

Antitumor effects of deguelin on H460 human lung cancer cells *in vitro* and *in vivo*: Roles of apoptotic cell death and H460 tumor xenografts model

Jing-Gung Chung, Yu-chieh Hsu and Rick Sai-Chuen Wu

China Medical University Hospital, Taiwan

Deguelin, a naturally occurring rotenoid of the flavonoid family, is known to be an Akt inhibitor, to have chemopreventive activities and anti-tumor effect on several cancers. In this study, we investigated to elucidate the effect of deguelin on apoptotic pathways in human lung cancer cells and on the anti-tumor effect in lung cancer xenograft nu/nu mice. *In-vitro* studies, we found that deguelin induced cell morphological changes, decreased the percentage of viability through the induction of apoptosis in H460 lung cancer cells. Deguelin-triggered apoptosis in H460 cells was also confirmed by DAPI staining, DNA gel electrophoresis and Annex V-FITC staining and these effects are dose-dependent manners. We also found that deguelin promoted the Ca^{2+} production and activation of caspase-3 but decrease the level of $\Delta\Psi_m$ in H460 cells. Western blots indicated that the protein levels of cytochrome c, AIF, and pro-apoptotic Bax and Bak protein were increased, but the anti-apoptotic Bcl-2 and BCL-X were decreased that may led to apoptosis in H460 cells after exposure to deguelin. It was also confirmed by confocal laser microscope examination shown that deguelin promoted the release of AIF from mitochondria to cytosol.

In-vivo studies, we found that in immunodeficient nu/nu mice bearing H460 tumor xenografts showed that the deguelin significantly suppressed tumor growth. Deguelin might be a potential therapeutic agent for treatment of lung cancer in future.

Biography

Jing-Gung Chung has completed his Ph.D. at the age of 36 years from University of Mississippi Medical School and postdoctoral studies from University of Michigan. He is the chairman of Department of Biological Science and Technology, China Medical University, Taichung 404, Taiwan, R.O.C. He has published more than 250 papers in reputed journals and serving as an editorial board member of *International Journal of Oncology and Anticancer research*.

jgchung@mail.cmu.edu.tw