Indole-3-carbinol induces apoptosis through p53 and activation of caspase-8 pathway in lung cancer A549 cells.

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Source

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Abstract

Indole-3-carbinol (I3C) has anti-tumor effects in various cancer cell lines. However, the anti-tumor effect of I3C on human lung cancers has been rarely reported. We investigated the anti-tumor effects and its mechanism of I3C on human lung carcinoma A549 cell line. Treatment of the A549 cells with I3C significantly reduced cell proliferation, increased formations of fragmented DNA and apoptotic body, and induced cell cycle arrest at G0/G1 phase. I3C increased not only the protein levels of cyclin D1, phosphorylated p53, and p21 but also the expression of Fas mRNA. Cleavage of caspase-9, -8, -3 and PARP also was increased by I3C. Treatment with wortmannin significantly suppressed both I3C-induced Ser15 phosphorylation and accumulation of p53 protein. The inhibition of caspase-8 by z-IETD-FMK significantly decreased cleavage of procaspase-8,-3 and PARP in I3C-treated A549 cells. Taken together, these results demonstrate that I3C induces cell cycle arrest at G0/G1 through the activation of p-p53 at Ser 15 and induces caspase-8 mediated apoptosis via the Fas death receptor. This molecular mechanism for apoptotic effect of I3C on A549 lung carcinoma cells may be a first report and suggest that I3C may be a preventive and therapeutic agent against lung cancer.

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