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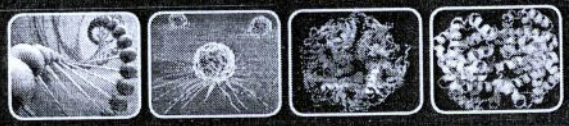

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Synergistic cytotoxic interaction of the HDAC inhibitor SAHA with the natural compound parthenolide in MDA-MB231 breast cancer cells.

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The histone deacetylase inhibitor SAHA is widely used as an anti-tumor agent and is approved as "Vorinostat" for the treatment of cutaneous T-cell lymphoma. Here we investigate whether combinations of SAHA with the natural compound parthenolide (PN) exert synergistic cytotoxic effects on triple negative breast cancer MDA-MB231 cells. After 20h of treatment with 5μM SAHA alone cells appeared viable but reduced in the number and enlarged. Cell cycle analysis by flow cytometry indicated that SAHA induced G2/M arrest. In addition SAHA increased the production of ROS and stimulated autophagic process, as suggested by positivity to mono-dansyl cadaverin, enhanced expression of beclin-1 and conversion of microtubule-associated protein light chain 3-I (LC3-I) to LC3-II. The addition of 12 μM PN to cells pre-treated for 20 h with 5μM SAHA markedly reduced cell proliferation in a synergistic manner. This effect seemed to be a consequence of induction of apoptosis, as suggested by positivity to annexin V staining and activation of caspase-3. Moreover, treatment with SAHA/PN combination induced the decrease in the level of Bcl-2 and the release of cytochrome c into the cytosol. Collectively, our results suggest the existence of a synergistic interaction between SAHA and PN, even though the exact mechanism has not yet defined.

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