Genes linked to energy metabolism and immunoregulatory mechanisms are associated with subcutaneous adipose tissue distribution in HIV-infected men.

OBJECTIVE: Genetic studies may help explain abnormalities of fat distribution in HIV-infected patients treated with antiretroviral therapy (ARV).

METHODS: Subcutaneous adipose tissue (SAT) volume measured by MRI in the leg, the lower trunk, the upper trunk, and the arm was examined in 192 HIV-infected White men, ARV-treated from the Fat Redistribution and Metabolic Change in HIV infection study. Single-nucleotide polymorphisms were assayed using the Illumina Human CNV370-quad beadchip. Multivariate and univariate genome-wide association analyses of the four SAT depots were implemented in PLINK software adjusted for age and ARV duration. Functional annotation analysis using Ingenuity Systems Pathway Analysis tool was carried out for markers with P lower than 10\(^{-3}\) near known genes identified by multivariate analysis.

RESULTS: Loci (rs10504906, rs13267998, rs921231) in or near the anion exchanger solute carrier family 26, member 7 isoform a (SLC26A7) were strongly associated with the upper trunk and the arm SAT (9.8\times10\(^{-7}\) \leq P < 7.8\times10\(^{-6}\)). Loci (rs193139, rs7523050, rs1761621) in and near a gene-rich region including G-protein-signaling modulator 2 (GPSM2) and syntaxin-binding protein 3 (STXBP3) were significantly associated with the lower body SAT depots.
Genes linked to energy metabolism and immunoregulatory mechanisms are associated with subcutaneous adipose tissue distribution in HIV-infected men. (9.9×10(-7) ≤P<9.5×10(-6)). GPSM2 is associated with cell division and cancer whereas STXBP3 is associated with glucose metabolism in adipocytes. Ingenuity Systems Pathway Analysis identified atherosclerosis, mitochondrial function, and T-cell-mediated apoptosis as processes related to SAT volume in HIV-infected individuals (P<5×10(-3)).

CONCLUSION: Our results are limited by the small sample size and replication is needed; however, this genomic scan uncovered new genes associated with metabolism and inflammatory pathways that may affect SAT volume in ARV-treated HIV-infected patients.

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