# 微小 RNA16 抑制肺癌細胞增生之研究 = Micro RNA16 inhibit lung cancer cell proliferation


## 石文昭、蔡孟

E-mail: 9806537@mail.dyu.edu.tw



**摘 要**

microRNAs是一群小片段的RNA，它的長度約18~24個核?・艦B不會被轉譯為蛋白質。生物體的運作伴隨而來的是一連串的調控作用，而microRNA更是這其中的要角，像是胚胎的發育、細胞分化、細胞周期的調控等等都可以發現microRNA參與其中。腫瘤的形成就是因為細胞在生物體中並沒有受到正常的調控，所以才會無限制的增生或是轉移；而近年來更陸續的發現乳癌、直腸癌、前列腺癌及神經膠母細胞瘤中都可以發現到microRNA的異常表現，但是在肺癌與microRNA之間的研究文獻則較少。因此本研究要分析與肺癌相關之microRNA，其中包含了miR-16、miR-24、miR-494等等不同的microRNA；進一步分析不同肺癌細胞株的結果顯示，若與正常支氣管上皮細胞相比，miR-16在肺癌細胞中的表現量往往都較正常細胞來的低。我們分別在CL1-5肺腺癌細胞中建立了兩個miR-16表現系統：pSilencerTM3.1-miR16與pcDNATM6.2-miR16。透過已建立完成的表現系統分析，我們發現miR-16大量表現的細胞株pSilencer3.1-miR16-A7、A19與pcDNA6.2-miR16-G16、G17細胞的生長速率會受到抑制達50%；但是對肺腺癌細胞的移動(migration)以及侵入(invasion)能力則不會有明顯的改變。接著透過二維電泳(2-D electrophoresis)的分析以及電腦軟體的預測，我們想找出在肺癌細胞中受到miR-16調控的基因；目前為止我們利用上述兩種方法找到了兩個可能的目標基因，分別是NYGGF4和ALDOA 。研究microRNA與癌症將有助於我們瞭解癌症的發生機制及癌症的治療，甚至是作為一個分子標記與預防癌症的再復發。



關鍵詞 : 微小RNA ; 微小RNA16 ; 肺癌 ; 癌細胞侵入 ; 癌轉移


**目錄**

## 參考文獻

1. 衛生署，97年死因統計結果分析。 2. Bartel DP (2004) MicroRNAs: genomics, biogenesis, mechanism, and function. Cell 116: 281-297. 3. Boffetta P (2006) Human cancer from environmental pollutants: the epidemiological evidence. Mutat Res 608: 157-162. 4. Bottoni A, Piccin D, Tagliati F, Luchin A, Zatelli MC, et al. (2005) miR-15a and miR-16-1 down-regulation in pituitary adenomas. J Cell Physiol 204: 280-285. 5. Bushati N, Cohen SM (2008) MicroRNAs in neurodegeneration. Curr Opin Neurobiol 18: 292-296. 6. Calin GA, Croce CM (2006) MicroRNA signatures in human cancers. Nat Rev Cancer 6: 857-866. 7. Carthew RW, Sontheimer EJ (2009) Origins and Mechanisms of miRNAs and siRNAs. Cell 136: 642-655. 8. Chan JA, Krichevsky AM, Kosik KS (2005) MicroRNA-21 is an antiapoptotic factor in human glioblastoma cells. Cancer Res 65: 6029-6033. 9. Chen C, Ridzon DA, Broomer AJ, Zhou Z, Lee DH, et al. (2005) Real-time quantification of microRNAs by stem-loop RT-PCR. Nucleic Acids Res 33: e179. 10. Chu CY, Rana TM (2007) Small RNAs: regulators and guardians of the genome. J Cell Physiol 213: 412-419. 11. Cimmino A, Calin GA, Fabbri M, Iorio MV, Ferracin M, et al. (2005) miR-15 and miR-16 induce apoptosis by targeting BCL2. Proc Natl Acad Sci U S A 102: 13944-13949. 12. Collins LG, Haines C, Perkel R, Enck RE (2007) Lung cancer: diagnosis and management. Am Fam Physician 75: 56-63. 13. Deng CX (2009) SIRT1, is it a tumor promoter or tumor suppressor? Int J Biol Sci 5: 147-152. 14. Doench JG, Sharp PA (2004) Specificity of microRNA target selection in translational repression. Genes Dev 18: 504-511. 15. Du J, Yang S, An D, Hu F, Yuan W, et al. (2009) BMP-6 inhibits microRNA- 21 expression in breast cancer through repressing deltaEF1 and AP-1. Cell Res 19: 487-496. 16. Eulalio A, Huntzinger E, Izaurralde E (2008) Getting to the root of miRNA-mediated gene silencing. Cell 132: 9-14. 17. Fan D, Ma C, Zhang H (2009) The molecular mechanisms that underlie the tumor suppressor function of LKB1. Acta Biochim Biophys Sin (Shanghai) 41: 97-107. 18. Fire A, Xu S, Montgomery MK, Kostas SA, Driver SE, et al. (1998) Potent and specific genetic interference by double-stranded RNA in Caenorhabditis elegans. Nature 391: 806-811. 19. Gillies JK, Lorimer IA (2007) Regulation of p27Kip1 by miRNA 221/222 in glioblastoma. Cell Cycle 6: 2005-2009. 20. Griffiths-Jones S, Saini HK, van Dongen S, Enright AJ (2008) miRBase: tools for microRNA genomics. Nucleic Acids Res 36: D154-158. 21. Hamaguchi T, Iizuka N, Tsunedomi R, Hamamoto Y, Miyamoto T, et al. (2008) Glycolysis module activated by hypoxia-inducible factor 1alpha is related to the aggressive phenotype of hepatocellular carcinoma. Int J Oncol 33: 725-731. 22. Hayashita Y, Osada H, Tatematsu Y, Yamada H, Yanagisawa K, et al. (2005) A polycistronic microRNA cluster, miR-17-92, is overexpressed in human lung cancers and enhances cell proliferation. Cancer Res 65: 9628-9632. 23. Jemal A, Siegel R, Ward E, Hao Y, Xu J, et al. (2008) Cancer statistics, 2008. CA Cancer J Clin 58: 71-96. 24. Jemal A, Thomas A, Murray T, Thun M (2002) Cancer statistics, 2002. CA Cancer J Clin 52: 23-47. 25. Kefas B, Godlewski J, Comeau L, Li Y, Abounader R, et al. (2008) microRNA-7 inhibits the epidermal growth factor receptor and the Akt pathway and is down-regulated in glioblastoma. Cancer Res 68: 3566-3572. 26. Ko YC, Huang YL, Lee CH, Chen MJ, Lin LM, et al. (1995) Betel quid chewing, cigarette smoking and alcohol consumption related to oral cancer in Taiwan. J Oral Pathol Med 24: 450-453. 27. Lee RC, Feinbaum RL, Ambros V (1993) The C. elegans heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. Cell 75: 843-854. 28. Lee S, Gang J, Jeon SB, Choo SH, Lee B, et al. (2007) Molecular cloning and functional analysis of a novel oncogene, cancer-upregulated gene 2 (CUG2). Biochem Biophys Res Commun 360: 633-639. 29. Lu M, Zhang Q, Deng M, Miao J, Guo Y, et al. (2008) An analysis of human microRNA and disease associations. PLoS One 3: e3420. 30. Mountain CF, Lukeman JM, Hammar SP, Chamberlain DW, Coulson WF, et al. (1987) Lung cancer classification: the relationship of disease extent and cell type to survival in a clinical trials population. J Surg Oncol 35: 147-156. 31. Nicoloso MS, Spizzo R, Shimizu M, Rossi S, Calin GA (2009) MicroRNAs--the micro steering wheel of tumour metastases. Nat Rev Cancer 9: 293-302. 32. Novakova J, Slaby O, Vyzula R, Michalek J (2009) MicroRNA involvement in glioblastoma pathogenesis. Biochem Biophys Res Commun. 33. Parkin DM, Bray FI, Devesa SS (2001) Cancer burden in the year 2000. The global picture. Eur J Cancer 37 Suppl 8: S4-66. 34. Rintala-Maki ND, Goard CA, Langdon CE, Wall VE, Traulsen KE, et al. (2007) Expression of RBM5-related factors in primary breast tissue. J Cell Biochem 100: 1440-1458. 35. Rosti G, Bevilacqua G, Bidoli P, Portalone L, Santo A, et al. (2006) Small cell lung cancer. Ann Oncol 17 Suppl 2: ii5-10. 36. Selaru FM, Olaru AV, Kan T, David S, Cheng Y, et al. (2009) MicroRNA-21 is overexpressed in human cholangiocarcinoma and regulates programmed cell death 4 and tissue inhibitor of metalloproteinase 3. Hepatology 49: 1595-1601. 37. Sleeman J, Schmid A, Thiele W (2009) Tumor lymphatics. Semin Cancer Biol. 38. Travis WD, Travis LB, Devesa SS (1995) Lung cancer. Cancer 75: 191-202. 39. Urbich C, Kuehbacher A, Dimmeler S (2008) Role of microRNAs in vascular diseases, inflammation, and angiogenesis. Cardiovasc Res 79: 581-588. 40. Venturini L, Battmer K, Castoldi M, Schultheis B, Hochhaus A, et al. (2007) Expression of the miR-17-92 polycistron in chronic myeloid leukemia (CML) CD34+ cells. Blood 109: 4399-4405. 41. Wang B, Zhang M, Ni YH, Liu F, Fan HQ, et al. (2006) Identification and characterization of NYGGF4, a novel gene containing a phosphotyrosine-binding (PTB) domain that stimulates 3T3-L1 preadipocytes proliferation. Gene 379: 132-140.