ATG4B

ATG4B stimulates autophagy by promoting autophagosome formation through reversible modification of ATG8. We identify ATG4B as a substrate of mammalian sterile20-like kinase (STK) 26/MST4. MST4 phosphorylates ATG4B at serine residue 383, which stimulates ATG4B activity and increases autophagic flux. Inhibition of MST4 or ATG4B activities using genetic approaches or an inhibitor of ATG4B suppresses autophagy and the tumorigenicity of glioblastoma (GBM) cells. Furthermore, radiation induces MST4 expression, ATG4B phosphorylation, and autophagy. Inhibiting ATG4B in combination with radiotherapy in treating mice with intracranial GBM xenograft markedly slows tumor growth and provides a significant survival benefit. Our work describes an MST4-ATG4B signaling axis that influences GBM autophagy and malignancy, and whose therapeutic targeting enhances the anti-tumor effects of radiotherapy [1)].

1)
Huang T, Kim CK, Alvarez AA, Pangeni RP, Wan X, Song X, Shi T, Yang Y, Sastry N, Horbinski CM, Lu S, Stupp R, Kessler JA, Nishikawa R, Nakano I, Sulman EP, Lu X, James CD, Yin XM, Hu B, Cheng SY. MST4 Phosphorylation of ATG4B Regulates Autophagic Activity, Tumorigenicity, and Radioresistance in Glioblastoma. Cancer Cell. 2017 Dec 11;32(6):840-855.e8. doi: 10.1016/j.ccell.2017.11.005. PubMed PMID: 29232556.