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重组TNF-α慢病毒感染的脐血间质干细胞对胃癌移植瘤生长的抑制作用

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马贵亮 张学斌 朱新红 李杨 毛伟征

青岛市市立医院 普外科，山东 青岛 266071;无棣县人民医院 普外科，山东 无棣 251900;青岛市市立医院 普外科，山东 青岛 266071;青岛市市立医院 普外科，山东 青岛 266071;青岛市市立医院 普外科，山东 青岛 266071

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摘要：

目的：以脐血间质干细胞（umbilical cord blood mesenchyme stem cell，UCBMSC）作为肿瘤坏死因子-α（tumor necrosis factor-alpha，TNF-α）载体，研究重组TNF-α慢病毒Lv-TNF-α感染的UCBMSC对胃癌移植瘤生长的抑制作用。方法：人胃癌细胞SGC-7901注射到裸鼠腹股沟皮下建立胃癌移植瘤裸鼠模型。将表达TNF-α的重组慢病毒Lv-TNF-α和对照慢病毒Lv-EGFP分别感染UCBMSC后获得Lv-TNF-α感染的UCBMSC（UCBMSC-TNF-α）以及Lv-EGFP感染的UCBMSC（UCBMSC-EGFP）。荷瘤裸鼠随机分为3组：分别注射UCBMSC-TNF-α、UCBMSC-EGFP及生理盐水（NaCl），观察注射后瘤体生长情况，RT-PCR和ELISA方法分别测定各组胃癌组织中TNF-α mRNA和蛋白的表达；H-E染色观察瘤体的坏死情况。结果：成功建立SGC-7901胃癌细胞裸鼠移植瘤模型。治疗后三组荷瘤裸鼠肿瘤体积分别为（0.51±0.27）、（0.64±0.36）和（1.21±0.80）cm 3，UCBMSC-TNF-α组肿瘤体积最小（F=3.88，P<0.05）；RT-PCR法检测结果显示，3组荷瘤裸鼠肿瘤组织TNF-α mRNA分别为（1.92±0.12）、（1.21±0.26）、（0.81±0.22），UCBMSC-TNF-α组TNF-α mRNA表达量最大（F= 54.82，P< 0 01）；ELISA法检测结果显示，3组荷瘤裸鼠肿瘤组织TNF-α蛋白表达分别为（148.29±3.76）、（78.22±6.24）、（42.80±3 02）pg/ml，MSC-TNF-α组表达量最大（F=694.54，P<0.01）；H-E染色病理切片显示，UCBMSC-TNF-α治疗组肿瘤坏死面积最大。结论：TNF-α转基因UCBMSC可通过旁分泌TNF-α抑制胃癌的生长。

关键词：慢病毒 TNF-α 脐血间质干细胞 转基因治疗 胃癌

Inhibitory effect of umbilical cord blood mesenchymal stem cells infected with reconstructed lentivirus-TNF-α on growth of gastric cancer transplantation tumors

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MA Gui-liang ZHANG Xue-bin ZHU Xin-hong LI Yang MAO Wei-zheng

Department of General Surgery, Qingdao Municipal Hospital, Qingdao 266071, Shandong, China;Department of General Surgery, Wudi County Hospital, Wudi 251900, Shandong, China;Department of General Surgery, Qingdao Municipal Hospital, Qingdao 266071, Shandong, China;Department of General Surgery, Qingdao Municipal Hospital, Qingdao 266071, Shandong, China;Department of General Surgery, Qingdao Municipal Hospital, Qingdao 266071, Shandong, China

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Abstract:

Objective:To study the inhibitory effect of umbilical cord blood mesenchymal stem cells (UCBMSCs) infected with reconstructed lentivirus-TNF-α on growth of gastric cancer transplantation tumors, based on UCBMSC as a TNF-α carrier. Methods: The human gastric cancer SGC-7901 cells were injected into nude mice subcutaneously groin. The model of transplanted SGC-7901 cells in nude mice was set up. The reconstructed lentivirus (Lv-TNF-α) and empty lentivirus (Lv-EGFP) were added to UCBMSC, and UCBMSC-TNF-α cells and control UCBMSC-EGFP cells were obtained. Tumor-bearing nude mice were separated into three groups randomly: a UCBMSC-TNF-α group, an UCBMSC-EGFP group and a NaCl group. The nude mice in these three groups were injected around the tumor with UCBMSC-TNF-α cells, UCBMSC-EGFP cells or NaCl. The transplanted gastric cancer volume and weight was observed; the expressions of TNF-α mRNA and protein in the three groups were determined by RT-PCR and ELISA; and the necrosis areas in the tumors were observed by H-E staining. Results: The transplantation tumor model was established in the nude mice successfully. The transplanted tumor average volume in the three groups were (0.51±0.27), (0.64±0.36) and (1.21± 0.80) cm 3, and the transplanted tumor average volume in the UCBMSC-TNF-α group was minimum (F=3.88, P<0 05); The expressions of TNF-α mRNA in the three groups were (1.92±0.12), (1.21±0.26) and (0.81±0.22), and the expression of TNF-α mRNA in the UCBMSC-TNF-α group was maximum (F=54.82, P<0.01); The expressions of TNF-α protein in the three groups were (148.29±3.76), (78.22±6.24) and (42.80±3.02) pg/ml, and the expression of TNF-α protein in the UCBMSC-TNF-α group was maximum (F=694.54, P<0.01); H-E stained biopsy revealed that the largest tumor necrosis was in the UCBMSC-TNF-α treatment group. Conclusion: Transgenic UCBMSCs can paracrine TNF-α, which has an inhibitory effect on gastric cancer.

Keywords:lentivirus TNF-α umbilical cord blood mesenchymal stem cell transgenosis therapy gastric cancer

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