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Germline HVR-II mitochondrial polymorphisms associated with breast cancer in Tunisian women

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ABSTRACT. A high incidence of somatic mtDNA polymorphisms has been reported in a wide variety of human cancers; some of them have been proposed as markers for the early detection of breast cancer. However, little attention has been paid to the potential of germline mitochondrial sequence variations as genetic risk factors for cancer. We performed a case-control study of 70 unrelated Tunisian women with breast cancer and 80 healthy age- and gender-matched blood donors, taking into account clinicopathological data, to evaluate germline polymorphism of mitochondrial HVR-II region as a genetic risk factor for breast cancer. Through direct sequencing, we detected 351 polymorphisms in controls and 248 variants in patients, with 47 and 39 segregating sites, respectively. In both groups, more than 50% of the polymorphisms were due to four variants: 315 ins C, 309 ins C, 263 A>G, and 73 A>G. The

HVR-II sequences were also classified into haplotypes on the basis of the polymorphisms. Fifty-nine different haplotypes were found, 20 of them shared between patients and controls. Both groups had specific haplotypes, 18 in breast cancer patients and 21 in controls. Statistical analysis revealed a weak protective effect against breast cancer risk for two mitochondrial polymorphisms - 152 T>C (odds ratio (OR) = 0.33, 95% confidence interval (CI) = 0.12-0.91) and 263 A>G (OR = 0.17, 95%CI = 0.06-0.47). In contrast, an increased risk of breast cancer was detected for the 315+C haplotype (OR = 11.66, 95%CI = 1.44-252.23). We conclude that mitochondrial variants can affect breast cancer risk. More extensive studies, involving different types of cancer and patients with different genetic makeup, will be required to improve our understanding of the effects of germline mtDNA polymorphisms on carcinogenesis.

Key words: Breast cancer; mtDNA; Polymorphism; D-loop

