

Variant Alleles in XRCC1 Arg194Trp and Arg399Gln Polymorphisms Increase Risk of Gastrointestinal Cancer in Sabah, North Borneo

ABSTRACT

Background: The XRCC1 protein facilitates various DNA repair pathways; single-nucleotide polymorphisms (SNPs) in this gene are associated with a risk of gastrointestinal cancer (GIC) with inconsistent results, but no data have been previously reported for the Sabah, North Borneo, population. We accordingly investigated the XRCC1 Arg194Trp and Arg399Gln SNPs in terms of GIC risk in Sabah. Materials and Methods: We performed genotyping for both SNPs for 250 GIC patients and 572 healthy volunteers using a polymerase chain reaction-restriction fragment length polymorphism approach. We validated heterozygosity and homozygosity for both SNPs using direct sequencing. Results: The presence of a variant 194Trp allele in the Arg194Trp SNP was significantly associated with a higher risk of GIC, especially with gastric and colorectal cancers. We additionally found that the variant 399Gln allele in Arg399Gln SNP was associated with a greater risk of developing gastric cancer. Our combined analysis revealed that inheritance of variant alleles in both SNPs increased the GIC risk in Sabah population. Based on our etiological analysis, we found that subjects ≥ 50 years and males who carrying the variant 194Trp allele, and Bajau subjects carrying the 399Gln allele had a significantly increased risk of GIC. Conclusions: Our findings suggest that inheritance of variant alleles in XRCC1 Arg194Trp and Arg399Gln SNPs may act as biomarkers for the early detection of GIC, especially for gastric and colorectal cancers in the Sabah population.