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IFATS collection: Adipose stromal cells adopt a proangiogenic phenotype under the influence of hypoxia.

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Evolving evidence suggests a possible role for adipose stromal cells (ASCs) in adult neovascularization, although the specific cues that stimulate their angiogenic behavior are poorly understood. We evaluated the effect of hypoxia, a central mediator of new blood vessel development within ischemic tissue, on proneovascular ASC functions. Murine ASCs were exposed to normoxia (21% oxygen) or hypoxia (5%, 1% oxygen) for varying lengths of time. Vascular endothelial growth factor (VEGF) secretion by ASCs increased as an inverse function of oxygen tension, with progressively higher VEGF expression at 21%, 5%, and 1% oxygen, respectively. Greater VEGF levels were also associated with longer periods in culture. ASCs were able to migrate towards stromal cell-derived factor (SDF)-1, a chemokine expressed by ischemic tissue, with hypoxia augmenting ASC expression of the SDF-1 receptor (CXCR4) and potentiating ASC migration. In vivo, ASCs demonstrated the capacity to proliferate in response to a hypoxic insult remote from their resident niche, and this was supported by in vitro studies showing increasing ASC proliferation with greater degrees of hypoxia. Hypoxia did not significantly alter the expression of endothelial surface markers by ASCs. However, these cells did assume an endothelial phenotype as evidenced by their ability to tubularize when seeded with differentiated endothelial cells on Matrigel. Taken together, these data suggest that ASCs upregulate their proneovascular activity in response to hypoxia, and may harbor the capacity to home to ischemic tissue and function cooperatively with existing vasculature to promote angiogenesis.