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Vitamin K3 triggers human leukemia cell death through hydrogen peroxide generation and histone hyperacetylation.

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Source

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Abstract

Vitamin K3 (VK3) is a well-known anticancer agent, but its mechanism remains elusive. In the present study, VK3 was found to simultaneously induce cell death, reactive oxygen species (ROS) generation, including superoxide anion (O2*-) and hydrogen peroxide (H2O2) generation, and histone hyperacetylation in human leukemia HL-60 cells in a concentration- and time-dependent manner. Catalase (CAT), an antioxidant enzyme that specifically scavenges H2O2, could significantly diminish both histone acetylation increase and cell death caused by VK3, whereas superoxide dismutase (SOD), an enzyme that specifically eliminates O2*-, showed no effect on both of these, leading to the conclusion that H2O2 generation, but not O2*- generation, contributes to VK3-induced histone hyperacetylation and cell death. This conclusion was confirmed by the finding that enhancement of VK3-induced H2O2 generation by vitamin C (VC) could significantly promote both the histone hyperacetylation and cell death. Further studies suggested that histone hyperacetylation played an important role in VK3-induced cell death, since sodium butyrate, a histone deacetylase (HDAC) inhibitor, showed no effect on ROS generation, but obviously potentiated VK3-induced histone hyperacetylation and cell death. Collectively, these results demonstrate a novel mechanism for the anticancer activity of VK3, i.e., VK3 induced tumor cell death through H2O2 generation, which then further induced histone hyperacetylation.

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