

同源箱基因 Oct-4 在人類睪丸生殖細胞腫瘤中所扮演的角色探討

Role of Homeobox Gene Oct-4 in Human Testicular Germ Cell Tumors

中文摘要

睪丸生殖細胞腫瘤是一種常見於 15-34 歲男性的惡性腫瘤。依據組織型態可將睪丸生殖細胞腫瘤區分為兩大類：精細胞癌類與非精細胞癌類。在睪丸生殖細胞腫瘤中的精細胞癌與胚胎癌已被證實會表現出一胚胎幹細胞之標誌 - 同源箱基因 *Pouf1* (*Oct-4*)。Oct-4 蛋白已知參與調控幹細胞之自體更新及分化的重要因子；然而 Oct-4 在生殖細胞瘤中所扮演的角色尚未清楚。

我們利用睪丸生殖細胞腫瘤之病理組織與 NCCIT 和 NT2 細胞株來探討 Oct-4 蛋白在生殖細胞腫瘤中所扮演的角色。本論文中相對於比較人類胚胎幹細胞，我們證實了 Oct-4 蛋白不但高度表現於 NCCIT 細胞株、NT2 細胞株和精細胞癌組織中，同時也由細胞核轉移到細胞質中表現。我們進一步利用 bisulfite 來修飾胚胎幹細胞細胞株、NCCIT 細胞株和 NT2 細胞株之 DNA，並以甲基化專一性聚合-連鎖反應偵測 Oct-4 基因 5' 端上游 -1069~-776 及 -623~-356 區域中之 CpG 位置甲基化之差異，我們的結果暗示著這些甲基化差異性是 Oct-4 蛋白在癌細胞株過度表現的原因之一，不過仍須更加進一步研究。

我們在精細胞癌與胚胎癌中所觀察到 Oct-4 蛋白高度表現與表現位置轉移的，推測 Oct-4 基因表現的調控與癌症生成具有高度的關連性。未來將進一步研究 Oct-4 基因高度表現與其基因甲基化的關連性，及蛋白質轉移到細胞質之機制及作用。

英文摘要

Testicular germ cell tumors (TGCTs) are the most common malignant neoplasms of testis in men at ages of 15-34 years. TGCTs are histologically classified into seminoma and non-seminoma, or combination of the two types. Seminoma and embryonic carcinoma (non-seminoma) have been shown to exhibit a unique pattern of gene expression same as embryonic stem cells (ES), such as Oct-4. In ES, Oct-4 protein is known to be the master regulator to participate in controlling stem cell self-renew and differentiation. In seminoma and embryonal carcinoma, Oct-4 protein was also recognized as a diagnosis marker recently; however, the role of Oct-4 protein in germ cell tumor has not been clarified.

To characterize the role of Oct-4 in germ cell tumorigenesis, we examined the expression pattern of Oct-4 protein in TGCTs. In this thesis, by collection patient's tissues, NCCIT and NT2 cell lines and using immunohistological staining and Western blotting, we demonstrated the Oct-4 protein is highly expressed in human seminoma and embryonic carcinoma. Interestingly, the localization of Oct-4 protein in

these tumor cells is not only in nucleus but also in cytoplasm. Furthermore, we demonstrated the relative expression level of Oct-4 mRNA among hES, NCCIT and NT2 cell lines by quantitative PCR; and the DNA methylation profile of the 5'-upstream region of the Oct-4 gene (-1069~-776 and -623~-356) was also examined by methylation specific PCR.