山东大学学报(医学版) 2010, 48(6) 67-71 DOI: ISSN: 1671-7554 CN: 37-1390/R

论文

SPK1/S1P信号途径对人肝癌耐药细胞株BEL-FU凋亡、侵袭力及耐药特性的影响

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摘要：

目的 研究利用N,N,-二甲基鞘氨醇（dimethyl sphingosine，DMS）干涉鞘氨醇激酶1/1-磷酸鞘氨醇（SPK1/S1P）信号后对人肝癌耐药细胞株BEL-FU的凋亡、侵袭能力及耐药特性的影响。方法 利用不同浓度的DMS处理人肝癌耐药细胞株BEL-FU，观看凋亡形态变化，检测凋亡发生；并用transwell小室模型测定侵袭力；Western blot杂交检测多药耐药相关蛋白1（MRP1）表达的变化。结果 随着DMS浓度的升高，细胞凋亡率增加，浓度组与对照组及各浓度组间比较差异均有统计学意义（P<0.01），且呈剂量依赖效应；同时可观察到侵袭力减弱，各浓度组穿膜细胞数、抑制率与对照组比较及组间比较差异均有统计学意义（P<0.01），且呈剂量依赖效应；MRP1蛋白表达量明显减少，浓度组与对照组比较差异均有统计学意义（P<0.05）。结论 SPK1/S1P信号和肝癌细胞的侵袭和耐药密切相关，利用DMS干涉SPK1/S1P信号能引起人肝癌耐药细胞株BEL-FU的凋亡、降低其侵袭力并且克服其耐药。

关键词： 信号转导;肝肿瘤；细胞凋亡;侵袭;多药耐药相关蛋白

Effects of SPK1/S1P signal pathway on the apoptosis, invasiveness and multidrug resistance characteristics of human hepatocellular carcinoma cell line BEL-FU

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Abstract:

Objective To evaluate the role of SPK1/S1P signal pathway in the apoptosis, invasiveness and multidrug resistance characteristics of the human hepatocellular carcinoma cell line BEL-FU after using the dimethyl sphingosine (DMS) to interfere the SPK1/S1P signal. Methods Treated with different concentrations of dimethyl sphingosine (DMS) in the human hepatocellular carcinoma cell line BEL-FU, the morphologic change, apoptosis of cells, invasion of cells and expression of multidrug resistance-related protein (MRP1) were observed by microscopy, flow cytometry, transwell chamber assay and western blot respectively. Results The apoptosis rate in every concentration group increased significantly compared with the control group(P<0.01), and there were significant differences among the concentration groups (P<0.01), in a dose-dependent manner. The number of invading cells decreased and the inhibitory rate of invasion increased significantly in the concentration groups compared with the control group, and there were significant differences among all the groups (P<0.01), in an apparent dose-dependent manner. The MRP1 expression level was significantly suppressed by DMS, and there were significant differences between concentration groups and the control group（P<0.05）. Conclusion The SPK1/S1P signal is closely associated with the invasion and multidrug resistance of the human hepatocellular carcinoma cell line BEL-FU. The SPK1/S1P signal pathway interfered by DMS can induce the apoptosis, reduce the invasiveness and inhibit expression of MRP1 of the human hepatocellular carcinoma cell line BEL-FU.

Keywords: Signal transduction; Liver neoplasms； Apoptosis; Invasion; Multidrug resistance-associated protein

收稿日期 2010-01-26 修回日期 网络版发布日期

DOI:

基金项目:

山东省自然科学基金资助课题（T2006C53）。

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