人類同源箱基因 OTEX 之功能性研究

Functional Characterization of Human Homeobox Gene OTEX

中文摘要

TPX1(Testis- Pairlike-Homeobox-1)爲先前在分析另一個人類同源箱基因 TSX1 時，在其上游 30 kb 處一個未被人發現的同源箱基因，我們進而購入並定序一個含有 750 bp 的 EST clone 而命名之，但這個基因去年 2002 年分別由德國 Christoph 等人及美國 Wayen 等人發表並命名爲 OTEX (Ovary-Testis-Epididymus Homeobox Gene)及 hPEPP1，因此我們之後即以第一篇發表之 OTEX 稱之。我們已得知 OTEX 在睪丸、副睪、攝護腺及卵巢中皆有表現，而且進一步發現 OTEX 只在人類存在，這個結果說明 OTEX 可能是在演化後期才出現之基因，也暗示其在人類生理功能上之重要性。目前我們也了解 OTEX 在 2 株不同的前列腺癌細胞 (LNCaP 及 PC-3)有表現，初步結果顯示 OTEX 會受到雄性素之刺激而增加其表現量。我們對 OTEX 上游 1 kb 區域進行搜尋時，也發現在接近 1 kb 之位置有一可能的雄性素受器結合位(ARE)，而雄性素(androgen)是導致前列腺癌之關鍵，因此我們希望藉提高 OTEX 在前列腺癌細胞株（LNCaP 和 PC 3）及綠猴腎細胞株 (COS 7) 之表現程度，來進一步觀察細胞內前列腺癌相關基因受影響的情形，及其他正常基因的改變。目前利用強啓動子（pEF）帶領 OTEX cDNA 在細胞內大量表現，初步結果發現有 OTEX 暫時性大量表現之細胞，似乎有較高之增殖性，暗示 OTEX 與前列腺癌之生長相關性。

英文摘要

A pair-like homeobox gene OTEX (Ovary-Testis-Epididymis-homeoboX) was identified through genomic DNA sequence alignment with a previously isolated homeobox gene TSX1. OTEX gene is localized on the human X chromosome and expressed in testis, epididymis, prostate, ovary and brain. No ortholog of OTEX gene has been identified in mouse genome through intensive GenBank search and cDNA library screening. Zoo blot analysis further confirmed that OTEX is only present in human genome. The results suggested that OTEX is appeared in a later period of the evolution, and may be involved in an important genetic regulation of the human physiology. OTEX expression is also identified in both LNCaP and PC3 prostate cancer cell lines, and the expression was stimulated dramatically following androgen treatment. Proscran was used to search binding motif of upstream and intron 1 of OTEX gene, and an ARE site was identified in the upstream region. Since androgen is crucial to the development of prostate cancer, we change the expression level of OTEX in the LNCaP cell lines, to elucidate the potential role of OTEX in prostate

cancer. Both transgenic overexpression and RNA interference were induded in our strategy. OTEX was transfected into PC-3 and COS 7 cell lines to understand the effect of OTEX in other cell lines. From the preliminary result, we found that OTEX overexpression seem enhanced the cell proliferation, which imply a correlation between OTEX and prostate cancer.