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HIV-1 INFECTION ALTERS MITOCHONDRIAL, METABOLIC AND ADIPOCYTOKINE GENE EXPRESSION IN SUBCUTANEOUS ADIPOSE TISSUE

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OBJECTIVES: The aetiopathogenic bases of HIV-1/highly active antiretroviral treatment (HAART)-associated lipodystrophy (HALS) are poorly known. However, this syndrome indicates that adipose tissue is highly sensitive to either HIV-1 infection, antiretroviral drugs or their combination. To distinguish among these aspects, a gene expression study was followed to establish major disturbances in adipose tissue from patients under different conditions.

METHODS: We assessed by quantitative real-time PCR (TaqMan, Applied Biosystems) the expression of marker genes corresponding to mitochondrial function, adipocyte differentiation and metabolism, and adipocytokines in subcutaneous adipose tissue (abdominal biopsies) from healthy controls, untreated HIV-1-infected patients, and HIV-1-infected patients treated with HAART with or without HALS.

RESULTS: Subcutaneous adipose tissue from HIV-1-infected patients contained lower concentrations of the mRNA of the mitochondrial DNA-encoded cytochrome *c* oxidase subunit II than that of controls. These concentrations decreased further in association with HAART and HALS. The expression of nuclear genes coding for mitochondrial proteins, for peroxisome proliferators-activated receptor-γ, and for adipocyte-specific markers was reduced in HIV-1- infected patients, treated or not, with respect to controls. In contrast, mRNA concentrations of uncoupling protein-3 and preadipocyte factor-1 increased in lipodystrophic HAART-treated patients. The genes coding for adipocytokines were strongly affected: tumour necrosis factor-α was upregulated whereas

adiponectin and leptin were downregulated in HIV-1-infected patients, treated or not. Thus, most of the alterations of gene expression were already present when naïve patients were compared with controls. Minor changes were associated with HAART or with the diagnosis of HALS.

CONCLUSIONS: Major disturbances in adipose tissue gene expression are already present in untreated HIV-1-infected patients, thus indicating a major role of HIV-1 infection itself in eliciting adipose tissue alterations that produce HALS.

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