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• 計畫英文名稱	Study of the Molecular Mechanism of Cancer-Specific Inhibitory Effect of Magnolol
• 主管機關	行政院國家科學委員會
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• 中文關鍵字	厚朴酚；抗癌作用；分子機轉；肝癌；大腸癌
• 英文關鍵字	Magnolol；Anticancer effect；Molecular mechanism；Hepatoma；Colon cancer
• 中文摘要	Magnolol 曾被報告有抗癌作用.我們發現用 100 μM magnolol 可以引發肝癌及大腸癌細胞產生細胞凋亡而對牙齦 fibroblast 及 HUVEC 則不產生細胞凋亡.我們發現 magnolol 引發肝癌細胞產生細胞凋亡主要有以下步驟:(1)增加細胞內鈣(2)增加 cytochrome c 由粒腺體轉移到細胞質中(3)活化 caspase3,8 及 9(4)抑制 bcl-2 之表現.給肝癌細胞預處理 phospholipase c 抑制劑(U73122)或鈣離子螯合劑 BAPTA-AM 可抑制 magnolol 引發之細胞內鈣增加,而抑制 caspase 8 及 9 之活化及抑制肝癌細胞產生細胞凋亡.肝癌細胞預處理 ZB-4(Fas receptor antagoist)可抑制 magnolol 引發之 caspase 8 活化及抑制肝癌細胞產生細胞凋亡.我們發現以上步驟是 magnolol 引發肝癌細胞產生細胞凋之步驟而細胞內鈣,Fas,及 cytochrome c 居間作調控
• 英文摘要	Magnolol has been reported to have anticancer activity. In this study we found that treatment with 100 μM magnolol induced apoptosis in cultured human hepatoma (Hep G2) and colon cancer (COLO 205) cell lines but not in human untransformed gingival fibroblasts and human umbilical vein endothelial cells. Our investigation of apoptosis in Hep G2 cells showed a sequence of associated intracellular events that included (a) increased cytosolic-free Ca 2+ ; (b) increased translocation of cytochrome c (Cyto c) from mitochondria to cytosol; (c) activation of caspase-3, caspase-8, and caspase-9; and (d) downregulation of bcl-2 protein. Pretreatment of the cells with phospholipase C inhibitor, 1-[6-[[(17b)-3-methoxyestra-1,3,5(10)-trien-17-yl]amino]hexyl]-1 H-pyrrole-2,5-dione, or intracellular chelator of Ca 2+ , 1,2-bis(2-aminophenoxy)ethane-N,N, N',N' -tetraacetic acid acetoxymethyl ester, inhibited the subsequent magnolol augmentation of [Ca 2+]i and also the activation of caspase-8 and caspase-9, so that the occurrence of apoptosis in those cells was greatly reduced. Pretreatment of the cells

with ZB4 (which disrupts the Fas response mechanism) also decreased the subsequent magnolol-induced caspase-8 activation and reduced the occurrence of apoptosis. We interpreted these findings to indicate that the above-listed sequence of intracellular events led to the apoptosis seen in Hep G2 cells and that [Ca2+]i , Cyto c, and Fas function as intracellular signals to coordinate those events.