

Worsening of Obesity and Metabolic Status Yields Similar Molecular Adaptations in Human Subcutaneous and Visceral Adipose Tissue: Decreased Metabolism and Increased Immune Response

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Abstract:

Context: It is not known whether biological differences reported between sc adipose tissue (SAT) and visceral adipose tissue (VAT) depots underlie the pathogenicity of visceral fat.

Objective: We compared SAT and VAT gene expression according to obesity, visceral fat accumulation, insulin resistance, and presence of the metabolic syndrome.

Design: Subjects were assigned into four groups (lean, overweight, obese, and obese with metabolic syndrome).

Setting: Subjects were recruited at a university hospital.

Patients: Thirty-two women were included.

Main Outcome Measures: Anthropometric measurements, euglycemic-hyperinsulinemic clamps, blood analyses, and computed tomography scans were performed, and paired samples of SAT and VAT were obtained for DNA microarray-based gene expression profiling.

Results: Considering the two fat depots together, 1125 genes were more and 1025 genes were less expressed in lean compared with metabolic syndrome subjects. Functional annotation clustering showed, from lean to metabolic syndrome subjects, progressive down-regulation of metabolic pathways including branched-chain amino acid, fatty acid, carbohydrate, and mitochondrial energy metabolism and up-regulation of immune response genes involved in toll-like receptor, TNF, nuclear factor- κ B, and apoptosis pathways. Metabolism and immune response genes showed an opposite correlation with fat mass, fat distribution, or insulin resistance indices. These associations were similar in SAT and VAT, although about 1000 genes showed differential expression between SAT and VAT.

Conclusions: The increase in adiposity and the worsening of metabolic status are associated with a coordinated down-regulation of metabolism-related and up-regulation of immune response-related gene expression. Molecular adaptations in SAT prove as discriminating as those in VAT.

Full text: <https://doi.org/10.1210/jc.2010-1575>

