



Michael Stewart^{1,} Aditi Kuchi², Jiande Wu², David Otohinoyi², Mahir Rahman³ and Chindo Hicks²

Introduction

- Despite remarkable progress in treatment, ovarian cancer remains the leading cause of death among (OC)gynecological malignancies in women in the US and globally.
- Because of their compromised immune system, women diagnosed with OC are at high risk of COVID-19.
- Thus, the COVID-19 pandemic has presented new challenges in clinical management of OC.
- Sadly, the molecular mechanisms underlying the association between the two deadly diseases have not been elucidated.
- There is an urgent need to address this unmet medical need.

Objective/Hypothesis

- **Objective:** Discover a signature of genes, network states & signaling pathways associating OC outcomes and COVID-19.
- Hypothesis: Genomic alterations in women diagnosed with OC and COVID-19 could lead to measurable changes associating the two diseases and affecting therapeutic decision making, and that these alterations affect molecular networks and signaling pathways, which in turn affect prognostic outcomes.

Materials and Methods

Table 1. Distribution and characteristics of the original data sets used in
 the investigation.

	COVID-19	9 (n=51)	OC	Immur	
# of Probes	19,4	72	6	1,661	
Sample Type	COVID-19	Control	Dead	Alive	
# of Samples	38	13	229	146	

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

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

Xavier University of Louisiana¹, Department of Genetics and the Bioinformatics Program, Louisiana State University Health Sciences Center, School of Medicine², Haynes Academy for Advanced Studies³

Project Design



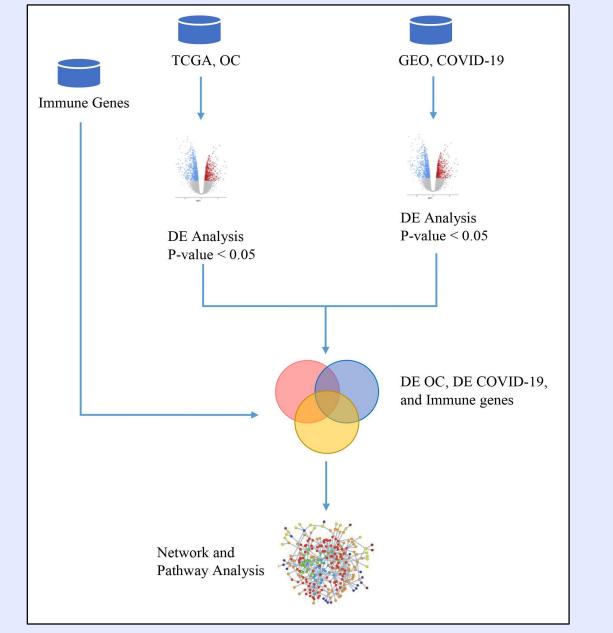


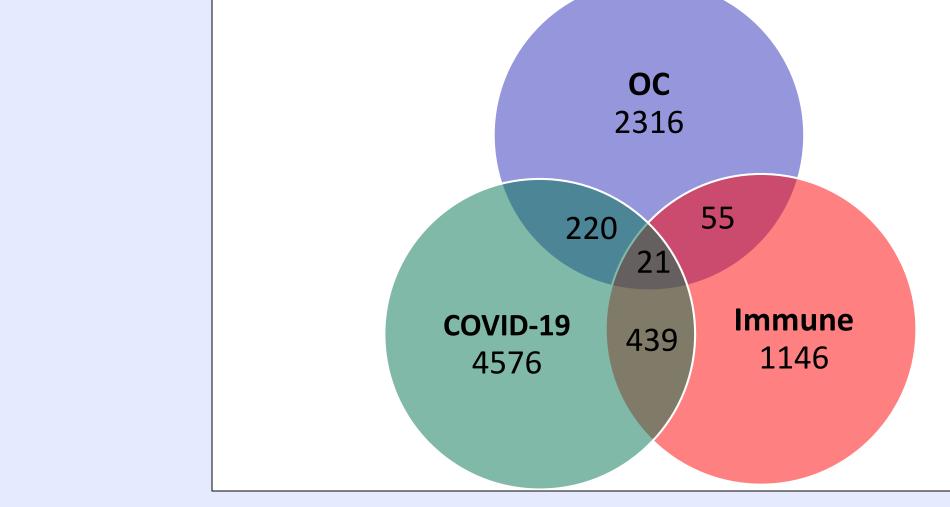
Figure 1. Project design and analysis workflow.

Data Analysis

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

Results

Figure 2. Three-way Venn diagram displaying gene signatures associated with OC, COVID-19, both diseases and immune-responsive.

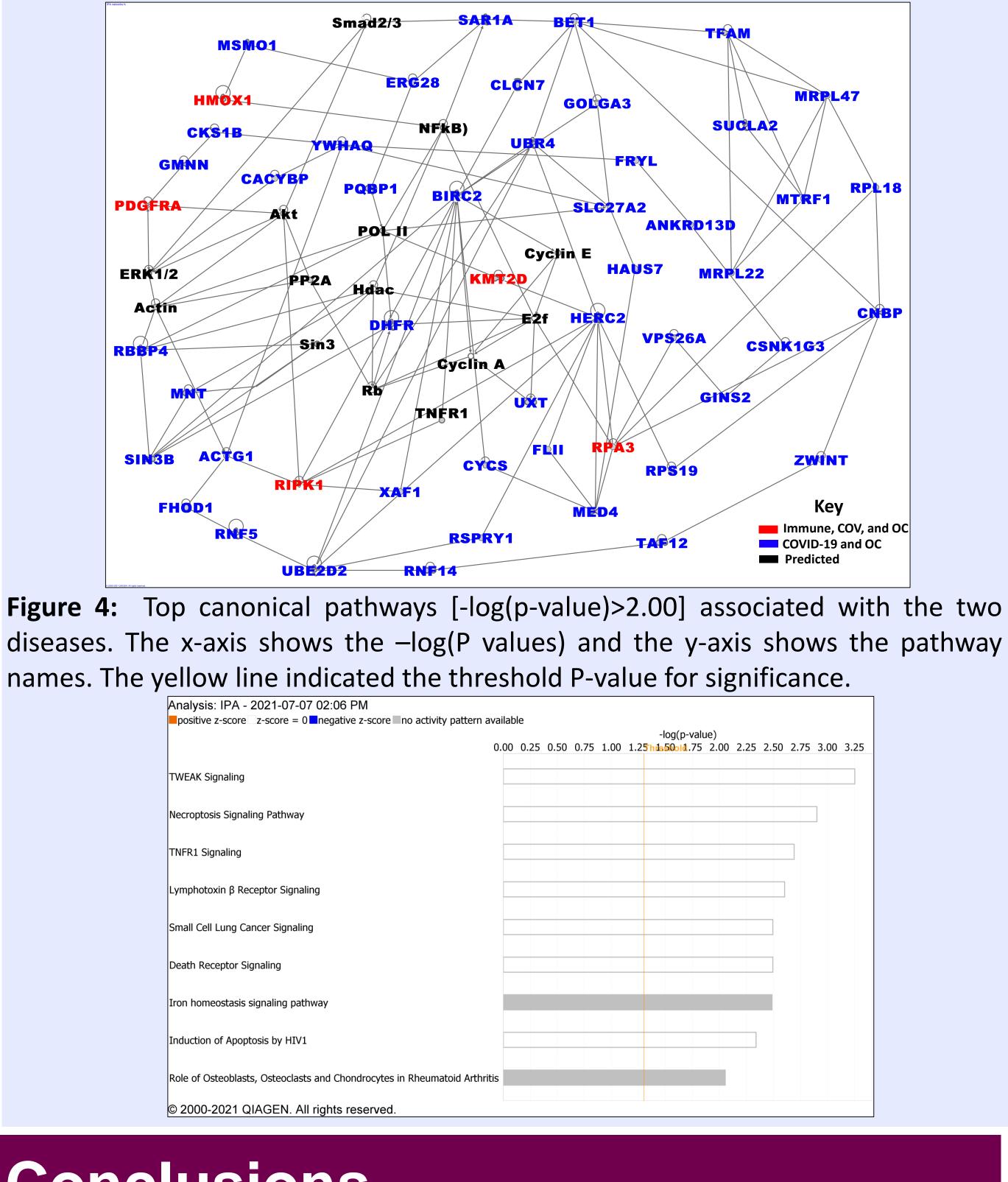


- •Discovered a signature of **2,612** genes associated with OC. •Discovered a signature of **5,298** genes associated with COVID-19.
- •Discovered a signature of 241 genes associating OC with COVID-19.
- •Validation using immune responsive genes revealed a signature of **21** immune regulated genes associated with both OC and COVID-19.

This research project was supported by Award Number: DBI-2051440 through the National Science Foundation (NSF), Research Experiences for Undergraduates (REU) Program, **LSUHSC-School of Medicine and the Bioinformatics and Genomics Program.**

Network and Pathway Analysis

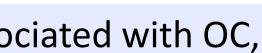
Figure 3. Molecular networks associating COVID-19 and OC. Genes in blue represent genes associated with both COVID-19 and OC. Genes in red represent genes associated with COVID-19, OC, and the immune system. Genes in black represent genes that are highly predicted to be associated with the two diseases.



positive z-score z-score = 0 negative z-score no activity pattern available	ilabl	е		
0.	00	0.25	0.50	0.75
TWEAK Signaling				
Necroptosis Signaling Pathway				
TNFR1 Signaling				
Lymphotoxin β Receptor Signaling				
Small Cell Lung Cancer Signaling				
Death Receptor Signaling				
Iron homeostasis signaling pathway				
Induction of Apoptosis by HIV1				
Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Arthritis				
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Conclusions

- Discovered signature of genes unique to each disease (OC, COVID-19)
- Discovered a signature associated with both diseases.
- Discovered networks and signaling pathways associating the two diseases.
- Results suggest pathways crosstalk between OC and COVID-19.
- Integrative bioinformatics analysis is a powerful approach to elucidating the genomic landscape of OC and COVID-19.
- Further research is recommended to validate the results in women diagnosed with both diseases.





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There is an urgent need to address this unmet medical need.

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- Omnibus (GEO).
- (TCGA).

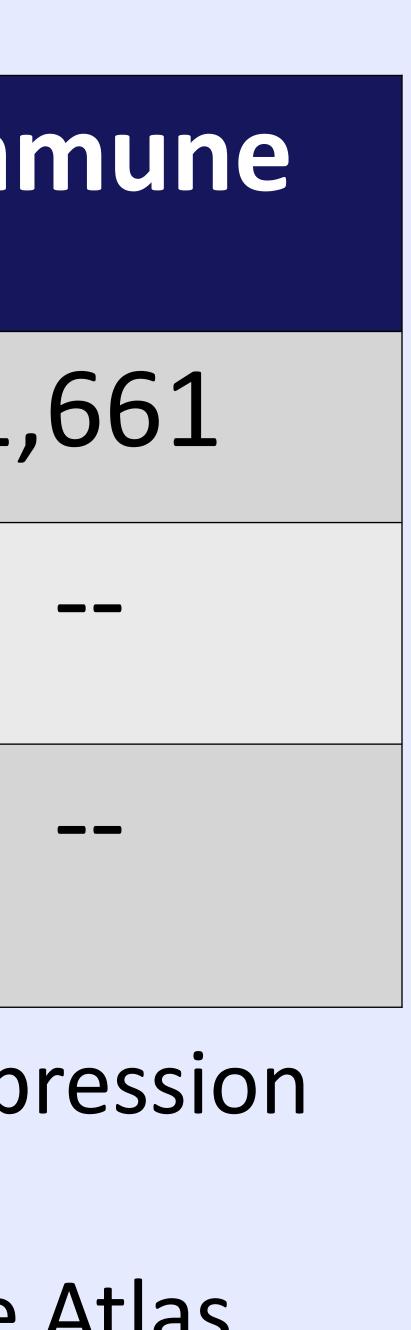
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Gene Expression (KINA-Seq) and clinical data on COVID-19 obtained from the Gene Expression

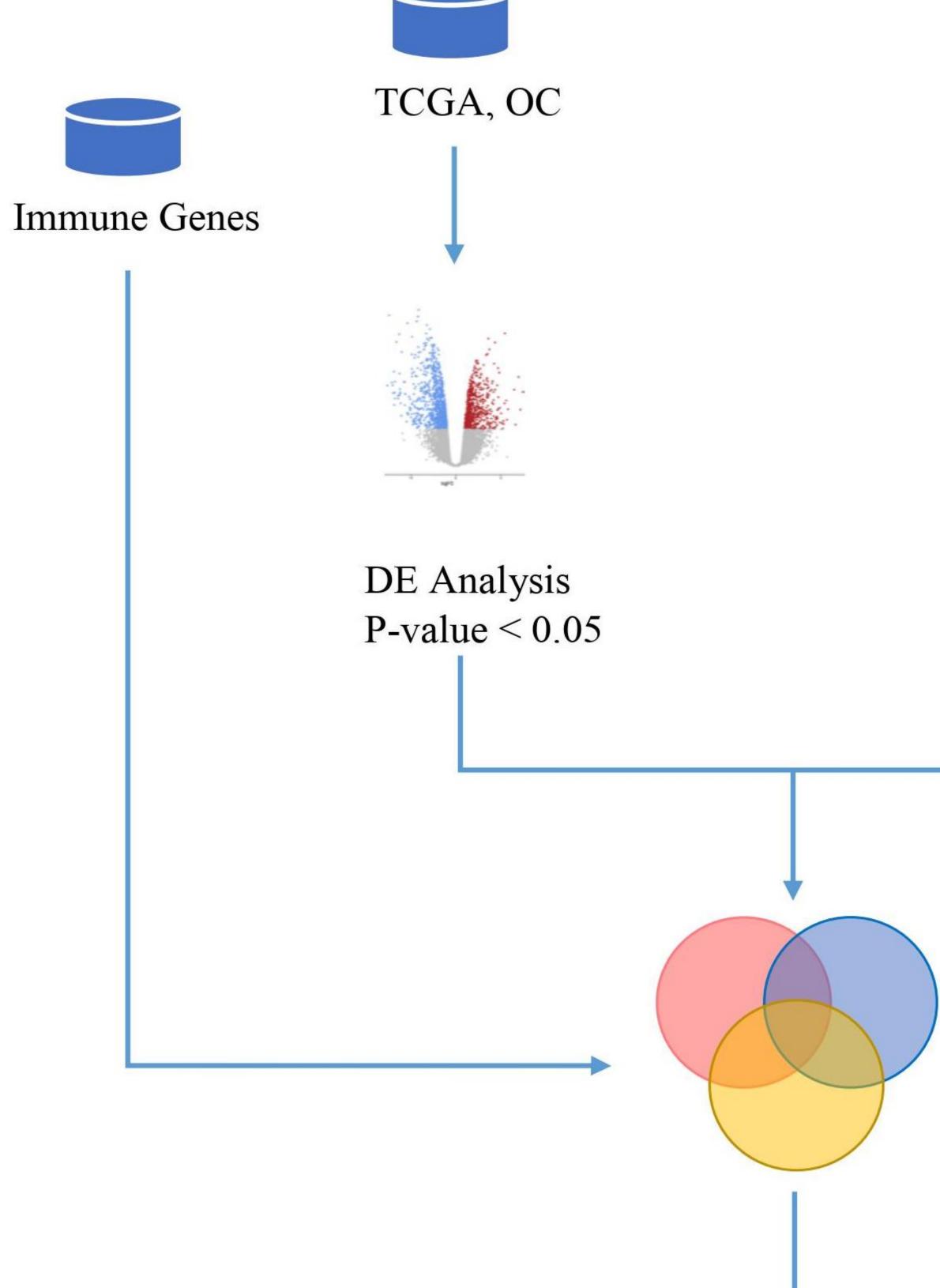
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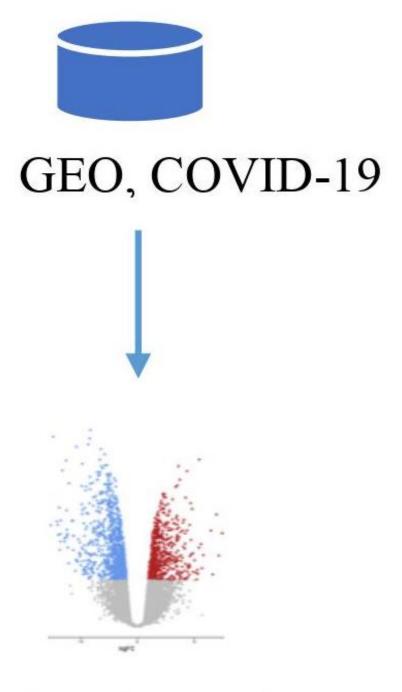
Project Design

Figure 1. Project design and execution workflow.



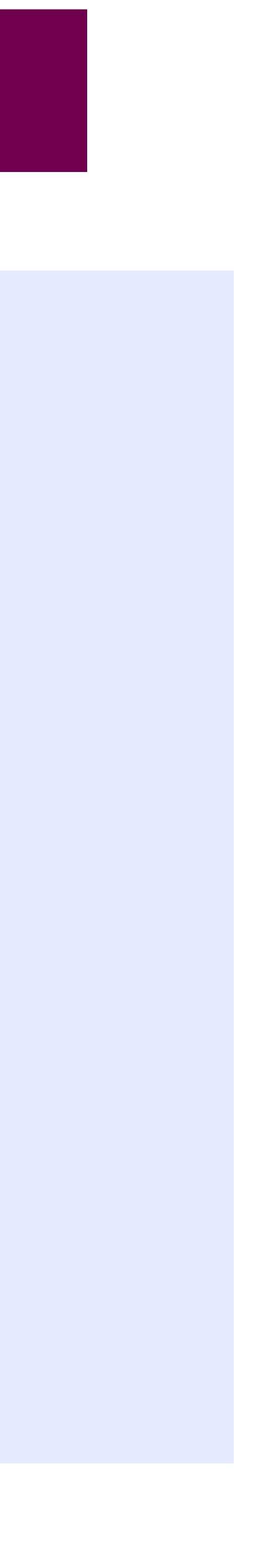
Network and Pathway Analysis





DE Analysis P-value < 0.05

DE OC, DE COVID-19, and Immune genes



(P<0.05).

signature for association with both diseases.

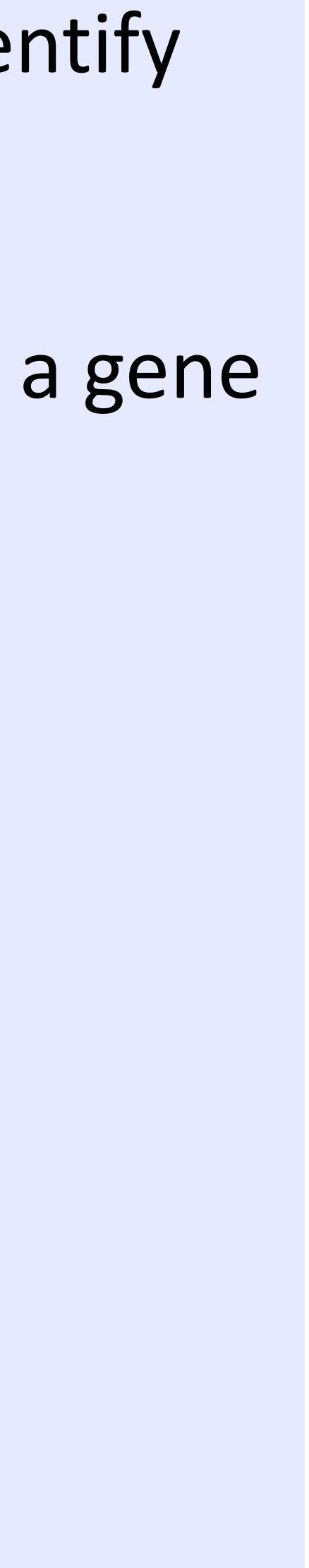
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Data Analysis

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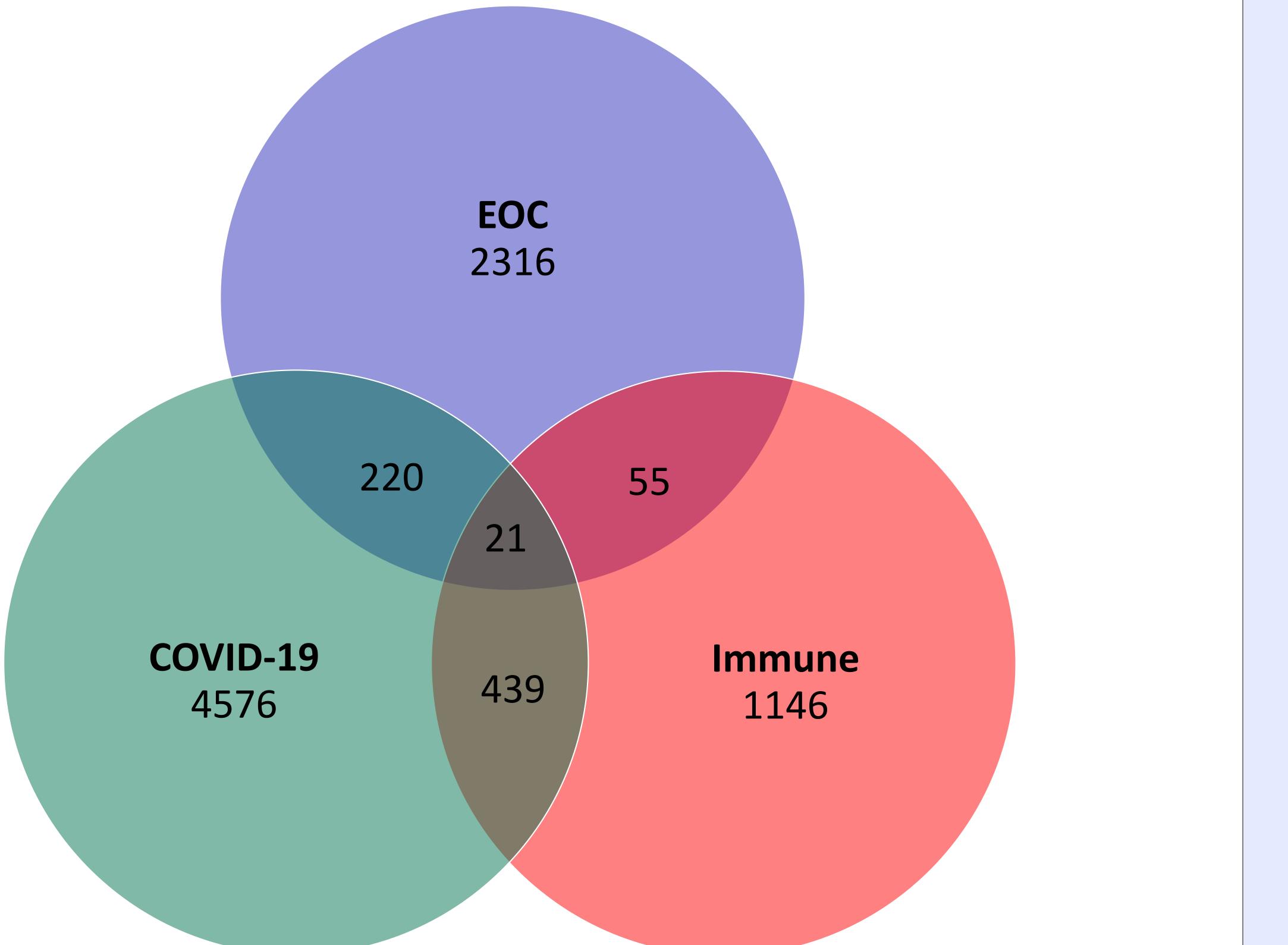
signatures of genes associated with each disease (OC, COVID-19)



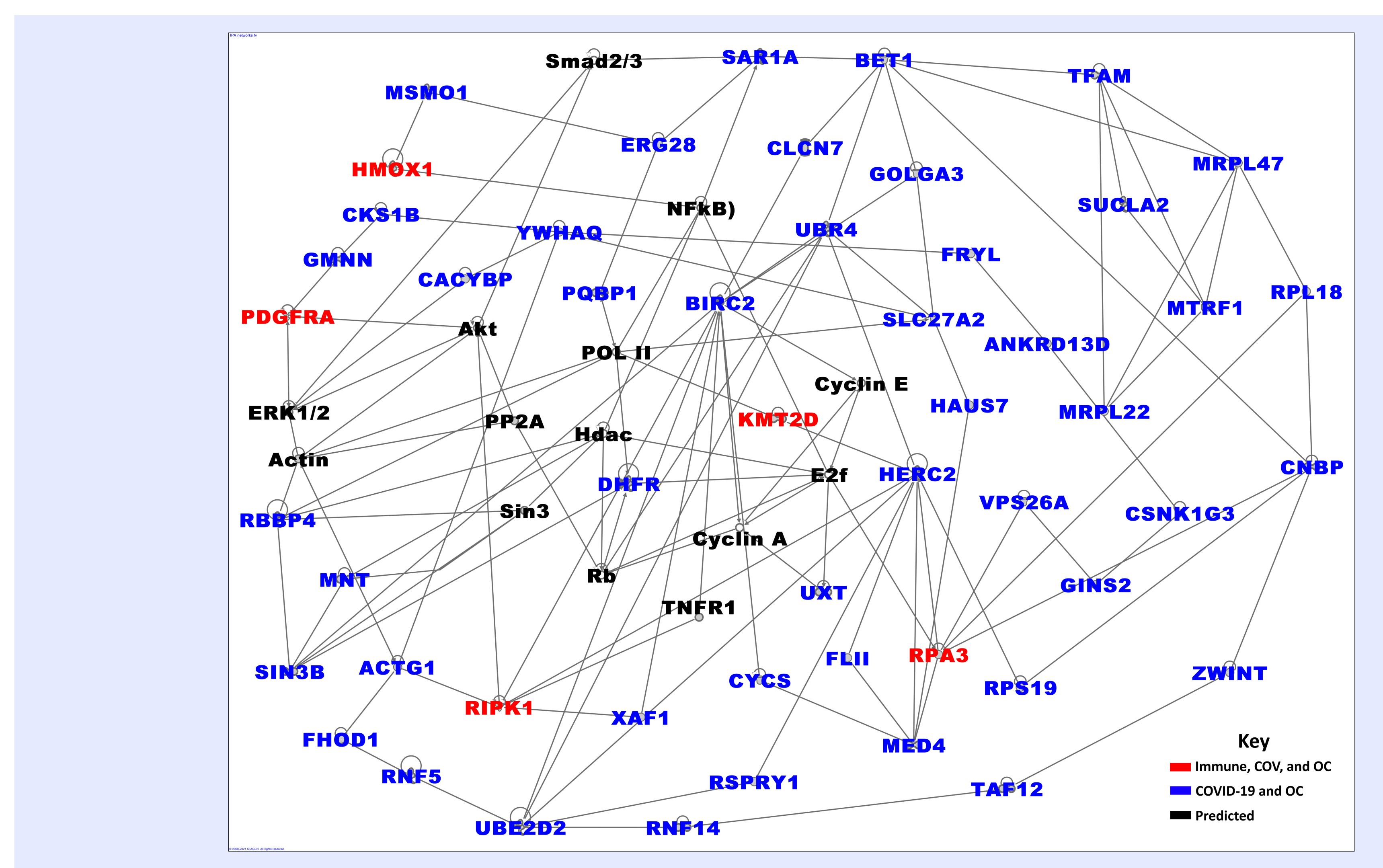
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Figure 3. Figure 3 displays commonalities between the following three groups: DEGs for OC, DEGs for COVID-19 and immuneresponse genes. The 220 genes shared between OC and COVID-19 as well as the 21 genes shared by all three groups were used for network and pathway analysis.

Discovery of Gene Signatures







predicted to associate the two diseases.

Network and Pathway Analysis

Figure 3. Molecular networks associating COVID-19 and OC. Genes in blue represent genes that are associated with both COVID-19 and OC. Genes in red represent genes that are associated with COVID-19 and OC and the immune system. Genes in black represent genes that are highly

Network and Pathway Analysis

positive z-score z-score = 0 negative z-score no activity pattern available

TWEAK Signaling

Necroptosis Signaling Pathway

TNFR1 Signaling

Lymphotoxin β Receptor Signaling

Small Cell Lung Cancer Signaling

Death Receptor Signaling

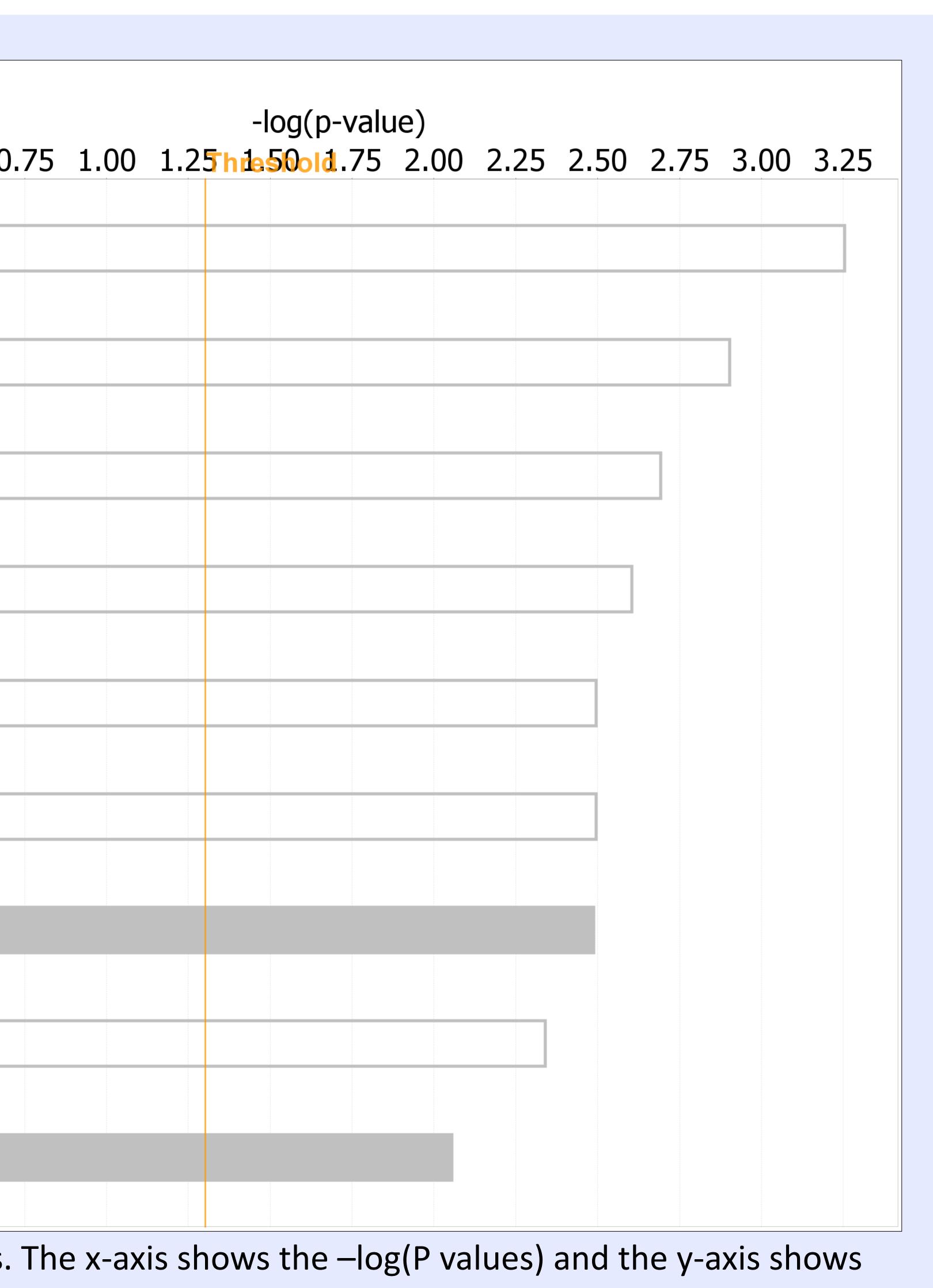
Iron homeostasis signaling pathway

Induction of Apoptosis by HIV1

Role of Osteoblasts, Osteoclasts and Chondrocytes in Rheumatoid Ar

Figure 5: Signaling pathways [-log(P-value)>2.00] associated with the two diseases. The x-axis shows the –log(P values) and the y-axis shows the pathway names. The yellow line indicates the threshold P-value for significance.

0.	00	0.	25	0.	50	0.	
rthritis							
with the two diseases							



- diseases.

- diagnosed with both diseases.

Conc usions

•Discovered a signature associated with both diseases. Discovered networks and signaling pathways associating the two

 Results suggest pathways crosstalk between OC and COVID-19. Integrative bioinformatics analysis is a powerful approach to elucidating the genomic landscape of OC and COVID-19. •Further research is recommended to validate the results in women

- Discovered signature of genes unique to each disease (OC, COVID-19)

