

Effects of p53, p21 and CCND1 Single Nucleotide Polymorphism on Breast Cancer Susceptibility

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Abstract—Breast cancer incidence rates are increasing by up to 5% per year in urban areas of India. It is critical to detect breast cancer at an early stage for better prognosis and disease free survival. p53, p21 and CCND1 genes are involved in cell cycle control and their mutations/ polymorphism influences the breast cancer susceptibility.

A case- control study involving 115 breast cancer patients attending BRA-IRCH, AIIMS, New Delhi and even number of control samples from unrelated normal healthy women without a family history of cancer, was carried out. Polymorphism namely SNP93 (C to A) in p21 gene was detected using gene sequencing while PCR-RFLP approach was used to detect Pro72Arg and G870A polymorphism in p53 and CCND1 gene, respectively.

Neither SNP93C nor SNP93A allele of p21 was found associated significantly with breast cancer risk in total cohort. Arg allele found to be somewhat more common in breast cancer than in the controls, but the association failed to reach statistical significance, OR 1.896 (p-value (p=) 0.136). Significant protective association of p53 heterozygous arginine variant with breast cancer was found in total cohort. ORs for Arg/Pro (G/C) genotype in total, premenopausal and postmenopausal women were 2.63 (p=0.0002), 1.96 (p-value 0.06) and 5.55 (p=0.0002), respectively. Arg/Arg (G/G) genotype was associated significantly with breast cancer risk in total and postmenopausal women with ORs 1.97 (p= 0.009) and 3.25 (p= 0.01), respectively. A/A genotype in CCND1 found associated significantly with the breast cancer risk in total and premenopausal women with ORs 2.29 (p= 0.006) and 2.31 (p= 0.04), respectively. G/G and G/A genotype were not associated significantly with the breast cancer risk. No evidence of p21 codon 231 polymorphism with an increased breast cancer risk was found in our study. However, Arg allele found to be prevalent in patients than in the controls. A significant association of GG allele in p53 Arg72Pro with breast cancer risk was observed in total and postmenopausal women. A significant protective association of p53 heterozygous arginine variant with breast cancer was found in total cohort. A/A genotype in CCND1 found associated significantly with the breast cancer risk in total and premenopausal women. However further studies among different ethnic populations across India are required to assess the associations of these SNPs with breast cancer risk.

Keywords: p53; p21, CCND1; SNP; Breast Cancer.