CD74 在癌症轉移中所扮演的角色

Potential Role of CD74 in Cancer Metastasis

中文摘要

CD74 爲 major histocompatibility complex class II invariant chain，是第二類非多形性穿膜的醣化蛋白，在抗原呈現的過程中爲 MHC class II 的護衛蛋白。近年來的研究發現 CD74 亦爲一個傳訊分子，可以傳遞使細胞增生存活的訊息。最近也證實了 CD74 除了表現在抗原呈現細胞上以外，在許多的肉瘤上也都有 CD74 的表現，像是腎癌、肺癌、胃癌及胸腺來源的肉瘤等等。但是，對於 CD74 和腫瘤惡化的關係目前卻不是很清楚。

利用 subtractive hybridization 的方式比對肺癌轉移及原位肺癌病人的 cDNA library 發現，CD74 的基因表現與肺癌的轉移有關。首先我們利用免疫組織染色觀察肺癌病人的組織切片確認了在腫瘤細胞相對於鄰近的正常細胞 CD74 的確有過度表現的現象。但奇怪的是，在 15 株肺部相關的細胞株(包含正常及肺癌細胞株)中，利用 RT-PCR 及 Western blotting 都沒有觀察到 CD74 的表現。我們利用 PCR 的方法以及用 Western blotting 分析處理過甲基轉移脢抑制劑的細胞株來確認這些細胞中的CD74基因沒有被剔除，而其mRNA的不表現也不是因爲DNA被甲基化的關係。同時，我們建構了兩個 CD74 的 isoforms－p33 及 p35，並利用兩株不同侵襲能力的肺癌細胞株—低侵襲力的 CL1-0 細胞及高侵襲力的 CL1-5-F4 細胞來作爲細胞模式。將 CD74 p33 過度表現在 CL1-5-F4 細胞中可以更加強細胞的爬行和侵襲能力，但在 CL1-0 則沒有觀察到這個現象。而過度表現 CD74 p35 則不論在 CL1-0 或 CL1-5-F4 細胞中對於細胞的爬行、侵襲以及生長能力都沒有影響。我們推測，CD74 可能是一個協同因子能夠幫助惡性腫瘤的惡化。

英文摘要

CD74 (major histocompatibility complex class II invariant chain) is a type II transmembrane protein which was thought to function mainly as an MHC class II chaperone during antigen presentation. Recently, CD74 was reported to have a role as a signaling molecule for cell survival. In addition to its expression on antigen-presenting cells, it is expressed by sarcomas of renal, lung, gastric, and thymic origin and by certin sarcomas. However, little is known for the relationship in CD74 and tumor malignancy.

CD74 gene is originally cloned out from a cDNA library by subtracting metastatic tumors from primary tumors of a patient with lung adenocarcinoma. Our immunohistochemical study confirmed its overexpression on the tumor parts of patients with lung cancer as compared to the tumor-adjacent normal counterparts.

Intriguingly, no expression of CD74 was observed in 15 lung cancer or normal-like cell lines by RT-PCR and Western blotting analysis. We demonstrated that absence of CD74 mRNA or protein expression is not due to gene deletion or DNA methylation through PCR and Western blotting analysis of 5-aza-2'-deoxycytidine (inhibitor of DNA methyltransferase) – treated cells. We constructed two isoforms of CD74, p33 and p35, and use low-/ high-invasive lung cancer cell line, CL1-0 and CL1-5-F4, as cell model. Overexpression of CD74 p33 in a high-invasive lung cancer cell line, CL1-5-F4, could further increase its migration and invasion ability, but the phenomenon was not observed in low-invasive lung cancer cell line, CL1-0. However, overexpression of CD74 p35 in both CL1-0 and CL1-5-F4 cells did not affect cell migration, invasion, and cell growth. Therefore, these data suggested that CD74 may play a co-factor which promote tumor malignancy.