ABSTRACT

OBJECTIVE::

We evaluated genetic variants in 51 candidate genes encoding proteins that interact with HIV-1 during the virus life cycle for association with HIV-1 outcomes in an African cohort.

METHODS::

Using a nested case-control study within a cohort of heterosexual HIV-1 serodiscordant couples, we genotyped 475 haplotype-tagging (tagSNPs) and 18 Single Nucleotide Polymorphisms (SNPs) previously associated with HIV-1 transmission and/or progression (candidate SNPs) in 51 host genes. We used logistic and Cox proportional hazards regression with adjustment for sex, age, and population stratification to detect SNP associations with HIV-1 acquisition, plasma HIV-1 set-point, and a composite measure of HIV-1 disease progression. Significance thresholds for tagSNP, but not candidate SNP, associations were subjected to Bonferroni correction for multiple testing.

RESULTS::

We evaluated 491 HIV-1 infected and 335 HIV-1 uninfected individuals for 493 SNPs, 459 of which passed quality control filters. Candidate SNP PPIA rs8177826 and haplotype tagging SNP SMARCB1 rs6003904 were significantly associated with HIV-1 acquisition risk (odds ratio [OR] = 0.14, p=0.03, and 2.11, pcorr= 0.01, respectively). Furthermore, the TT genotype for CCR5 rs1799988 was associated with a mean 0.2 log10 copies/mL lower plasma HIV-1 RNA set-point (p = 0.04). We also identified significant associations with HIV-1 disease progression for variants in FUT2 and MBL2.

CONCLUSION::

Using a targeted gene approach, we identified variants in host genes whose protein products interact with HIV-1 during the virus replication cycle and were associated with HIV-1 outcomes in this African cohort.