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论著

低氧对人脐带间充质干细胞活性和内皮分化能力的影响及VEGF的干预作用

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摘要:

目的: 探讨低氧对人脐带间充质干细胞(hUC-MSCs)的活性及向内皮细胞分化能力的影响,并进一步探索外源性VEGF对低氧损伤的保护作用。方法: 在体外对hUC-MSCs进行分离培养。对hUC-MSCs的形态学和表型特征进行分析。在添加/不添加50 ng/mL VEGF的情况下,对hUC-MSCs分别进行不同时间的低氧诱导后,对细胞凋亡率、ROS生成及细胞增殖能力进行检测,并对hUC-MSCs的内皮分化能力进行评估。结果: 低氧诱导早期(6, 12 h),hUC-MSCs的凋亡及ROS生成显著增加,增殖能力显著下降;晚期(24,72 h),细胞的增殖及凋亡水平与对照组间无明显差异;高浓度(50 ng/mL)外源性VEGF抑制低氧诱导早期出现的凋亡增加及增殖下降;外源性VEGF存在的情况下,低氧诱导14 d,hUC-MSCs表达早期内皮细胞表型,并能获得部分内皮细胞功能。结论: 低氧早期造成hUC-MSCs急性损伤,晚期通过逐步适应恢复细胞活性并保持了其分化潜能。VEGF能够保护急性缺氧对细胞的损伤,并能诱导其向内皮样细胞分化。

关键词: 间充质干细胞 低氧 血管内皮生长因子 分化 细胞凋亡 增殖

Role of hypoxia in viability and endothelial differentiation potential of UC-MSCs and VEGF interference

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Abstract:

Objective: To investigate the effect of hypoxia on cell viability and the endothelial differentiation potential in human umbilical cord derived mesenchymal stem cells (UC-MSCs), and to assess the in vitro protective role of VEGF under low oxygen tension.
Methods: MSCs were isolated from human umbilical cords and cultured in vitro. The morphological and phenotypic characterizations of human UC-MSCs were analyzed. The hypoxia induction was performed with or without the presence of 50 ng/mL of VEGF for different lengths of time. The cell proliferation, apoptosis, and reactive oxygen species (ROS) generation were assessed. Meanwhile, the endothelial differentiation potential of the UC-MSCs was measured.
Results: An increased apoptosis and ROS generation but reduced proliferation rate were observed at early stages (6, 12 h) after transferring the UC-MSCs from the atmospheric condition to the hypoxia condition. However, the UC-MSCs presented equal proliferation and apoptosis levels under hypoxic condition as compared with those under the atmospheric condition at the later stages (24, 72 h). A high concentration of exogenous VEGF (50 ng/mL) attenuated the increased apoptosis and inhibited the proliferation of UC-MSCs, induced by a short-term hypoxia treatment. After 14 days of exogenous VEGF induction under the hypoxia condition, the UC-MSCs acquired an early endothelial phenotype consisting of a mature endothelial molecule and some endothelial functions.
Conclusion: UC-MSCs progressively adapt to hypoxia in a step-by-step manner and maintain differentiation potential under hypoxia condition. VEGF can protect the UC-MSCs from cell damage and induce a differentiation of UC-MSCs toward endothelial lineage under hypoxic conditions.

Keywords: mesenchymal stem cells hypoxia VEGF differentiation apoptosis proliferation
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