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细胞因子诱导的杀伤细胞逆转耐顺铂肺腺癌细胞系A549/DDP耐药性的研究

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Cytokine-induced Killer Cells Modulate Cisplatin Resistance in the A549/DDP Cell Line

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摘要 观察细胞因子诱导的杀伤细胞 (cytokine induced killer, CIK) 对耐顺铂 (DDP) 人肺腺癌细胞系A549/DDP的耐药逆转作用及其逆转A549/DDP耐药的可能机制。方法: A549/DDP与CIK细胞采用Transwell非接触共培养。四氮唑兰比色法 (MTT法) 验证A549/DDP的DDP耐药性及检测共培养前后A549/DDP对DDP耐药性的变化。RT-PCR法筛选A549与A549/DDP有差异表达的基因作为检测耐药性变化的观察指标, 并检测共培养前后A549/DDP中基因表达水平的变化; Western blot检测A549及共培养前后A549/DDP中基因蛋白水平的变化。结果: A549/DDP的耐药系数为14.5, 具有较强的DDP耐药性。RT-PCR筛选出A549与A549/DDP表达有差异的耐药相关基因为谷胱甘肽转移酶 (glutathione-S-transferase, GST- π) 基因、人类铜离子转运蛋白 (human copper transporter 1, hCTR1) 基因, A549/DDP中GST- π 表达量明显增加, hCTR1表达量明显降低。与CIK细胞共培养后, A549/DDP对DDP的耐药性明显下降, 共培养20h后耐药逆转倍数约为4.93倍, 细胞内GST- π 基因及蛋白水平的表达明显降低 ($P < 0.05$)。结论: CIK细胞对A549/DDP有逆转DDP耐药的作用, 其机制可能与下调GST- π 基因及蛋白水平的表达有关。

关键词: 化疗耐药 细胞因子诱导的杀伤细胞 肺腺癌 GST- π hCTR1

Abstract: To observe the effects of cytokine-induced killer cells (CIKs) on the reversal of cisplatin (DDP) resistance in the DDP-resistant human lung adenocarcinoma cell line A549/DDP. Methods: The cisplatin resistance of the A549/DDP cell line was validated and the drug sensitivity of A549/DDP indirectly cocultured with CIKs was determined with an MTT assay. The expression levels of the relative resistance genes of A549, A549/DDP, and A549/DDP co-cultured with CIK were determined via semiquantitative RT-PCR. The expression levels of relative resistance proteins were determined via western blot analysis. Results: The resistant index of A549/DDP to A549 was 14.5. The GST- π expression levels were increased in A549/DDP than in A549, but hCTR1 was contrary ($P < 0.05$). The cisplatin resistance of A549/DDP cocultured with CIK was decreased, and its GST- π expression was decreased ($P < 0.05$). Conclusion: CIK could reverse the cisplatin resistance of A549/DDP by inhibiting the expression of GST- π .

Key words: Drug resistance Cytokine-induced killer Lung adenocarcinoma GST- π hCTR1

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