

## 论著

### TGF- $\alpha$ 诱导前列腺癌DU145细胞神经内分泌分化和增强DU145对顺铂的化疗耐药性

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**摘要:** 目的:研究TGF- $\alpha$ 是否具有EGF相似的可诱导前列腺癌DU145细胞发生神经内分泌分化(neuroendocrine differentiation, NED)的作用,并探讨TGF- $\alpha$ 诱导的前列腺癌DU145细胞神经内分泌分化对肿瘤化疗耐药性的影响。方法:将接受不同培养液处理的DU145细胞分为3组:2%FBS组、2%FBS+TGF- $\alpha$  5 ng/mL组和2%FBS+TGF- $\alpha$ 10 ng/mL组。显微镜下观察TGF- $\alpha$ 处理后DU145细胞的形态变化;Real time RT-PCR法检测神经特异性烯醇化酶(neuron-specific enolase, NSE) mRNA的表达水平;Western印迹检测NSE, P-糖蛋白(P-glycoprotein, P-gp), 多药耐药相关蛋白1(multiple drug resistance protein, MRP1)和Bcl-2蛋白的表达水平。流式细胞术分析TGF- $\alpha$ (5  $\mu$ g/mL)处理后DU145细胞周期的变化;MTT比色法测定TGF- $\alpha$ (5  $\mu$ g/mL)对DU145细胞顺铂化疗耐药性的影响。结果:同2%FBS组相比,2%FBS+TGF- $\alpha$ 处理组的DU145细胞出现多形性,细胞伪足伸出;NED标志物NSE mRNA的表达水平升高,分别为上调了(3.6 $\pm$ 0.5)倍( $P$ <0.05)和(10.1 $\pm$ 0.1)倍( $P$ <0.01);细胞的NSE, Bcl-2和MRP1蛋白的表达水平也明显增加,但未检测到P-gp蛋白的表达;同时, TGF- $\alpha$ (5  $\mu$ g/mL)处理后DU145细胞的G<sub>1</sub>期细胞比例降低, S期和G<sub>2</sub>/M期细胞比例升高;顺铂的化疗耐药性增加。结论:TGF- $\alpha$ 也可诱导前列腺癌DU145细胞神经内分泌分化增强,从而进一步增强DU145细胞对顺铂的化疗耐药性。

**关键词:** 前列腺癌DU145细胞 转化生长因子 神经内分泌分化

### TGF- $\alpha$ increases neuroendocrine differentiation and strengthens chemoresistance in prostate cancer DU145 cells

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**Abstract:** Objective: To study whether TGF- $\alpha$  possesses similar EGF effect of enforcing neuroendocrine differentiation (NED) in prostate cancer cell line DU145 and determine the influence of NED induced by TGF- $\alpha$  on chemoresistance.

**Methods:** DU145 cells were divided into 3 groups: a group with 2% FBS, a group with 2% FBS+TGF- $\alpha$  5 ng/mL and a group with 2%FBS+TGF- $\alpha$  10 ng/mL. Morphological change in DU145 cells was observed after TGF- $\alpha$  treatment. Expression levels of NSE mRNA were detected with real time RT-PCR. Western blot was used to detect the expression levels of protein NSE, P-gp, MRP1 and Bcl-2. Cell cycles of DU145 cells in the 3 groups were examined with flow cytometry. MTT assay was used to evaluate the influence of TGF- $\alpha$  in chemoresistance.

**Results:** Compared with DU145 cells cultured with 2% FBS, cells treated with 2% FBS+TGF- $\alpha$  were pleomorphic and pseudopodia extended. The expression level of NSE mRNA upregulated to (3.6 $\pm$ 0.5) folds ( $P$ <0.05) and (10.1 $\pm$ 0.1) folds ( $P$ <0.01). Western blot showed that the expression levels of protein NSE, Bcl-2, and MRP1 increased after treatment with different concentrations of TGF- $\alpha$ ; P-gp was not detected. The proportion of DU145 cells in phase G<sub>1</sub> decreased; proportions of cells in phase S and phase G<sub>2</sub>/M were increased after TGF- $\alpha$  treatment (5  $\mu$ g/mL). At the same time, chemoresistance of DU145 cells to cisplatin increased.

**Conclusion:** TGF- $\alpha$  can increase NED in DU145 cells and enforce the chemoresistance to cisplatin.

**Keywords:** prostate cancer cell line DU145 transforming growth factor neuroendocrine differentiation

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