Functional analyses reveal the greater potency of preadipocytes compared with adipocytes as endothelial cell activator under normoxia, hypoxia, and TNFalpha exposure.

Abstract:
Obesity is associated with a state of chronic low-grade inflammation. Immune cells accumulate in white adipose tissue (WAT). The vascular endothelium plays an interactive role in these infiltration and inflammatory processes. Mature and hypertrophic adipocytes are considered as the major adipogenic cell type secreting proinflammatory cytokines in WAT. In contrast, the proinflammatory capacity of preadipocytes and their role in endothelial cell activation have been neglected so far. To gain new insights into this molecular and cellular cross-talk, we examined the proinflammatory expression and secretion of normoxia, hypoxia, and TNFalpha-treated human preadipocytes and adipocytes (SGBS cells) and their impact on human microvascular endothelial cell (HMEC-1) function. In this study, stimulation of HMEC-1 with conditioned media (CM) from preadipocytes increased endothelial ICAM-1 expression and monocyte adhesion but not adipocyte-CM. After hypoxia and TNFalpha stimulation of SGBS cells, adipocyte-CM induced andpreadipocyte-CM enhanced the monocyte adhesion. Concordantly, the expression of proinflammatory adipokines was considerably higher in preadipocytes than in adipocytes. SGBS-CM upregulated the phosphorylation of three MAPK pathways, STAT1/3, and c-Jun in HMEC-1, whereas the NF-kappaB
pathway was not affected. Inhibitor experiments showed that monocyte/endothelial cell-cell adhesion and endothelial ICAM-1 expression was JNK and JAK-1/STAT1/3 pathway dependent and revealed IL-6 as a major mediator in CM increasing monocyte/endothelial cell-cell adhesion via the STAT1/3 pathway. Our study shows that preadipocytes rather than adipocytes operate as potent activators of endothelial cells. This can be enhanced in preadipocytes and induced in adipocytes by TNFalpha and hypoxia in a manner similar to what may occur in WAT in the etiology of obesity.