INVESTIGATING MARKERS OF CELLULAR AGING IN HUMAN IMMUNODEFICIENCY VIRUS INFECTED AND UNINFECTED ADULTS

by

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Abstract

Background: Despite successful combination antiretroviral therapy (cART), people living with HIV have shorter lifespans than the general population. Leukocyte telomere length (LTL) and mitochondrial DNA (mtDNA) oxidative damage are two frequently studied markers of aging that have recently been linked. Telomerase extends telomeres in highly proliferative tissues and is believed to play a protective role against oxidative stress in mitochondria. Given that both HIV and cART have the potential to accelerate cellular aging processes, we sought to measure LTL and mtDNA apparent oxidative damage (AOD) in the context of HIV infection and treatment.

Methods: Demographic and clinical data and whole blood were collected from adults aged 19-75 enrolled in a prospective cohort on HIV therapy and aging (CARMA). LTL were measured by qPCR. Variables statistically correlated with LTL on univariate analysis ($p<0.15$) were candidates for a multivariate model. A subset of subjects with LTL data was selected to explore the relationship between LTL and mtDNA AOD, as measured by a quantitative long PCR based assay.

Results: Of the 395 study participants, 58% were HIV infected, 76% were women, and 71% were current or previous smokers. In a multivariate model of all participants, older age, HIV infection, active hepatitis C virus (HCV) infection, and smoking were associated with shorter LTL. Smoking was associated with shorter LTL only in HIV uninfected subjects. Among the latter, age and smoking were independently related to shorter LTL. In contrast, in two models among HIV infected individuals, age and having either active HCV or a peak HIV plasma viral load ≥100,000 copies/ml were associated with shorter LTL. Other HIV disease or cART parameters were unrelated to LTL. In the 115 subjects for whom mtDNA AOD was measured, there was no relationship between AOD and age, HIV status or LTL.

Conclusions: HIV infection was independently associated with shorter LTL in this cohort and this was related to peak viremia. Future studies should examine the effects of early HIV and HCV therapy, as well as smoking cessation, on LTL. The mtDNA AOD results suggest that more validation work is needed for use of this assay with clinical samples.