P70

THE CHANGES OF WHOLE GENOME METHYLATION PROFILES IN MUTATION CARRIERS OF BRCA1 GENE

Erdoğan S (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Avşar M (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Tuncer M (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Ödemiş A D (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Kılıç S (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Kuru G (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)
Yazıcı H (Istanbul Univesrity, Oncology Institute, Cancer Genetics Department Istanbul, Turkey)

Introduction - Purpose : BRCA1 and BRCA2 genes are the most important tumor suppressor genes involved in DNA repair mechanism. It is known that germline mutations in these two genes increase the risk of breast and ovarian cancer. In our study, the role of whole genome methylation changes had been investigated in ovarian cancer patients with and without BRCA1 mutation.

Methods - Tools : DNA samples of monozygotic twins and their healthy siblings which were prepared for BRCA1/2 genetic analysis has been used for methylation analysis. 500 ng of DNA was modified using bisulphite reaction. Methylation array profile of all samples were analyzed with the "Infinium MethylationEPIC BeadChip" on the iSCAN platform for 850000 genes in Illumina. Raw data was obtained from the samples displayed after loading the chip. In order to minimize the statistical error rate, background corrections, filtering, transformation and normalization of the data were performed. Data analyzes were performed using the Illumina GenomeStudio Methylation Module software. Results: Our study group was consisted of total five cases which of one is ovarian cancer with a BRCA1 mutation and a healthy case with negative BRCA1 mutation. We have found that 68,05% of CpG sites are hypermethylated. In these regions, the number of regions founded hyper methylated are 6091. According to USCS gene region feature category, 17% of hyper methylated CpG sites are located at 5' UTR region, 19,5% at Transcription Start Site-1500, 26,7% at Transcription Start Site-200, 3,3% at 1st Exon, 0,1% Exon boundary, 16,2% at gene body, 16,6% at intergenic site, 0,6% at 3' UTR region

Findings : Our study showed that the mutated BRCA1 gene was effected methylation level of different genes in whole genome. Our findings showed that biomarker potential of hyper methylated genes can be investigated in large breast and ovarian cancer cohort in future research.This is the first study in the literature that has been analyzed the whole genome methylation levels in ovarian cancer patients with and without BRCA1 mutation.

Discussion : The project was supported by the scientific research department of Istanbul University with 59477 project number and approved by Ethics Committee of Istanbul University: Approval number: 1552.

Keywords: Whole genome methylation, BRCA1 gene mutation, monozygotic twins, ovarian cancer