XPD and XRCC1 polymorphisms and risk of nasopharyngeal cancer.

ABSTRACT

Introduction: According to the National Cancer Registry, nasopharyngeal carcinoma (NPC) is the third most common cancer among men in Peninsular Malaysia in 2006. Published evidence has shown that variation in certain DNA repair genes alter individual cancer risk and that the DNA repair system plays a crucial role in maintaining the integrity of the human genome. Xeroderma pigmentosum complementation group D (XPD)/Excision Repair Cross-Complementing group 2 (ERCC2) encodes a helicase, which participates in nucleotide excision repair. This variant allele of polymorphism XPD Lys751Gln has been associated with increased DNA adduct levels, and with low DNA repair capacity. X-ray Cross Complementing group 1 (XRCC1) is a protein involved in base excision repair pathway. The Arg280His is located in the proliferating cell nuclear antigen binding region. Published reports have suggested that the Arg280His variant protein is defective in its efficient localization of a damaged site in the chromosome, thereby reducing the cellular base excision repair efficiency. In this study, we investigate the possible association of these two polymorphisms with an increased risk of developing NPC in the Malaysian population.

Methods: A molecular epidemiological study using hospital based case-control study design. SNP genotyping was carried out using PCR-RFLP method.

Discussion: In this preliminary study, a total of 113 cases and 130 controls were analyzed. For XRCC1 codon 280 polymorphisms, an OR of 1.34 was observed among individuals with Arg/His and His/His genotype (95% CI, 0.62-2.87; P=0.457, adjusted for age, sex and ethnicity). There was no significant association between XRCC1 Arg280His and the risk of NPC. For XPD codon 751, an OR of 1.99 was observed (95% CI=0.95-4.17; P=0.06). Although not statistically significant, there is a trend of increased risk of NPC nearly two times higher among homozygous wild type (Lys/Lys) compared with heterozygous (Lys/Gln) genotype. To our knowledge, there have been no documented studies of the association of XPDLys751Gln and nasopharyngeal carcinoma risk. Funding: Financial support from Ministry of Science, Technology and Innovation (MOSTI) for E-Science Fund grant.

Keyword: NPC; Polymorphisms; XPD; XRCC1.