THE STUDY OF GENOMIC VARIATION OF BRCA GENES IN THE ALBANIAN POPULATION

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According to the Global Cancer Observatory, breast cancer is the most commonly cancer in women in Europe and Albania. The BRCA 1 and BRCA 2 are two essential tumour suppressor genes with a central role in the homologous recombination repair (HRR) pathway. According to many studies on genome populations, BRCA genes are considered polymorphic and revealed approximately 70.000 variants. Also, they suggest that BRCA variants are highly deleterious in damaging BRCA function, causing genome instability and increased cancer risk, affecting mostly breast and ovaries. This study aims to investigate the spectrum of BRCA1 and BRCA2 genetic variants in female Albanian population and to analyze the mutations significance from an evolutionary perspective. This is the first study conducted in Albania for the identification of BRCA gene variants, part of an ongoing project on Biomarkers in Rare Genetic Diseases in Albania, of the NanoAlb research group. The national screening of women for breast cancer is done through imaging techniques at Obstetrics and Gynecological University Hospital (Queen Geraldina), in Tirana, Albania (almost 600 tests/year). This allows the coordination of the work, through examinations and/or interviews, to identify the target group (with family breast cancer history). BRCA gene variants will be identified through Multiplex Ligation Probe Assay (MLPA) and fragment analysis will be done with SeqStudio genetic analyser. This variants will be compared with the documented identified variants in gnomAD browser database (recently ExAC data is available in the gnomAD browser) and BRCA Exchange data, to define the pathogenic variants. Actually, a family of 6 women members, already identified by MLPA assay with a deletion in exon 11 of BRCA1 gene, will be included in the positive control group. These tests demonstrated the existence of an autosomal dominant pattern of inheritance of the breast cancer cases, that is already confirmed by other studies. Furthermore, extensive studies suggest that BRCA genes vary by ethnicity. This is very important to study in Albanian population, as this country has its unique genetic, linguistic, and cultural features. Evolution factors contributed to this ethnic specificity, which include the positive selection imposed on human BRCA genes, the adaptation of different ethnic populations to their living environment, the bottleneck and founder effects, will also be involved in this study. As the studies suggest, this investigation is of highly importance in providing genetic evidences to understand the relationship between human evolution and cancer risk. Finally, this study may contribute to provide an overview of Albanian population for the BRCA variation genes and a comprehensive reference for clinical applications in the era of precising medicine.

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