SCE 0706 Public Evidence Appendix

Mitochondrial transfer

Literature review date: September 10, 2026

Controlling principle. Mitochondrial transfer is a specific mechanistic hypothesis; direct organelle movement, route, persistence, functional causality, and human relevance must be demonstrated rather than inferred from improved metabolic markers alone.

Mechanistic evidence map

Domain	What is evaluated	Interpretive boundary
Tunneling nanotubes	Direct cell-to-cell membrane bridges, actin dependence, organelle movement, donor/recipient identity, and persistence.	A visible nanotube or moving fluorescent signal does not by itself prove viable mitochondrial transfer or functional integration.
EV-associated transfer	Mitochondrial DNA, protein, RNA, fragments, or mitochondria-containing extracellular particles and their uptake.	Detection of mitochondrial material in an EV preparation does not establish intact-organelle transfer; contamination and nonvesicular material must be excluded.
Functional consequences	Oxidative phosphorylation, ATP production, membrane potential, respiration, survival, and metabolic rescue.	Improved metabolism after coculture supports the hypothesis only if transfer is shown to be causally necessary for the effect.
Evidence limitations	Tracking artifacts, label transfer, cell fusion, phagocytosis, route ambiguity, dose, biodistribution, persistence, and human in-vivo relevance.	Most evidence remains preclinical; experimental transfer should not be equated with established clinical benefit.

Key evidence conclusions

Observation is not causality. Direct tracking, route discrimination, and experiments that block transfer are stronger than simple colocalization or metabolic improvement.

Transferred material must be characterized. Whole mitochondria, mitochondrial fragments, proteins, DNA, RNA, and vesicle-associated cargo are biologically different and should not be conflated.

Function and persistence matter. A transferred organelle must remain sufficiently intact and functional to contribute meaningfully to recipient-cell metabolism.

Human relevance remains the translational boundary. Frequency, organ distribution, persistence, recipient-cell targeting, dose-response, safety, and contribution to clinical outcomes remain incompletely defined.

Principal references

1. Spees JL, Olson SD, Whitney MJ, Prockop DJ. Mitochondrial transfer between cells can rescue aerobic respiration. Proc Natl Acad Sci U S A. 2006;103:1283-1288.

2. Islam MN, Das SR, Emin MT, et al. Mitochondrial transfer from bone-marrow-derived stromal cells to pulmonary alveoli protects against acute lung injury. Nat Med. 2012;18:759-765.

3. Jackson MV, Morrison TJ, Doherty DF, et al. Mitochondrial transfer via tunneling nanotubes is an important mechanism by which mesenchymal stem cells enhance macrophage phagocytosis. Stem Cells. 2016;34:2210-2223.

4. Phinney DG, Di Giuseppe M, Njah J, et al. Mesenchymal stem cells use extracellular vesicles to outsource mitophagy and shuttle microRNAs. Nat Commun. 2015;6:8472.

5. Relevant contemporary literature concerning mitochondrial transfer, tunneling nanotubes, extracellular-vesicle-associated mitochondrial material, organelle tracking, functional rescue, and methodological limitations.