Late Outgrowth Endothelial Cells Derived From Wharton's Jelly in Human Umbilical Cord Reduce Neointimal Formation After Vascular Injury: Involvement of Pigment Epithelium-derived Factor

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摘要

Abstract

OBJECTIVE: The number of endothelial progenitor cells (EPCs) that can be obtained from adult bone marrow and peripheral blood to treat cardiovascular diseases is limited. The goal was to examine the endothelial potential of Wharton jelly in human umbilical cord (WJC)-derived stem cells and evaluate their potential to affect neointimal formation after vascular injury. METHODS AND RESULTS: Mesenchymal cells (MCs) were isolated from WJC and cultured in endothelial growth medium. Differentiation into late outgrowth endothelial cells (WJC-OECs) was demonstrated by incorporation of acetylated low-density lipoprotein and expression of the endothelial-specific markers. Transplantation of these cells into wire-injured femoral arteries in mice led to rapid reendothelialization. At 4 weeks after injury, the neointima/media area ratio was reduced and strong expression of pigment epithelium-derived factor (PEDF) compared to saline-or MC- or cord blood-OEC-treated mice. WJC-OECs-conditioned medium has an extremely strong capacity to inhibit the migration and proliferation of smooth muscle cells. The effects were inhibited by neutralizing antibody for PEDF and by siRNA silencing of PEDF. CONCLUSIONS: We firstly demonstrated the presence of a cell population within WJC that has the potential to differentiate into OECs. Transplantation of WJC-OECs may play a crucial role in reestablishing endothelial integrity in injured vessels, thereby inhibiting neointimal hyperplasia. These findings have implications for a novel and practical cell-based therapy for vascular diseases.