

## EGCG对人耐药口腔表皮样癌细胞株耐药逆转的实验

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### MDR-reversing Effect of (-)epigallocatechin-3-gallate on Human MDR Cell Lines KBV200

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#### 摘要

目的 研究EGCG对人多药耐药口腔癌细胞KBV200的细胞毒增敏作用及裸鼠移植瘤的抑瘤作用。方法 MTT法检测药物对细胞的毒性作用, 流式细胞术分别检测细胞P糖蛋白的表达, HPLC检测细胞内VCR浓度, 采用KB和KBV200细胞分别种植同一裸鼠左、右腋下, 观察用药后体重、抑瘤率的变化。RT-PCR检测瘤组织mdr1的表达。结果 EGCG在100mg·L<sup>-1</sup>以下剂量对两株肿瘤细胞的抑制率均小于10%, EGCG与VCR联合应用可明显提高VCR的细胞毒作用; EGCG联合VCR作用后KBV200细胞内VCR浓度升高, P糖蛋白的表达下降; EGCG可增加VCR对KBV200的抑瘤作用, 可降低瘤组织MDR1的表达量。结论 EGCG可增强VCR对多药耐药肿瘤细胞KBV200的细胞毒作用, 机制可能与降低MDR1-mRNA、P-gp表达, 提高细胞内药物浓度有关。

关键词: 多药耐药 P糖蛋白 耐药逆转剂 鳞癌

Abstract: Objective Experiments were carried out to examine the potential of EGCG(epigallocatechingallate) as a multidrug resistance (MDR) reversal agents. Methods MTT assay was used to detect cytotoxicity of EGCG and vincristine (VCR). Intracellular concentration of VCR was detected by high performance liquid chromatography (HPLC). Flow cytometry was used to determine the expression of P-gp. In a BALB/C-nu/nu mouse model, cells of drug-sensitive KB and KBV200 (MDR) cell lines were inoculated to yield tumors in opposite flanks. EGCG and VCR were injected to the peritoneal of nude mice with carcinoma xenografts. MDR1 mRNA expression was observed with reverse-transcriptase PCR. Results Survival of cells incubated with EGCG at 75 mg/l for 72 h was over 80%. EGCG at 8 mg/l almost completely reversed resistance to VCR in KBV200 cells and produced a 13.0-fold reversal of MDR. It increased intracellular concentration of VCR in KBV200 cells while not influence that in KB cells. In KBV200 xenograft model, neither EGCG nor VCR inhibited tumor growth. However, VCR and EGCG combined inhibited tumor growth by 72.8%. EGCG inhibited MDR1 expression and augmented accumulation of VCR in KBV200 cells. Conclusion The results suggest that EGCG is a potent MDR-reversing agent in vitro and in vivo. The mechanism is probably associated with down-regulating the expression of MDR1 and P-gp. So that increases the concentrations of anticancer drug in tumor cells.

Key words: Multidrug resistance P-glycoprotein Resistance reversal agents Squamous cell carcinoma

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