Interleukin-10 (IL-10) pathway: genetic variants and outcomes of HIV-1 infection in African American adolescents.

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Abstract

BACKGROUND: Immunological and clinical outcomes can vary considerably at the individual and population levels during both treated and untreated HIV-1 infection. Cytokines encoded by the interleukin-10 gene (IL10) family have broad immunomodulatory function in viral persistence, and several SNPs in the IL10 promoter sequence have been reported to influence pathogenesis or acquisition of HIV-1 infection.

METHODOLOGY/PRINCIPAL FINDINGS: We examined 104 informative SNPs in IL10, IL19, IL20, IL24, IL10RA and IL10RB among 250 HIV-1 seropositive and 106 high-risk seronegative African American adolescents in the REACH cohort. In subsequent evaluation of five different immunological and virological outcomes related to HIV-1 infection, 25 SNPs were associated with a single outcome and three were associated with two different outcomes. One SNP, rs2243191 in the IL19 open reading frame (Ser to Phe substitution) was associated with CD4(+) T-cell increase during treatment. Another SNP rs2244305 in IL10RB (in strong linkage disequilibrium with rs443498) was associated with an initial decrease in CD4(+) T-cell by 23 ± 9% and 29 ± 9% every 3 months (for AA and AG genotypes, respectively, compared with GG) during ART-free period. These associations were reversed during treatment, as CD4(+) T-cell increased by 31 ± 0.9% and 17 ± 8% every 3 months for AA and AG genotype, respectively.

CONCLUSIONS/SIGNIFICANCE: In African Americans, variants in IL10 and related genes

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might influence multiple outcomes of HIV-1 infection, especially immunological response to HAART. Fine mapping coupled with analysis of gene expression and function should help reveal the immunological importance of the IL10 gene family to HIV-1/AIDS.

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