Abstract

Objective:

We evaluated the association of single nucleotide polymorphisms (SNPs) in *TLR*s with infant HIV-1 acquisition and viral control.

Design:

Infant HIV-1 outcomes were assessed in a Kenyan perinatal HIV-1 cohort.

Methods:

Infants were genotyped for six candidate and 118 haplotype-tagging polymorphisms in *TLRs* 2, 3, 4, 7, 8, and 9, *MYD88* and *TIRAP*. Cox proportional hazards and linear regression were performed to assess associations with time to HIV-1 acquisition, time to infant mortality, and peak viral load.

Results:

Among 368 infants, 56 (15%) acquired HIV-1 by month 1 and 17 (4.6%) between 1 and 12 months. Infants with the *TLR9* 1635A (rs352140) variant were more likely to acquire HIV-1 by 1 month [hazard ratio=1.81, 95% confidence interval (CI)=1.05–3.14, P=0.033] and by 12 months (hazard ratio=1.62, CI=1.01–2.60, P =0.044) in dominant models adjusted for maternal plasma HIV-1 RNA level and genetic ancestry. Among 56 infants infected at 1 month of age or less, at least one copy of the *TLR9* 1635A allele was associated with a 0.58 $\log_{10}$ copies/ml lower peak viral load (P=0.002). Female infants with at least one copy of the *TLR8* 1G (rs3764880) variant had a 0.78 $\log_{10}$ copies/ml higher peak viral load (P=0.0009) and having at least one copy of the C allele for a haplotype tagging *TLR7* variant (rs1634319) was associated with a 0.80 $\log_{10}$ copies/ml higher peak viral load in female infants (P=0.0003).

Conclusion:

In this African perinatal cohort, we found several *TLR* polymorphisms associated with HIV-1 acquisition and progression. Defining mechanisms for these *TLR* associations may inform HIV-1 prevention strategies that leverage innate responses.