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• 計畫中文名稱	環境中氧化氮與亞硝基化合物之毒理學研究－氧化氮基因毒性分子機制之探討(II)
• 計畫英文名稱	Studies on the Molecular Mechanisms of Genotoxicity of Nitric Oxide (NO) (II/III)
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• 研究人員	何元順；林仁混 Ho, Yuan-Soon；Lin, Jen-Kun
• 中文關鍵字	一氧化氮；細胞凋亡；基因毒性；抗氧化劑
• 英文關鍵字	Nitric oxide (NO)；Apoptosis；Genotoxicity；Antioxidant
• 中文摘要	有報告指出,NO 可以攻擊細胞內核酸進而使其產生突變,或染色體異常。由我們第一年的研究結果更證實了,NO 可以使細胞 DNA 損傷,並造成細胞凋亡。經我們第一年的研究結果亦證實,NO 確實能誘發細胞內 P53 與 P21/WAF1/CIP1 的表現增強,這些基因的變化,明顯地將影響許多與細胞週期有關的基因如:Bcl-2、Bax、mdm-2、GADD-45...etc,而 Bax 基因會受到 NO 的刺激而活化,反之 bcl-2 則受抑制。 除此之外,我們在第二年的研究結果亦發現,某些自然界的抗氧化物(如 L-N-acetylcysteine、curcumin 等)可以有效防止 NO 所造成的細胞死亡。這些抗氧化物質主要的作用機制是增加細胞內部許多抗氧化蛋白如 Glutathione,bcl-2 等大量激增。另一方面則使 Bax 蛋白表現減少,因此細胞存活率大增。
• 英文摘要	It has been demonstrated that nitric oxide (NO) can promote apoptosis in human cancer cells. To test the protective effects of antioxidants, (L-N-Acetyl-Cysteine, LNAC) or free radical spin traps (5,5-dimethyl-1-pyrroline-N-oxide, DMPO, and 2,2,6,6-tetra-methyl-1-piperidinyloxy, TMPO) against NO-induced apoptosis, a human colon cancer cell line (COLO 205) subjected to NO and the survival rate was evaluated both with and without antioxidant therapy. LNAC arrested the development of progression of apoptosis in COLO 205 cells in a dose dependent manner, promoted long term survival, and prevented internucleosomal DNA cleavage induced by NO. The intracellular level of Glutathione (GSH) was found to be elevated in cells after exposure to LNAC. The bax protein levels were elevated by NO treatment and this effect was blocked by LNAC. On the other hand, the bcl-2 oncoprotein level in the LNAC pretreated cells was significantly elevated in a time dependent manner compared to cells that received NO pretreatment. In summary, our results suggest that the protective effect of LNAC might be linked to its inducement of increases in

cellular glutathione and bcl-2 protein levels and to its suppression of cellular bax protein in treated cells.