Genetic Epidemiology of Breast cancer in Thai women

Suleeporn Sangrajrang
Research Division, National Cancer Institute, Bangkok, Thailand

ABSTRACT

Breast cancer is the first leading cancer among Thai women and the incidence still increasing. Although there are well established risk factors, such as age at first child’s birth, nulliparity, and family history of breast cancer, the etiology of breast cancer is still not completely known, particularly in Thailand.

There are many single nucleotide polymorphisms (SNPs) in human genome that alter the activity of key enzymes. High-throughput molecular method can be used to associate with specific diseases in case-control studies and provide clues to causation. To evaluate the role of genetic polymorphisms of selected gene and gene-environment interactions in breast cancer, we conducted a case-control study with 554 cases and 572 controls. Cases were all new incident breast cancer patients histopathologically diagnosed in the National Cancer Institute in Bangkok and in Khon Kaen University hospital, and Khon Kaen General Hospital during the period of May 2002 - March 2004. Controls were randomly selected from healthy women that visited patients admitted to the same hospitals for diseases than breast or ovarian cancer, who were matched to cases on age (± 5 years) and residence.

Selected genes included are those involved in estrogen synthesis and metabolism (CYP1A1, CYP1A2, CYP1B1, CYP17, CYP19, CYP2C9, CYP2C19, ESR1, PGR, ERRG, COMT, NQO1, HSD17B1, HSD17B2, AhR), folate and alcohol metabolism (MTR, MTRR, MTHFR, TYMS, ADH1C, ALDH2, GSTP1, NAT1, NAT2, CYP2E1, DRD2, DRD3, SLC6A4), DNA repair (hOGG1, APE1, XRCC1, XRCC2, XRCC3). Genetic polymorphism were determined by PCR, PCR-RFLP, light-cycler and 5'-nuclease assay (Taqman). Some SNPs showed significantly different distribution between case and control. For example, we found that CYP1A2, CYP2C19, AhR genotypes were associated with an increased risk of breast cancer, while a protective effect of CYP17, CYP1B1, ERRG genotype were found. For genetic polymorphism of DNA repair enzyme, we found that APE1 showed a significant protective effect of breast cancer risk. Further more, subgroup analysis based on menopausal status revealed increased breast cancer risk in postmenopausal women and OGG1 polymorphism. Diploptype analysis of XRCC1 (codon 194, 280, 399) revealed that CGA/CGA carriers had an increased risk of breast cancer compared with carriers of the wild type CGG/CGG. When the joint effect of XRCC1, APE1 and OGG1 polymorphism were evaluated, individuals homozygous for two or three risk allele were associated with breast cancer risk.

In conclusion, these results suggest that genetic polymorphisms of some selected penetrance genes in individual susceptibility to breast cancer development in Thai Women.