Association of chemokine receptor gene (CCR2-CCR5) haplotypes with acquisition and control of HIV-1 infection in Zambians.

BACKGROUND: Polymorphisms in chemokine (C-C motif) receptors 2 and 5 genes (CCR2 and CCR5) have been associated with HIV-1 infection and disease progression. We investigated the impact of CCR2-CCR5 haplotypes on HIV-1 viral load (VL) and heterosexual transmission in an African cohort. Between 1995 and 2006, cohabiting Zambian couples discordant for HIV-1 (index seropositive and HIV-1 exposed seronegative {HESN}) were monitored prospectively to determine the role of host genetic factors in HIV-1 control and heterosexual transmission. Genotyping for eight CCR2 and CCR5 variants resolved nine previously recognized haplotypes. By regression and survival analytic techniques, controlling for non-genetic factors, we estimated the effects of these haplotypic variants on a) index partner VL, b) seroconverter VL, c) HIV-1 transmission by index partners, d) HIV-1 acquisition by HESN partners.

RESULTS: Among 567 couples, 240 virologically linked transmission events had occurred through 2006. HHF*2 homozygosity was associated with significantly lower VL in seroconverters (mean beta = -0.58, log10 P = 0.027) and the HHD/HHE diplotype was associated with significantly higher VL in the seroconverters (mean beta = 0.54, log10 P = 0.014) adjusted for age and gender in multivariable model. HHD/HHE was associated with more rapid acquisition of infection by the HESNs (HR = 2.0, 95% CI = 1.20-3.43, P =
0.008), after adjustments for index partner VL and the presence of genital ulcer or inflammation in either partner in Cox multivariable models. The HHD/HHE effect was stronger in exposed females (HR = 2.1, 95% CI = 1.14-3.95, P = 0.018).

CONCLUSIONS: Among Zambian discordant couples, HIV-1 coreceptor gene haplotypes and diplotypes appear to modulate HIV-1 VL in seroconverters and alter the rate of HIV-1 acquisition by HESNs. These associations replicate or resemble findings reported in other African and European populations.

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