Desmocollin-2 (DSC2)基因在肺腺癌細胞中之生物功能及其下游調控機制之研究 = The Studies of Biological Function and Downstre

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摘 要

肺癌是目前國人死亡率最高的疾病之一，肺癌的轉移是導致病患死亡的主因，而肺癌的治療上又缺乏診斷轉移的生物指標，因此肺癌的轉移一直都是大家努力研究的目標。Desmosome (橋粒)是細胞與細胞黏附的主要結構之一，許多研究認為Desmosome在訊息傳遞亦扮演重要的角色。Desmocollin-2 (DSC2)是一種跨膜蛋白為Desmosome主要組成蛋白之一，分布於大部分的上皮細胞。近年來研究指出DSC2在大腸直腸癌、胃癌和食道癌都的研究證明DSC2表現減少與癌細胞的增生、轉移、侵入有關。然而DSC2基因與肺癌的關係性及在肺癌細胞中所扮演的角色尚未清楚。因此本研究探討DSC2是否會影響肺癌細胞的功能。首先利用即時定量PCR和西方墨點法分析DSC2在CL1-0、CL1-5和A549肺癌細胞株mRNA與蛋白質的表現量，結果顯示DSC2在CL1-0的表現量比CL1-5和A549高出許多。初步確定DSC2在不同肺癌細胞株表現會有差異。所以我們利用CL1-0細胞株藉由shRNA的方式抑制DSC2之後分析DSC2基因對細胞功能的影響。結果證明抑制DSC2之後會促進肺癌細胞增生、遷移和侵入能力，並且細胞會產生Epithelial to mesenchymal transition (EMT)現象。這表示DSC2在腫瘤發展中扮演一個重要的角色。為了瞭解DSC2是如何影響肺癌細胞增生、遷移和侵入能力，我們利用Microarray assay方法分析發現DSC2可能藉由調節：1. MMP10、SHISA3、NDRG1和SLIT2表現可能影響細胞轉移。2. Desmosome的其他組成蛋白JUP、PKP2、DSP、DSC3、DSC1和DSG2表現則影響細胞黏附及移動能力。3. EGFR和DLC1表現可能影響細胞生長。4. IL18和SOX4表現可能影響細胞凋亡。本研究針對DSC2在肺癌中的調控機制的探討對於未來肺癌病人的治療與管理是有很大的幫助。

關鍵詞 : DSC2、肺癌、增生、轉移、侵入、EMT、Microarray

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