**The Mechanism of Protease Inhibitor Induced Dyslipidemia and Lipodystrophy**

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**Background:** Treatment with HAART is frequently accompanied by dyslipidemia and insulin resistance. In animal studies involving ritonavir, a commonly prescribed protease inhibitor linked to dyslipidemia in humans, the inhibition of proteasome degradation of the activated sterol regulatory element binding proteins (SREBPs) results in the accumulation of activated SREBPs that function as transcription factors for lipid biosynthetic pathway enzymes.
**Objective:** To analyze lipid metabolism genes in HIV-infected individuals with proven dyslipidemia on ritonavir-containing HAART (Group A), HIV+s not taking therapy (Group B) and HIV- volunteers (Group C).
**Methods:** Participants (n=20) underwent 6 mm skin biopsies to obtain subcutaneous adipose samples from the thigh and abdomen. Blood samples were analyzed by ultracentrifugation quantification of total cholesterol, triglycerides, LDL, and HDL. Additional testing was performed for Apo A/B, hs-CRP, insulin, glucose, leptin and adiponectin by standard enzymatic methods. Adipose tissue samples will be analyzed for mRNA levels by RT-PCR for SREBP, FAS, SCD and related lipid biosynthetic genes.
**Results:** Fifteen HIV+ (Group A=10 / Group B = 5) and 5 HIV- (Group C) participated. Demographic characteristics included a median age of 43 years; 2 women; and 5 African-Americans. The median total cholesterol was 236, 204, & 162 mg/dL for groups A, B & C, respectively (P=0.06). The median triglyceride levels were 284, 128, & 86 mg/dL for groups A, B & C, respectively (P=0.003). There no differences in the levels of insulin, adiponectin, LDL, HDL or apoA1. There were significant differences between group comparisons in the levels of glucose, leptin, apo B, hs-CRP, remnant lipoproteins, Lp(a), and VLDL.
**Conclusions:** We successfully selected groups with differences in metabolic parameters. Gene experiments are currently in progress to explain the observed differences in metabolic phenotypes. HIV infection and antiretroviral therapy likely alter lipid metabolism consistent with a higher risk for atherosclerotic heart disease.