Perivascular Cells

Prof. Steven S. Saliterman
Department of Biomedical Engineering, University of Minnesota
http://saliterman.umn.edu/

Perivascular cells

Pharmacology & Therapeutics 171 (2017) 83–92

Contents lists available at ScienceDirect

Pharmacology & Therapeutics

journal homepage: www.elsevier.com/locate/pharmthera

Associate editor: P. Madeddu

Perivascular cells and tissue engineering: Current applications and untapped potential

Elisa Avolio [a,*], Valeria V. Alvino [a], Mohamed T. Ghorbel [b], Paola Campagnolo [c,**]

[a] Division of Experimental Cardiovascular Medicine, Bristol Heart Institute, University of Bristol, United Kingdom
[b] Division of Congenital Heart Surgery, Bristol Heart Institute, University of Bristol, United Kingdom
[c] School of Biosciences and Medicine, University of Surrey, Guildford, United Kingdom

Vascular Anatomy

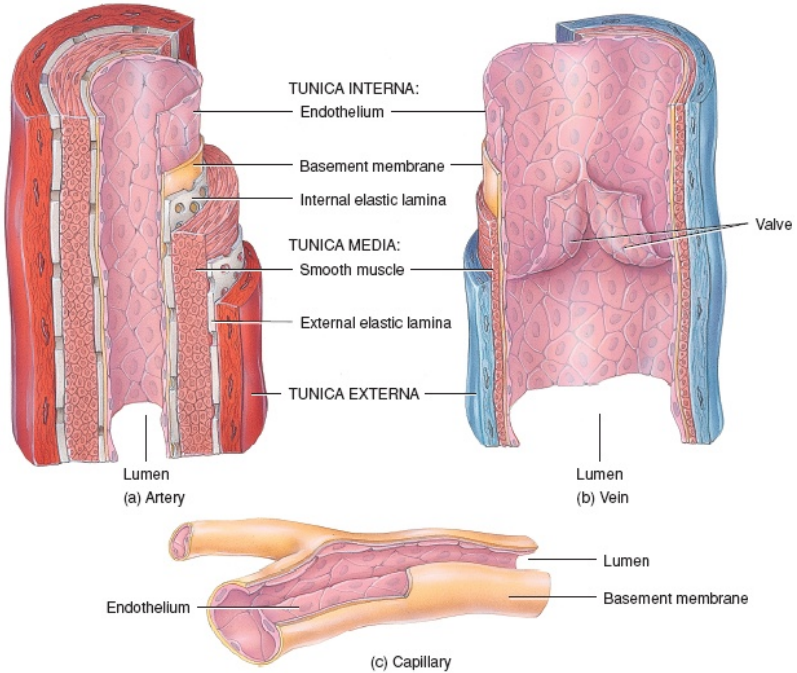
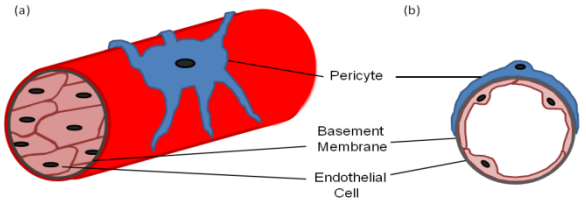


Image Courtesy of John Wiley & Sons

- The walls of all blood vessels, except capillaries, consists of three layers named *tunica intima*, *tunica media* and *tunica adventitia (tunica externa).*
- The latter contain fibroblasts, collagen and nerves.
- Blood vessels are formed early on during embryogenesis from the mesoderm in a process known as *vasculogenesis*.
- Pericytes surround the endothelium as part of the basement membrane.



Mills, S. J., A. J. Cowin, and P. Kaur. "Pericytes, Mesenchymal Stem Cells and the Wound Healing Process." *Cells* 2, no. 3 (2013): 621-34.

Pericytes

- Pericytes have stem cell-like properties and are seemingly able to differentiate into adipocytes, chondrocytes, osteoblasts and granulocytes, leading them to be identified as mesenchymal stem cells (MSCs).
- They increase ECs proliferation/survival and migration.
- They release a large variety of GFs and cytokines.
- They may accelerate wound healing.
- There are several markers, none unique, and vary with location and time.

Mills, S. J., A. J. Cowin, and P. Kaur. "Pericytes, Mesenchymal Stem Cells and the Wound Healing Process." *Cells* 2, no. 3 (2013): 621-34.

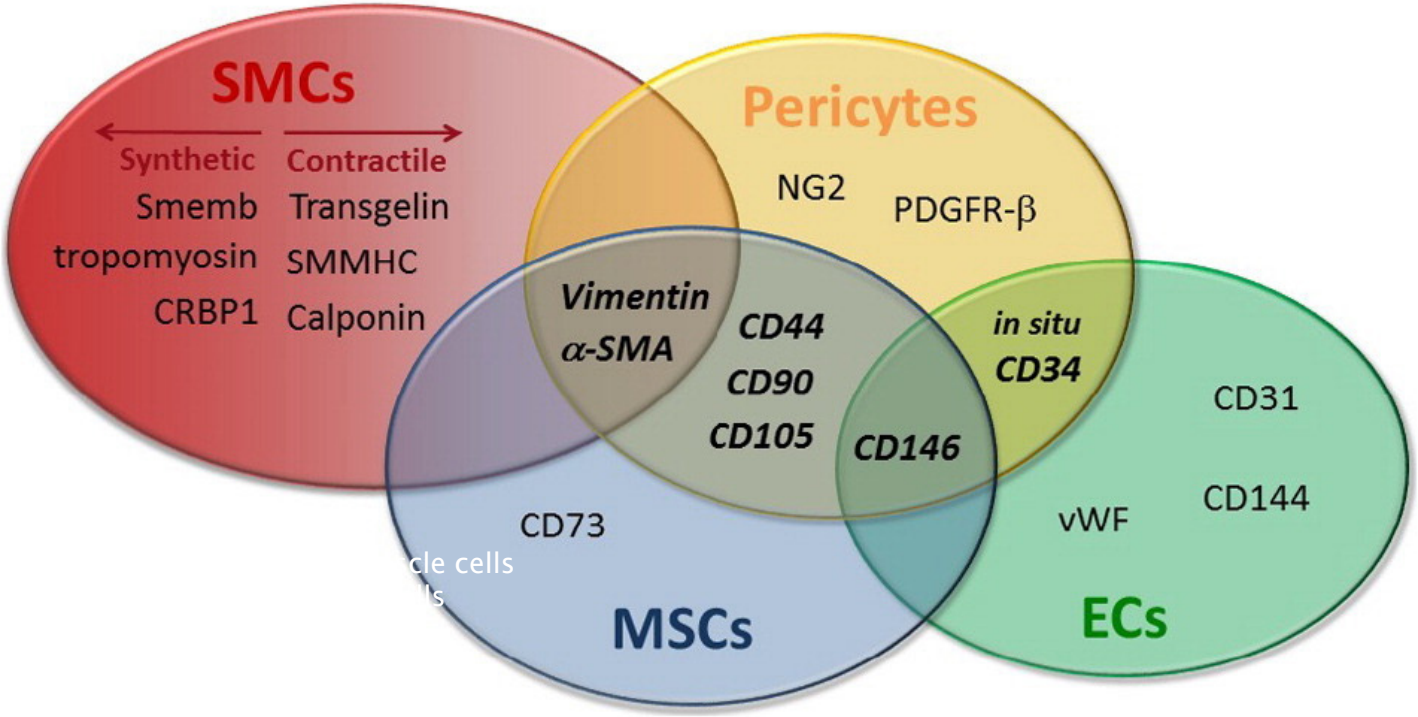
Marker Expression

Table 1
Comparison of marker expression between mesenchymal stem cells (MSCs), vascular smooth muscle cells (SMCs), pericytes and endothelial cells (ECs).

Cell type	Source	Phenotype	References
MSCs	Bone marrow, adipose tissue, peripheral blood, other tissues	CD44+/CD90+/CD105+/CD73+/CD146+/CD34−/CD45−/CD14−	Hass et al. (2011)
SMCs	Arteries, veins	Synthetic: vimentin+/Smemb+/tropomyosin+/CRBP1+ Contractile: α-SMA+/Transgelin+/SMMHC+	Wanjare, Kusuma, and Gerecht (2014)
Pericytes and pericyte-associated cells	Capillaries/microvessels from various tissues	NG2+/PDGFRβ+/vimentin+ CD146+or−/CD34+or− CD44+/CD90+/CD105+/CD73+/CD31−/CD45−/CD56−	Campagnolo et al. (2010) Chen et al., (2015) Avolio, Meloni, et al. (2015)
ECs	Vascular intima	CD31+/CD144+/vWF+/CD34+/CD45−	Bompais et al. (2004)

Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

Expressed Markers & Overlap



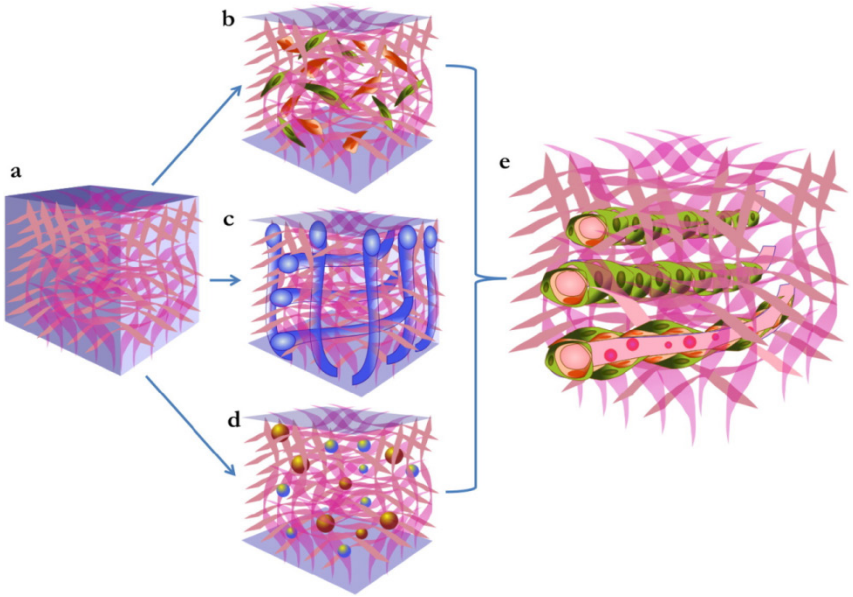
Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

Table 2
Characteristics of pericytes and pericyte-associated isolated from different sources.

Pericytes and source	Strategy of isolation	Phenotype in culture	Characteristics/functions	References
Saphenous vein pericytes (SVPs), from saphenous vein	CD34 +/CD31 − magnetic bead selection	*Positive:* NG2, PDGFRβ, CD44, CD90, CD105, CD73, VIMENTIN *Negative:* CD146, CD45, CD31	Stabilization/control, blood vessel permeability, blood pressure, vasculogenesis, angiogenesis; Physiological/pathological repair process.	Campagnolo et al. (2010)
Cardiac pericyte-associated (CPs), from neonatal atrium/ventricle	CD34 +/CD31 − magnetic bead selection	*Positive:* NG2, PDGFRβ, CD44, CD90, CD105, CD73 *Negative:* CD146, CD45, CD31	Angiogenesis, ECM protein secretion.	Avolio, Rodriguez-Arabaolaza, et al. (2015)
Myocardial pericytes (MPs), from fetal/adult hearts	CD146 +/CD34 −/CD45 −/CD56 −/CD117 − Fluorescent activated cell sorting	*Positive:* NG2, PDGFRβ, CD44, CD90, CD105, CD73, VIMENTIN, CD146 *Negative:* CD34, CD45, CD31	Angiogenesis; vascular permeability control; blood flow regulation; trophic functions; ECM protein secretion.	Chen et al. (2015)
Skeletal muscle pericytes (SkPs), from Skeletal muscle	CD146high/CD34 − Fluorescent activated cell sorting	*Positive:* CD146 *Negative:* CD34, CD45, CD144, CD56, CD31	Myogenic potential; Role in muscle ontogeny and regeneration; Promote assembling of new vasculature in skeletal muscle. Control of BBB integrity	Crisan et al. (2008)
Brain pericytes (BPs), from brain microvasculature	Cloning and morphology	*Positive:* PDGFRβ, α-SMA, 3G5, RGS5, MHC I-II *Negative:* CD45, vWF	Regulation of microvessel architecture; ECM protein secretion; Regulation of capillary diameter and blood flow; Phagocytic functions.	Bouchard et al. (1997) Winkler, Bell, and Zlokovic (2011)
Liver pericytes (LPs) from hepatic tissue	Density gradient or Fluorescent sorting based on endogenous retinol or Liver explant outgrowth	*Positive:* α-SMA, NG2, DESMIN, GFAP	Retinol transport and storage; TGFβ-dependent ECM regulation; Angiogenesis and sinusoidal remodelling.	Friedman and Roll (1987); Matsuura et al. (1989) Blazejewski et al. (1995) Yokoi et al. (1984) Friedman (2008)
Dental pulp pericytes (DPPs), from dental pulp	STRO1 + magnetic bead selection	*Positive:* STRO-1, CD146, 3G5, α-SMA *Negative:* vWF	High proliferative potential; Regeneration of mineralized structure as bone and dentin; Support hematopoiesis.	Shi and Gronthos (2003) Alliot-Licht et al. (2005)

Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

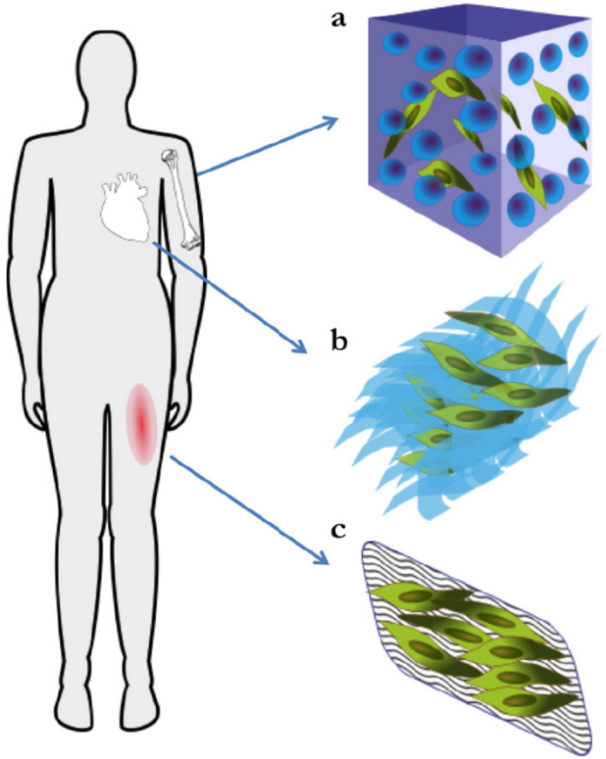
Strategies for Vascularization



a) Uniform vascularization.
b) Combination of the material with cells able to support angiogenesis.
c) Design of the scaffold structure reproducing vascular like-structures that will act as a guide for the angiogenic process.
d) Incorporation of angiogenic factors during the manufacture of the graft.
e) The result should be a vascularized graft in which new-formed vessels are mature and functionally competent.

Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

Perivascular Cells for Damaged Tissues

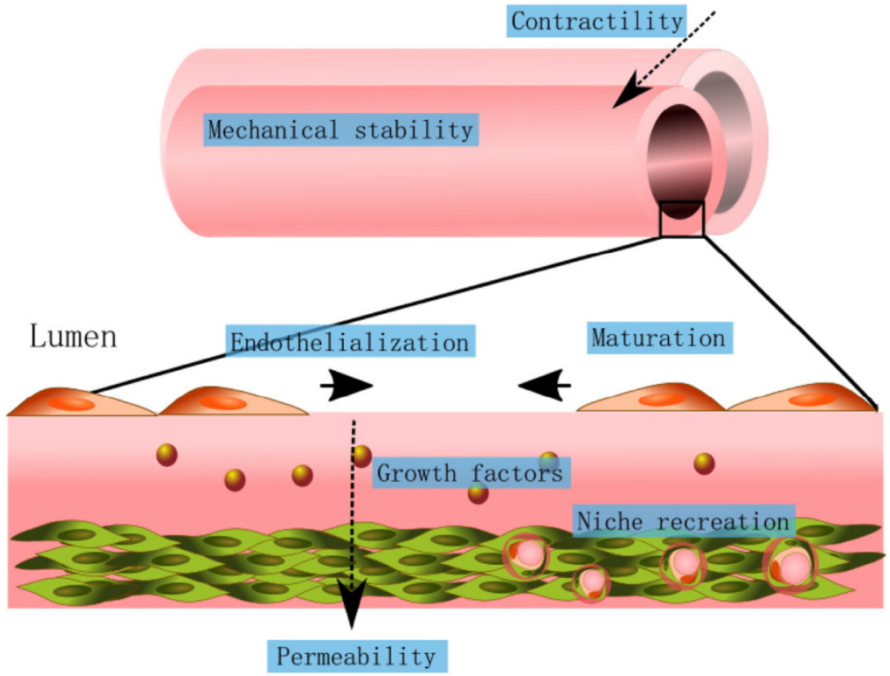


a) Bone reconstruction was achieved by incorporating PCs in 3D scaffolds.
b) Heart patches obtained by stacking multilayers of PCs combined grown on matrix substrate were devised for myocardial infarction.
c) Topical application of dermal patches containing PCs improved skin wound healing.

Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

Role of Perivascular Cells in TE Grafts

1. The seeding of vascular grafts with perivascular cells increases their contractility and mechanical properties, regulating permeability.
2. The release of growth factors by the perivascular cells regulates endothelialization and endothelial cell function.
3. Additionally, perivascular cells contribute to the reconstitution of the perivascular niche, favoring the long-term graft success.



Avolio, E., V. V. Alvino, M. T. Ghorbel, and P. Campagnolo. "Perivascular Cells and Tissue Engineering: Current Applications and Untapped Potential." *Pharmacology & Therapeutics* 171 (Mar 2017): 83-92.

Summary

- Pericytes have stem cell-like properties and are mesenchymal stem cells.
- They promote vessel growth and stability.
- May in the future be useful for vascular graft repopulation, and skeletal and cardiac muscle grafts.
- May be an alternative to bone marrow mesenchymal stem cells (BMSCs) for bone regeneration.