# Anti-cancer mechanisms of curcumin in temozolomide-resistant glioblastoma cells

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## ABSTRACT

Glioblastoma (GBM) is a WHO grade IV glioma and the most common malignant, primary brain tumour with a 5-year survival under 10%. The current standard treatment for GBM patients is surgical resection, followed by concurrent temozolomide (TMZ) and radiotherapy. Despite the significant advances in diagnostic and therapeutic approaches, GBM remains largely resistant to treatment. With increasing drug resistance, the introduction of phytochemicals into current GBM treatment has become a potential strategy to combat GBM. Phytochemicals possess multifarious bioactivities with multitarget sites and comparatively marginal toxicity. Among them, curcumin is the most studied compound described as a potential anticancer agent due to its multi-targeted signalling/molecular pathways properties in GBM. This study aims to elucidate the anti-cancer mechanisms of curcumin in LN-18, a TMZ-resistant GBM cell line. The cytotoxicity effects of curcumin were investigated using the MTT assay, while the apoptotic effects were evaluated using flow cytometry assay. The differentially expressed proteins (DEPs) in curcumin-treated cells were determined using LC-MS/MS analysis, with further protein classification and pathway analysis. Curcumin demonstrated lower IC50 values compared to TMZ with a significant greater anti-proliferative effect. Flow cytometric analysis further confirmed that the curcumin treatment significantly increased the total apoptotic cell populations compared to the untreated control cells. Protein classification and pathway analysis revealed that DEPs regulated by curcumin were associated with protease activity, protein-binding activity modulators, and scaffold/adaptor proteins, and were highly enriched in the top regulated pathway: the WNT signalling pathway. These findings suggest that curcumin exerts its anticancer effects through anti-proliferative and pro-apoptotic activities, potentially mediated by regulating WNT signalling pathways in LN-18, TMZ-resistant GBM cells.

Keywords: Glioblastoma, curcumin, tmz-resistant, cancer treatment, differentially expressed proteins (DEPs)