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Novel diterpene derivatives induced apoptosis in human lung cancer cell lines in p53 independent mechanism

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Lung cancer has been identified as the most lethal form of cancer today. We designed and screened 16 diterpene derivatives for their cytotoxic activties in H1299 human large cell lung carcinoma cells that are null for p53, normal lung epithelial cell lines (NL-20). Our data indicated that Diterpene derivatives 9 and 15 decreased cell proliferation and induced apoptosis in H1299 lung cancer cells more than normal lung epithelial NL-20 cells. Flow cytometric analysis showed that both Diterpene derivatives 9 and 15 arrested the H1299 cells in G1 phase which is further confirmed by increased expression level of p21. Moreover, both diterpene derivatives increased caspase-9 activitiy and the induction of apoptosis was significantly reduced after treating cells with caspase-9 inhibitor LEHD-CHO. Both Diterpene derivatives increased Caspase 3 activities and induced Parp-1 cleavage in H1299 cells. Based on previous results, we have identified two novel diterpenes derivatives which provoked apoptosis lung cancer cells by arresting cells in G1 phase and increasing caspase-9 and caspase-3 activities. The above findings demonstrate that diterpene derivative 9 and 15 induces apoptosis in H1299 cells in p53-indpendent mechanisms which merits further development.

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