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雷公藤甲素对肺癌A549/DDP细胞多药耐药的逆转作用及机制

The effects and mechanisms of triptolide to reverse the multi-drug resistance of A549/DDP lung cancer

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中文摘要:

【】 目的：探讨雷公藤甲素对肺癌A549/DDP多药耐药的逆转作用及机制。方法：雷公藤甲素作用于肺癌A549/DDP细胞后,应用MTS法检测细胞生长抑制率,流式细胞术检测细胞内罗丹明-123(Rhodamine-123,Rh-123)及细胞表面P-糖蛋白(P-glycoprotein,P-gp)表达,应用Western blot法和real time PCR检测肿瘤细胞多药耐药蛋白 (MDR1)和肺耐药相关蛋白(LRP)表达变化,应用报告基因技术检测细胞NF-κB启动子活性,应用Western blot法检测肿瘤细胞Akt磷酸化。结果：雷公藤甲素可提高肺癌A549/DDP细胞药物敏感性,经2μM和10μM雷公藤甲素作用后,顺铂逆转倍数(RF)分别为2.09倍和2.93倍,肿瘤细胞中Rh-123含量分别提高了1.38倍和2.88倍,P-gp表达分别是对照组的57.1%和32.1%,MDR1和LRP蛋白表达水平显著下降,MDR1 mRNA表达分别是对照组的64.2%和22.6%,LRP mRNA表达分别是对照组的54.8%和34.7%, NF-κB启动子活性分别是对照组的55.6%和23.6%,Akt磷酸化水平显著下降。结论：雷公藤甲素可逆转肺癌A549/DDP细胞多药耐药性,提高肿瘤细胞药物敏感性,抑制药物外排,降低细胞MDR1和LRP表达,其机制可能与抑制Akt磷酸化水平,下调NF-κB启动子活性有关。

英文摘要:

Object: To investigate the effects and mechanisms of triptolide to reverse the multi-drug resistance of lung cancer cell line A549/DDP. Methods: After treating A549/DDP cells with triptolide, we determined the cells proliferation inhibition ratio by MTS assay, the intracellular concentration of rhodamine-123 (Rh-123) and cells surface expression of p-glycoprotein (P-gp) by flow cytometry, the expression of multi-drug resistance protein (MDR1) and lung resistance related protein (LRP) by western blot and real time PCR, and the activity of NF-κB by report gene system. We also determined the phosphorylation of Akt by western blot. Results: Treatment with triptolide was able to increase the drug sensitivity of A549/DDP cells. After treatment with 2 or 10 μM triptolide, the reverse folds (RF) to cisplatin were

2.09and 2.93, respectively. The intracellular concentration of Rh-123 was elevated by 1.38 and 2.88 folds, and the P-gp level was 57.1% and 32.1% of the control, respectively. The expression of MDR1 and LRP was downregulated significantly. Accordingly, the mRNA level of MDR1 was 64.2% and 22.6% of control, and the mRNA level of LRP was 54.8% and 34.7% of control, respectively. Furthermore, the transcriptional activity of NF-κB was reduced to 55.6% and 23.6% of the control, and the phosphorylation of Akt was also decreased significantly. Conclusions: Triptolide was potential to reverse the multi-drug resistance of A549/DDP, increase its drug sensitivity. Triptolide could inhibit the drug efflux, downregulate the expresson of MDR1 and LRP. The possible mechanisms were inhibition of Akt phosphorylation and NF-κB activity by triptolide.