# ENDOTHELIAL PROGENITOR CELLS FOR ORGANOGENESIS

Takayuki Asahara [1,2],

[1] *Institute of Biomedical Research and Innovation, Kobe JAPAN,*
, [2] *Tokai University School of Medicine, Isehara, Kanagawa, JAPAN,*

Recently the regenerative potential of stem cells has been under intense investigation. In vitro, stem and progenitor cells possess the capability of self-renewal and differentiation into organ-specific cell types. In vivo, transplantation of these cells may reconstitute organ systems, as shown in animal models of diseases. In contrast, differentiated cells do not exhibit such characteristics. Human endothelial progenitor cells (EPCs) have been isolated from the peripheral blood of adult individuals, expanded in-vitro and committed into an endothelial lineage in culture. The transplantation of these human EPCs has been shown to facilitate successful salvage of limb vasculature and perfusion in athymic nude mice with severe hindlimb ischemia, while differentiated endothelial cells (human microvascular endothelial cells) failed to accomplish limb-saving neovascularization .

These experimental findings call into question certain fundamental concepts regarding blood vessel growth and development in adult organisms. Postnatal neovascularization has been previously considered synonymous with proliferation and migration of pre-existing, fully differentiated ECs resident within parent vessels, i.e. angiogenesis. The finding that circulating EPCs may home to sites of neovascularization and differentiate into ECs in situ is consistent with “vasculogenesis”, a critical paradigm for establishment of the primordial vascular network in the embryo.

Recent progress in stem cell biology widened the therapeutic application of human EPCs/ CD34+ cells for another category of regenerative medicine. Eghbali-Fatourechi et al first identified circulating osteocalcin (OC)-positive cells in adult human, demonstrating osteogenic gene expression and mineralized nodule formation in vitro and representing bone formation in vivo. Chen et al identified osteoblast (OB) precursor cells in human BM CD34+ cells. Tondreau et al reported potential of G-CSF-mobilized PB CD133+ cells as mesenchymal stem cells contributing to osteogenesis in vitro. Long et al successfully induced in vitro osteogenic differentiation of human BM CD34+ cells. These findings strongly suggest therapeutic usefulness of BM-derived CD34+ cells for osteogenesis as well as vasculogenesis. We quite recently reported that human circulating CD34+ cells, systemically transplanted into immunodeficient rats with non-healing fracture, were recruited into fracture sites, developed a favorable environment for fracture healing by enhancing vasculogenesis and osteogenesis and finally led to functional recovery from fracture. This animal study demonstrating efficacy of transplantation of CD34+ cells may encourage application of the cell-based therapy in patients with unhealing fracture in the future clinical trial.

Reference

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