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研究论文

介导多药耐药的ABC转运蛋白超家族与MTX耐药性的关系研究

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摘要 细胞耐药性的产生是导致肿瘤化疗失败的重要因素，尤其是多药耐药是目前研究的一个重点。ABC转运蛋白超家族成员介导药物的外排，与多药耐药密切相关。为了解该家族成员与MTX耐药的相关性，进一步探讨MTX的耐药机制，应用SuperArray基因芯片对MTX耐药前后编码ABC转运蛋白超家族成员的mdr1、mrp1、mrp2、mrp3、mrp5、mrp6和abcg2 7个基因进行检测，并对MRP1和MRP5蛋白表达进行了验证。结果显示，与MTX耐药性相关的ABC转运蛋白超家族成员主要为多药耐药相关蛋白，其中mrp1和mrp5呈现高表达，并且，在MTX抗性细胞中，MRP5在mRNA及蛋白水平的表达均明显增强，提示其在MTX耐药机制中起重要作用，可能为潜在的药物作用靶点。

关键词 多药耐药 ABC转运蛋白超家族 MTX耐药性 SuperArray Western blot mrp1 mrp5

分类号 Q356

Study on the Relationship Between the Resistance to MTX and the Transport Protein Superfamily of ATP-binding Cassette that Induces Multiple Drug Resistance

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Abstract

Abstract: A major problem, especially the multidrug resistance, in chemotherapy was the resistance to the chemotherapeutic agents. ATP-binding cassette transporter superfamily that mediated the efflux of drugs was involved in multidrug resistance. In order to understand the relationship between the resistance to MTX and the transport protein superfamily of ATP-binding cassette, and to investigate the mechanism of resistance to MTX, the study detected the expressions of mdr1, mrp1, mrp2, mrp3, mrp5, mrp6 and abcg2 that encoded the transport proteins by SuperArray analysis and the expressions of MRP1and MRP5 proteins by Western blot analysis. The results showed that the multidrug resistance proteins were the chief member of ATP-binding cassette transporter superfamily related to resistance to MTX. And the high expression levels of mrp1 and mrp5 were detected. Moreover, it revealed by SuperArray analysis that expression of mrp5 in MTX-resistant cells was significantly higher than that in normal mouse cells. Besides, corresponding excessive expression of MRP5 protein in MTX-resistant cells was also confirmed by Western blot. So, MRP5 could play important roles in the resistance to MTX and would be a new potential drug target.

Key words 多药耐药 ABC转运蛋白超家族 MTX耐药性 SuperArray Western blot mrp1 mrp5

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