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MAPPING THE GENOMIC AND IMMUNOMIC LANDSCAPE OF TRIPLE NEGATIVE BREAST CANCER USING MULTI-OMICS AND SEQUENCE DATA

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ABSTRACT: Triple-negative breast cancer (TNBC) is the most aggressive form of breast cancer with a very poor prognosis and survival rate. Over the last decade considerable efforts have been directed at molecular classification of subtypes of TNBC. Advances in high-throughput genotyping and the recent surge in next generation sequencing technologies have enabled discovery of germline and recurrent somatic mutations driving the disease phenotypes. More recently, there has been growing interest in understanding the role of the immune system in TNBC. However, multi-omics data have not been integrated with immunomic data to map the genomic and immunomic landscape of TNBC. The objective of this study is to map the genomic and immunomic Landscape of TNBC using publicly available multi-omics data. The hypothesis is that genomic and immunomic alterations in immune modulated miRNAs and genes containing germline and recurrent somatic mutations could led to measurable changes affecting molecular networks, biological pathways, and therapeutic decision making. To address this issue, we integrated miRNA and gene expression data from over 500 TNBC patients diagnosed with immune activated and immune suppressed clinical phenotypes, with genotype and sequence information to map the genomic and immunomic landscape of TNBC. We performed supervised and unsupervised analysis to identify immune modulated miRNA signatures and miRNA-mediated gene signatures, molecular networks and biological pathways. Additionally, we conducted enrichment analysis to identify molecular networks and biological pathways enriched for germline and recurrent somatic mutations. We discovered immune modulated miRNA signatures, miRNA-mediated gene signatures, molecular networks and biological pathways enriched for germline and recurrent somatic mutations involved in TNBC. Among the identified pathways included p53, NF-kB, BRCA, apoptosis and DNA repair signaling pathways. The results show that integrative analysis provides a powerful approach for establishing putative functional bridges between the genome and the immunome in TNBC.

Key Words: TNBC genomics immunomics miRNA gene expression mutations

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