
Abstract

The region of human chromosome 6 containing the MHC has been identified as influencing asthma and atopy (allergy) by several genome-wide searches. The MHC contains many genes with potential effects on innate and specific immunity. As a first step in dissecting MHC influences on asthma and its underlying quantitative phenotypes, we have examined the HLA-DRB1 locus in a population sample consisting of 1004 individuals from 230 families from the rural Australian town of Busselton. The locus was strongly associated with the (log(e)) total serum IgE concentration, accounting for 4.0% of the sigma(2) (variance) in that trait (multi-allelic test, P=0.00001). The locus also influenced specific IgE titres to common allergens (multi-allelic tests, 2.8% sigma(2) for the house dust mite allergen Der p I, P=0.0013; 3.0% of sigma(2) for Der p II, P=0.0007; and 2.1% of sigma(2) for the cat allergen Fel d I, P=0.014). No associations were found to the categorical phenotype of asthma, or to the quantitative traits of peripheral blood eosinophil counts and bronchial hyper-responsiveness. Transmission disequilibrium tests excluded genetic admixture as a cause of false-positive findings. The results indicate that HLA-DRB1 alleles modulate the total serum IgE concentration and IgE responses to allergens, but do not account for the previous observations of linkage of asthma to the MHC.