Fatty Acid Profiles Altered by HIV Infection Persist Despite Suppressive Antiretroviral Therapy (ART) and are Associated with Immune Activation in the ACTG 5248 Study

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Abstract

Background

HIV infection and ART alter lipid profiles. Among HIV-infected (HIV+) populations the concentrations of various lipid classes (i.e. ceramides, lysophosphatidylcholine, LPC) and their saturated (SaFAs), monounsaturated (MUFA), and polyunsaturated fatty acid (PUFA) composition are related to inflammation and cardiovascular disease risk. Associations among changes in the lipidome and immune activation in persons initiating ART have not been described.

Methods

Plasma concentrations (µM) of lipid species (N=1,300) and FA composition (mol%) were measured by differential mobility spectroscopy (TrueMass Complex Lipid Panel, Metabolon), and markers of inflammation were measured by ELISA in plasma samples from HIV+ participants initiating raltegravir (RAL) based ART (N=35, baseline and week 48), and from HIV-individuals (N=13) of similar demographics. Analyses (paired t-tests, 2-sample t-tests, and Pearson correlations) were exploratory.

Results

Compared to levels in HIV- donors, the plasma concentrations of multiple lipid species are altered in HIV+ persons pre-ART (32.2% increased, 4.9% decreased, p<0.05) and at 48 weeks of ART (29.6% increased, 2.2% decreased, p<0.05). Levels of PUFAs (including 18:3, 20:4, and 20:5) are enriched in HIV+ compared to HIV doner pre-ART (p<0.01); levels of these PUFA species increased by 48 weeks of ART. Levels of SaFAs (including 16:0 and 18:0) tend to be enriched in HIV+ participants (pre-and post-ART). Levels of palmitic acid (16:0) were positively correlated with sCD14, and the composition of LPC is enriched for SaFAs (18:3, 216 µM, 184 µM, p<0.003, p<0.001), and the composition of LPC is enriched for SaFAs (16:0 and 18:0) among HIV+ individuals. Also at baseline and week 48, several LPC molecules containing SaFAs were positively correlated with sCD14, D-dimer, and TNFR1 (p<0.01, for all) and levels of PUFA containing LPC (18:3, 20:5, 22:5, 22:6) were positively correlated with CD4 counts and inversely correlated with sCD14 and IL-6 (all p<0.01).

Conclusions

The composition of the lipidome is altered in HIV-infection and changes with ART. Alterations in SaFAs were generally associated with inflammatory markers and may contribute to immune activation and comorbid disease pathogenesis.

Table 1: Demographic information

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Figure 1. Plasma levels of lipid species are altered by HIV infection and by ART. Blood samples were collected in EDTA-containing tubes were centrifuged prior to thawing and analyzed in batch. Measurement of the concentration and composition of approximately 1,300 lipid metabolites was performed by Metabolon (TrueMass Complex Lipid Panel, Metabolon, Research Triangle Park, North Carolina, U.S.A.).