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Resveratrol triggers apoptosis through regulating ceramide metabolizing genes in human k562 chronic myeloid leukemia cells.

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Source

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Abstract

Resveratrol, an important phytoalexin in many plants, has been reported to have cytotoxic effects on various types of cancer. Ceramide is a bioactive sphingolipid that regulates many signaling pathways, including cell growth and proliferation, senescence and quiescence, apoptosis, and cell cycle. Ceramides are generated by longevity assurance genes (LASS). Glucosylceramide synthase (GCS) and sphingosine kinase-1 (SK-1) enzymes can convert ceramides to antiapoptotic molecules, glucosylceramide, and sphingosine-1-phosphate, respectively. C8:ceramide, an important cell-permeable analogue of natural ceramides, increases intracellular ceramide levels significantly, while 1-phenyl-2-decanoylamino-3-morpholino-1-propanol (PDMP) and SK-1 inhibitor increase accumulation of ceramides by inhibiting GCS and SK-1, respectively. Chronic myelogenous leukemia (CML) is a hematological disorder resulting from generation of BCR/ABL oncogene. In this study, we examined the roles of ceramide metabolizing genes in resveratrol-induced apoptosis in K562 CML cells. There were synergistic cytotoxic and apoptotic effects of resveratrol with coadministration of C8:ceramide, PDMP, and SK-1 inhibitor. Interestingly, there were also significant increases in expression levels of LASS genes and decreases in expression levels of GCS and SK-1 in K562 cells in response to resveratrol. Our data, in total, showed for the first time that resveratrol might kill CML cells through increasing intracellular generation and accumulation of apoptotic ceramides.