Abstract

BACKGROUND:

The immunologic findings that most consistently correlate with resistance in human schistosomiasis are high levels of IgE and low levels of IgG4. We have genotyped gene and promoter polymorphisms of cytokines associated with regulation of these isotypes in a cohort of men occupationally exposed to Schistosoma mansoni in western Kenya and evaluated their patterns with respect to resistance and susceptibility to reinfection after treatment and cure with praziquantel (PZQ).

METHODOLOGY/PRINCIPAL FINDINGS:

In this cohort, polymorphisms in IL-4 (-590T high IgE), IL-13 (-1055T high producer) and IFN-gamma (+874A high producer) demonstrated several correlations with resistance to reinfection. Resistance to reinfection was significantly correlated with the heterozygous IL-4 -590 genotype C/T (OR 3.5, [CI 1.2, 10.2]) compared to T/T. Among men with a homozygous IL-13 genotype CC/TT, having a T allele at the IFN-gamma +874 position increased the odds of resistance relative to individuals with the IFN-gamma +874 A/A genotype (OR = 17.5 [CI 3.0, 101.5]). Among men with homozygous A/A IFN-gamma genotype, the heterozygous IL-13 genotype C/T was associated with resistance relative to the homozygous C/C or T/T genotypes (OR = 22.5 [CI 3.5, 144.4]). No increases in odds of resistance were found in relation to the IL-13 genotype among those with a T allele in the IFN-gamma gene or in relation to the IFN-gamma genotype among those with a heterozygous IL-13 genotype. Calculation of the attributable proportion of resistance showed a significant synergistic interaction between IL-13 -1055 C/T and IL-4 -590 C/T.

CONCLUSIONS:

The identified polymorphisms do not by themselves confer resistance or susceptibility, but we propose that these genotypes allow the resistant phenotype to be developed and expressed upon suitable immune exposure. Based on the literature, these polymorphisms contribute to the regulation of their respective cytokines, likely leading to downstream differences in the production and interrelationships of critical defense mechanisms.