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姜黄素对人多发性骨髓瘤ARH-77细胞外源性凋亡通路的影响 点此下载全文

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摘要：

目的：探讨姜黄素（curcumin，Cur）对人多发性骨髓瘤ARH-77细胞外源性凋亡通路的影响。方法：ARH-77细胞经6.25、12.5、25、50、100、200 μmol/L Cur处理12、24、48 h，MTT法检测Cur对ARH-77细胞增殖的抑制作用，Hoechst 33258染色法观察Cur处理24 h后ARH-77细胞凋亡的形态学改变，流式细胞术检测ARH-77细胞周期和Fas/FasL、TRAIL/TRAIL-R的表达，分光光度法检测ARH-77细胞caspase-8的活性。结果：Cur对ARH-77细胞的增殖有时间和剂量依赖的抑制作用。25 μmol/L Cur处理ARH-77细胞可观察到凋亡小体，Cur阻滞细胞周期于G 0/G 1期，并且有凋亡峰。其促凋亡作用呈浓度依赖性，6.25、12.5、25 μmol/L Cur作用24 h后，ARH-77细胞凋亡率均显著高于对照组\[（10.35±0.35）%、（14.35±1.34）%、（ 36.65±1.06）% vs （3.83±0.32）%， F =500.432， P =0.000\]；实验组细胞内caspase 8的活化程度均显著高于对照组\[（0 223±0.018）、（0.263±0.019）、（0.240±0.035） vs （0.154±0.007）； F =9.059， P =20.03\]。12.5 μmol/L Cur作用24 h后，ARH-77细胞表面Fas\[（99.05±0.49）% vs （92.10±0.70）%， t =15.404， P =0.000\]、FasL \[（9.05±0.78）% vs （1.73±1 19）%， t =9.487， P =0.008\]、TRAIL\[（1.35±0.07）% vs （0.55±0.07）%， t =-11.317， P =0.008\]、DR4、DcR1和DcR2的表达均显著升高，DR5表达显著降低\[（0.95±0.07）% vs （7.70±0.29）%， t =32.742， P =0.001\]；进一步提升Cur浓度至25 μmol/L，却降低了DcR1\[（4.35±1 20）% vs （14.25±0 21）%； t =5.692， P =0.008\]及DcR2\[（0.75±0.21）% vs （1.65±0 71）%； t =11.470， P =0.03\]的表达。结论：Cur能明显抑制人多发性骨髓瘤ARH-77细胞的增殖，其机制可能与激活外源性凋亡通路从而诱导细胞凋亡有关。

关键词：姜黄素 多发性骨髓瘤 凋亡通路 Fas TRAIL

Effect of curcumin on extrinsic apoptosis pathway in human multiple myeloma cell ARH-77 Download Fulltext

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Abstract:

Objective:To investigate the influence of curcumin (Cur) on the extrinsic apoptosis pathway of human multiple myeloma cell line ARH-77. Methods: ARH-77 cells were treated with Cur at 6.25, 12.5, 25, 50, 100 and 200 μmol/L. At 12, 24 and 48 h after treatment, cell viability was analyzed by MTT assay and growth inhibition was accordingly calculated. At 24 h after treatment, changes in the cell morphology were assessed by Hoechst 33258 staining, cell cycle progression and levels of Fas/FasL and TRAIL/TRAIL-R were analyzed by flow cytometry, and the activity of caspase 8 was determined by colorimetry. Results: Cur significantly inhibited the growth of ARH-77 cells in a time- and dose-dependent manner. At 24 h after treatment, Cur induced apoptosis in ARH-77 cells in a dose-dependent manner; the percentage of apoptotic cells was (10.35±0.35)% at 6.25 μmol/L, (14 35±1.34)% at 12.5 μmol/L and (36.65±1 06)% at 25 μmol/L, significantly higher than that in untreated control cells (\[3.83±0.32\]%, P <0.01). Apoptotic bodies and cell cycle arrest at the G 0/G 1 phase were seen in ARH-77cells treated with 25 μmol/L Cur. Caspase 8 activity was significantly higher in ARH-77 cells treated with Cur at 6.26 μmol/L(0.223±0.018), 12.5 μmol/L (0.263±0.019), or 25.0 μmol/L (0.240±0.035) than in untreated control cells (0.154±0.007) (P <0.05). Compared with the non-treatment control, 24 h Cur treatment at 6.25 μmol/L significantly increased the protein levels of Fas (\[99.05±0.49\]% vs \[92.10±0.7\]%, P =0.000), FasL (\[9.05±0.78\]% vs \[1.73±1.19\]%, P =0 008), TRAIL (\[1.35±0.07\]% vs \[0.55±0.07\]%, P =0.008), DR4, DcR1 and DcR2 but significantly decreased DR5 (\[0.95±0.07\]% vs \[7.70±0.29]%, P =0.001). The effect of Cur on DcR1 (\[4.35±1.20\]% vs \[14.25±0.21\]%, P =0.008) and DcR2 (\[0.75±0.21\]% vs \[1.65±0.71\]%, P =0.03) were more pronounced at 25.0 μmol/L than at 12.5 μmol/L. Conclusion: Cur is able to inhibit the growth of ARH-77 cells through activating the extrinsic apoptosis pathway and thereby may offer a potential therapeutic agent for multiple myeloma.

Keywords:curcumin multiple myeloma apoptosis pathway Fas TRAIL

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