

论著 基因芯片技术检测鼻咽癌紫杉醇耐药及耐药逆转相关基因的表达

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摘要:

目的:比较药物处理前后鼻咽癌亲本细胞系CNE-1及鼻咽癌紫杉醇耐药细胞系CNE-1/Taxol的基因表达差异, 试图发现与鼻咽癌紫杉醇耐药及耐药逆转相关的基因。**方法:**使用基因芯片检测药物处理前后6组细胞系之间的基因表达差异, 运用多重筛选和针对已知耐药相关基因的具体分析相结合的方式进行分析。**结果:**经过多重筛选, 筛选出297个差异表达的基因; 比较亲本细胞, 在耐药细胞中上调或下调超过5倍的有17个基因。通过对已知耐药相关基因的分析, 结果显示: 具有药物转运作用的ATP结合盒家族中多药耐药基因(MDR1)在各组细胞中都未出现阳性表达; P450家族中CYP1A1在亲本细胞中不表达, 在耐药细胞中出现较强的阳性表达, 经紫杉醇处理后, 其表达进一步大幅下调, 顺铂处理后其表达下调; 肿瘤坏死因子家族中在耐药细胞系表达下调, 经顺铂处理后出现逆向表达增强的基因有TNFAIP1, 3和TNFRSF12A, 21; caspase家族出现差异表达的基因有caspase-4和caspase-6; β -微管蛋白II在耐药细胞中表达下调; TSP1在耐药细胞中表达明显下调, 经紫杉醇处理后, 表达进一步下调, 但是, 经顺铂作用后, 其表达明显上调。**结论:**可能与鼻咽癌紫杉醇耐药及耐药逆转相关的基因有: 经过多重筛选得到的297个差异表达的基因、CYP1A1、部分肿瘤坏死因子家族成员以及另外17个在亲本细胞和耐药细胞之间表达差异超过5倍的基因; 结合全部基因数据的多重筛选和已知耐药相关基因的具体分析研究肿瘤细胞耐药及耐药逆转机制是比较理想的方法。

关键词: 鼻咽癌 多药耐药 耐药逆转 基因芯片

Differential expression of taxol resistance and taxol resistance reversal related genes in nasopharyngeal carcinoma by cDNA microarray

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Abstract:

Objective: To compare the difference in gene expression profiles between parental cell line and drug resistant cell line (CNE-1 and CNE-1/taxol) pre-treated or treated by drugs, and search for genes related to taxol resistance and reversal of taxol resistance phenotype. **Methods:** cDNA microarray was used to detect the difference in gene expression profiles between 6 groups of cells. Combination of multiple filtering genes and detailed analysis of documented resistance genes were used to analyze the data. **Results:** Through multiple filtering, 297 differentially expressed genes were screened. The expression of 17 genes was increased or decreased more than 5 folds in CNE-1/taxol compared with CNE-1. Through analyzing documented drug-resistant genes, MDR1 expression was not detected in each group. CYP1A1, one of P450 family members, was not expressed in CNE-1, but significantly increased expressions was found in CNE-1/taxol and these increased expressions were restored by cisplatin. The expression level of some members of tumor necrosis factor family was decreased in CNE-1/taxol and restored by cisplatin, including TNFAIP1, 3 and TNFRSF12A, 21. The differentially expressed members in the caspase family were caspase-4 and caspase-6. The expression of β -tubulin II was down-regulated in CNE-1/taxol. TSP1 was obviously down-regulated in CNE-1/taxol compared with CNE-1, and a more significant down-regulation of TSP1 was found when treated by taxol. However, it was greatly up-regulated after cisplatin treatment in CNE-1/taxol. **Conclusion:** Some genes are probably related to taxol resistance and reversal of taxol resistance in NPC cells: 297 differentially expressed genes detected by multiple filing, CYP1A1, some members of TNF family and another 17 genes whose differential expression is more than 5 folds between parental cell line and drug resistant cell line. Combination of multiple filtering genes and detailed analysis of documented resistance genes is a good method to study drug resistance and reversal of drug resistance in carcinoma cells.

Keywords: nasopharyngeal carcinoma multidrug resistance drug resistance reversal cDNA microarray

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基金项目:

国家自然科学基金(30471874,30772403)。

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参考文献:

- [1] 褚玉敏, 谭国林, 马艳红. 人鼻咽癌紫杉醇耐药细胞株CNE-1/Taxol的建立及其机制初探 [J]. 中国耳鼻咽喉颅底外科杂志, 2007, 13(6): 411-414. CHU Yumin, TAN Guolin, MA Yanhong. Establishment of a paclitaxel-resistant human nasopharyngeal carcinoma cell line and study of its mechanisms [J]. Chinese Journal of Otorhinolaryngology-skill Base Surgery, 2007, 13(6): 411-414.
- [2] Peng X, Li W, Tan G. Reversal of taxol resistance by cisplatin in nasopharyngeal carcinoma by upregulating thrombospondin-1 expression [J]. Anticancer Drugs, 2010, 21(4): 381-388.
- [3] Li C, Wong WH. Model-based analysis of oligonucleotide arrays: Expression index computation and outlier detection [J]. Proc Natl Acad Sci USA, 2001, 98(1): 31-36.
- [4] Lih CJ, Wei W, Cohen SN. TXR1: a transcriptional regulator of thrombospondin-1 that modulates cellular sensitivity to taxanes [J]. Genes Dev, 2006, 20(15): 2082-2095.
- [5] van Amerongen R, Berns A. TXR1-mediated thrombospondin repression: a novel mechanism of resistance to taxanes? [J]. Genes Dev, 2006, 20(15): 1975-1981.
- [6] Fetisova EK, Avetisian AV, Iziumov DS, et al. Multidrug resistance P-glycoprotein inhibits the antiapoptotic action of mitochondria-targeted antioxidant SkQR1 [J]. Tsitologija, 2011, 53(6): 488-97.
- [7] Robey RW, Lin B, Qiu J, et al. Rapid detection of ABC transporter interaction: potential utility in pharmacology [J]. J Pharmacol Toxicol Methods. 2011, 63(3): 217-22.
- [8] 彭小伟, 贺广湘, 李维, 等. ATP结合盒转运体基因在鼻咽癌紫杉醇耐药细胞中的表达 [J]. 中国耳鼻咽喉颅底外科杂志, 2008, 14(1): 15-20. PENG Xiaowei, HE Guangxiang, LI Wei, et al. Expression of ATP-binding cassette transporters in a paclitaxel-resistant nasopharyngeal carcinoma cell line [J]. Chinese Journal of Otorhinolaryngology-skill Base Surgery, 2008, 14(1): 15-20.
- [9] Yu LJ, Matias J, Scudiero DA, et al. P450 enzyme expression patterns in the NCI human tumor cell line panel [J]. Drug Metab Dispos, 2001, 29(3): 304-312.
- [10] Wang JF, Chou KC. Molecular modeling of cytochrome P450 and drug metabolism [J]. Curr Drug Metab, 2010, 11(4): 342-346.
- [11] Szliszka E, Krol W. The role of dietary polyphenols in tumor necrosis factor-related apoptosis inducing ligand (TRAIL)-induced apoptosis for cancer chemoprevention [J]. Eur J Cancer Prev, 2011, 20(1): 63-69.
- [12] Stein U, Walther W, Lauren M, et al. Tumor necrosis factor alpha and expression of the multidrug resistance-associated genes LRP and MRP [J]. JNCI, 1997, 89(11): 807-813.
- [13] Oguma K, Oshima H, Oshima M. Inflammation, tumor necrosis factor and Wnt promotion in gastric cancer development. Future Oncol, 2010, 6(4): 515-26.
- [14] Roy S, Bayly CI, Gareau Y, et al. Maintenance of caspase-3 proenzyme dormancy by an intrinsic "safety catch" regulatory tripeptide [J]. Proc Natl Acad Sci USA, 2001, 98(11): 6132-6137.
- [15] Haber M, Burkhart CA, Regl DL, et al. Altered expression of M beta2, the class II beta-tubulin isotype, in a murine J7442.2 cell line with a high level of taxol resistance [J]. J Biol Chem, 1995, 270

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1. 罗晨, 何小鹏, 赵艳, 张志杰, 李官成. 人源性鼻咽癌抗独特型单链抗体基因G22真核表达载体的构建及表达鉴定[J]. 中南大学学报(医学版), 2008,33(01): 16-20
2. 洪继东, 廖遇平, 袁君, 魏瑞, 王学伟, 毛海娇. 44例儿童青少年鼻咽癌临床和预后分析[J]. 中南大学学报(医学版), 2008,33(08): 723-726
3. 张海霞, 王连生. 多态变异对药物转运体活性影响及其临床意义[J]. 中南大学学报(医学版), 2008,33(08): 765-769
4. 钟宇, 唐瑶云, 谢常宁, 赵素萍. HRE1.Egr-1.yCDglyTK融合自杀基因前药系统对鼻咽癌放射增敏作用的体外实验[J]. 中南大学学报(医学版), 2008,33(02): 110-114
5. 陈进伟, 陶师, 骆蓉, 张广森, 徐运孝. Puerarin逆转K562/AO2耐药的分子机制[J]. 中南大学学报(医学版), 2008,33(03): 216-221
6. 林秀梅; 谢兆霞; 祝焱; 祝平安; 李薇; . 急性白血病多药耐药相关蛋白及P糖蛋白表达与临床耐药的关系[J]. 中南大学学报(医学版), 2002,27(6): 522-
7. 曾朝阳; 熊炜; 李小玲; 张必成; 李桂源; . 鼻咽癌相关基因文献数据库的建立及分析[J]. 中南大学学报(医学版), 2003,28(1): 1-
8. 侯德富; 贺智敏; 杨芳; 陈主初; . 人鼻咽上皮细胞CYP2E1 cDNA克隆及序列分析[J]. 中南大学学报(医学版), 2003,28(2): 107-
9. 王梦昌 刘陕西 刘蓬勃 .

雄黄对多发性骨髓瘤细胞株RPMI 8226细胞基因表达谱的作用

[T]. 中南大学学报(医学版), 2006.31(01): 24-27

10. 易红 杨轶轩 汤参娥 陈主初 张桂英 肖志强.

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[T]. 中南大学学报(医学版), 2006.31(03): 340-344

11. 徐婧 邱元正 唐瑶云 田勇泉 肖献忠 赵素萍.

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[T]. 中南大学学报(医学版), 2006.31(05): 706-709

12. 张梅春 胡成平 陈琼 夏莹.

Survivin反义寡核苷酸治疗耐顺铂人肺腺癌细胞裸鼠移植瘤的实验研究

[T]. 中南大学学报(医学版), 2006.31(05): 717-722

13. 任勇亚. RNA干扰抑制MDR1表达并逆转Bel7402/5-Fu肝癌细胞耐药性的研究[J]. 中南大学学报(医学版), 2006,31(06): 872-876

14. 黄程辉¹, 曹培国¹, 谢兆霞². MCF-7/Adr细胞mdr-1基因启动子甲基化和组蛋白乙酰化状态与多药耐药的关系[J]. 中南大学学报(医学版), 2009,34(05): 369-374
15. 彭芳, 汤参娥, 李茂玉, 李萃, 程爱兰, 李峰, 张鹏飞, 李美香, 肖志强, 陈主初. 应用激光捕获显微切割技术纯化的鼻咽癌蛋白质表达谱的建立[J]. 中南大学学报(医学版), 2009,34(06): 481-486