

论文

KB细胞耐药株的建立及其耐药机制的探讨

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摘要:

用对长春新碱(VCR)敏感的KB细胞为亲本,通过诱变剂甲基磺酸乙酯刺激,然后在培养液中加入浓度递增的CVR,得到耐药细胞株KB_{V200}。此细胞株对VCR的耐受程度约为KB细胞的175倍。对其它抗肿瘤药物如紫杉醇、秋水仙碱和阿霉素等也有不同程度的交叉耐药性。进一步研究表明,KB_{V200}对³H-VCR的蓄积明显减少,且耐药基因(mdr1)表达增加。钙通道阻滞剂维拉帕米(Ver)可增加KB_{V200}对³H-VCR的蓄积和对VCR的敏感性。这些结果提示,KB_{V200}耐药的机制可能是由于mdr1基因表达增加,产生过量的p-糖蛋白,使药物外排增多所致。

关键词: KB细胞 多药耐药 长春新碱 mdr1基因

VINCRI STINE-RESI STANT HUMAN KB CELL LI NE AND MECHANI SM OF MULTI DRUG RESI STANCE

XH Zbang;FY Zhang;XJ Ji and ZY Li

Abstract:

A multidrug-resistant(mdr)clone of human cancer KB cells was isolated by step-wise selection on exposure to increasing doses of vincristine. The final clone ,KB_{V200} ,obtained after ethylmethane sulfonate(EMS)mutagenesis showed 175-fold higher resistance to vincristine than did KB cells. The cells were also cross-resistant to taxol, colchicine and adriamycin. Cellular accumulation of vincristine in KB_{V200} was decreased to less than one-fifth of that in KB. To determine the presence of mdr 1 mRNA in KB_{V200} and KB ,total cellular RNAs from each cell line were analyzed by means of slot blot hybridization. The result showed that the mdr 1 gene had been highly expressed in KB_{V200}. In addition , verapamil, a calcium channel blockers ,was shown to increase VCR accumulation in KB_{V200} and reverse the vincristine resistance. All these results demonstrate that the mechanism of KB_{V200} cell resistance to multiple drugs resulted from increased expression of mdr 1 gene and brought about over production of P-glycoprotein and increased the efflux of drugs.

Keywords: Multidrug resistance Vincristine Mdr 1 gene KB cells

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