

Characterization of hASC Adhesion Under Static and Flow Conditions

BAILEY AM, AMOS PJ, KATZ AJ, PEIRCE SM.

Department of Biomedical Engineering, University of Virginia, Charlottesville, VA

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Introduction: Although previous studies have shown that i.v.-injected human adipose-derived stromal cells (hASCs) have the ability to travel through the circulation and home to remote sites of tissue injury, there has been no previous work addressing their functional adherence to endothelial ligands and extracellular matrix proteins. Furthermore, cultured hASCs are responsive to hypoxia and, when injected in vivo, partially recover ischemic hindlimbs in animal models. Here, we characterize the differential adhesion characteristics of hypoxic versus normoxic cells. This will lead to a better understanding of the mechanisms of mobilization and extravasation of native hASCs, present at a site of injury in fat depots, to nearby vasculature, and may offer a mode through which to increase the efficiency of targeted therapeutic cell delivery.

Methods: Early passage hASCs were isolated, and expanded in culture under normoxic or hypoxic (0% oxygen) conditions for 48 hours before performing adhesion assays in parallel plate flow chamber at a flow rate of 1 dyne/cm² (cells assayed at P=2). Either Type 1 Collagen, fibronectin, fibrinogen, V-CAM1, I-CAM1, E-selectin, P-selectin, or L-selectin was absorbed to the bottom plate of the chamber, and the cells were tested for their ability to initially capture to the surface under flow conditions and for their ability to firmly adhere under static conditions. Interactions were interpreted as being either positive or negative, while the frequency of capture events was quantified.

Results: The control TWEEN, fibrinogen, E and L-selectins failed to adhere either cell population under static or laminar flow conditions. Type I collagen and fibronectin positively adhered both cell populations under laminar flow and static conditions (100% of cells adhered), although only weak evidence for initial capture events and firm adhesion on P-selectin by 23% and on I-CAM1 by 83%. In contrast, on V-CAM1 substrates, the frequency of capture events was unchanged while the incidence of firmly adhered cells increased significantly with hypoxic pre-conditioning (77% increase in cell adherence).

Conclusions: These results suggest that hASCs can functionally bind to substrates presented by the endothelium in the presence of a physiologically relevant flow field. Furthermore, hASCs appear to alter their functional surface expression of adhesion molecules in response to hypoxia.