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论著

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

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摘要

目的：分析MCF-7/Adr及MCF-7细胞mdr-1基因启动子甲基化和组蛋白乙酰化状态，初步探讨乳腺癌多药耐药的表观遗传机制。 方法：用甲基化敏感PCR技术检测两个细胞系mdr-1基因启动子甲基化状态。实时定量PCR技术检测DNA甲基转移酶（DNA methyltransferases，DNMTs) mRNA及组蛋白去乙酰化酶（histone deacetylases，HDACs) mRNA的表达。光密度值法检测组蛋白H3和H4乙酰化水平。结果：MCF-7细胞mdr-1基因启动子呈现高甲基化，MCF-7/Adr细胞mdr-1基因启动子呈现低甲基化。与MCF-7细胞比较，MCF-7/Adr细胞DNMT1，DNMT3a及DNMT3b mRNA表达显著下降(P＜0.05)。MCF-7/Adr细胞组蛋白H3和H4乙酰化水平较MCF-7细胞明显升高(P＜0.01)。与MCF-7细胞比较，MCF-7/Adr细胞HDAC1，HDAC2，HDAC7及SIRT1 mRNA的表达显著下降(P＜0.01)。 结论：mdr-1基因启动子低甲基化、组蛋白H3和H4高乙酰化、DNMTs mRNA及HDACs mRNA低表达可能是介导MCF-7/Adr细胞MDR形成的重要表观遗传学因素。

关键词 乳腺癌； 多药耐药； 基因；甲基化；组蛋白；乙酰化

分类号

Relation of promoter methylation of mdr-1 gene and histone acetylation status with multidrug resistance in MCF-7/Adr cells

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Abstract

Objective To analyze the mdr-1 gene promoter methylation and histone acetylation status in both MCF-7/Adr and MCF-7 cells and to preliminarily explore the epigenetic mechanism of multidrug resistance in breast cancer. Methodsmdr-1 gene promoter methylation status of the 2 cell lines was detected by methylation-sensitive PCR. mRNA expression of DNA methyltransferases (DNMTs) and histone deacetylases (HDACs) was detected by real-time quantitative PCR. Acetylation level of histone H3 and H4 was examined by optical density assay. ResultsPromoter hypermethylation of mdr-1 gene was observed in MCF-7 cells whereas hypomethylation was found in MCF-7/Adr cells. Expression of DNMT1,DNMT3a, and DNMT3b mRNA in MCF-7/Adr cells significantly decreased compared with that of MCF-7 cells (P＜0.05). H3 and H4 histone acetylation levels of MCF-7/Adr cells were obviously higher than those of the MCF-7 cells (P＜0.01). Expression of HDAC1，HDAC2，HDAC7, and Sirtuin type 1 (SIRT1)mRNA in MCF-7/Adr cells was significantly reduced (P＜0.05).ConclusionHypomethylation of the promoter region of mdr-1 gene, high H3 and H4 histone acetylation, and low mRNA expression of DNMTs and HDACs may be important epigenetic factors for the development of MDR in MCF-7/ Adr cells.

Key words breast cancer；multidrug resistance；gene；methylation；histone；acetylation

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