

## Novel diterpene derivative induced apoptosis in Melanoma cells via sphingomyelinase and ERK signaling

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In this study, we designed and synthesized novel diterpene derivative to be investigated for anticancer activities. Our initial screening showed that our novel derivative was cytotoxic against Melanoma cells. Our data revealed that diterpene derivative reduced proliferation and induced apoptosis in Melanoma cells. Flow cytometric analysis showed that our novel diterpene derivative increased the percent of Melanoma cells in G1 phase which is confirmed by increased expression levels of p21. Novel diterpene derivative increased expression level of p53 and bax at both protein and mRNA levels and reduced expression level of STAT-3, Bak, Bad and Mdm2. Finally, it increased sphingomyelinase signaling and ceramide formation as well as its downstream targets ERK1/2, p38 and JNK. The induction of apoptosis by our novel diterpene derivative was dramatically reduced siRNAs targeting acid sphingomyelinase or acid ceramidase. Inhibition of ERK1/2 with PD98059 exerted markedly reduced the novel diterpene-induced apoptosis in Melanoma cells, p38 inhibition with SB203580 slightly lessened apoptosis and inhibition of JNK with SP600125 had no significant effect on diterpene derivative-induced apoptosis. These results indicate that our novel diterpene derivative induced the activation of sphingomyelinase signaling and that ERK played a pivotal role in induction of apoptosis in Melanoma cells. In vivo studies and molecular docking experiments are now in progress for further anticancer investigations.

### Biography

Ahmed M Malki has completed his Ph.D in Molecular Oncology at the age of 30 years from Edison Institute of Biotechnology, Ohio University in USA and He completed postdoctoral studies from University of California Berkeley, USA. He is the director of Molecular therapeutics laboratory, City of Research and Technology applications. He is currently an associate professor of Molecular Biology in Alexandria University; he has published more than 15 papers in reputed journals and serving as an editorial board member of Journal of Genetic Syndromes and Gene Therapy, African Journal of Biochemistry Research and Biotechnology and Molecular Biology Reviews. He also received Best Research Award, Global Breast Cancer conference, 2011, Seoul, South Korea.

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