# Calvatia lilacina Protein-Extract Induces Apoptosis through Glutathione Depletion in Human Colorectal Carcinoma Cells

邱仲峰

Jwu-Guh Tsay;King-Thom Chung;Chung-Hung Yeh;Wan-Ling Chen;Chi-Hung Chen;Martin Hsiu-Chu Lin;Fung-Jou Lu;Jeng-Fong Chiou;Ching-Hsein Chen

摘要

**Abstract**

This paper reports that a novel protein extract isolated from Calvatia lilacina (CL) can induce cell death against four types of human colorectal cancer cells. Importantly, CL was shown to be free of apoptotic effects against normal rat liver cells. We have also identified that CL-induced glutathione (GSH) depletion is the major contributor responsible for the apoptotic cell death induction of SW 480 cells, as evidencd by the observation that exogenously added N-acetylcysteine (NAC), or GSH, but not vitamin C, could offer a near complete protection of CL-treated cells against apoptotic cell death. Furthermore, the participation of reactive oxygen species (ROS) evoked a drop in the transmembrane potential ($\Delta \Psi_m$) in the CL-induced apoptotic cell death. This observation can only be deemed as a minor pathway due to the fact that cyclosporine A (CyA) could only partially rescue the CL-treated cells from apoptotic cell death. Likewise, despite the fact that CL could induce the upregulation of Bax, its knockdown via siRNA (48 h) failed to completely mitigate apoptotic cell death, indicating that its role in this apoptotic process was insignificant. To further explore the possible underlying mechanism associated with CL-induced GSH depletion, we proceeded to determine the effect of CL on the cellular $\gamma$-glutamylcysteine synthetase ($\gamma$-GCS), a rate-limiting enzyme responsible for GSH biosynthesis, and demonstrated that indeed $\gamma$-GCS could be repressed by CL. Taken together, we report here for the first time that the anticancer effect of CL on human colorectal cancer cells is mediated through GSH depletion mechanism rather than a ROS-mediated killing process. This functional attribute of CL can thus provide the basis for the strategic design of a treatment of colorectal cancer