SCE 0704 Public Evidence Appendix

Angiogenesis

Literature review date: September 9, 2026

Controlling principle. Therapeutic angiogenesis requires more than new endothelial structures; vascular growth must mature into stable, functional perfusion, while pathological angiogenesis remains a product- and patient-specific safety consideration.

Mechanistic evidence map

Domain	What is evaluated	Interpretive boundary
Endothelial-cell activation	Migration, proliferation, survival, barrier behavior, adhesion molecules, and vascular-structure formation.	Tube formation or proliferation in vitro supports mechanism but does not establish functional vessels in vivo.
Vascular growth factors	VEGF, fibroblast growth factors, angiopoietins, HGF, PDGF, and coordinated signaling networks.	Presence of a growth factor does not establish functional sufficiency or clinical benefit.
Pericyte interactions	Pericyte recruitment, attachment, mural-cell support, basement membrane organization, and microvascular remodeling.	Early endothelial sprouts without supporting cells may remain unstable, leaky, or regress.
Vessel maturation	Lumen formation, stabilization, permeability, perfusion, structural integration, and durability.	Microvessel density alone does not prove useful blood flow or tissue oxygen delivery.
Pathological angiogenesis risks	Unwanted vascular growth in settings such as tumors or proliferative retinal disease.	Proangiogenic signaling may be beneficial or harmful depending on product, dose, route, timing, tissue, and patient biology.

Key evidence conclusions

New vascular structures are not synonymous with functional perfusion. Mature vessels require stabilization, appropriate permeability, integration with the circulation, and useful blood flow.

Angiogenesis is network-driven. No single detected growth factor establishes the magnitude, durability, or clinical relevance of an angiogenic response.

Timing and context matter. Hypoxia, inflammation, tissue injury, dose, route, product characteristics, and recipient biology can alter the vascular response.

Potential benefit and risk must both be evaluated. The same broad proangiogenic biology that may support ischemic repair could be undesirable in settings where abnormal vascular growth is harmful.

Principal references

1. Galipeau J, Sensebé L. Mesenchymal stromal cells: clinical challenges and therapeutic opportunities. Cell Stem Cell. 2018;22:824-833.

2. Caplan AI, Correa D. The MSC: an injury drugstore. Cell Stem Cell. 2011;9:11-15.

3. Phinney DG, Pittenger MF. Concise review: MSC-derived exosomes for cell-free therapy. Stem Cells. 2017;35:851-858.

4. Carmeliet P, Jain RK. Molecular mechanisms and clinical applications of angiogenesis. Nature. 2011;473:298-307.

5. Relevant contemporary literature concerning MSC/EV endothelial signaling, vascular growth factors, pericyte biology, vessel maturation, perfusion, and pathological angiogenesis.