

hASCs in a Rat Mesenteric Model of Angiogenesis:
Positional, Histomorphic, and Functional Evidence of a Perivascular Phenotype

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INTRODUCTION: Human adipose-derived stromal cells (hASCs) have been shown to differentiate into endothelial cells, form vascular-like sprouts in matrigel, enhance neovascularization in an ischemic hindlimb model, and secrete angiogenic and anti-apoptotic growth factors, suggesting a potential for this cell population in therapeutic vascularization. In a rat model of angiogenesis, we investigate, at the single cell level, the potential of hASCs to contribute to microvascular remodeling when injected *in vivo*, and we have found that injected hASCs migrate to the abluminal surface of microvessels, alter their cell morphology to conform to the curvature of the microvessel in a manner that is consistent with perivascular cell behavior, augment vascular density, and express perivascular cell markers.

METHODS: Human ASCs and lung fibroblasts were isolated, expanded in culture, labeled with the fluorescent marker DiI, and injected into adult nude rat mesenteries stimulated to undergo microvascular remodeling via Compound 48-80, a mast cell degranulating agent that induces inflammation. 10, 30, and 60 days after cell injection, mesenteric tissues were harvested and processed with immunohistochemical techniques to determine hASC quantity, positional fate in relation to microvessels, expression of endothelial and perivascular cell markers, as well as vascular density.

RESULTS: After 60 days, 29% of total hASCs exhibited perivascular morphologies compared to 11% of injected human lung fibroblasts (hLFs). Total vascular density was increased 46% in tissues treated with hASCs over age-matched controls that did not receive cell injections. Some hASCs exhibiting perivascular morphologies also expressed markers characteristic of vascular pericytes: smooth muscle α -actin (10%) and NG2 (8%).

CONCLUSIONS: This study demonstrates that hASCs can exhibit perivascular morphology when injected *in vivo*, express pericyte lineage markers, and contribute to increases in microvascular density during angiogenesis associated with inflammation.