Abstract

The major histocompatibility complex (MHC) is known to have a role in the development of non-melanoma skin cancer (NMSC), although the genes and mechanisms involved have yet to be determined. To identify the susceptibility locus for NMSC within the MHC, we used a collection of well-defined polymorphic microsatellite markers from the Human leucocyte antigen (HLA) region for an association analysis of 150 cases with NMSC and 200 healthy controls selected from the Busselton population in Western Australia. High-resolution mapping was undertaken using a total of 40 highly polymorphic markers located at regular intervals across the HLA region (3.6Mb). Polymerase chain reaction (PCR) analysis was initially performed on pooled DNA markers to detect those markers that showed different allele profiles. Statistically significant differences in allelic frequencies (differentiating alleles) were found between cases and controls at three polymorphic microsatellite loci within a 470-kb genomic susceptibility region ranging between 6 kb centromeric of the HLA-B gene and intron 5 of the DDR gene. Interestingly, this genome region corresponded completely with the psoriasis-susceptibility locus. The three differentiating alleles and another four markers outside the susceptibility region were then PCR tested by individual genotyping of cases and controls. The newly identified susceptibility locus for NMSC within the MHC was found to be significantly different between the cases and controls by comparisons of allele frequencies at the three differentiating loci estimated from DNA pools and then confirmed by individual genotyping. This is the first study using high density microsatellite markers to localize a NMSC susceptibility region within the human genome.