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Hypoxia is a potential risk factor for chronic inflammation and adiponectin reduction in adipose tissue of *ob/ob* and dietary obese mice

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Abstract:

Chronic inflammation and reduced adiponectin are widely observed in the white adipose tissue in obesity. However, the cause of the changes remains to be identified. In this study, we provide experimental evidence that hypoxia occurs in adipose tissue in obese mice and that adipose hypoxia may contribute to the endocrine alterations. The adipose hypoxia was demonstrated by a reduction in the interstitial partial oxygen pressure (PO_2), an increase in the hypoxia probe signal, and an elevation in expression of the hypoxia response genes in *ob/ob* mice. The adipose hypoxia was confirmed in dietary obese mice by expression of hypoxia response genes. In the adipose tissue, hypoxia was associated with an increased expression of inflammatory genes and decreased expression of adiponectin. In dietary obese mice, reduction in body weight by calorie restriction was associated with an improvement of oxygenation and a reduction in inflammation. In cell culture, inflammatory cytokines were induced by hypoxia in primary adipocytes and primary macrophages of lean mice. The transcription factor NF- κ B and the TNF- α gene promoter were activated by hypoxia in 3T3-L1 adipocytes and NIH3T3 fibroblasts. In addition, adiponectin expression was reduced by hypoxia, and the reduction was observed in the gene promoter in adipocytes. These data suggest a potential role of hypoxia in the induction of chronic inflammation and inhibition of adiponectin in the adipose tissue in obesity.

Key-words: Partial oxygen pressure, obesity, type 2 diabetes, insulin resistance