Pericyte Dynamics during Angiogenesis: New Insights from New Identities

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Introduction
Vascular pericytes were first discovered in 1873 by the French physiologist, Charles Marie-Benjamin Rouget, and defined as 'Rouget cells. Zimmerman introduced the term pericyte in 1923, describing them as a periendothelial support cell that wraps around the length of microvessels [1]. While the presence of pericytes in the microcirculation has been long-documented, their functional roles and importance in microvascular physiology have been largely underinvestigated. In more recent years, clarification of their versatile functionality has thrust them into the spotlight. Due to their putative influence on endothelial cells (ECs), pericytes have become a research area of growing interest and are increasingly being evaluated as potential targets for proangiogenic or antiangiogenic therapies.

Vascular pericytes are still defined morphologically as periendothelial support cells that elongate around endothelial cells (ECs) and are functionally associated with regulating vessel stabilization, vessel diameter and EC proliferation. During angiogenesis, bidirectional pericyte-EC signaling is critical for capillary sprout formation. Observations of pericytes leading capillary sprouts also implicate their role in EC guidance. As such, pericytes have recently emerged as a therapeutic target to promote or inhibit angiogenesis. Advancing our basic understanding of pericytes and developing pericyte-related therapies are challenged, like in many other fields, by questions regarding cell identity. This review article discusses what we know about pericyte phenotypes and the opportunity to advance our understanding by defining the specific pericyte cell populations involved in capillary sprouting.
guish specific pericyte subpopulations has limited (1) our understanding of how pericytes directly influence EC dynamics and (2) the development of pericyte-targeted angiogenic therapies. For example, pericytes have been shown to both stabilize and promote capillary sprouting. This apparent dual role motivates the following questions. Do specific subtypes of pericytes exist? Do pericytes change their phenotype in order to perform specific functions? In EC biology, specialized cell types are exemplified by the discovery of tip cells versus stalk cells during angiogenesis [7]. The tip cell paradigm highlights the potential for two neighboring cell types to be delineated by their phenotype and function. In the context of pericyte biology, determining the spatial and temporal phenotypic differences along angiogenic vessels versus mature vessels represents an equal opportunity to add new insight and perspective.

Common pericyte markers include smooth muscle α-actin (SMA), desmin, vimentin, PDGFR-β and neuron-glial antigen 2 (NG2). However, these markers identify multiple cell populations along the entire hierarchy of microvascular networks and are not angiogenesis-specific [3, 8, 9]. What is equally challenging is that pericyte marker expression varies across a network and per tissue. In this review, we propose a new paradigm for pericyte biology wherein transient expression patterns by pericyte subtypes during angiogenesis can potentially be used to distinguish pericyte functionality. In the first half of this review, we briefly summarize the current understanding of pericyte physiology and function. In the second half, we introduce the potential for defining functionally distinct pericyte subpopulations, by discussing the temporal expression dynamics of two neural molecules, NG2 and class III β-tubulin, by pericytes in the adult microcirculation.

### Pericyte Dynamics Involved in Angiogenesis

Vascular pericytes are critical players in the microcirculation and their various functions are comprehensively covered by multiple reviews [3, 10–13]. However, the mapping of specific pericyte functions and downstream mechanisms to specific pericyte dynamics remains elusive. Pericytes are defined morphologically as cells within the basement membrane that elongate along the long axis of capillaries, and wrap around ECs with shorter processes [3, 14]. Direct interdigitations protrude from pericytes into ECs at their interface, and endothelial processes reciprocate [15]. Pericytes are functionally associated with the regulation of blood vessel diameter, vessel permeability, EC proliferation, angiogenesis and even leukocyte recruitment [11, 14, 16–18]. Recent evidence shows that pericytes mediate capillary diameter by contraction in response to electrical or neurotransmitter stimulation [19], implicating pericytes as highly localized modulators of blood flow. Lack of pericyte recruitment leads to endothelial hyperplasia and increased vascular permeability [6, 20], associating pericytes with vessel stability and maturation.

Work in the pericyte biology field has established several mechanisms that regulate pericyte-endothelial communication [3, 11, 13]. The prominent signaling pathways are PDGF-B/PDGFR-β, angiopoietin 1 (Ang1)/Tie2 and transforming growth factor-β (TGF-β) [21], which regulate pericyte recruitment, EC viability and mural cell differentiation, respectively [22]. Pericytes can also influence the local extracellular matrix (ECM) to guide endothelial migration by modulating deposition of basement membrane proteins [23]. As pericytes have been linked to microvascular function, it makes sense that their coverage is heterogeneous among organs depending on the needs of the local tissue environment. In the brain, for example, a high density of pericytes tightly regulates the blood-brain barrier as a selectively permeable fortification which prevents fluctuations in the sensitive environment of the central nervous system (CNS). Pericyte coverage in skeletal muscle, however, may be as low as one pericyte for every 100 ECs [2]. Liver (stellate cells) and kidney pericytes are specialized to aid parenchymal functions. Recently, pericytes of both organs have garnered attention for their central role in liver and kidney fibrosis [24–26].

Alterations in pericyte coverage are not surprisingly linked to multiple pathologies. In the case of diabetic retinopathy, the disassociation of pericytes from ECs has been associated with uncontrolled angiogenesis [12]. Decreased pericyte coverage in the brain causes neurodegeneration [27]. This is similar to a tumor growth scenario, in which loose pericyte coverage leads to vascular dysfunction [28, 29]. Pericytes contribute to angiogenesis during tumor vascularization. However, loss of pericytes or abnormal pericyte function in tumors increases vessel permeability and decreases vessel integrity, which enhances tumor metastatic potential [28, 30]. These examples illustrate the dual role of pericytes in regulating angiogenesis and vessel integrity.

During angiogenesis, pericyte dynamics include recruitment, ECM modulation, paracrine signaling and direct interactions with ECs (fig. 1) [3]. They have also been
shown to lead sprouting ECs and bridge the gaps between two sprouting segments in some cases [31, 32]. ECs of newly forming vessels recruit pericytes by secreting PDGF-B [4, 5]. Manipulating pericyte investment by altering recruitment to the endothelium can cause lethal microvascular dysfunction, deviate vascular patterning during development and affect the formation of new vessels during physiological and pathological angiogenesis [3, 33]. As previously mentioned, this can be attributed to pericyte regulation of EC proliferation. Recent work has also identified pericytes as important players in regulating basement membrane organization. During developmental vascular assembly, pericytes catalyze deposition of basement membrane proteins including collagen IV, laminin and fibronectin [11]. Pericyte actomyosin-mediated contraction can modulate the local mechanical environment for adjacent ECs [34]. EC behavior can also be mediated by direct connections between the two cell types via N-cadherin adhesions [13, 35], pericyte NG2 binding to β1 integrins on ECs [29, 36] and, potentially, connexin 43 [37, 38]. Furthermore, pericyte-EC interactions induce changes in the expression of ECM-binding integrins by both cell types, which are necessary for investment in newly formed matrix [39]. Once vascular tubes are assembled, the pericyte-derived tissue inhibitor of metalloproteinase-3 (TIMP-3) prevents proteolysis of matrix proteins [40].

Because of their necessity in microvascular remodeling and proximity to ECs, pericytes have emerged as a cellular target to manipulate angiogenesis [41–43]. For example, the inhibition of PDGFR-β in tumors depletes pericytes and disrupts tumor vasculature, which curbs tumor growth [44]. Conversely, increasing pericyte coverage via Ang2 inhibition can represent an antiangiogenic tumor therapy [45]. Pericytes have been implicated in preventing tumor metastasis [28, 30], and depletion of pericytes in vascular retinopathy leads to hypervascularization and blindness [33]. The therapeutic potential for pericytes can also be exemplified by considering the similarities between pericytes and mesenchymal stem cells (MSCs) [46–51] (a concept that will be revisited in the next section) and appreciating that the delivery of MSCs represents a viable approach for pericyte-targeted angiogenic therapies [43]. The success of this approach has been well documented [43]. Therapeutically delivered MSCs have been convincingly shown to acquire pericyte characteristics and stabilize aberrant angiogenesis in various models of normal and pathological vessel remodeling. Still, the exact mechanisms that regulate pericyte and MSC physiology in these scenarios remain unclear, and understanding the pericyte (and MSC) subtypes that contribute to angiogenesis and vessel stabilization will open new avenues for therapeutic manipulation of the microvasculature.

While it is clear that pericyte-EC interactions play a crucial role in establishing and maintaining a normal microcirculation, questions about pericyte mechanisms, especially during angiogenesis in the adult, remain. Determining phenotypic differences between the pericytes on angiogenic vessels and mature vessels may provide insight as to the varying functions of pericytes across the microvasculature. However, pericyte-specific phenotypes remain elusive, and recent studies document the overlap between pericytes and multiple other cell types. Interestingly, pericytes have even been suggested to display multipotency similar to stem cells. Many questions certainly also remain regarding pericyte lineage, yet in the
midst of any debate, the recognition of their phenotypic
dynamics offers a valuable opportunity to discover new
pericyte spatial and temporal identities that define spe-
cific cell subpopulations.

**Pericyte Identity**

**Pericyte Phenotypic Markers**

Pericyte heterogeneity and plasticity have been major
barriers to further elucidating scenario-specific pericyte
mechanisms. Common pericyte markers include NG2,
SMA, desmin, vimentin and PDGFR-β, but their expres-
sion is not specific to pericytes [3]. Desmin and PDGFR-β
are expressed by SMCs and interstitial fibroblasts [52].
SMA identifies vascular SMCs and myofibroblasts [53].
NG2 can identify macrophages, glial cells and various
types of tumor cells [36, 54, 55]. Additionally, the expres-
sion of these markers and their overlap vary among peri-
cyte populations along the hierarchy of a network (fig. 2)
[9, 56]. Further complicating the issue of pericyte identifi-
cation, expression of the various markers differs, depend-
ing on species, tissue and even developmental stage. As
just one example, pericytes along microvessels in a devel-
opling chicken embryo stain positive for SMA, but this is
not the case for mouse retina [3]. Since other cell types
express all of the above markers, a pericyte cannot be ubiq-
uitously identified by any one marker. Observational data
suggest that at least a population of pericytes is derived
from interstitial fibroblasts [57], and, consequently, peri-
cytes are often thought of as a plastic cell type somewhere
between SMCs and fibroblasts.

The phenotypic state of a pericyte, indeed, seems to
 correlate with pericyte maturation. In the adult rat mes-
entery, pericytes along capillaries lacked SMA compared
to assuming more contractile cells along precapillary
arterioles and postcapillary venules [9, 56]. As another
example, Song et al. [42] demonstrated that only a sub-
population of PDGFR-β+ perivascular progenitor cells in
tumors expressed more mature pericyte markers (i.e.
NG2, desmin or SMA). In support of their progenitor na-
ture, the isolated PDGFR-β+ cells were able to differen-
tiate into the more mature NG2+ or SMA+ phenotypes
after culture. When cultured along with ECs, the progen-
itor cells displayed the ability to differentiate into des-
min+ cells. The results of their study support the concept
that pericyte specific phenotypes are dependent on their
local environment and suggest the need to better under-
stand the temporal and spatial functional importance of
pericyte subpopulations during angiogenesis. Recogni-
tion of pericyte phenotype dynamics represents an op-
portunity to expand our understanding of how pericyte
markers relate to different cell states.

Considering pericyte identity or, more appropriately,
the lack of identity, forces one to appreciate their pheno-
typic heterogeneity and overlaps with other cell types.
The versatility and plasticity of pericytes is maybe best
exemplified by their relationship with MSCs. The fate of
various stem cell populations in vivo [42, 58–61] suggests
that MSCs can differentiate into pericytes. Intriguingly,
pericytes have also been implicated to be a source of mul-
tipotent stem cells [46] and have the ability to differen-
tiate into osteogenic [47], macrophage/dendritic [48] and
neural lineages [49]. The derivation of stem cells from the
perivascular niche in multiple tissues [50, 51] further sup-
ports the stem cell nature of pericytes. Regardless of the
origin or fate of pericytes, elucidating their specific roles
in vessel stabilization versus capillary sprouting requires
further spatial and temporal characterization of pericyte
identities during angiogenesis.

In the rest of this review, we will focus on how we can
apply what we know about the overlaps between pericytes
and neural cells to discover new pericyte subpopulations
and their potential specialized functions during angio-
genesis.
Pericyte Marker Overlap with Neural Cells

In recent years, NG2, a marker of glial progenitor cells in the CNS, has become the most common marker for pericytes [62]. NG2 is a membrane spanning chondroitin proteoglycan and its expression in the CNS identifies oligodendrocyte progenitor cells [36] during development. NG2+ progenitor cells are also capable of producing astrocytes depending on the culture environment in vitro [36] with such a capability being confirmed for a small population of astrocytes in vivo [63]. In the microcirculation, NG2 identifies perivascular cells along arteries (fig. 2), capillaries and capillary sprouts, and is transiently upregulated along remodeling venules during angiogenesis [8, 64]. The identification and use of NG2 as a pericyte marker highlights the emerging area of microvascular research focused on the link between vascular and neural patterning [65–69]. This link is supported at the molecular level when considering growth inhibitors in the CNS such as ephrins, semaphorins, NG2, neuropilins and Nogo [55]. In the vascular system, these molecules also appear to play regulatory roles in the guidance of capillary sprouts and have helped define the functional differences between endothelial tip versus stalk cells. Neural molecules, like ephrin B2, EphB4 and the neuropilins have also been largely used as the gold standards for identifying arteriole versus venous EC identity [65, 66, 70–72]. Altogether, a coordinated link between neural and vascular patterning is just beginning to be characterized, and this offers an exciting new perspective on the study of adult microvascular remodeling.

We have shown that NG2 expression in adult rat mesenteric microvascular networks identifies perivascular cells along capillaries and arterioles, but not venules [8]. During microvascular network growth, NG2 expression by pericytes is upregulated along venules. Interestingly, this upregulation of NG2 is transient, and temporally correlates with capillary sprouting [64]. The transient expression pattern of NG2 during angiogenesis stresses the need to understand different functions of pericytes on unstimulated (i.e. quiescent) versus angiogenic vessels (fig. 3) and is consistent with NG2 expression by various tissue-specific precursor cell types during development, including oligodendrocytes, immature chondroblasts, osteoblasts and keratinocyte progenitor cells [36, 54]. A temporal specific NG2 phenotype might also exist for developing cardiomyocytes and skeletal muscle [54]. More than a pericyte marker, NG2 seems to be a marker of a dynamic cell type and indicator of a cell state. NG2 is thought to be expressed by partially differentiated progenitor cells and is downregulated upon differentiation [36]. This general description is consistent with the observation of NG2 expression by oligodendrocyte progenitor cells, but not oligodendrocytes in the CNS during development and consistent with the view that pericytes are plastic cell types with progenitor potential. Our laboratory has also observed strong NG2 immunolabeling along nerves in adult rat mesenteric networks [8, 73]. Nerves were identified by typical nerve morphology and by the expression of protein gene product 9.5 (PGP 9.5), tyrosine hydroxylase, neurofilament and class III β-tubulin. Whether NG2 is actually expressed by the peripheral axons in the rat mesentery has still to be investigated. Work by Rezajooi et al. [74] suggests that NG2 expression might not be associated with the axons at all, but rather perineurial or endoneurial fibroblasts involved in axon ensheathment. Nonetheless, the expression of NG2 by glial progenitor cells and along nerves in the adult further highlights the overlap between vascular pericytes and neural cell types. And the common use of NG2 as a pericyte marker and its characterization raises the question of whether other neural phenotypic markers identify pericytes during angiogenesis.

Class III β-tubulin is a potential candidate and, like NG2, is another marker of neural progenitor cells in the
CNS and peripheral nerves in the adult [75, 76]. Class III β-tubulin is one of seven β-tubulin isotypes that forms α/β-tubulin heterodimers with six α-tubulin isotypes during microtubule assembly, and is most commonly used as a marker of neural phenotypes [77]. During development in the CNS, class III β-tubulin is transiently expressed by glial precursor cells, and in adults it is expressed by peripheral nerves [77]. Outside the nervous system, class III β-tubulin expression by tumor cells correlates with increased metastasis and resistance to tubulin-binding agents [78, 79]. All taken together, the expression patterns of class III β-tubulin are similar to NG2. So, it was not unexpected that class III β-tubulin does identify vascular pericytes. What was surprising was when and where class III β-tubulin identified pericytes. In unstimulated adult rat mesenteric networks, class III β-tubulin is nerve-specific and absent along arterioles, venules and capillaries [80]. After the networks are stimulated to undergo angiogenesis, class III β-tubulin is expressed by pericytes along these vessel types, and is subsequently downregulated to unstimulated levels after capillary sprouting [80]. These observations suggest that class III β-tubulin is a potential marker of angiogenic pericytes (fig. 4). To our knowledge, the regulator of G-protein signaling 5 (RGS-5) is the only other potential pericyte marker that has been reported to transiently correlate with an angiogenic or activated state [81].

Human brain pericytes in vitro also express class III β-tubulin (fig. 5). The positive expression of class III β-tubulin by tumor cells and pericytes in vitro suggests a potential issue with using just class III β-tubulin expression as an indicator of a neural phenotype. For example, stem cell differentiation into nerves has been confirmed, in part, based on class III β-tubulin expression as an indicator of a neural phenotype. For example, stem cell differentiation into nerves has been confirmed, in part, based on class III β-tubulin expression [82, 83]. However, our observations show that class III β-tubulin can be expressed by pericytes and is not nerve-specific. We have also confirmed that human placenta-derived pericytes, human mesenchymal stem cells, and mouse embryonic stem cells also express class III β-tubulin in vitro (data not shown). Since mesenchymal stem cells might be a source of vascular pericytes in adult tissues [58] and, vice versa, vascular pericytes can be induced to exhibit multipotent stem cell activity [49], we speculate that class III β-tubulin is indeed more than a nerve marker in vivo and potentially identifies a precursor cell population. Regardless, class III β-tubulin represents an exciting biomarker of cells in an active state and, in the context of pericytes, represents a potential phenotype related to the functions involved in angiogenesis.

**Fig. 4.** Pericyte differentiation during angiogenesis. This represents an example of the phenotype change of pericytes from an unstimulated (nonangiogenic) to an angiogenic scenario in adult rat mesenteric microvascular networks. In unstimulated microvascular networks, class III β-tubulin labeling is nerve-specific and does not identify perivascular cells along PECAM-positive arterioles, venules (V) or capillaries (c). During angiogenesis, perivascular cells along all vessels change their phenotype to become class III β-tubulin-positive (arrows). The transient upregulation of class III β-tubulin by pericytes during angiogenesis highlights the potential for specialized pericyte subpopulations. Scale bars: 25 μm.
Do Pericyte Subpopulations Play Functional Roles?

The concept of specialized subpopulations of vascular pericytes forces the integration of studies using pericyte markers to identify pericytes and studies focused on elucidating the functional roles of those markers. NG2 is sometimes referred to as a marker of angiogenic pericytes along capillaries [31, 62] because it typically colocalizes with pericytes along all capillaries and capillary sprouts. In support of the angiogenic classification, we have demonstrated that NG2 is dramatically upregulated along venules during angiogenesis, implicating its involvement in capillary sprouting [64]. Importantly, NG2 is more than just a marker, and its identification led to its discovery as a regulator of capillary sprouting. NG2-binding of PDGF-AA and basic fibroblast growth factor (bFGF) [84, 85], as well as the kringle domains of plasminogen, which is important for the activation of latent TGF-β [86], implicates its role as a regulator of local angiogenic growth factor presentation. NG2 expression has also been shown to orient with actin stress fibers in a linear array and has been linked to downstream Rho-Rac signaling [54, 87]. Another possible role for NG2 is manipulation of the local ECM environment as a receptor for type VI collagen [88]. The soluble form of the proteoglycan promotes EC motility and angiogenesis via engagement of galectin-3 and α3β1 integrin [89], suggesting a direct interaction between NG2-expressing perivascular cells and neighboring ECs. Transmembrane signaling between the two cell types is further supported by NG2 knockdown pericyte-EC coculture models. Pericyte-specific NG2 inhibition can reduce β1 integrin activation by ECs and EC tube formation, junction formation and permeability [29].

The functional importance of this proteoglycan has been demonstrated in vivo with the use of ng2−/− mice and functional blocking antibodies [90, 91]. Genetic deletion
or blockade of NG2 in hypoxia-induced microvascular growth in the retina and bFGF-induced growth in the cornea resulted in fewer vessels [91]. NG2 antibody inhibition in rat mesenteric microvascular networks has been shown to inhibit bFGF and vascular endothelial growth factor (VEGF)-induced sprout formation [92]. During tumor angiogenesis, NG2 has been shown to sequester angiostatin, increasing the tumor growth rate [93]. Further advocating the functional role of NG2, tumors in mice with pericyte-specific NG2 deletion display a highly

**Fig. 6.** Class III β-tubulin regulates pericyte migration. **a-c** Class III β-tubulin and DAPI nucleic acid labeling in the human brain-derived pericytes 6 h after a scratch wound was applied. Scale bars: 200 μm. Inhibition of class III β-tubulin was confirmed qualitatively by the reduction in class III β-tubulin-positive cells (c) compared to the control groups (a, b). **d** Quantification of scratch closure for the control sham, control siRNA and class III β-tubulin target siRNA groups. At 72 h (24 h transfection + 48 h for gene suppression to manifest), each monolayer was scratched and imaged. After 6 h, scratches were imaged again, and the change in the scratch area was blindly quantified for 8 wells per group (n = 8 per group). Scratch wound closure fractions were compared using a one-way ANOVA followed by a Student Newman-Keuls pairwise comparison test. *p < 0.05 represents significant differences from the control sham group. + p < 0.05 represents significant differences from the control siRNA group. **e** Fraction of the fraction of class III β-tubulin-positive cells inside the initial scratch area compared to the general population outside the scratch area (n = 8 per group). Statistical comparison between the 2 groups was made using a Student’s t test. CTRL = Control. *p < 0.05 represents a significant difference. **f** Example of class III β-tubulin and DAPI nucleic acid labeling along the leading edge of a scratch wound in the target siRNA group. Class III β-tubulin-positive versus class III β-tubulin-negative cells were more prone to migrate into the wound area. The asterisks indicate class III β-tubulin-negative cell nuclei. Arrows indicate class III β-tubulin-positive cells. Scale bar: 50 μm.
vascular networks during angiogenesis (fig. 4).

Upregulation by pericytes in adult rat mesenteric micro-
tro together with our observations of class III β-tubulin
expression in vitro. Both issues will prove critical for applying
the class III β-tubulin siRNA group was 35% smaller
compared to the nontargeting control siRNA group (0.45 ±
0.04 vs. 0.69 ± 0.06; p = 0.002) and 27% smaller than the
sham control group (0.45 ± 0.04 vs. 0.62 ± 0.02; p = 0.009;
fig. 6d). In the class III β-tubulin siRNA treatment groups,
cells were both positive and negative for class III β-tubulin,
indicating that the siRNA knockdown effect was not ho-
mogeneous. Class III β-tubulin+ cells were frequently
found leading migration into the scratch area in the target
siRNA groups (fig. 6e, f). The effect of class III β-tubulin
inhibition on the scratch wound closure is consistent with
reports by others [94] that have shown that class III β-
tubulin in vitro can influence cell motility and prolifera-
tion. Our results in the context of pericytes suggest
that expression of class III β-tubulin by pericytes during
angiogenesis would influence their ability to be recruited
to newly forming capillary sprouts. Undoubtedly, further
follow-up studies including various pericyte sources and
additional assays are required, but the preliminary results
do motivate the need to understand the different roles of
specific pericyte subpopulations. If we can define specific
pericyte subpopulations, as in the endothelial tip versus
stalk cell scenario, then we might be able to differenti-
ate the importance of one pericyte type as opposed to an-
other.

Summary

Pericytes are essential for angiogenesis and vessel maturation.
Their specific mechanisms during these processes
remain unclear due to the heterogeneity of pericyte
identities across individual microvascular networks and
different tissues. Although this has been a barrier in
the past, transient pericyte phenotypes during capillary
sprouting suggest that subpopulations perform specific
angiogenic functions. The transient expression of NG2
and class III β-tubulin implicate two neural phenotypes
in pericyte function during angiogenesis. Correlating
known angiogenic dynamics with such subpopulations
represents an opportunity to pinpoint specialized peri-
cyte functions based on phenotype, or else target pericyte
mechanisms for therapeutic benefits. Accordingly, defin-
ing specific pericyte subpopulations involved in angiogen-
esis versus vessel maturation will be advantageous,
and maybe compulsory, for future studies that aim to elu-
cidate pericyte mechanisms. As we attempt to focus on
specific spatial and temporal pericyte subpopulations, the
need for tunable model systems will emerge. The devel-
oment of such in vivo and ex vivo systems that enable

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pericytes to be dynamically probed within intact microvascular networks will help advance our understanding of pericyte identity [29, 92]. In the meantime, the discoveries of different pericyte subpopulations offer new foundations for the future.

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References

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