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三氧化二砷诱导K562细胞凋亡与其抑制Evi-1表达有关

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摘要 背景与目的： 探讨三氧化二砷(As2O3)诱导K562细胞凋亡的分子机制。 材料与方法： 分别以1、2、4、8 μmol/L的As2O3诱导K562细胞凋亡，每隔24 h采用光镜和电镜观察细胞形态变化，MTT观察细胞增殖抑制率，流式细胞仪检测细胞凋亡率，RT-PCR检测Evi-1mRNA表达率，ELISA检测细胞内JNK蛋白。 结果：As2O3对K562细胞增殖具有明显的抑制作用，且呈剂量-时间关系；1、2、4、8 μmol/L的As2O3可使K562细胞发生凋亡，在本实验时间段内随着作用时间的延长细胞凋亡逐渐升高，诱导细胞凋亡的最佳浓度为4 μmol/L；在此过程中K562细胞的Evi-1基因表达下调，JNK蛋白表达增多，两者跟As2O3浓度存在剂量-时间关系。 结论：As2O3通过抑制K562细胞Evi-1表达，从而激活JNK信号传导途径，促进细胞凋亡，这可能是As2O3促进K562细胞凋亡的机制之一。

关键词 三氧化二砷； 慢粒细胞系, K562； Evi-1； JNK

Suppressed Evi-1 Gene Expression: a Possible Mechanism of Arsenic Trioxide Inducing Apoptosis in K562 Cells

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Abstract BACKGROUND & AIM: To investigate a possible mechanism of arsenic trioxide-induced apoptosis in K562 cells. MATERIAL AND METHODS: The K562 cells were treated with As2O3 at 1, 2, 4, 8 μmol/L. Light and transmission electron microscope were used to examine the morphologic changes of K562 cells every 24 hours. Methyl thiazolyl tetrozolium (MTT) was used to establish the dose-effect curves of cell proliferation and apoptotic rates were measured by flow cytometry(FCM),RT-PCR was used to detect the expression of Evi-1 mRNA and cellular JNK was detected by ELISA. RESULTS: MTT test showed K562 cell proliferation was significantly inhibited by As2O3 in time and dose-dependent fashion. Marked apoptosis was detected by FCM in K562 cells after treatment by As2O3 at 1,2,4, 8 μmol/L and increased in a time-dependent manner within 48 hours and the optimal concentration was 4 μmol/L. As2O3 could down-regulate significantly the expression of Evi-1 mRNA and up-regulate JNK protein in K562 cells in time- and dose-dependent manner. CONCLUSION: As2O3 could obviously inhibit the expression of Evi-1 mRNA and activate JNK signal transduction pathway, which may be a possible mechanism of As2O3 inducing apoptosis in K562 cells.

Keywords arsenic trioxide chronic myelogenous leukemia cell line K562 ecotropic virus integration site1 c-jun terminal kinase

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