# Dutomycin induces autophagy and apoptosis by targeting the serine protease inhibitor SERPINB6

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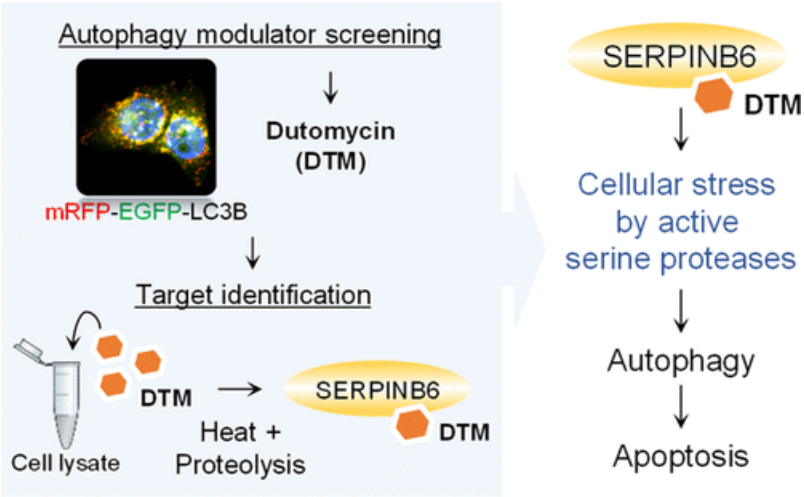
Autophagy plays an important role in maintaining tumor cell progression and survival in response to metabolic stress[1]. Thus, the regulation of autophagy can be used as a strategy for anticancer therapy[2]. Here, we report dutomycin (DTM) as a novel autophagy enhancer that eventually induces apoptosis due to excessive autophagy. Also, human serine protease inhibitor B6 (SERPINB6) was identified as a target protein of DTM, and its novel function which is involved in autophagy was studied for the first time. We show that DTM directly binds SERPINB6 and then activates intracellular serine proteases, resulting in autophagy induction. Inhibitory effects of DTM on the function of SERPINB6 were confirmed through enzyme- and cell-based approaches, and SERPINB6 was validated as a target protein using siRNA-mediated knockdown and an overexpression test. In a zebrafish xenograft model, DTM showed a significant decrease in tumor area. Furthermore, the present findings will be expected to contribute to the expansion of novel basic knowledge about the correlation of cancer and autophagy by promoting active further research on SERPINB6, which was not previously considered the subject of cancer biology.




**References**

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