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Muscle mitochondrial DNA and RNA copy number/cell are reduced in treatment-naïve HIV-infected people, regardless of glucose in/tolerance

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BACKGROUND: Mitochondrial DNA (mtDNA) depletion may be a mediator of metabolic syndromes in HIV-infected people treated with highly active antiretroviral therapy (HAART). Skeletal muscle is mt-rich and the primary site for glucose disposal.

HYPOTHESIS: Muscle mtDNA depletion is associated with HIV-metabolic syndromes.

METHODS: We quantified muscle mtDNA and mtRNA copy number per cell in vastus lateralis muscle samples (10mg) obtained after an overnight fast from 13 HIV-infected subjects with impaired glucose tolerance (HIV+IGT), 10 HIV+ with normal glucose tolerance (HIV+NGT), 12 HIV-seronegative controls (CTRL), and correlated these with parameters of glucose lipid, and amino acid metabolism measured during a hyperinsulinaemic– euglycaemic clamp, NRTI use and serum markers of inflammation.

RESULTS: In comparison with CTRL, muscle mtRNA and mtDNA copies/cell were lower ($P < 0.05$) in HIV+NGT (–40 and –23%) and HIV+IGT (–38 and –29%), but not different between HIV+NGT and HIV+IGT. In comparison with CTRL, muscle mtRNA and mtDNA copies/cell were lower in treatment-naïve subjects and those on AZT- 3TC- or d4T-ddI-based regimens, but similar among these HIV-infected participants. Non-parametric bivariate correlations suggested that muscle mtRNA copies/cell was modestly associated with the duration of HIV-infection ($r = -0.34$, $P = 0.016$), serum C-reactive protein levels ($r = -0.40$, $P = 0.007$), and mildly associated with glucose disposal parameters (carbohydrate oxidation; $r = 0.20$, $P = 0.09$, and insulin sensitivity; $r = 0.23$, $P = 0.06$). For mtDNA, non-parametric bivariate correlations were modest for serum

triglycerides ($r=-0.36$, $P=0.003$), total cholesterol ($r=-0.34$, $P=0.004$), and serum IL-6 levels ($r=-0.36$, $P=0.01$), and mild for glucose disposal rate measured at high insulin levels (570–660 pM; $r=0.23$, $P=0.06$).

CONCLUSIONS: Lower mtDNA and mtRNA levels predict a reduced capacity of muscle mt to synthesize proteins, regardless of glucose in/tolerance status. Although not definitive in this cross-sectional study, the mediator(s) of muscle mtDNA and mtRNA depletion appear more related to HIV-associated factors and less related to metabolic syndromes or HAART components.

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