



- [Immune Recovery And Wellness – www.ImmuneClinic.com](http://www.ImmuneClinic.com)
- [More Clinical Research – www.ImmuneClinic.com/research](http://www.ImmuneClinic.com/research)

Critical role of reactive oxygen species and mitochondrial membrane potential in Korean mistletoe lectin-induced apoptosis in human hepatocarcinoma cells.

Kim WH, Park WB, Gao B, Jung MH.

Division of Metabolic Disease, Department of Biomedical Science, National Institutes of Health, Seoul, South Korea.

Viscum album L. coloratum agglutinin (VCA), isolated from Korean mistletoe, is a strong inducer of apoptosis in a variety of tumor cells; however, the underlying molecular mechanisms responsible are not clear. Here, we show that VCA induces apoptotic killing, as demonstrated by DNA fragmentation, Hoechst 33258 staining, terminal deoxynucleotidyl transferase dUTP nick-end labeling assay, and flow cytometry analysis in hepatocarcinoma Hep3B cells. VCA treatment results in a significant increase in reactive oxygen species (ROS) and loss of mitochondrial membrane potential ($\Delta\psi$). Furthermore, treatment with the antioxidant N-acetyl-L-cysteine reduces ROS induction by VCA, preventing apoptosis in Hep3B cells, indicating that oxidative stress is involved in VCA-mediated cell death. Our results also show rapid changes in mitochondrial transition permeability, Bax translocation, cytochrome c release, caspase-3 activity, and poly(ADP-ribose) polymerase degradation in Hep3B cells occurring in VCA-induced apoptosis. There is much evidence that implicates c-Jun NH₂-terminal kinase (JNK) activation with apoptosis in a variety of cellular and animal models. In this study, we show that VCA induces JNK phosphorylation, which is abolished with pretreatment with a JNK inhibitor. Moreover, Hep3B cells overexpressing JNK1 or stress-activated protein kinase kinase (SEK1) seem to be more susceptible to cell death from ROS and loss of $\Delta\psi$ induced by VCA, whereas expression of dominant-negative JNK1 or SEK1 in Hep3B cells do not. These data suggest that JNK phosphorylation may be a major regulator involved in VCA-induced apoptosis. Together, these results suggest that VCA induces apoptosis by inducing ROS production and a loss of $\Delta\psi$, in which JNK phosphorylation plays a critical role in these events.

PMID: 15340045 [PubMed - in process]