Abstract

The role of Akt3 in prostate cancer metastasis is not well understood. We investigated if Akt3 is involved in the regulation of migration and invasion of prostate cancer cells. We selected stable overexpression Akt3 clones of PC-3 androgen receptor (AR)-negative androgen-independent human prostate cancer cells. Overexpression of Akt3 suppressed cell migration and invasion as determined by the transwell and wound-healing assays. Using In Vivo Imaging System (IVIS) and Immunohistochemistry (IHC), we observed that overexpression of Akt3 suppressed cancer metastasis of PC-3 cells in nude mice orthotopic model. Western blot analysis for PC-3 cells indicated that alteration of Akt3 protein suppressed the protein abundance of epithelial-mesenchymal transition (EMT) marker protein vimentin, Snail, Ncadherin, and Slug. Meta-analysis of PubMed GEO profile data of 81 normal prostate tissues, 6 BPH tissues, 13 PIN tissues, 104 primary prostate tumors, and 51 metastatic prostate tumors indicated that Akt3 mRNA expression level was lower in metastatic prostate tumors as compared to primary prostate tumors. These observations suggested that overexpressed Akt3 regulates the migration and invasion of prostate cancer cells via adjustment of protein abundance and subcellular distribution of certain EMT marker proteins. Targeting Akt3 may be a potential treatment for prostate cancer metastases.

摘要

Akt3 在攝護腺癌中高度轉移的癌細胞所扮演的角色，與功能尚未被了解。我們去研究 Akt3 是否會參與在攝護腺癌細胞中的轉移和侵襲，和 Akt3 所扮演的角色。我們利用 Meta-analysis of PubMed GEO profile data 發現 Akt3 的 mRNA expression 與正常組織相比都是比較低的，因此我們先利用 androgen receptor (AR)-negative androgen-independent 的 PC-3 人類攝護腺癌細胞，篩選有穩定高度表現 Akt3 的細胞株進行往後的實驗。

我們利用 transwell 和 wound healing assays 去觀察細胞的轉移和侵襲我們發現高度表現 Akt3 會去抑制細胞的轉移和侵襲。我們把細胞以原位注射的方式打到老鼠的前列腺，再利用非侵入式活體觀察系統(IVIS)觀察，發現隨時間的增加，老鼠體內高度表現 Akt3 的細胞株相較於控制組有明顯的抑制細胞轉移到其他器官。再利用免疫組織染色，使用 Ki-67 抗體去確認癌細胞是否轉移到其他器官，我們發現控制組的癌細胞有轉移到器官，高度表現 Akt3 的細胞幾乎沒有轉移到其他的器官，甚至原位的癌細胞也變少。 Akt3 可以抑制攝護腺癌細胞的轉移，可能是透過 Epithelial-Mesenchymal Transition (EMT)，我們利用高度表現 Akt3 去看 EMT 相關蛋白質的表現，發現 vimentin, Snail, N-cadherin, Slug，都有明顯的被抑制表現。 Akt3 在攝護腺癌中可以去抑制類的攝護腺癌細胞的轉移和侵襲， Akt3 未來也許可以成為一個治療攝護腺癌的標靶。