

Understanding DNA Methylation patterns in Breast Cancer

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Breast Cancer is the most frequently diagnosed cancer among women worldwide. According to the estimates of the American Cancer Society, 231,840 new cases of invasive breast cancer will be diagnosed in US women in 2015. Early diagnosis of breast cancer relies on extensive understanding of the molecular mechanisms underlying its development and progression. In addition to the genetic and hormonal risk factors that are responsible for breast carcinogenesis, other factors such as life-styles, environmental and nutritional factors also plays a part in development of this complex disease. The study of these factors which modifies the genome without altering the DNA sequence is termed as cancer epigenetics. DNA methylation is an extensively studied epigenetic dysregulation which governs cell differentiation, and other aberrancies which can steer cells towards a malignant phenotype. This heritable, tissue- and species-specific DNA modification primarily occurs at cytosine-guanine (CpG) dinucleotides and often causes silencing of gene expression. Since altered DNA methylation patterns are commonly observed in various types of malignancies including Breast cancer, it is a potential target to investigate for diagnosis and prognosis of cancer. The main aim of our study was to identify DNA methylation pattern in Breast cancer patients and correlate it with the disease progression. We evaluated 5 Breast tumor samples and 2 Breast normal samples (Stages II and III) obtained from The Cancer Genome Atlas. The DNA from the samples were Bisulfite sequenced which provides the whole-genome coverage at a single-nucleotide resolution and is considered the gold-standard approach for quantitative measurement of DNA methylation level. The mapped bisulfite reads were processed to obtain the methylation ratio of all cytosine positions. The data was analyzed to identify the differentially methylated positions on all chromosomes. The results of our study shows that 97.3% of the differentially methylated positions overlap with intergenic regions, 0.1% in promoter regions and remaining in the exon and intronic regions. Out of 160803 differentially methylated positions, 139579 positions were hypo-methylated and 21224 were hyper-methylated positions. We observed that majority of the differentially methylated positions are were hypo-methylated which traditionally affects gene transcription. Highest number of hypo-methylated and hyper- methylated positions were observed on chromosome 1 and 5 respectively. As per our study NR5A2, BCAS3, PRR11, VMP1, PBX1 are the top 5 genes which are aberrantly methylated in Breast cancer patients.

