Mapping the Genomic Landscape of TNBC and COVID-19

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Introduction

- Triple-negative breast cancer (TNBC) is the most aggressive form of breast cancer, representing 15 to 20% of all newly diagnosed breast cancers annually.
- Clinically, it is defined as tumors lacking expression of the estrogen receptor (ER), progesterone receptor (PR), and the human epidermal growth factor-2 (HER-2).
- TNBC patients are at high risk of COVID-19, and those affected tend to have poorer clinical outcomes.
- Sadly, the molecular mechanisms linking TNBC and COVID-19 have not been characterized.

Objective/Hypothesis

- **Objective:** Discover a signature of genes, networks and signaling pathways associating TNBC and COVID-19.
- **Hypothesis:** Genomic alterations in women diagnosed with TNBC and COVID-19 could lead to measurable changes associating the two diseases, and these alterations affect gene regulatory networks and signaling pathways driving the association between the two diseases.

Materials/Methods

- Gene expression and clinical data on TNBC were obtained from The Cancer Genome Atlas (TCGA).
- Gene expression and clinical data on COVID-19 were obtained from the Gene Expression Omnibus (GEO).
- Immune responsive genes were obtained from Illumina.
- Figure 1 shows project design and execution workflow.

Table 1. Distribution of samples.

Data	TNBC	COVID-19	Immune
Genes	60,483	19,473	1,661
# Cases	115	38	-
# Controls	113	13	-

Experimental Design

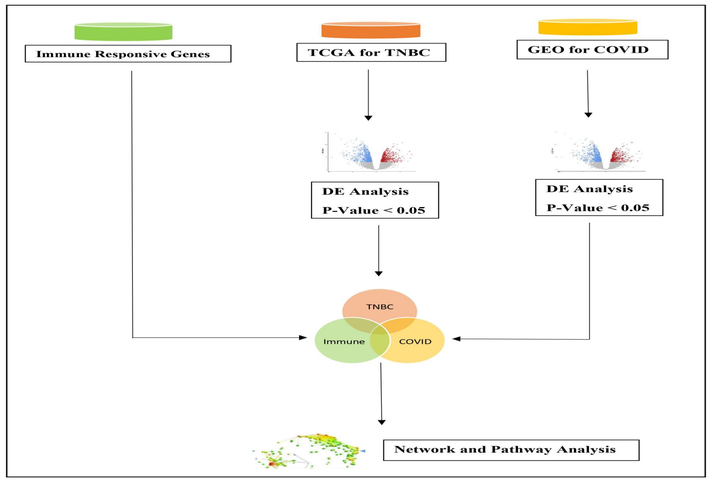

Figure 1. Experimental design and analysis workflow.

Data Analysis

- Performed supervised analysis comparing cases to controls to identify signatures of genes associated with each disease (TNBC, COVID-19) ($P<0.05$).
- Merged and evaluated the two signatures of genes to discover gene signature for association with both diseases.
- Pathway analysis to discover networks and signaling pathways.

Results

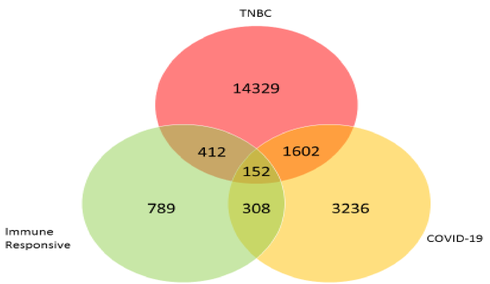

Figure 2. Differentially expressed (DE) genes associated with TNBC, COVID-19, both diseases, and genes validated for immune responsiveness.

Gene Signatures

- Signature of genes associated with TNBC = **16,495**.
- Signature of genes associated with COVID-19 = **5,298**.
- Signature of genes associating the two diseases = **1,754**
- Signature of immune genes associated with both diseases = **152**.

Top Canonical Pathways

- Mitotic Roles of Polo-Like Kinase
- Kinetochore Metaphase Signaling Pathway
- Cyclins and Cell Cycle Regulation

Networks

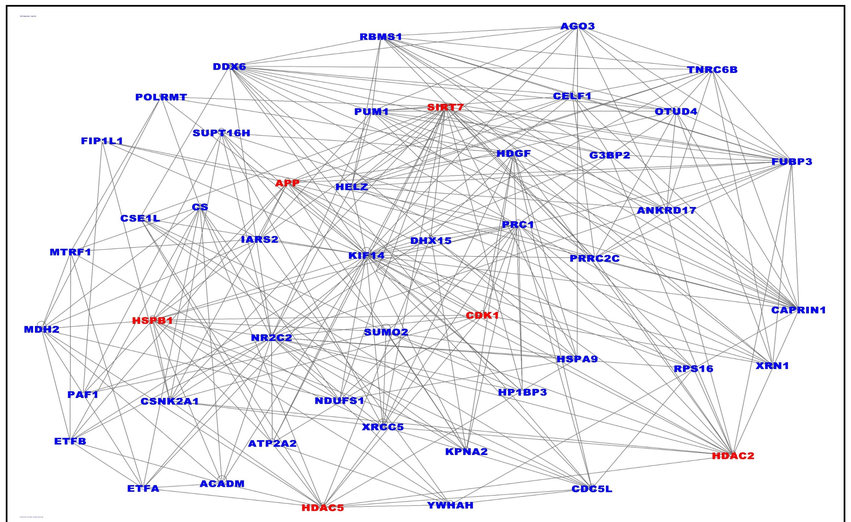

Figure 3. Gene regulatory networks for genes associated with both COVID-19 and TNBC (blue font), and genes associated with both diseases and immune system (red font).

Conclusions

- Discovered signatures of genes unique to COVID-19 and TNBC.
- Discovered a signature of genes associated with both TNBC and COVID-19.
- Discovered gene regulatory networks and signaling pathways associating the two diseases.
- Results suggest crosstalk between pathways involved in COVID-19 and pathways involved in TNBC.
- Integrative bioinformatics analysis is a powerful approach to mapping the genomic landscape of TNBC and COVID-19.
- Further research is recommended to validate the results in women diagnosed with both diseases.

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