【P-66】

Genotype-Phenotype Relationship between Genetic Polymorphisms of Selected DNA Repair Genes and DNA Repair Capacity

Kyoung-Mu Lee[1], Ji-Yeob Choi[1], Changwon Kang[2], Changsoo Kang[2], Sue Kyung Park[3], Hyangsook Kim[4], Byungchan Ahn[4], Hyunmi Cho[5], Dae-Yeon Cho[5], Keun-Young Yoo[1], Myung-Hee Shin[6], Dong-Young Noh[7], Sei-Hyun Ahn[8], Qingyi Wei[9] and Daehee Kang[1]

Departments of [1]Preventive Medicine & [7]General Surgery, Seoul National University College of Medicine, Cancer Research Institute, [2]Department of Biological Sciences, KAIST, [3]Department of Preventive Medicine, Konkuk University College of Medicine; [4]Departments of Microbiology and Genetic Engineering, College of Natural Science, Ulsan University; [5]Clinical Research Institute, Labgenomics Co, Ltd, Doosan Engineering Center; [6]Department of Preventive Medicine, Sungkyunkwan University College of Medicine; [8]Department of Surgery, Ulsan University College of Medicine; [9]Department Epidemiology-189, University of Texas, M.D. Anderson Cancer Center

Objectives : Genotype-phenotype relationship between genetic polymorphisms of DNA repair genes and DNA repair capacity was evaluated in case-control study. Selected DNA repair genes included are those involved in double strand break repair (*XRCC2, XRCC4, XRCC6, LIG4, RAD51, RAD52),*base excision repair (*LIG1*), nucleotide excision repair (*ERCC1*), and mismatch repair (*hMLH1*)

Methods : The subjects were consisted of histologically confirmed breast cancer cases (n=56) and controls (n=48) with no present or previous history of cancer admitted to Asan Medical Center from February to December, 2002. Information on demographic characteristics and other information were collected by interviewed questionnaire. Genetic polymorphisms (*XRCC2* 31479G/A, *XRCC4* 921G/T, *XRCC6* 1796G/T, *LIG4* 1977T/C, *RAD51* 135G/C, 172G/T, *RAD52* 2259C/T, LIG1 583A/C, *ERCC1* 8092A/C, 354C/T, *hMLH1* 5' region -93G/A, 655A/G) were determined by matrix-assisted laser desorption/ionization time of flight (MALDI-TOF) mass spectrometry. DNA repair capacity (%) was measured by the host-cell reactivation assay. The variation of DNA repair capacity by genotypes was evaluated by the analysis of covariance (ANCOVA) adjusting for age and family history.

Results : The *XRCC2* 31479G/A, *XRCC6*1796 G/T, *LIG4* 1997T/C were not polymorphic

in Korean women, whereas the minor alleles of *XRCC2* 31479G/A (A: 0.08), *XRCC6* 1796G/T (T: 0.37), *LIG4*1997T/C (C: 0.16) were relatively high, showing the remarkable ethnic difference compared with Caucasian. *RAD51* GC or CC (OR=0.08, 95% CI=0.08-0.93), *RAD52* CT or TT (OR=2.88, 95% CI=1.02-8.08), *ERCC1* 3' UTR 8029 AC (OR=0.40, 95% CI=0.16-0.99), and *hMLH1*-93 GA or GG (OR=3.52, 95% CI=1.24-10.0) genotypes were associated with breast cancer risk. Significant difference in DNA repair capacity (%) was not found between cases (12.0±4.1) and controls (11.6±4.5). However, DNA repair capacitysignificantly differed by the genotypes of *RAD52* 2259C/T (CC: n=22, 12.5±4.2; CT: n=53, 10.8±3.8; TT: n=29, 13.1±4.7, p=0.04). A moderately decreasing trend as the number of A allele of *ERCC1* 3'UTR 8029 increased was also observed (CC: n=55, 12.3±4.8; AC: n=39, 11.2±3.5; AA: n=29, 9.13±2.9, p-for trend=0.09).

Conclusion : Our findings suggest that DNA repair capacity might be influenced by the genetic polymorphisms of DNA repair genes such as *RAD52* and *ERCC1*.

Keyword : gentic polymorphism, DNA repair capacity, breast cancer,