Abstract

Glioblastoma Multiforme (GBM) is the most aggressive and the most common primary brain tumor in adults. Temozolomide (TMZ) is the first line drug prescribed for GBM patients. However, its effectiveness is often hindered by the development of drug resistance leading to an incredibly low 5 year survival rate (Ortiz et al., 2021). One of the main challenges in treating GBM is the heterogeneity of tumors as the effectiveness of known treatment relies on the expression of key genes. Recent discovery of cuproptosis, a copper induced cell death pathway presents a possible treatment to TMZ resistant GBM patients as it is completely separate to the pathway targeted by administration of TMZ. This study aims to elucidate the effectiveness of cuproptosis against GBM as well as if the treatment is able to overcome the heterogeneity of GBM through cytotoxicity assay as well as determine the correlation between CRGs and cuproptosis sensitivity through QPCR. The results of this study finds that cuproptosis induction results in higher cytotoxicity than TMZ and that the cytotoxic effect of cuproptosis induction is affected more by the presence or absence of CRGs as alterations in individual CRGs do not affect the cytotoxicity. This study also finds that despite the variation in CRG expression, cuproptosis induction using Es-Cu remains more effective than TMZ in all cell lines tested.

Keywords: Glioblastoma Multiforme, Temozolomide Resistance, GBM Heterogeneity, Cuproptosis