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[1]黄剑波,罗鑫荣,孔令泉,等.PAQR3增强乳腺癌细胞SK-BR-3的表柔比星敏感性[J].第三军医大学学报,2013,35(16):1658-1662. Huang Jianbo,Luo Xinrong,Kong Lingquan,et al.PAQR3 enhances chemosensitivity of breast cancer cell line SK-BR-3 to epirubicin[J].J Third Mil Med Univ,2013,35(16):1658-1662.

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## PAQR3增强乳腺癌细胞SK-BR-3的表柔比星到:

《第三军医大学学报》[ISSN:1000-5404/CN:51-1095/R] 卷: 35 期数: 2013年第16期 页码: 1658-1662 栏目: 论著 出版日期: 2013-08-30

Title: PAQR3 enhances chemosensitivity of breast cancer cell

line SK-BR-3 to epirubicin

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关键词: 乳腺癌; PAQR3; 表柔比星; RAS/RAF/ERK; 化疗敏感性

Keywords: breast cancer; PAQR3; epirubicin; RAS/RAF/ERK;

chemosensitivity

分类号: R73-361;R737.9;R979.14

文献标志码: A

摘要: 目的 探讨PAQR3增强乳腺癌细胞对表柔比星的敏感性。 方

法 采用Real-time PCR比较ER、PR及HER2受体不同的4株乳腺癌细胞 (MDA-MB-231、MCF7、SK-BR-3及T47D)的PAQR3表达情况。在乳腺癌细胞SK-BR-3中转染人源性PAQR3全长表达质粒,设立对照组,观察比较转染PAQR3细胞组与空载质粒细胞组对表柔比星的敏感性,分别计算其所对应的IC<sub>50</sub>。通过细胞凋亡检测、Western blot探讨PAQR3增加表柔比星敏感性的机制。 结果 在4株乳腺癌细胞中,受体三

阴性细胞MDA-MB-231的PAQR3表达量最高,SK-BR-3与MCF7表达量相对较低:SK-BR-3过表达PAQR3后,其对表柔比星的化疗敏感性显著升

高,IC<sub>50</sub>显著降低[(25.33±0.94)μg/mL *VS* (17.72±1.11)μg/mL,

P<0.05], PAQR3本身并未促使SK-BR-3凋亡, 实验组与对照组的凋亡率

导航/NAVIGATE

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差异并无统计学意义(P>0.05)。但在同等浓度表柔比星的作用下,PAQR3促使SK-BR-3表达凋亡相关蛋白Cleaved Caspase-7,从而导致表柔比星抑制率增加,对Cleaved Caspase-3、Bcl-2、Bcl-xL表达则无影响。进一步分析发现,PAQR3可抑制乳腺癌化疗中表柔比星所致的ERK活化,因而促使乳腺癌细胞对表柔比星敏感。 结论 PAQR3可提高乳腺癌细胞对表柔比星的化疗敏感性,PAQR3表达可能与乳腺癌对表柔比星的敏感性相关。

Abstract:

Objective To investigate whether PAQR3 can enhance the chemosensitivity of breast cancer line to epirubicin, and the possibly underlying mechanisms. Methods The mRNA level of PAQR3 in 4 breast cancer cell lines (MDA-MB-231, MCF7, SK-BR-3 and T47D) with different statuses of ER, PR and HER2 receptors were analyzed by real-time PCR. The plasmid pEGFP-PAQR3 encoding full-length sequence of PAQR3 was transfected into the SK-BR-3 cells, and the cells transfected with empty vector pEGFP-C1 served as control. The inhibitory ratio and  $IC_{50}$  of epirubicin on the SK-BR-3 cells were observed and compared. Flow cytometry was used to analyze the cell apoptosis, and Western blotting to detect the expression of apoptosis- related genes. Among the 4 breast cancer cell lines, MDA-MB-231 cells Results who were positive to the above 3 receptors expressed the highest level of PAQR3, while the SK-BR-3 and MCF7 cells got the relatively lower levels. After transfected with plasmid pEGFP-PAQR3, the SK-BR-3 cells become more sensitive to epirubicin as compared to those transfected with pEGFP-C1 (P<0.05), and their IC $_{50}$  was obvious decreased (25.33 $\pm$ 0.94 vs 17.72 $\pm$ 1.11  $\mu$ g/mL, P<0.05). PAQR3 transfection had no effect on cell apoptosis (P>0.05), but when the cells were treated with the same doses of epirubicin, the expression of cleaved caspase-7 was significantly elevated in SK-BR-3 transfected with PAQR3, which contributed to the enhanced sensitivity to epirubicin. Nevertheless, no change of cleaved caspase-3, Bcl-2, and Bcl-xL was found. Furthermore, the anti-apoptotic activation of ERK by epirubicin was suppressed in SK-BR-3 transfected with PAQR3 compared with those transfected with empty vector, which explained their enhanced sensitivity to epirubicin. Conclusion PAQR3 enhances the chemosensitivity of breast cancer cells to epirubicin. In light of certain clinical findings, PAQR3 may be relative to the sensitivity of breast cancer to epirubicin.

## 参考文献/REFERENCES: