

基础医学

N-乙酰半胱氨酸对宫颈癌细胞紫杉醇耐药性的影响

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摘要:

目的 建立耐紫杉醇(PTX)宫颈癌细胞株, 观察N-乙酰半胱氨酸(NAC)对宫颈癌细胞紫杉醇耐药的影响。方法 用PTX处理并培养Hela细胞, 建立耐PTX宫颈癌细胞株Hela/PTX。观察和检测其细胞形态、细胞生长曲线、耐药指数、氧化还原状态及紫杉醇耐药基因1(Txr1)的表达。用NAC处理Hela/PTX细胞, 观察NAC对其PTX耐药的影响。结果 用PTX处理Hela细胞10个月后, 可获得在500μg/L PTX中生长状态良好的Hela/PTX细胞。Hela/PTX细胞体积偏大, 胞浆内颗粒较多, 群体倍增时间是亲代细胞的1.32倍, 对PTX具有显著耐药性, 耐药指数为122.69。与Hela细胞相比, Hela/PTX细胞有高水平的活性氧(ROS)和Txr1 mRNA, 但还原型谷胱甘肽(GSH)水平及超氧化物歧化酶、过氧化氢酶和谷胱甘肽过氧化物酶活性却有不同程度的降低, 而氧化型谷胱甘肽(GSSG)水平和GSH/GSSG比值则无明显变化。NAC处理后, Hela/PTX细胞ROS和Txr1 mRNA水平下降, 对PTX敏感性增加。结论 耐紫杉醇Hela/PTX细胞氧化还原状态失衡, Txr1表达增加。NAC能降低ROS水平, 减少Txr1表达, 可逆转其对PTX的耐受。

关键词: 宫颈肿瘤; 紫杉醇; 抗药性; N-乙酰半胱氨酸; 活性氧; 紫杉醇耐药基因1

Effects of N-acetylcysteine on resistance to paclitaxel in cervical carcinoma cells

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Abstract:

Objective To construct a paclitaxel (PTX)-resistant human cervical carcinoma cell line and observe the effects of N-acetylcysteine (NAC) on resistance to PTX in the cells. Methods Hela cells were treated with PTX to construct the PTX-resistant Hela/PTX cell line. The cell shape, cell growth curves and drug resistance index as well as the cellular redox state and the taxol resistance gene 1 (Txr1) expression were observed or determined. Hela/PTX cells were treated with NAC, and the effects of NAC on resistance to PTX in the cells were observed. Results After Hela cells were treated with PTX for 10 months, the PTX-resistant cervical carcinoma Hela/PTX cells could be obtained, which grew well in 500μg/L of PTX. Compared with Hela cells, the size of Hela/PTX cells was larger, and there were more cytoplasmic granules in them. The population doubling time for Hela/PTX cells was 1.32 times of that for Hela cells. Hela/PTX cells manifested a stronger resistance to PTX than Hela cells did with the resistance index of 122.69. They had higher levels of reactive oxygen species (ROS) and Txr1 mRNA, a lower level of reduced glutathione(GSH), and lower activities of superoxide dismutase, catalase and glutathione peroxidase than Hela cells. There was no significant difference between Hela/PTX and Hela cells in the level of oxidized glutathione (GSSG) or the GSH to GSSG ratio. After Hela/PTX cells were treated with NAC, the levels of ROS and Txr1 mRNA in them decreased, and they were more sensitive to PTX. Conclusion In Hela/PTX cells, which resisted to PTX, there was a redox imbalance, and the Txr1 transcripts increased. NAC could reduce the levels of ROS and Txr1 mRNA in Hela/PTX cells and reversed the sensitivity of them to PTX.

Keywords: Cervical neoplasms; Paclitaxel; Drug resistance; N-acetylcysteine; Reactive oxygen species; Taxol resistance gene 1

收稿日期 2012-11-13 修回日期 网络版发布日期

DOI:

基金项目:

山东省优秀中青年科学家科研奖励基金(2008BS03038)

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