

Variant toll-like receptor4 (Asp299Gly and Thr399Ile alleles) and toll-like receptor2 (Arg753Gln and Arg677Trp alleles) in colorectal cancer.

ABSTRACT

The innate immune system recognizes the presence of bacterial products through the expression of a family of membrane receptors known as Toll-like receptors (TLRs). Polymorphisms in TLRs have been shown to be associated with increased susceptibility to diseases such as inflammatory bowel disease. The aim of this study was to determine whether there was a correlation between polymorphisms of TLR4 (Asp299Gly; Thr399Ile) and TLR2 (Arg677Trp; Arg753Gln) genes and risk of colorectal cancer. DNA from 60 colorectal carcinoma patients from 3 major races in Malaysia (22 Malays, 20 Chinese and 18 Indians) and blood from 50 apparently healthy individuals were evaluated. Control group were matched to study group by race and age. The polymorphisms were determined by Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP). Genotyping results showed two out of sixty tumour specimens (3.3%) harbored both variant TLR4 Asp299Gly and Thr399Ile alleles. In contrast, DNA isolated from blood cells of 50 apparently healthy individuals harbored wild type TLR4. In the case of TLR2 Arg753Gln genotyping, all of the fifty normal and 60 tumours were of the wild type genotype. TLR2 Arg677Trp genotyping showed a heterozygous pattern in all samples. However, this may not be a true polymorphism of the TLR2 gene as it is likely due to a variation of a duplicated (pseudogene) region. There was only a low incidence (2/60; 3.3%) of TLR4 polymorphism at the Asp299Gly and Thr399Ile alleles in colorectal cancer patients. All normal and tumour samples harbored the wild type TLR2 Arg753 allele. Our study suggests that variant TLR4 (Asp299Gly and Thr399Ile alleles) as well as TLR2 (Arg753Gln allele) are not associated with risk of colorectal cancer.

Keyword: Colorectal cancer; Polymorphisms; Toll-like receptors.