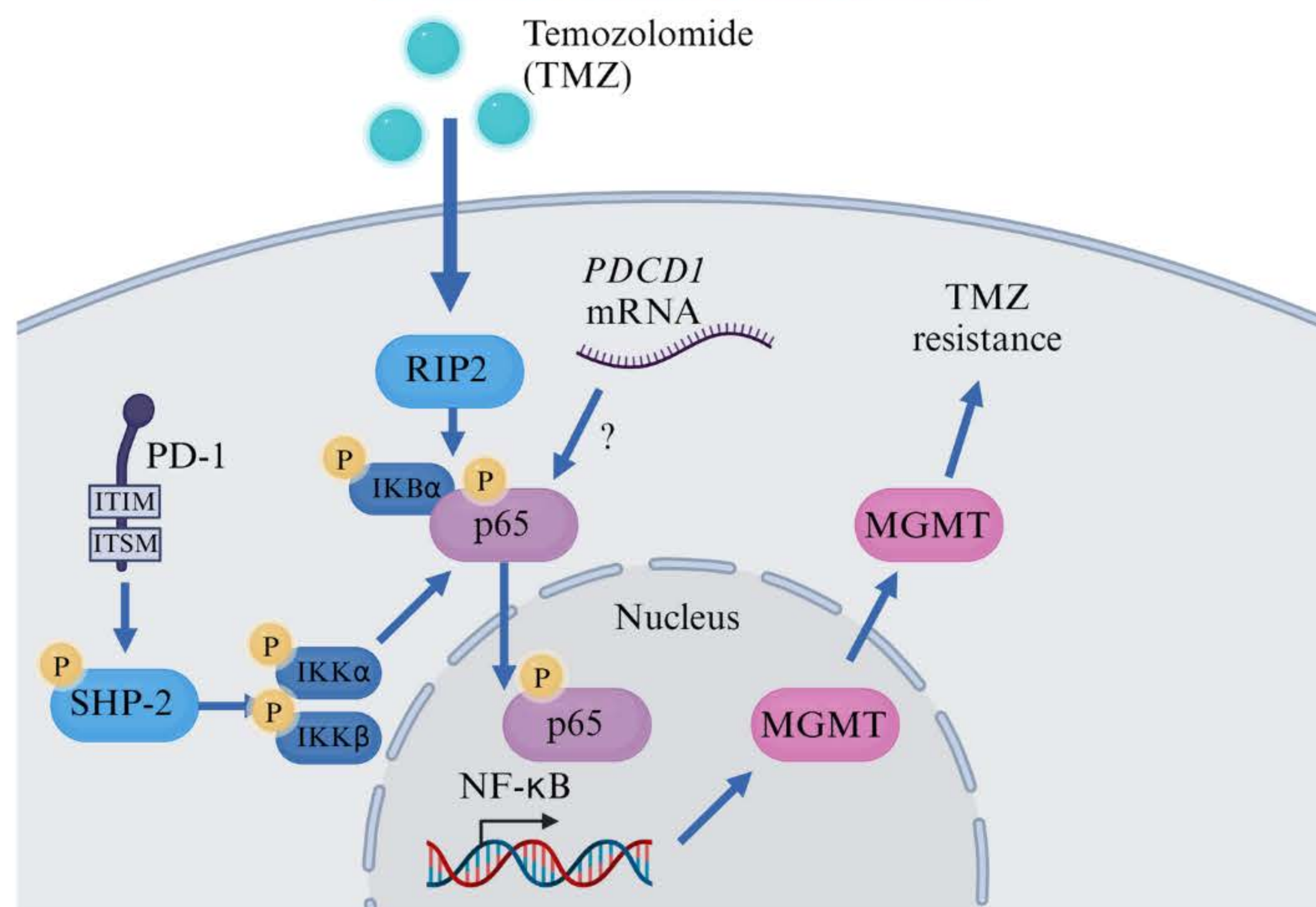


Fig. 1 Proposed mechanism of PD-1 protein and PDCD1 transcript in promoting TMZ resistance in GBM.

DATA ANALYSIS

High *PDCD1* transcript expression is associated with poorer survival, according to both the Chinese Glioma Genome Atlas (CGGA) ($p < 0.0001$ for survival probability = 0.05) (Fig. 2).

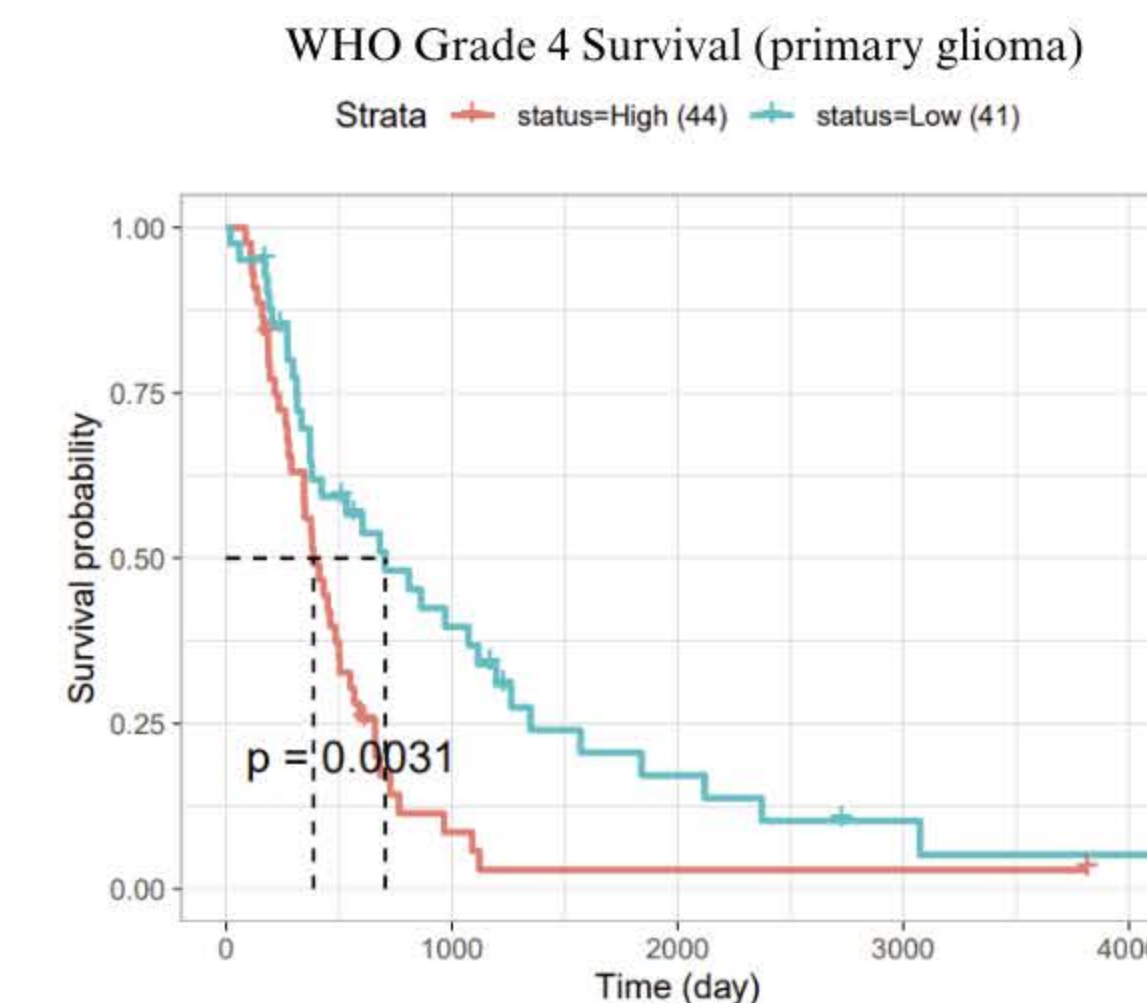


Fig. 2 Survival curves of patients with WHO grade 4 glioma with high and low mRNA expression of PDCD1 from CGGA.

METHODOLOGY

In vitro studies have been conducted using human GBM cell lines, U87 and U251, both TMZ-sensitive and resistant. PD-1 expression analysis was done using western blot, RT-qPCR, and immunofluorescence staining. Data analysis has been performed using PRISM.

RESULTS

Western blot demonstrates the presence of PD-1 proteins in both U87 and U251 cell lines. However, a similar level of PD-1 protein expression is found in both TMZ-sensitive (S) and TMZ-resistant (R) cell lines (Fig. 3a).

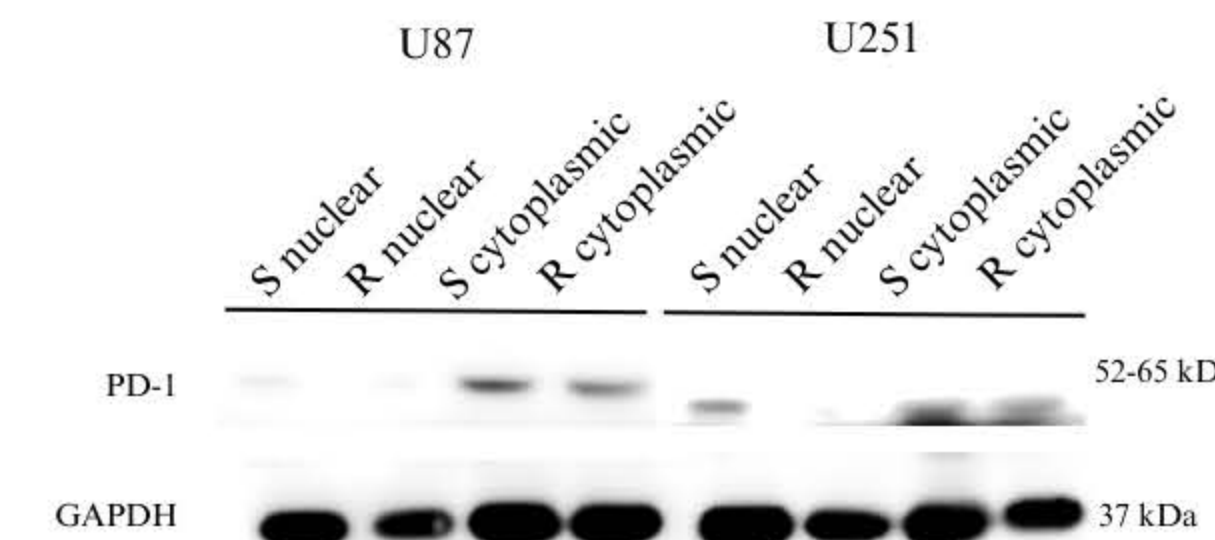


Fig. 3a PD-1 protein expression in different GBM cell lines.

However, RT-qPCR shows a significantly higher PDCD1 transcript expression in TMZ-resistant than TMZ-sensitive cell lines for U87 ($p < 0.0001$), while there is no significant difference in the expression levels in TMZ-resistant and TMZ-sensitive cell lines for U251 (Fig. 3b).

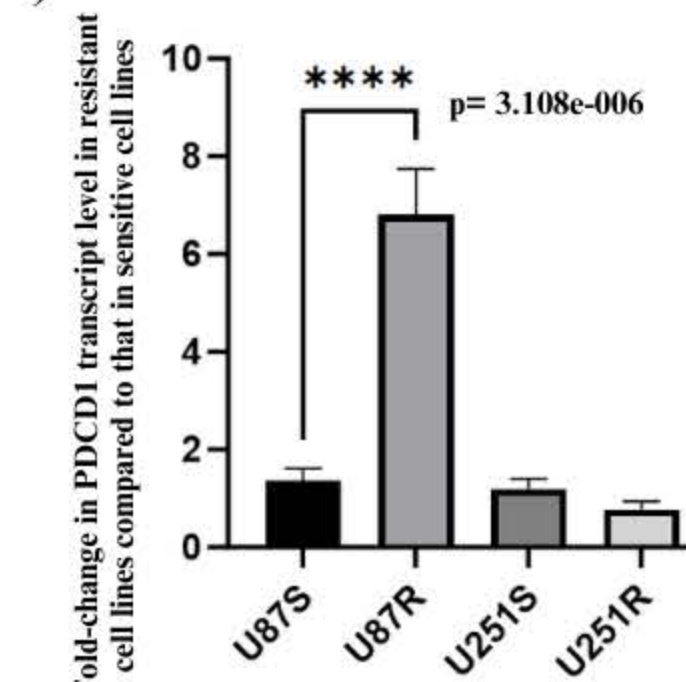


Fig. 3b Fold-change of PDCD1 transcript level in cell lines resistant to TMZ relative to that in cell lines sensitive to TMZ.

DISCUSSION

The experimental results suggest that PD-1 may play a role in contributing to TMZ resistance in certain differentiated human GBM cell lines. The difference between the PDCD1 transcript levels with relevance to TMZ resistance in U87 and U251 may be due to the differential gene expressions in the two cell lines. Further experiments, including knockdown of *PDCD1* and treatment with TMZ shall be done to verify the roles of *PDCD1* transcript and PD-1 protein in TMZ resistance and GBM proliferation.

CONCLUSION

PD-1 expression may play a role in contributing to TMZ resistance in certain human GBM cell lines and its protein/mRNA level may be a predictor of TMZ outcome in GBM.

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