UBE2C

Ubiquitin conjugating enzymes, also known as E2 enzymes and more rarely as ubiquitin-carrier enzymes, perform the second step in the ubiquitination reaction that targets a protein for degradation via the proteasome. The ubiquitination process covalently attaches ubiquitin, a short protein of 76 amino acids, to a lysine residue on the target protein. Once a protein has been tagged with one ubiquitin molecule, additional rounds of ubiquitination form a polyubiquitin chain that is recognized by the proteasome's 19S regulatory particle, triggering the ATP-dependent unfolding of the target protein that allows passage into the proteasome's 20S core particle, where proteases degrade the target into short peptide fragments for recycling by the cell.

Ubiquitin-conjugating enzyme E2C (UBE2C) is characterized as a crucial molecule in cancer cell growth that plays an essential role in the development of gliomas, but the detailed mechanisms have not been fully elucidated. In this study, we found that Forkhead box transcription factor M1 (FoxM1) overexpression increased UBE2C expression, whereas FoxM1 suppression inhibited UBE2C expression in glioma cells. In addition, high FoxM1/UBE2C expression was significantly correlated with poor prognosis in glioma. We subsequently demonstrated that UBE2C was a direct transcriptional target of FoxM1, and site-directed mutations markedly down-regulated UBE2C promoter activity. Moreover, UBE2C siRNA (si-UBE2C) significantly induced glioma cell autophagy and increased both mCherry-LC3 punctate fluorescence and LC3B-II/LC3-I expression. Notably, the si-UBE2C-induced decrease in cell viability was markedly inhibited by the autophagy inhibitor bafilomycin A1. The silencing of UBE2C resulted in a distinct inhibition of the PI3K-Akt-mTOR pathway, which functions in the negative modulation of autophagy. Collectively, our findings provide clinical and molecular evidence that FoxM1 promotes glioma progression by enhancing UBE2C transcription and that the inhibition of UBE2C partially induces autophagic glioma cell death. Thus, targeting the FoxM1-UBE2C axis has therapeutic potential in the treatment of gliomas [1)].

1)
Guo L, Ding Z, Huang N, Huang Z, Zhang N, Xia Z. Forkhead Box M1 positively regulates UBE2C and protects glioma cells from autophagic death. Cell Cycle. 2017 Aug 2:0. doi: 10.1080/15384101.2017.1356507. [Epub ahead of print] PubMed PMID: 28767320.