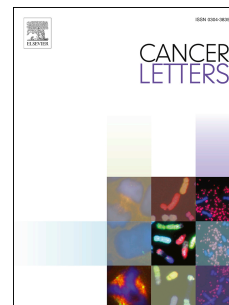


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Sulforaphane-N-Acetyl-Cysteine inhibited autophagy leading to apoptosis via Hsp70-mediated microtubule disruption

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Abstract

Sulforaphane-N-acetyl-cysteine (SFN-NAC) is a potential drug to inhibit human non-small cell lung cancer (NSCLC), but the underlying mechanisms are elusive. Here, we uncovered that SFN-NAC induced apoptosis via flow cytometer assay and transmission electron microscopy. Further, SFN-NAC increased LC3 II/LC3 I and the number of LC3 punctas, but Western blot showed that SFN-NAC inhibited cell autophagy in response to a co-treatment of Bafilomycin A1 and SFN-NAC. Furthermore, immunofluorescence staining and Western blot showed that SFN-NAC triggered microtubule disruption causing apoptosis via downregulating α -tubulin and phosphorylated ERK1/2-mediated Stathmin-1. Besides, SFN-NAC upregulated Hsp70 via phosphorylating ERK1/2. Confocal microscopy and immunoprecipitation assay showed that SFN-NAC promoted the colocalization and interaction of Hsp70 and α -tubulin; knockdown of Hsp70 enhanced SFN-NAC-induced microtubule disruption, lowered LC3 II/LC3 I and promoted apoptosis. Interestingly, tissue microarray analysis showed that the increased expression of either α -tubulin or Hsp70 correlated to NSCLC malignant grading, indicating that microtubule and Hsp70 are two key targets for SFN-NAC. These results will give us a new insight into SFN-NAC-induced apoptosis so that we develop more efficient therapeutics to treat NSCLC.

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