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• 計畫中文名稱	黑殭菌素及蘇力菌素抑制腫瘤細胞效果及抗腫瘤機制之探討
• 計畫英文名稱	Study of the Anti-tumor Effect and the Mechanism of Action on Destruxin B and Thuringiensin
• 主管機關	行政院國家科學委員會
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• 研究人員	劉正民 Liu, Cheng-Min
• 中文關鍵字	抗癌藥物; 黑殭菌素; 淋巴腫瘤細胞; 自然凋亡; 壞死現象; 訊號傳遞之路徑
• 英文關鍵字	Anti-tumor drug; Destruxin B; Lymphoma cell; Apoptosis
• 中文摘要	黑殭菌素 (Destruxin)是由昆蟲寄生性真菌(entomogenous fungi)之一的黑殭菌 (Metarhizium)所分泌出的毒素，在已分離出的三十餘種中，本研究中採用的是 Destruxin B 作爲抗腫瘤製劑。經發酵後自發酵液中抽取純化後，先以毛細管電泳及質譜儀鑑定其純度，純化出的 Destruxin B 以 Acetonitrile 爲溶劑配製。在本實驗中，我們採用 DBA/2 品系老鼠經 methylcholanthrene 所引導出的 L5178Y 淋巴癌細胞作反應。企圖了解 Destruxin B 對於對腫瘤細胞之生長影響。結果中發現 1.29 M 及 2.58 M 的 DB 對腫瘤細胞生長有顯著的抑制作用，當劑量超過 5.17 M 時有毒殺腫瘤細胞的作用。然而相同劑量的 DB 對正常脾臟細胞及纖維母細胞株則沒有抑制作用。利用流式細胞儀觀測藥物引發細胞週期停滯於 G2/M 時期，並進一步誘使其發生細胞凋亡的現象。此外，探討會影響細胞週期行進和調控細胞凋亡的相關蛋白表現，以了解 Destruxin B 作用下 L5178Y 細胞的分子機轉。最後再以 DBA/2 品系老鼠作 in vivo 試驗，了解其在體內抗癌的效果。本實驗冀望爲未來抗癌藥物開展一個新的領域。
• 英文摘要	Destruxin is a substance which secrete from fungus, Metarhizium. This substance is toxic to insect and has been used as an insecticide for decades. Over thirty species of destruxins have been isolated from different investigators. In this study, the purified destruxin B (DB) was tested for its in vitro and in vivo anti-tumor activities by using L5178Y lymphoma cells. This cell line was induced by methylcholanthrene from T lymphocytes of DBA/2 mice. The results indicated that DB suppresses L5178Y lymphoma cells growth dramatically even in the dose as low as 1.29 M. When doses of DB over 5.17 M, the dead tumor cells were found. The same doses range has no growth suppression or tumoricidal effect on either mouse spleen cells primary culture or NIH3T3 fibroblast cells. The results from flow cytometric analyses indicated that DB induced cell

cycle arrest at G2/M phase, consequently, caused cell apoptosis. The mechanisms of apoptosis were analyzed by Western blot. The results indicated that under DB treatment, the CDK1 (cdc2) protein expression was suppressed, p53 protein was increased and caspase 3 was activated. These results confirmed that previous growth suppression and flow cytometric results. The in vivo experiment was performed by implanting L5178Y lymphoma cells into DBA/2 mouse peritoneal cavity i.p. at dose of 230 g/kg. The results showed that the treated group of mice may extent their survival days at least for 2 weeks longer than that of control group. From both in vitro and in vivo experiment results, it has proven that DB may be as a potential candidate for future anti-tumor drug.