肿瘤防治研究 » 2012, Vol. 39 » Issue (8): 985-991 DOI: 10.3971/j.issn.1000-8578.2012.08.026

TopoⅡα、GST-π、P-gp对卵巢癌患者化疗反应及预后预测的体内外实验

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Value of TopoⅡα, GST-π and P-gp in Predicting Chemotherapeutic Response and Prognosis of Ovarian Cancer in vivo and in vitro

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全文: PDF (2790 KB) HTML (1 KB) 输出: BibTeX | EndNote (RIS) 背景资料

摘要

目的

研究TopoⅡα、GST-π、P-gp在卵巢癌耐药中的作用及其对化疗反应及预后的预测价值。方法免疫组织化学SP法检测TopoⅡα、GST-π、MDR-1/P-gp在80例上皮性卵巢癌组织中的表达,分析它们与化疗反应及预后的关系;RNA干扰封闭GST-π、MDR-1/P-gp在人卵巢癌耐药细胞中的表达,检测其逆转细胞耐药的可能性。结果TopoⅡα阴性和阳性患者的化疗反应无差异。

GST-π阴性患者的化疗疗效显著优于阳性者(P=0.009);P-gp阴性患者也较阳性者疗效好,但差异无统计学意义(P=0.059)。尽管Log-rank test显示 GST-π 或P-gp阴性患者的生存时间显著长于相应指标阳性患者,但Cox分析并未指示两者为独立预后因素 (P=0.682;P=0.101)。根据GST-π、P-gp的共同表达情况进一步分组分析显示,两者共同阴性的患者化疗有效率100%、85.7%生存至末次随访,GST-π、P-gp共同阴性预示较好的化疗反应及预后(P=0.012;P=0.000) 。体外实验显示,卵巢癌耐药细胞对多种化疗药物敏感度降低,同时GST-π、MDR-1/P-gp mRNA表达增高。结论GST-π及MDR-1/ P-gp在卵巢癌耐药中具重要作用,GST-π 或P-gp单独预测化疗反应及预后的效用有限,联合检测可提供较高临床价值，封闭两者表达可一定程度逆转卵巢癌细胞的耐药性。

关键词： 多药耐药 卵巢癌 谷胱甘肽-S-转移酶-&pi P-糖蛋白 拓扑异构酶Ⅱ&alpha

Abstract:

Objective

To assess the role of TopoⅡα,GST-π and P-gp in drug-resistance of ovarian cancer and their value as predictors of chemotherapeutic response and prognosis.MethodsThe expression of GST-π,P-gp and TopoⅡα in the surgical specimens were detected by immunohistochemistry and their relationship with the chemotherapeutic response and prognosis of the patients were analyzed.The expression of GST-π and MDR-1/P-gp in human ovarian cancer cells was silenced by RNA:to evaluate the feasibility of reversal MDR phenotype in the cells.

ResultsChemotherapeutic response was no difference with negative TopoⅡα and positive.Chemotherapeutic response was more favorable in patients with negative GST-π than in those with positive expression (P=0.009).Similar trend occurred with P-gp,though the difference was not significant (P=0.059).Although log-rank test showed a longer survival in patients with negative GST-π or P-gp (P=0.012;P=0.000),Cox hazard analysis did not indicate they could be regarded as prognostic predictors (P=0.682;P=0.101).However,when their co-expression status was taken into account,it was found that 100.0% patients with co-negative GST-π/P-gp responded well to chemotherapy and 85.7% patients were still alive until the evaluation.Co-negative GST-π /P-gp presented better

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chemotherapeutic response and prognosis (*P*=0.001;*P*=0.000).Furthermore,decreased drug sensitivity accompanied with overexpressed GST-π and P-gp level was found in MDR ovarian cancer cell lines.ConclusionGST-π and P-gp are involved in the forming of MDR in ovarian cancer.The reliability of MDR-1 and GST-π alone as indicators of chemotherapeutic response and prognosis is limited,and co-detection of their expression may provide a higher predictive value.
After silencing the expression of GST-π and P-gp by RNAi,the drug sensitivity of the MDR cells were increased.

Key words： Multidrug resistance Ovarian cancer Glutathione S-transferase-&pi P-glycoprotein Topoisomerase Ⅱ&alpha

收稿日期: 2011-09-16;

基金资助:

湖北省科技厅自然基金一般项目(2010CDB10902);湖北省妇幼保健院院课题基金资助项目(20922004)

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引用本文:

蔡鸿宁,陈慧君,吴绪峰等. TopoⅡα、GST-π、P-gp对卵巢癌患者化疗反应及预后预测的体内外实验[J]. 肿瘤防治研究, 2012, 39(8): 985-991.

Cai Hongning,Chen Huijun,Wu Xufeng et al. Value of TopoⅡα, GST-π and P-gp in Predicting Chemotherapeutic Response and Prognosis of Ovarian Cancer in vivo and in vitro[J]. Cancer Research on Prevention and Treatment, 2012, 39(8): 985-991.

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