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"Elucidation of the Genomic Landscape of Ovarian Cancer and COVID-19"

Background: Ovarian cancer (OC) remains one of the leading causes of death among women in the US and globally. Despite remarkable progress in clinical management of OC using chemotherapy and surgery, 5-year survival rates have only improved modestly over the past few decades. The outbreak of the COVID-19 pandemic has further complicated clinical management of OC patients. Chemotherapy treatment leads to a compromised immune system, which makes OC patents more susceptible to SARs-CoV-2 infections and poorer clinical outcomes. Therefore, there is an urgent need to understand the association between the two deadly diseases and the mechanisms driving clinical outcomes to enhance clinical management of OC patients during the COVID-19 pandemic. The objective of this investigation was to discover and characterize a signature of genes, network states and signaling pathways associating OC with COVID-19 and driving OC clinical outcomes. We hypothesized that genomic alterations in women diagnosed with OC and COVID-19 could lead to measurable changes associating OC outcomes with COVID-19 and that these alterations affect network states and signaling pathways, which drive poorer outcomes in OC patients with COVID-19.

Materials and Methods: We addressed the hypothesis using publicly available RNA-Seq data from women diagnosed with OC, comprising of 146 individuals who died and 229 individuals who survived, from The Cancer Genome Atlas (TCGA), and 38 women diagnosed with COVID-19 and 13 control samples from the Gene Expression Omnibus (GEO). We compared gene expression levels between dead and alive and between COVID-19 and controls. Genes associated with each disease were then evaluated for association with both diseases to identify a signature of genes associated with both diseases and predictive of OC clinical outcome. The signature was validated using genes experimentally confirmed and known to be involved in the immune system. Validated genes associated with both diseases were subjected to network and pathway analysis using Ingenuity Pathway Analysis software to discover network states and signaling pathways driving the two diseases and OC clinical outcome.

Results: Comparing gene expression levels between dead and alive revealed a signature of 2,612 significantly differentially (P<0.05) expressed genes predictive of clinical outcome in OC. Comparing gene expression levels between COVID-19 and controls revealed a signature of 5,298 significantly differentially (P<0.05) expressed genes associated with COVID-19. Evaluation of the two sets of genes revealed a signature of 241 genes shared between OC and COVID-19, including 21 genes known to be involved in the immune system. In addition, the investigation revealed signaling pathways associating the two diseases and driving OC outcomes, including: TWEAK, necroptosis, and TNFR1 signaling pathways.

Conclusion: The investigation revealed a signature of genes, molecular networks and signaling pathways associating OC and COVID-19 and driving OC clinical outcomes. Further research is recommended to define the molecular mechanisms underpinning the association between the two lethal diseases and driving clinical outcomes in OC patients affected by COVID-19.