Preliminary study of genetic alterations in Romanian patients with sporadic breast cancer

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Like other human cancers, breast cancer (BC) occurs when a buildup of genetic alterations in critical genes are progressive accumulated allowing cells to grow and divide uncontrollably. In most cases, BC is due to small number of highly penetrated mutations such as BRCA1/2 and much larger number of lower penetrates, inherited mutations also increasing the risk.

In this study, we investigated the somatic alterations in TP53 (exons 4-9 and flanking regions), PIK3CA (exons 1, 10, 21) and BRCA1/2 genes in 22 fresh BCs tissues and normal matched pair. The melting profile of PIK3CA gene was characterized using HRMA technique. The mutations in TP53 and PIK3CA genes were documented with Sanger sequencing, while mutations in BRCA1/2 genes were assessed using AmpliSeq BRCA1/BRCA2 Panel and PGM Sequencer. Aberrant melt profiles in PIK3CA gene were observed in 47.6% samples. Of them, 14.3% harbored mutations in exon 10 and 33.3% in exon 21. Parallel testing by Sanger sequencing confirmed mutations in 80% of the samples determined to be positive by the HRMA.

The frequency of TP53 somatic mutations was 27.3%. Of these, 83.3% were located in the DNA binding domain. Also, we identified 5 mononucleotide polymorphic variations, 3 of them were located in the coding regions.

When analyzed BRCA1/2 genes, we identified one nonsense mutation in BRCA2 gene (not reported in COSMIC catalogue), and no mutations in BRCA1 gene. Both genes were highly polymorphic: 43.5% of variations were located in BRCA1 gene and 56.5% in BRCA1 gene.

Our results are in line with those in international database. Variations of independently analyzed genes show a minor risk of developing BC, yet their cumulative effect increase the risk of disease development.

Our future goal is to enlarge the batch of patients and to analyze more genetic alterations (LOH, CNV, gene expression), in order to do a have a better picture of molecular abnormalities involved in the development of BC in Romania.

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