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## Piwil2重编程人成纤维细胞形成肿瘤干细胞的初步研究

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**Title:** Preliminary study of Piwil2 reprogramming human fibroblasts into cancer stem cells

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**关键词:** [Piwil2](#); [成纤维细胞](#); [肿瘤干细胞](#)

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**摘要:** **目的** 初步观察精原干细胞自我更新基因Piwil2重编程人成纤维细胞的细胞形态及功能特征变化,建立Piwil2调控肿瘤干细胞发生过程的细胞实验模型。**方法** 将携带Piwil2-GFP标记和空载目的基因GFP标记的慢病毒载体分别感染原代培养的小儿包皮成纤维细胞,筛选建立稳定表达Piwil2-GFP和GFP成纤维细胞系,观察细胞形态变化及肿瘤球形成过程,分析细胞染色体核型,进行裸鼠体内成瘤实验,RT-PCR、免疫组织化学进一步鉴定重编程后细胞的干细胞特征及三胚层分化的相关标志物。**结果** 转染后第5天, Piwil2-GFP 成纤维细胞开始由长梭形逐渐转变为圆形,第14天出现集落样生长状态,挑选集落重悬后培养形成类似“肿瘤球”样克隆,其细胞染色体核型呈超二倍体的异质性改变。“肿瘤球”样克隆裸鼠体内移植2周时100%形成肿瘤,肿瘤组织学及免疫组化鉴定为表达多种外胚层、中胚层及内胚层肿瘤标志物的恶性肿瘤,RT-PCR显示细胞及裸鼠肿瘤表达干细胞多能基因Oct-4、Nanog、Sox2,以及三胚层特征标志物。**结论** Piwil2重编程人成纤维细胞后的细胞具有干细胞及多潜能分化特性,以及显著的肿瘤细胞异质特性。

**Abstract:** **Objective** To observe the cell morphology and functional characteristics of human fibroblasts after reprogrammed by spermatogonial stem cell self-renewal

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gene Piwil2, and to construct an experimental cell model for studying cancer stem cells (CSC). **Methods** Lentiviral vectors carrying Piwil2-GFP and GFP were transferred into primary culture of human foreskin fibroblasts to establish the cell lines stably expressing Piwil2-GFP fusion protein and GFP after selected by puromycin. Cells morphological changes and formation of tumor spheroids were observed, chromosomal karyotypes were analyzed and tumor formation assay was operated in nude mice. The tumor characteristics, stem cell characteristics and the markers of three germ layers were identified by RT-PCR and immunohistochemistry. **Results** The morphology of Piwil2-GFP fibroblasts became round and smaller at the 5th day after transfection, and turned to be colony-like growth at the 14th day after transfection. The selected colony was resuspended in culture and appeared to form similar tumor spheroids. The cell karyotype showed hyperdiploid heterogeneity, and all the tumor spheroids-like colonies formed tumor after transplanted into nude mice for 2 weeks. It was identified by histology and immunohistochemistry assays as a malignant tumor that expressed the markers of three germ layers. RT-PCR showed that the cells and tumors in nude mice expressed stem cell pluripotent genes such as Oct-4, Nanog, Sox2 and the markers of three germ layers. **Conclusion** According to the cell morphology, molecular phenotype of stem cells and tumorigenic cell heterogeneity after Piwil2 reprogramming, the Piwil2-GFP fibroblasts seems to have stem cell and pluripotent differentiation characteristics and significant tumor cell heterogeneity. Therefore, fibroblasts after Piwil2 reprogramming may have CSC functionality, and can be used as a model for studying the process and mechanism of CSC occurrence.

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