ABSTRACT

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Regulation of autophagy as a therapeutic option in glioblastoma.

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Around three out of one hundred thousand people are diagnosed with glioblastoma multiforme, simply called glioblastoma, which is the most common primary brain tumor in adults. With a dismal prognosis of a little over a year, receiving a glioblastoma diagnosis is oftentimes fatal. A major advancement in its treatment was made almost two decades ago when the alkylating chemotherapeutic agent temozolomide (TMZ) was combined with radiotherapy (RT). Little progress has been made since then. Therapies that focus on the modulation of autophagy, a key process that regulates cellular homeostasis, have been developed to curb the progression of glioblastoma. The dual role of autophagy (cell survival or cell death) in glioblastoma has led to the development of autophagy inhibitors and promoters that either work as monotherapies or as part of a combination therapy to induce cell death, cellular senescence, and counteract the ability of glioblastoma stem cells (GSCs) for initiating tumor recurrence. The myriad of cellular pathways that act upon the modulation of autophagy have created contention between two groups: those who use autophagy inhibition versus those who use promotion of autophagy to control glioblastoma growth. We discuss rationale for using current major therapeutics, their molecular mechanisms for modulation of autophagy in glioblastoma and GSCs, their potentials for making strides in combating glioblastoma progression, and their possible shortcomings. These shortcomings may fuel the innovation of novel delivery systems and therapies involving TMZ in conjunction with another agent to pave the way towards a new gold standard of glioblastoma treatment.

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