LIGHT (TNFSF14) inhibits adipose differentiation without affecting adipocyte metabolism.

The member of the tumor necrosis factor family LIGHT (lymphotoxin-like inducible protein that competes with glycoprotein D for herpesvirus entry on T cells; TNFSF14 (tumor necrosis factor super family protein 14) is primarily expressed in lymphocytes, in which it induces the expression of pro-inflammatory cytokines and alterations of lipid homeostasis. Recently, the protein was shown to be upregulated in obesity and to induce cytokine secretion from adipocytes. Using an automated complementary DNA (cDNA) screen, LIGHT was identified to inhibit adipose differentiation. As cellular models for adipogenesis mouse 3T3-L1, human SGBS (Simpson-Golabi-Behmel syndrome) and primary human preadipocytes differentiated in vitro were used as well as primary human adipocytes to study adipocyte functions. Analysis of lipid deposition by Oil Red O staining, mRNA expression by quantitative reverse transcriptase-PCR, nuclear factor (NF)-κB activation as well as protein secretion by enzyme linked immunosorbent assay and Luminex technology was performed. LIGHT was found to inhibit lipid accumulation in the three models of preadipocytes in a dose-dependent manner without cytotoxic effects. This inhibition of differentiation was probably because of interference at early steps of adipogenesis, as early exposure during differentiation showed the
strongest effect, as assessed by decreased peroxisome proliferator-activated receptor-\(\beta\) (PPAR\(\beta\)) and CCAAT/enhancer-binding protein-\(\beta\) (C/EBP\(\beta\)) mRNA expression. In contrast to TNF\(\alpha\), basal and insulin-stimulated glucose uptake and lipolysis of terminally differentiated mature adipocytes were not altered in the presence of LIGHT. At a concentration sufficient to inhibit differentiation, secretion of proinflammatory cytokines was not significantly induced and NF-\(\kappa\)B activity was only modestly induced compared with TNF\(\alpha\). LIGHT is a novel inhibitor of human adipocyte differentiation without adversely influencing central metabolic pathways in adipocytes.