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INTERACTIONS BETWEEN T LYMPHOCYTES AND PREADIPOCYTES INCREASE HIV PRODUCTION AND APOPTOSIS OF LYMPHOCYTES AND BLOCK ADIPOCYTE DIFFERENTIATION

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BACKGROUND: Adipocyte depots are associated with lymph node aggregates, hence distinct functional interactions may occur between activated lymphocytes and adipocytes. We investigated the potential role of such interactions in the pathogenesis of HIV lipodystrophy.

METHODS: Primary human pre-adipocytes (stromal vascular cells) or 3T3-L1 mouse pre-adipocytes were incubated with uninfected or HIV-infected lymphocytes for varying durations, with or without direct contact, and HIV production, cell cycle characteristics, apoptosis and biochemical functions were measured.

RESULTS: Exposure of acutely HIV-infected T lymphocytes to human pre-adipocytes led to markedly increased HIV-1 production in the lymphocytes. Chronically HIV-infected lymphocytes exposed to pre-adipocytes underwent both a block in G2/M of the cell cycle and an increase in apoptosis. These effects were observed without direct contact between the pre-adipocytes and HIV-infected lymphocytes, as well as after exposure to conditioned media, indicating that the effects were mediated by soluble, secreted factors. There was no change in the viability of uninfected lymphocytes exposed to pre-adipocytes. After treatment with standard adipocyte differentiation factors, pre-adipocytes experienced a reversible block in differentiation when pre-exposed to lymphocytes, as demonstrated by a reduction in Oil Red O staining and quantitative adipocyte gene expression. These effects were observed in both human and murine pre-adipocytes, indicating that they were not due to direct HIV-1 infection. The same results

were observed with three different human T lymphocyte lines, but not with two human macrophage lines.

CONCLUSIONS: Significant interactions between preadipocytes and HIV-infected lymphocytes increase HIV-1 production, G2/M arrest of the cell cycle, as well as apoptosis in lymphocytes, and cause a marked differentiation block in pre-adipocytes. The interactions are mediated by soluble factors – potentially cytokines, adipokines or HIV-1 Vpr. Identifying these factors and specifying mechanisms of action are important for understanding the pathophysiology of HIV lipodystrophy.

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