432~437.雷公藤内酯醇对人胰腺癌PANC-1细胞的抑制作用及其可能的机制[J].孙运良,马建霞,吴红玉,满晓华,李淑德.中国肿瘤生物治疗杂志,2013,20(4)

雷公藤内酯醇对人胰腺癌PANC-1细胞的抑制作用及其可能的机制 点此下载全文

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基金项目：连云港市卫生局科研项目资助（No.1242）

DOI：10.3872/j.issn.1007-385X.2013.04.009

摘要：

目的： 通过体内外实验观察雷公藤内酯醇（triptolide，TPL）对人胰腺癌PANC-1细胞生长和凋亡的抑制作用，并分析其对Toll样受体4（Toll-like receptor 4，TLR4）、血管内皮细胞生长因子（vascular endothelial cell growth factor，VEGF）的表达和肿瘤血管生成的影响。 方法： 以0、20、40、80 ng/ml的TPL作用于PANC-1细胞，MTT法和流式细胞术分别检测TPL对 PANC-1细胞增殖和凋亡的影响，Western blotting检测TPL作用后PANC-1细胞中TLR4和VEGF的表达。建立PANC-1细胞裸鼠荷瘤模型并随机分为TPL组、PBS组，测量移植瘤的体积变化，治疗35 d后摘取瘤块，免疫组织化学方法检测移植瘤组织内TLR4、VEGF和CD31的表达，并计算微血管密度（microvessel density，MVD）。 结果： 与0 ng/ml组相比，PANC-1细胞经20、40和80 ng/ml的TPL处理24 h后，细胞凋亡率均显著升高\[（4.7±1.0）%、（10.5±2.0）%、（21.1±4.2）% vs （2.6±0 5）%， P <0.05或 P <0.01\]；48 h后，细胞增殖率均显著下降\[（68.0±5.3）%、（59.6±5.0）%、（51.6±4.2）% vs （99.6±5.2）%，均 P <0.01\]，并较相同浓度TPL处理24 h时显著降低（ P <0.05或 P <0.01）。80 ng/ml TPL组处理后PANC-1细胞中TLR4蛋白\[(20.2±4.7)% vs (57.5±6 3)%， P <0.01\]和VEGF蛋白\[(35.8±4.0)% vs (92.1±8.3)%， P <0.01\]的表达量显著低于未处理组。TPL治疗组第34天的裸鼠移植瘤体积显著小于PBS对照组\[（510.9±79.8） vs （1220.6±127.2）mm 3， P <0.01\]；TPL治疗组移植瘤组织内的TLR4、VEGF表达均显著低于PBS组\[（3.2±0.6） vs (6.7±1.1)，(3.7±0.7) vs (7.1±1.2)；均 P <0.01），其MVD也显著低于PBS组\[(12.2±4.0) vs (22.7±5.6)， P <0.01\]。 结论： TPL能够抑制人胰腺癌PANC-1细胞及其裸鼠移植瘤的生长，并促进PANC-1细胞凋亡，其机制可能与TPL抑制TLR4、VEGF表达及肿瘤血管生成有关。

关键词：雷公藤内酯醇 胰腺癌 Toll样受体4 血管内皮细胞生长因子 血管生成

Inhibitory effect of triptolide on human pancreatic cancer PANC-1 cells and its possible mechanism Download Fulltext

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Fund Project:Project supported by the Research Foundation of Health Bureau of Lianyungang （No.1242）

Abstract:

Objective: To observe the inhibitory effect of triptolide (TPL) on the proliferation and apoptosis of human pancreatic cancer PANC-1 cells in vitro and in vivo, and to analyze its impact on Toll-like receptor 4 (TLR4), vascular endothelial cell growth factor (VEGF) expression and tumor angiogenesis. Methods: PANC-1 cells were treated with 0, 20, 40 and 80 ng/ml TPL in vitro. MTT and flow cytometry were performed to detect the proliferation and apoptosis of PANC-1 cells treated by TPL, respectively. TLR4 and VEGF protein expression in PANC-1 cells were evaluated by Western blotting. PANC-1 tumor-bearing nude mice were established and randomly divided into two groups: TPL group and PBS group. The tumor volume was examined, and all the tumors were taken out at 35 days after treatment. The expression of TLR4, VEGF and CD31 in the xenograft tumors was detected by immunohistochemical staining, and the microvessel density (MVD) was calculated. Results: Compared with 0 ng/ml group, after treated with 20, 40 and 80 ng/ml TPL 24 h, the apoptosis rate of PANC-1 cells was significantly increased (\[4.7±1.0\]%, \[10.5±2.0\]%, \[21.1±4.2\]% vs \[2 6±0.5\]%, P <0.05 or P <0.01); after 48 h, the cell proliferation rate of PANC-1 cells was significantly decreased (\[68.0±5.3\]%, \[59.6±5.0\]%, \[51.6±4.2\]% vs \[99.6±5.2\]%; all P <0.01), and was also decreased compared with that in 24 h treated with the same dose. The expression of TLR4(\[20.2±4.7\]% vs \[57.5±6 3\]%, P <0 01) and VEGF(\[35.8±4.0\]% vs \[92.1±8.3\]%, P <0.01) in PANC-1 cells treated by 80 ng/ml TPL was decreased significantly than those of the untreated group. On day 34, the tumor volume of the TPL treatment group were reduced significantly than that of the PBS control group (\[510.9±79.8\] vs \[1 220.6 ±127.2\] mm 3, P <0 01). The expression of TLR4 (P <0.01) and VEGF in the xenograft tumor tissues of the TPL group were significantly lower than those of the PBS group (\[3.2±0.6\] vs \[6.7±1.1\], \[3.7±0.7\] vs 7.1±1.2; all P <0.01), also the MVD within the transplanted tumor in the TPL group was significantly decreased compared with the PBS group (\[12.2±4.0\] vs \[22 7±5.6\], P <0.01). Conclusion: TPL can inhibit the growth of pancreatic cancer PANC-1 cells and its xenografts tumor in nude mice, and induce apoptosis of PANC-1 cells. Its mechanism may be related to the inhibitory effect on TLR4 and VEGF expression and tumor angiogenesis.

Keywords:triptolide pancreatic cancer Toll-like receptor 4 vascular endothelial cell growth factor angiogenesis

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