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吡咯烷二硫氨基甲酸促进间充质干细胞参与糖尿病

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Title: PDTC promotes wound healing in STZ-reduced diabetic mice by mesenchymal stem cells

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关键词: 吡咯烷二硫氨基甲酸; 骨髓间充质干细胞; 核因子-κB; 糖尿病; 创面愈合

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摘要: 目的 观察NF-κB信号通路阻断剂吡咯烷二硫氨基甲酸在骨髓间充质干细胞移植治疗糖尿病小鼠创面愈合中的作用。 方法 分离培养GFP^+小鼠骨髓间充质干细胞。链脲佐菌素诱导C57小鼠糖尿病。小鼠背部制作直径6mm的皮肤缺损创面。实验动物分为4组：①NC 组：正常小鼠对照；②DC组：糖尿病小鼠对照；③MSC1组：糖尿病小鼠移植MSCs（每个创面2.5×10^5个细胞注射于创缘皮下）；④MSC2组：糖尿病小鼠移植MSCs，同时腹腔注射PDTC(50 mg/kg)。细胞移植后观察创面愈合情况，同时切取创面组织制备切片行HE染色、免疫组织化学染色。 结果 MSC2组小鼠创面的愈合率明显高于MSC1组和DC组（$P<0.05$）。HE染色发现MSC2组创面愈合过程及血管形成优于MSC1组和DC组。免疫组织化学VEGF检测显示创面形成第11天，MSC2组(33.51±2.40)的表达明显增强，与DC组(26.07±4.50)和MSC1组(18.71±7.14)相比较，差异显著($P<0.05$)。MSC2组NF-κB p65荧光强度（35.20±18.77）明显减弱，与DC组（130.64±

16.35）和MSC1组（56.80±16.35）相比，差异显著（*P*<0.05）。第14天创面中GFP荧光信号显示MSC2组创面中GFP^+阳性细胞IOD值（135.20±11.84）明显大于MSC1组（46.81±22.37），差异显著(*P*<0.05)。　　结论　　PDTC阻断NF-κB通路，能够促进骨髓间充质干细胞在糖尿病创面愈合中的作用，加速创面愈合。

Abstract:　Objective　To investigate the role of special inhibitor of NF-κB pathway, pyrrolidine dithiocarbamate (PDTC), in wound healing by transplanting bone marrow mesenchymal stem cells (MSCs) in STZ-reduced diabetic mice. Methods　The bone marrow MSCs from GFP transgenic mice were isolated and cultured. For C57BL/6 mice, diabetes was induced by multiple low-dose of STZ (50 mg/kg injection i.p, once a day for 5 consecutive days). A round dorsal skin defect, in a diameter of 6 mm, was made in the mice model. The experimental animals were divided into 4 groups, that is, normal control, diabetic control group, MSCs treatment group (receiving 2.5×10^5 MSCs per dose in 8 areas surrounding wound margin), MSCs+PDTC group (receiving 2.5×10^5 MSCs and injection i.p of PDTC). Wound healing was observed in 3, 7, 11, and 14 d after operation, and wound tissue was cut and observed by HE staining and immunohistochemical assay.　Results　The wound healing rate was significantly higher in MSCs+PDTC group than in MSCs treatment group and diabetic control group（*P*<0.05）. HE staining indicated that there was better vascular formation in the former than the 2 later groups. Immunohistochemical assay showed VEGF was expressed in MSCs+PDTC group (33.51±2.40) in 11 d after operation, significantly strongly than those in MSCs treatment group (18.71±7.14) and diabetic control group（26.07±4.50, P<0.05). While the expression of NF-kappa B expression was significantly reduced in MSCs+PDTC group （35.20±18.77）than in MSCs treatment group （56.80±16.35）and diabetic control group （130.64±16.35, *P*<0.05）. On the 14th day, GFP fluorescence signal was significantly stronger in MSCs+PDTC group（135.20±11.84） than in MSCs treatment group （46.81±22.37, *P*<0.05). Conclusion　PDTC could promote wound healing in diabetic mice treated with bone marrow MSCs by blocking NF-kappaB pathway.

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