

维甲酸联合曲古抑素诱导及治疗荷人甲状腺滤泡状癌裸鼠的实验研究

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【摘要】 目的 探讨全反式维甲酸(ATRA)和曲古抑素(TSA)对人甲状腺滤泡状癌细胞株(FTC-133)和荷人甲状腺滤泡状癌裸鼠(NMB-hFTC)肿瘤模型摄碘能力的影响。方法 不同量 ATRA、TSA 诱导 FTC-133 细胞: ATRA 1.0×10^{-6} mol/L ($A_{低}$ 组)、 1.0×10^{-4} mol/L ($A_{高}$ 组)、TSA 1.65×10^{-7} mol/L (T 组)、 $A_{低}$ + T 组、 $A_{高}$ + T 组和无水乙醇(对照组), 96 h 后行 HE 染色, 测定 FTC-133 细胞摄碘率; 制备 NMB-hFTC, 成瘤后分组: ATRA 组(2 mg/kg 灌胃)、TSA 组(10 mg/kg 腹腔注射)、联合组(ATRA + TSA, 用量同前)、对照组(生理盐水灌胃 + 腹腔注射, 均为 10 ml/kg), 剂量均按鼠体质量给予。给药 22 d 后, 腹腔注射 37 MBq ^{131}I , 分别于注射后 4、6、12 和 24 h 行 γ 显像, 测定体内生物分布; 显像后取肿瘤组织行 HE 染色观察细胞形态。实验结果采用 SPSS 13.0 软件进行单因素方差分析。结果 FTC-133 细胞摄碘率 $A_{低}$ + T 组、 $A_{高}$ + T 组分别为 $(23\ 885 \pm 616.0)$ 和 $(13\ 849 \pm 728.2)$ 计数 $\cdot \text{min}^{-1} \cdot 10^{-6}$ 细胞, 其他各组在 $(985 \pm 84.2) \sim (17\ 600 \pm 782.7)$ 计数 $\cdot \text{min}^{-1} \cdot 10^{-6}$ 细胞范围内, 各组间比较差异有统计学意义 ($F = 600.879, P < 0.001$)。 ^{131}I 注射后 6、12 和 24 h 联合组裸鼠种植瘤 % ID/g 分别为 $6.17 \pm 0.46, 9.34 \pm 0.61, 11.19 \pm 0.98$, 其余各组保持在 $(1.97 \pm 0.34) \sim (5.14 \pm 0.65)$ 之间; 肿瘤质量各组间比较差异有统计学意义 ($F = 3.723, P < 0.05$)。结论 ATRA 联合 TSA, 可增强 FTC-133 细胞和 NMB-hFTC 病灶的分化、摄碘能力, 达到增强 ^{131}I 杀死甲状腺癌病灶的协同作用。

【关键词】 甲状腺肿瘤; 肿瘤细胞, 培养的; 维甲酸; 曲古抑素 A; 小鼠, 裸

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【Abstract】 Objective To study the changes of iodine uptake of the follicular thyroid carcinoma cell line (FTC-133) and nude mice bearing human follicular thyroid carcinoma after the induction with all-trans retinoic acid (ATRA), trichostatin A (TSA) or ATRA combined with TSA. **Methods** After the induction with ATRA, TSA, or ATRA combined with TSA in different concentrations for 96 h, the iodine uptake of FTC-133 cells was observed. The concentrations for different groups were as follows: ATRA 1.0×10^{-6} mol/L (A_{low} group), ATRA 1.0×10^{-4} mol/L (A_{high} group), TSA 1.65×10^{-7} mol/L (T group), A_{low} + T group, A_{high} + T group and ethanol (control group). Cell quantities and morphology were observed by HE staining. FTC-133 cells were subcutaneously injected into nude mice. Twelve nude mice were randomly divided into 4 groups after tumor formation: ATRA group (2 mg/kg, intragastric administration), TSA group (10 mg/kg, intraperitoneal injection), combined therapy group (ATRA + TSA, the same doses as above) and saline control group (10 ml/kg, intragastric and intraperitoneal administration, respectively). Drugs were administered to the tumor-bearing mice according to the mouse body mass daily. At the 22nd day, the tumor-bearing mice were injected with 37 MBq ^{131}I intraperitoneally. The biodistribution of ^{131}I and gamma imaging were performed at 4, 6, 12 and 24 h after the injection respectively. Histopathological examinations of the tumor samples were taken after imaging completion. The results were analyzed by analysis of variance (ANOVA) with SPSS 13.0. **Results** The cellular iodine uptake were $(23\ 885 \pm 616.0)$ and $(13\ 849 \pm 728.2)$ counts $\cdot \text{min}^{-1} \cdot 10^{-6}$ cells in the A_{low} + T group and A_{high} + T group respectively, and the data were $(985 \pm 84.2) \sim (17\ 600 \pm 782.7)$ counts $\cdot \text{min}^{-1} \cdot 10^{-6}$ in the other groups ($F = 600.879, P < 0.001$). The % ID/g of tumor at 6 h was 6.17 ± 0.46 in the combined group and it increased to 9.34 ± 0.61 at 12 h and 11.19 ± 0.98 at 24 h. The % ID/g of tumor in the other groups were from (1.97 ± 0.34) to (5.14 ± 0.65) . The tumor qualities of the 4 groups were significantly different ($F = 3.723, P < 0.05$). **Conclusion** The iodine uptake of the tumor could be enhanced in the tumor-bearing mice administered with ATRA combined with TSA, a potential way for treating follicular thyroid carcinoma.

【Key words】 Thyroid neoplasms; Tumor cells, cultured; Tretinoin; Trichostatin A; Mice, nude