T-lymphocyte infiltration in visceral adipose tissue: a primary event in adipose tissue inflammation and the development of obesity-mediated insulin resistance.

BACKGROUND: Adipose tissue inflammation may play a critical role in the pathogenesis of insulin resistance (IR). The present study examined the role of lymphocytes in adipose tissue inflammation and IR. METHODS AND RESULTS: In a mouse model of obesity-mediated IR, high-fat diet (HFD) induced IR already after 5 weeks, which was associated with a marked T-lymphocyte infiltration in visceral adipose tissue. In contrast, recruitment of macrophages was delayed with an increase of MAC3-positive staining and F4/80 mRNA expression after 10 weeks of HFD, suggesting a dissociation of macrophage invasion into adipose tissue and IR initiation. In patients with type 2 diabetes, lymphocyte content in adipose tissue biopsies significantly correlated with waist circumference, a marker of IR. Immunohistochemical staining of human adipose tissue revealed the presence of mainly CD4-positive lymphocytes as well as macrophage infiltration. Most macrophages were HLA-DR-positive, reflecting activation through IFNγ, a cytokine released from CD4-positive lymphocytes.

CONCLUSIONS: Proinflammatory T-lymphocytes are present in visceral adipose tissue and may contribute to
local inflammatory cell activation before the appearance of macrophages, suggesting that these cells could play an important role in the initiation and perpetuation of adipose tissue inflammation as well as the development of IR.

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