lncRNA Gene Expression Profiling Analysis by TCGA RNA-Seq Data of Breast Cancer

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Abstract : Introduction: Breast cancer is a heterogeneous disease that can be classified in 4 subgroups using transcriptional profiling. The role of lncRNA expression in human breast cancer biology, prognosis, and molecular classification remains unknown. Methods and results: Using an integrative comprehensive analysis of lncRNA, mRNA and DNA methylation in 900 breast cancer patients from The Cancer Genome Atlas (TCGA) project, we unraveled the molecular portraits of 1,700 expressed lncRNA. Some of those lncRNAs (i.e, HOTAIR) are previously reported and others are novel (i.e, HOTAIRM1, MAPT-AS1). The lncRNA classification correlated well with the PAM50 classification for basal-like, Her-2 enriched and luminal B subgroups, in contrast to the luminal A subgroup which behaved differently. Importantly, estrogen receptor (ESR1) expression was associated with distinct lncRNA networks in lncRNA clusters III and IV. Gene set enrichment analysis for cis- and trans-acting lncRNA showed enrichment for breast cancer signatures driven by breast cancer master regulators. Almost two third of those lncRNA were marked by enhancer chromatin modifications (i.e., H3K27ac), suggesting that lncRNA expression may result in increased activity of neighboring genes. Differential analysis of gene expression profiling data showed that lncRNA HOTAIRM1 was significantly down-regulated in basal-like subtype, and DNA methylation profiling data showed that lncRNA HOTAIRM1 was highly methylated in basal-like subtype. Thus, our integrative analysis of gene expression and DNA methylation strongly suggested that lncRNA HOTAIRM1 should be a tumor suppressor in basal-like subtype. Conclusion and significance: Our study depicts the first lncRNA molecular portrait of breast cancer and shows that lncRNA HOTAIRM1 might be a novel tumor suppressor.

Keywords : lncRNA profiling, breast cancer, HOTAIRM1, tumor suppressor

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