ESTROGEN METABOLISM RELATED GENES AND BREAST CANCER RISK: A CASE CONTROL STUDY IN THAI WOMEN

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Background: Although the incidence of breast cancer in the South-East Asia is substantially lower than found in Europe or North America, it does represent the most frequent cancer in Thai women and rates are increasing. Estrogen and its metabolites are believed to play important roles in breast cancer and its determinant include both genetic and lifestyle factors.

Purpose: The objective of the study is to investigate association of breast cancer risk in Thailand with genetic polymorphisms in several genes involved in estrogen synthesis and metabolism. Methods: Five hundred and seventy patients with histopathologically confirmed breast cancer and 497 controls were included in the present study. Forty single nucleotide polymorphisms (SNPs) in the CYP1A1, CYP1A2, CYP1B1, CYP17, CYP19, CYP2C9, CYP2C19, AhR, ESR1, PGR, ERRG, COMT, HSD17B1, HSD17B2, EPHX1, and NQO1 genes were genotyped. Associations of genotypes with breast cancer risk were evaluated using multivariate logistic regression.

Results: Heterozygote carriers of SNPs in CYP2C19 (rs4917623), AhR (rs2066853), ERRG (rs1857407) and homozygote carriers of SNPs in CYP1A2 (rs762551), CYP2C19 (rs4917623), ERRG (rs945453) had altered risk of developing breast cancer. In addition, a stratified analysis by menopausal status indicated that the association of the CYP1A2 (rs762551) and CYP17 (rs743572) polymorphisms with breast cancer risk were mainly evident in premenopausal, while those of CYP1B1 (rs162556) and ERRG (rs1857407) significant in postmenopausal women.

Conclusion: These findings suggest that CYP1A2, CYP2C19, AhR, ERRG, CYP17 and CYP1B1 polymorphisms may play an important role in estrogen metabolism and modify individual susceptibility to breast cancer in Thai women.