Genetic Variants Associated With Nasopharyngeal Carcinoma Susceptibility in Malaysian Chinese

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Nasopharyngeal carcinoma (NPC) is a complex multi-factorial disease with a distinct geographical and racial distribution. In endemic regions, NPC is closely associated with Epstein-Barr virus infection, environmental and genetic factors. In Malaysia, the incidence of NPC is higher in Chinese compared to Malays and Indians. We conducted case-control studies to identify genetic variants associated with NPC in Malaysian Chinese. The number of cases and controls were 444 and 481, respectively. Among the candidate genes investigated, two loci were associated with NPC susceptibility namely SPLUNC1 and CYP2E1. Further analysis of the associated SNPs in SPLUNC1 by electrophoretic mobility shift and luciferase reporter assays led to the identification of a functional variant in an enhancer of SPLUNC1 that might alter its transcriptional activity. A genome-wide association study was also performed using 600,077 autosomal SNPs in 184 NPC cases and 236 controls. The top 106 SNPs ($P < 1.0 \times 10^{-4}$) were later genotyped in an additional 260 cases and 245 controls. We identified multiple susceptibility loci which are consistent with other reports highlighting the strong association of the MHC I region with NPC susceptibility.