

## **RUTIN INCREASES THE EFFICACY OF TEMOZOLOMIDE IN GLIOBLASTOMA VIA AUTOPHAGY INHIBITION**

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The chemotherapeutic agent temozolomide (TMZ) is commonly used in glioblastoma (GBM) therapy, but patients usually have a poor prognosis. Rutin, a citrus flavonoid ecglycoside found in edible plants, has neuroprotection and anticancer activities. This study aims to investigate the efficacy of rutin in combination with temozolomide and the underlying mechanisms. In vitro viability assay demonstrated that rutin alone had generally low cytotoxic effect, but it was able to enhance the efficacy of TMZ in a dose-dependent manner. An in vivo xenograft study also showed that tumor volumes were significantly decreased in mice under combination treatment as compared to TMZ alone. Moreover, western blot analysis showed that TMZ activated JNK activity to induce protective response autophagy, while rutin blocked JNK activation, resulting in decreased autophagy and increased apoptosis, suggesting that rutin enhances TMZ efficacy via inhibition of JNK-mediated autophagy. Overall, these results indicate that the combination rutin with TMZ could improve the therapeutic efficacy of GBM.