

# Endothelial progenitor cell

Endothelial [progenitor cell](#) (or EPC) is a term that has been applied to multiple different cell types that play roles in the regeneration of the endothelial lining of blood vessels. Despite the history and controversy, the EPC in all its forms remains a promising target of regenerative medicine research.

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The importance of [flow shear stress](#) (SS) on the differentiation of [endothelial progenitor cells](#) (EPCs) has been demonstrated in various studies. [Cholesterol](#) retention and MicroRNA regulation have been also proposed as relevant factors involved in this process, though [evidence](#) regarding their regulatory roles in the differentiation of EPCs is currently lacking.

In a study Li et al. on high [shear stress](#) (HSS)-induced differentiation of EPCs, they investigated the importance of [ABCA1](#), an important regulator in cholesterol efflux, and miR-25-5p, a potential regulator of endothelial reconstruction. They first revealed an inverse correlation between miR-25-5p and ABCA1 expression levels in EPCs under HSS treatment; their direct interaction was subsequently validated by a dual luciferase reporter assay. Further studies using [flow cytometry](#) and qPCR demonstrated that both miR-25-5p overexpression and ABCA1 inhibition led to elevated levels of specific markers of [endothelial cells](#) (ECs), with concomitant down-regulation of [smooth muscle cell](#) (SMC) markers. Finally, knockdown of ABCA1 in EPCs significantly promoted tube formation, which confirmed the conjecture. This current results suggest that miR-25-5p might regulate the differentiation of EPCs partially through targeting ABCA1, and such a mechanism might account for HSS-induced differentiation of EPCs <sup>1)</sup>.

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Garbuzova-Davis et al., evaluated via electron microscopy the ability of transplanted human [bone marrow endothelial progenitor cells](#) (hBMEPCs) to repair the BBB in adult Sprague-Dawley rats subjected to transient middle cerebral artery occlusion (tMCAO).  $\beta$ -galactosidase pre-labeled hBMEPCs were intravenously transplanted 48 hours post-tMCAO. Ultrastructural analysis of microvessels in non-transplant stroke rats revealed typical BBB pathology. At 5 days post-transplantation with hBMEPCs, stroke rats displayed widespread vascular repair in bilateral striatum and motor cortex, characterized by robust cell engraftment within capillaries. hBMEPC transplanted stroke rats exhibited near normal morphology of endothelial cells, pericytes, and astrocytes, without detectable perivascular edema. Near normal morphology of mitochondria was also detected in endothelial cells and perivascular astrocytes from transplanted stroke rats. Equally notable, they observed numerous pinocytic vesicles within engrafted cells. Robust engraftment and intricate functionality of transplanted hBMEPCs likely abrogated stroke-altered vasculature. Preserving mitochondria and augmenting pinocytosis in cell-based therapeutics represent a new neurorestorative mechanism in BBB repair for stroke. <sup>2)</sup>.

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EPCs transplantation can participate in the reparative procedure of the [neovascularization](#) in oxygen-induced retinopathy (OIR) <sup>3)</sup>.

The relative increase in [angiopoietin 2](#) activity in [brain tumors](#) may result in the creation of a pro-angiogenic environment that enhances the recruitment of putative [bone marrow](#)-derived [endothelial progenitor cell](#) into the tumor's developing vascular tree <sup>4)</sup>.

1)

Li Z, Li JN, Li Q, Liu C, Zhou LH, Zhang Q, Xu Y. miR-25-5p regulates endothelial progenitor cell differentiation in response to shear stress through targeting ABCA1. *Cell Biol Int*. 2021 May 4. doi: 10.1002/cbin.11621. Epub ahead of print. PMID: 33945659.

2)

Garbuzova-Davis S, Haller E, Lin R, Borlongan CV. Intravenously Transplanted Human Bone Marrow Endothelial Progenitor Cells Engraft Within Brain Capillaries, Preserve Mitochondrial Morphology, and Display Pinocytotic Activity Towards BBB Repair in Ischemic Stroke Rats. *Stem Cells*. 2017 Jan 31. doi: 10.1002/stem.2578. [Epub ahead of print] PubMed PMID: 28142208.

3)

Wang D, Zhang B, Shi H, Yang W, Bi MC, Song XF, Zhang C, Cheng JH, Hao JL, Song E. Effect of endothelial progenitor cells derived from human umbilical cord blood on oxygen-induced retinopathy in mice by intravitreal transplantation. *Int J Ophthalmol*. 2016 Nov 18;9(11):1578-1583. PubMed PMID: 27990359.

4)

Udani V, Santarelli J, Yung Y, Cheshier S, Andrews A, Kasad Z, Tse V. Differential expression of angiopoietin-1 and angiopoietin-2 may enhance recruitment of bone-marrow-derived endothelial precursor cells into brain tumors. *Neurol Res*. 2005 Dec;27(8):801-6. PubMed PMID: 16354539.

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