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• 中文關鍵字	尼古丁; 乳癌; 抽菸		
• 英文關鍵字	NIC; Breast cancer; Nicotinic receptor		
• 中文摘要	1982 年起迄今二十餘年來，國人罹患乳癌的發生率急速增加了近 50-100%(Huang et al., 2001)且婦女罹患乳癌的年紀明顯較西方國家婦女要早很多(Cheng et al.,2000; Chie et al., 1995)。國人的研究發現女性乳癌發生與環境因子有密切相關如環境中少量藥物殘存(Chang et al.,2003)，荷爾蒙(避孕藥)或藥物濫用(Chie et al., 1998)，婦女抽菸或接觸二手煙等(Wu et al., 2002)。然而國人乳癌的發生與上述因子是否有關，並未獲得直接證實。本實驗室先期結果證實 1.乳癌病人癌組織中尼古丁受體($\alpha 9$-nAChR) mRNA 表現高於正常組織。2.這些病人有接觸或抽菸習性。3.乳癌細胞內 $\alpha 9$-nAChR 基因受到女性荷爾蒙(estrogen, E2)調控。		
• 英文摘要	Nicotine [3-(1-methyl-2-pyrrolidinyl)-pyridine], a major alkaloid in tobacco, has been implicated as playing a role in carcinogenesis. Our previous study showed that cigarette smoking promoted inflammation-associated lung adeno-carcinoma formation in vivo and in vitro, and MAPK plays an important role in this process. In the present study, we aimed to investigate whether NIC and its specific nicotinic acetylcholine receptor (nAChRs) could stimulate breast cancer cell proliferation and tumour growth and the possible mechanisms involved. We first demonstrated that the $\alpha 5$ and $\alpha 9$ nAChRs were detected in both the MCF-7 and MDA-MB-231 breast cancer cell lines. We further study the expression of the nAChR mRNA levels in breast tumour tissues collected from over-hundred cases of breast cancer patients in Taiwan and found that the $\alpha 9$ subunit of the nAChR was more significant in tumour tissue than in normal tissue. Western blotting analysis demonstrated that the Akt-regulated proteins were the major signalling pathway that involved in breast cancer cell proliferation stimulated by NIC treatment. Constructively express $\alpha 9$-nAChR knock		

down breast cancer cell line caused a similar result as treatment with LY294002, a Akt/protein kinase B (PKB) inhibitor, it was not only blocked PKB down stream signal but also reduced the tumour formation and growth in vitro-soft agar assay and growth curve and in vivo-mude mice tumour formation assay. Another important carcinogenic factor was found to be Estrogen (E2) which directly bound alpha9-nAChR promoter binding site at -44 bp and produced more mRNA expression in breast can cell line. Thus, this study provides evidence for a novel signalling route coupling the stimulation of alpha9 nAChR to the activation of PKB dependent manner, which implied that the alpha9-nAChR may play some important role 3 involved in NIC-mediated breast tumour carcinogenesis.