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Introduction

- Despite remarkable progress in treatment, ovarian cancer (OC) remains the leading cause of death among 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

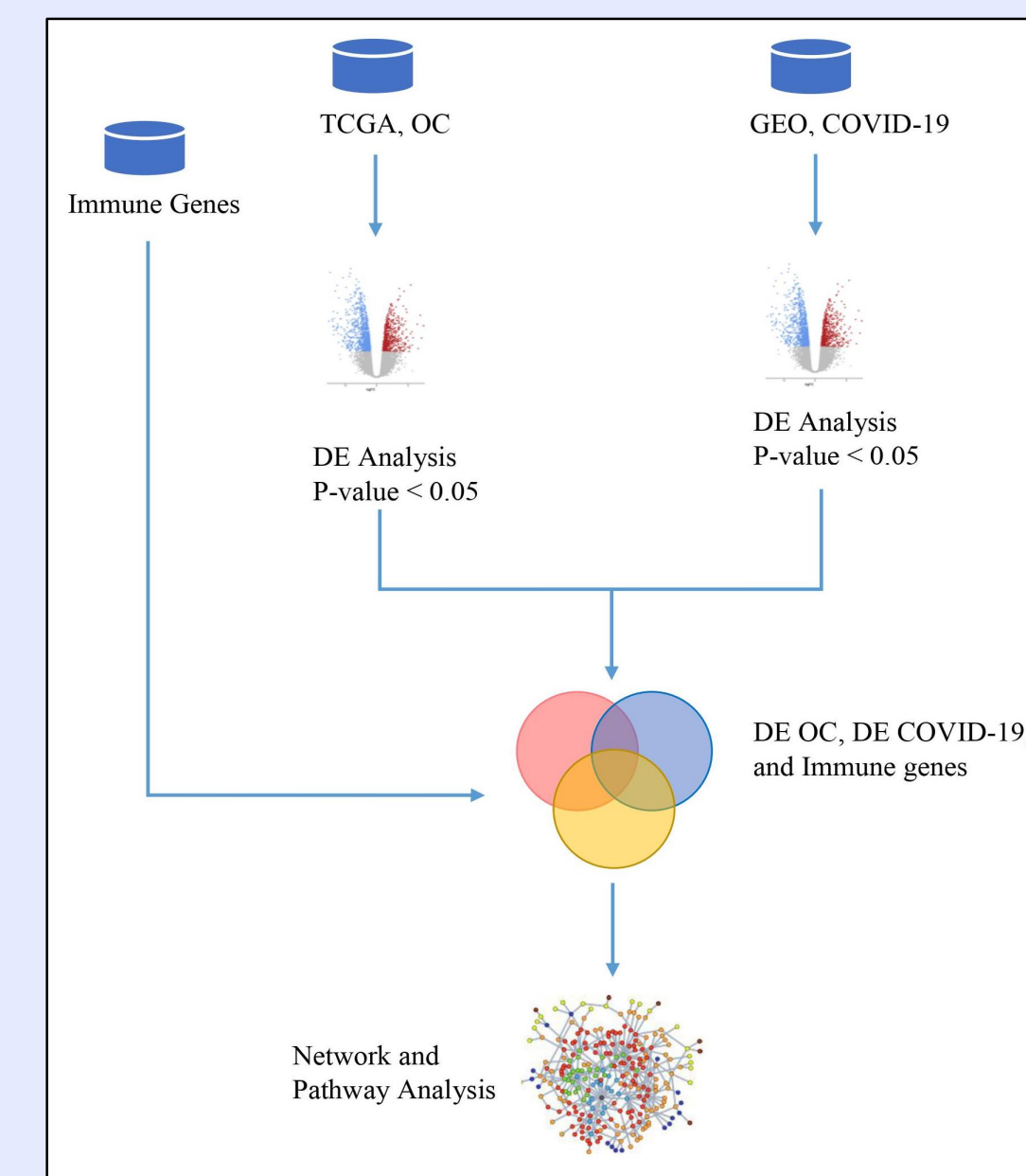
Table 1. Distribution and characteristics of the original data sets used in the investigation.

	COVID-19 (n=51)		OC (n=375)		Immune
# of Probes	19,472		60,483		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.

Project Design

Figure 1. Project design and analysis workflow.

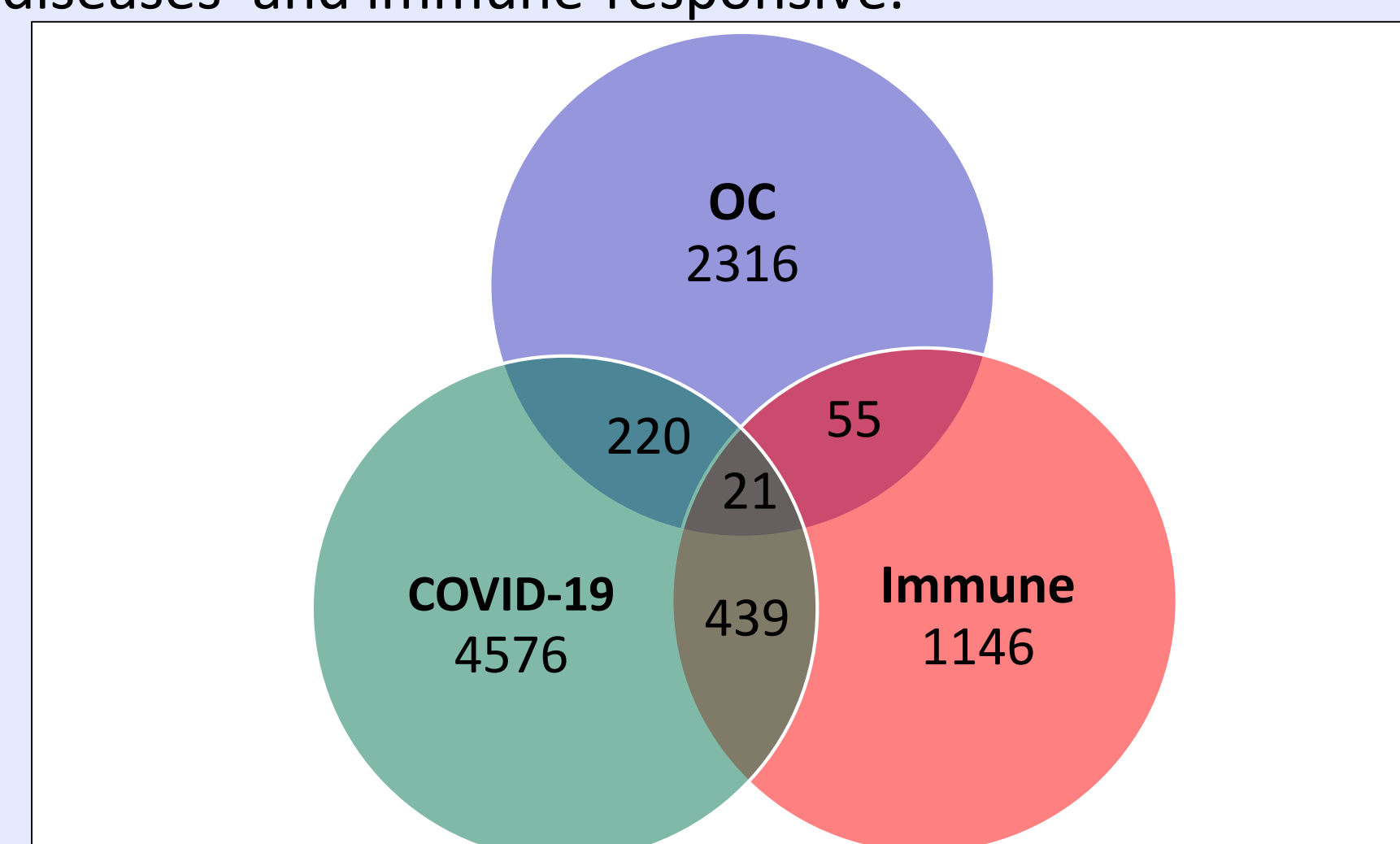


Data Analysis

- 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.

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.

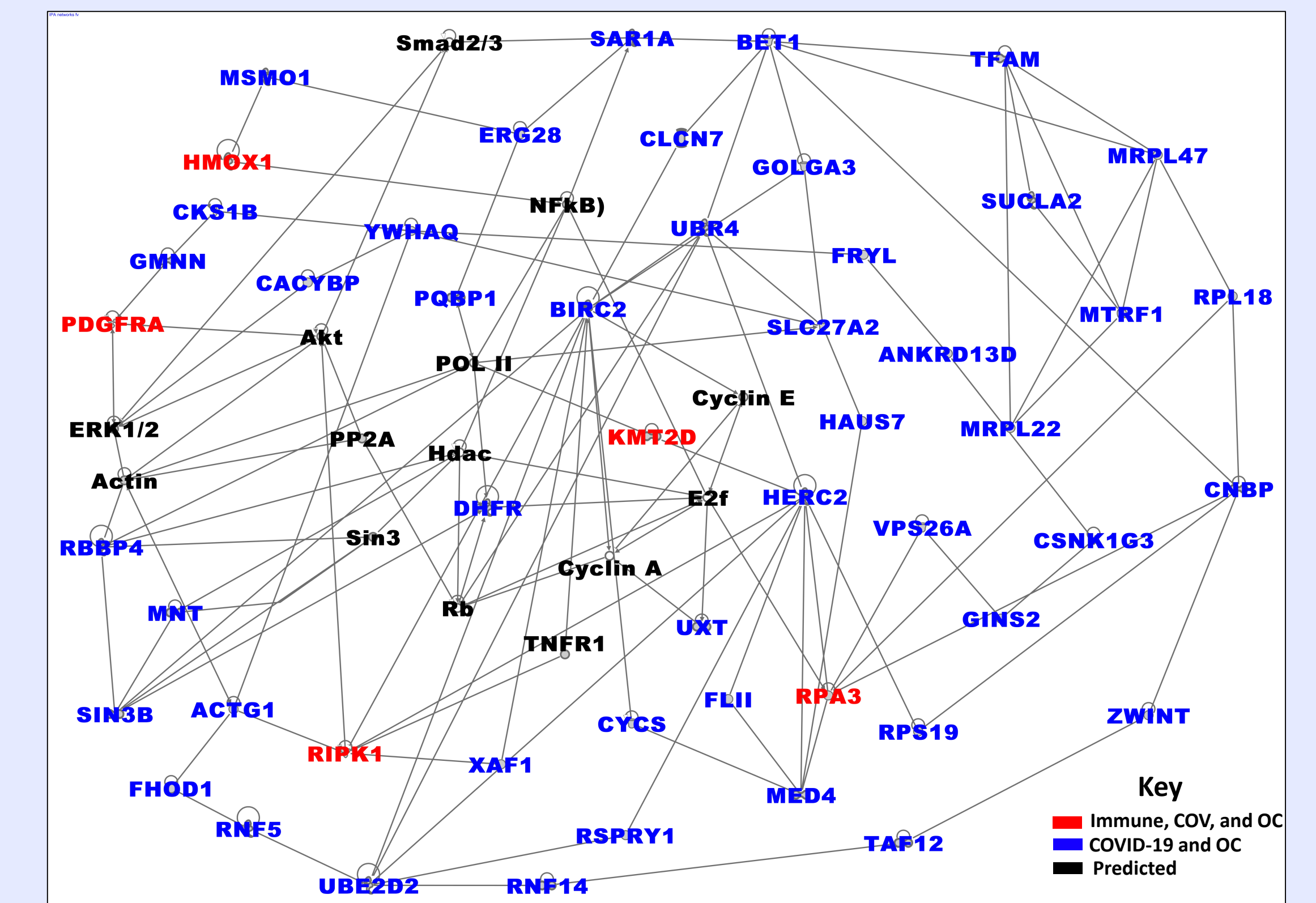
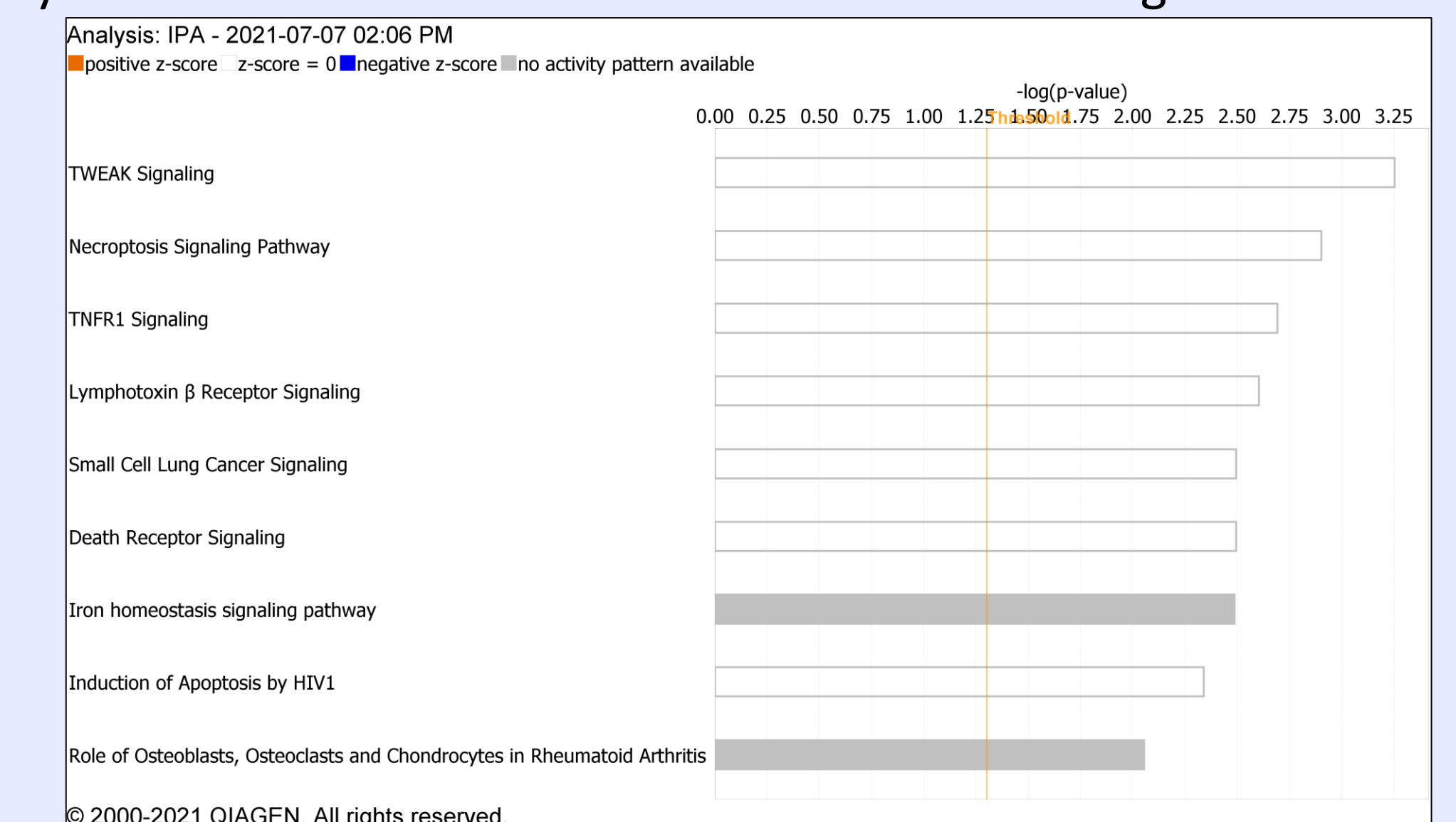


Figure 4. Top canonical pathways [$-\log(p\text{-value}) > 2.00$] associated with the two diseases. The x-axis shows the $-\log(P\text{ values})$ and the y-axis shows the pathway names. The yellow line indicated the threshold P-value for significance.



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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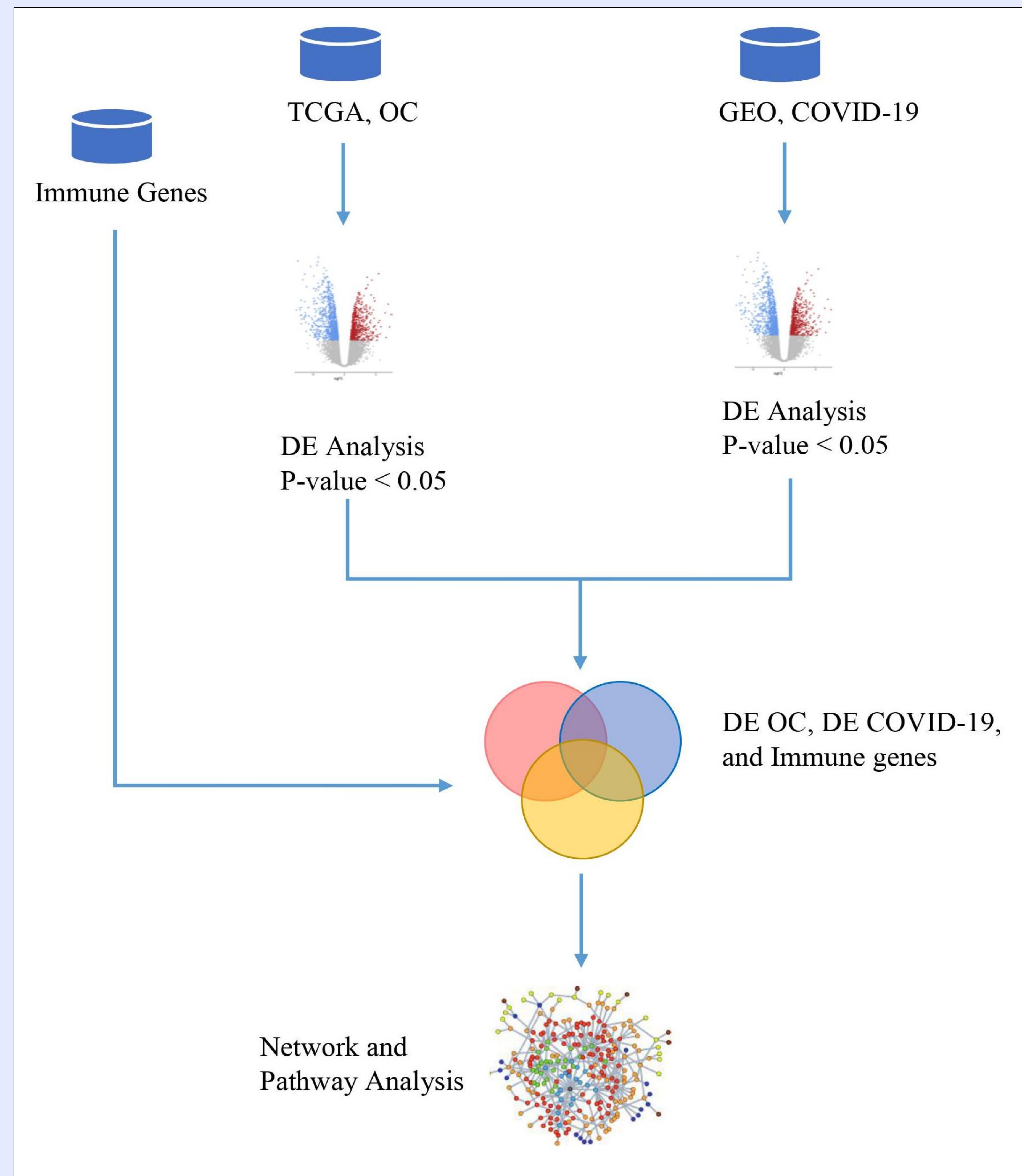
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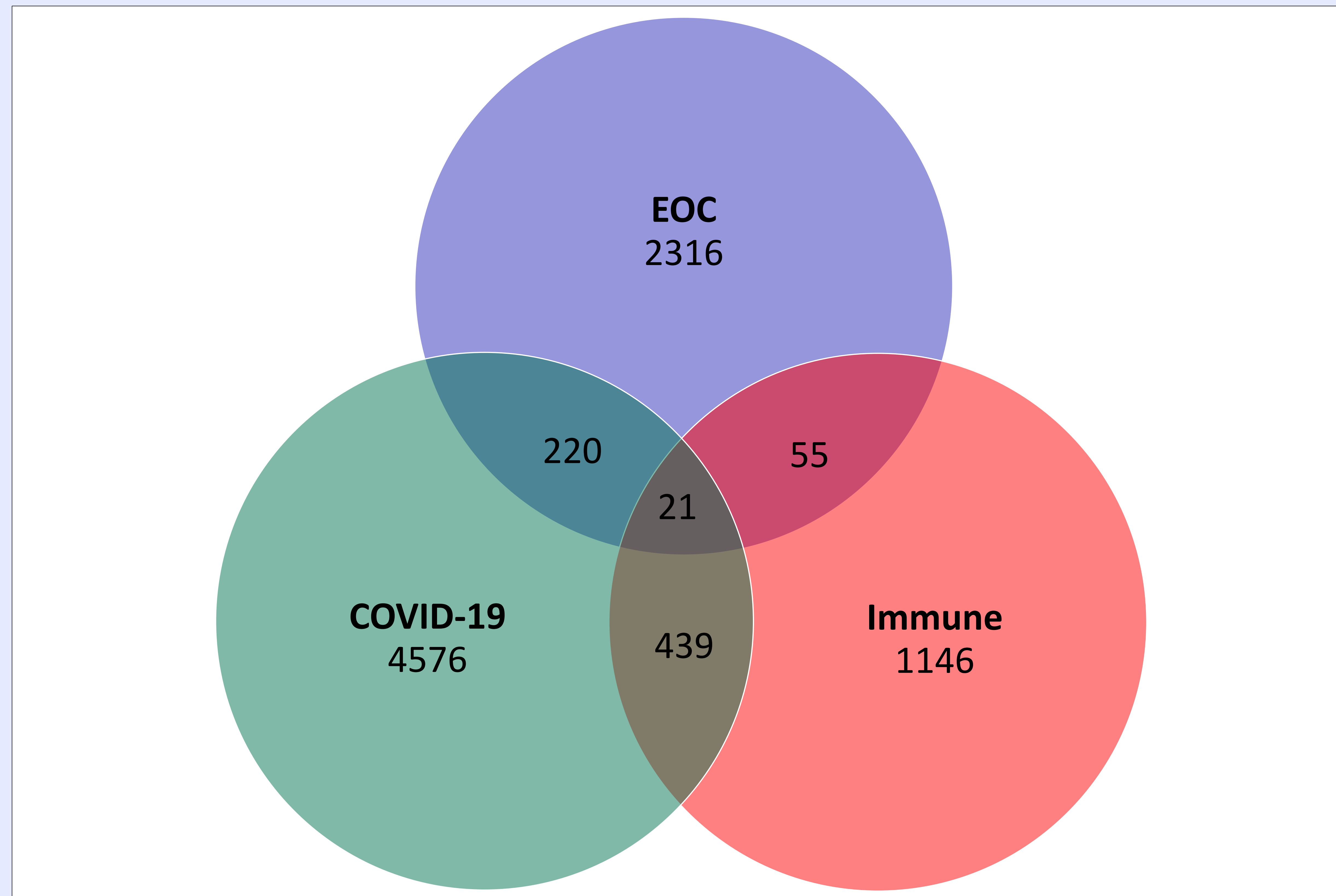


Figure 3. Figure 3 displays commonalities between the following three groups: DEGs for OC, DEGs for COVID-19 and immune-response genes. The 220 genes shared between OC and COVID-19 as well as the 21 genes shared by all three groups were used for network and pathway analysis.

Network and Pathway Analysis

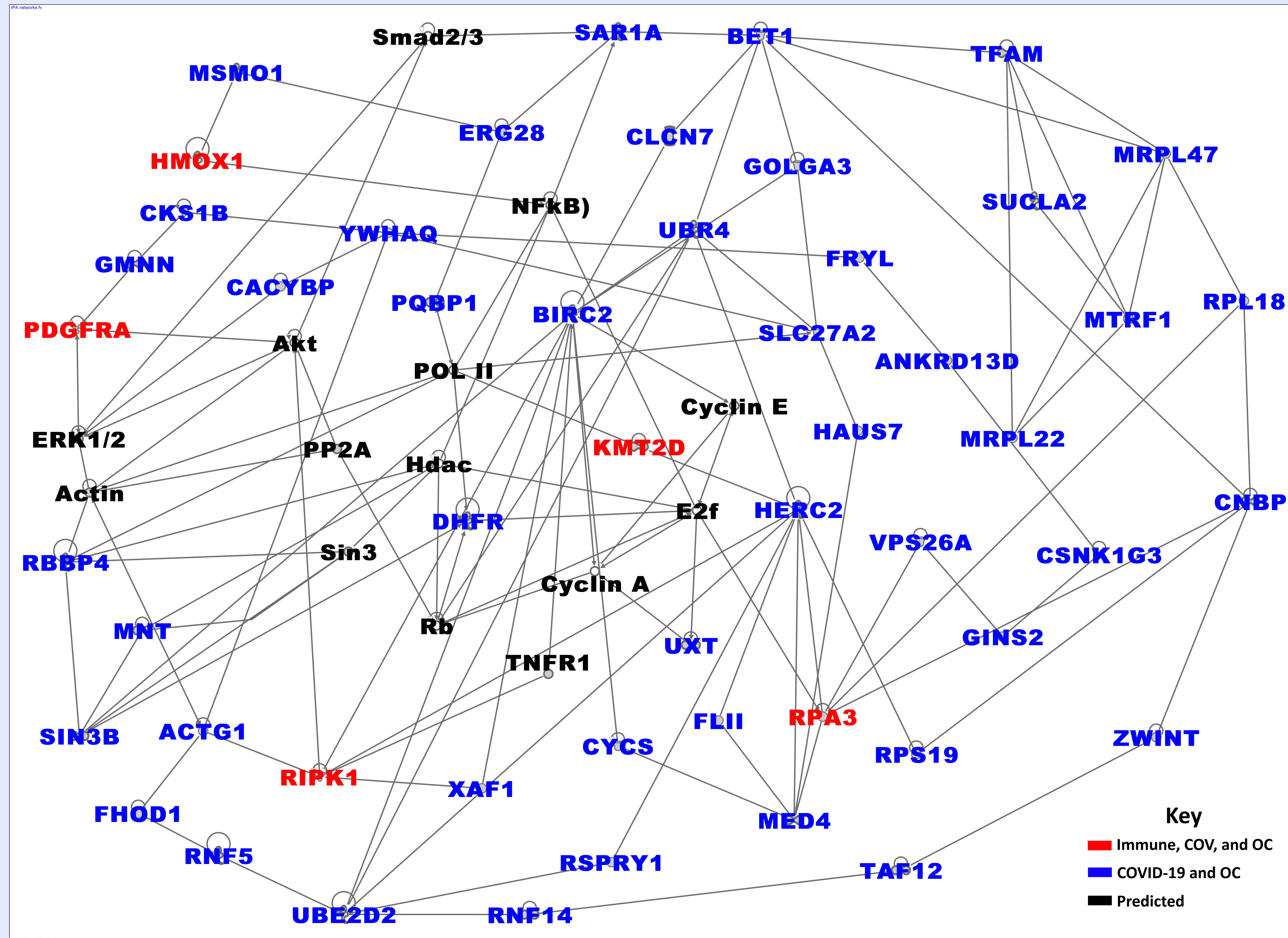


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Network and Pathway Analysis

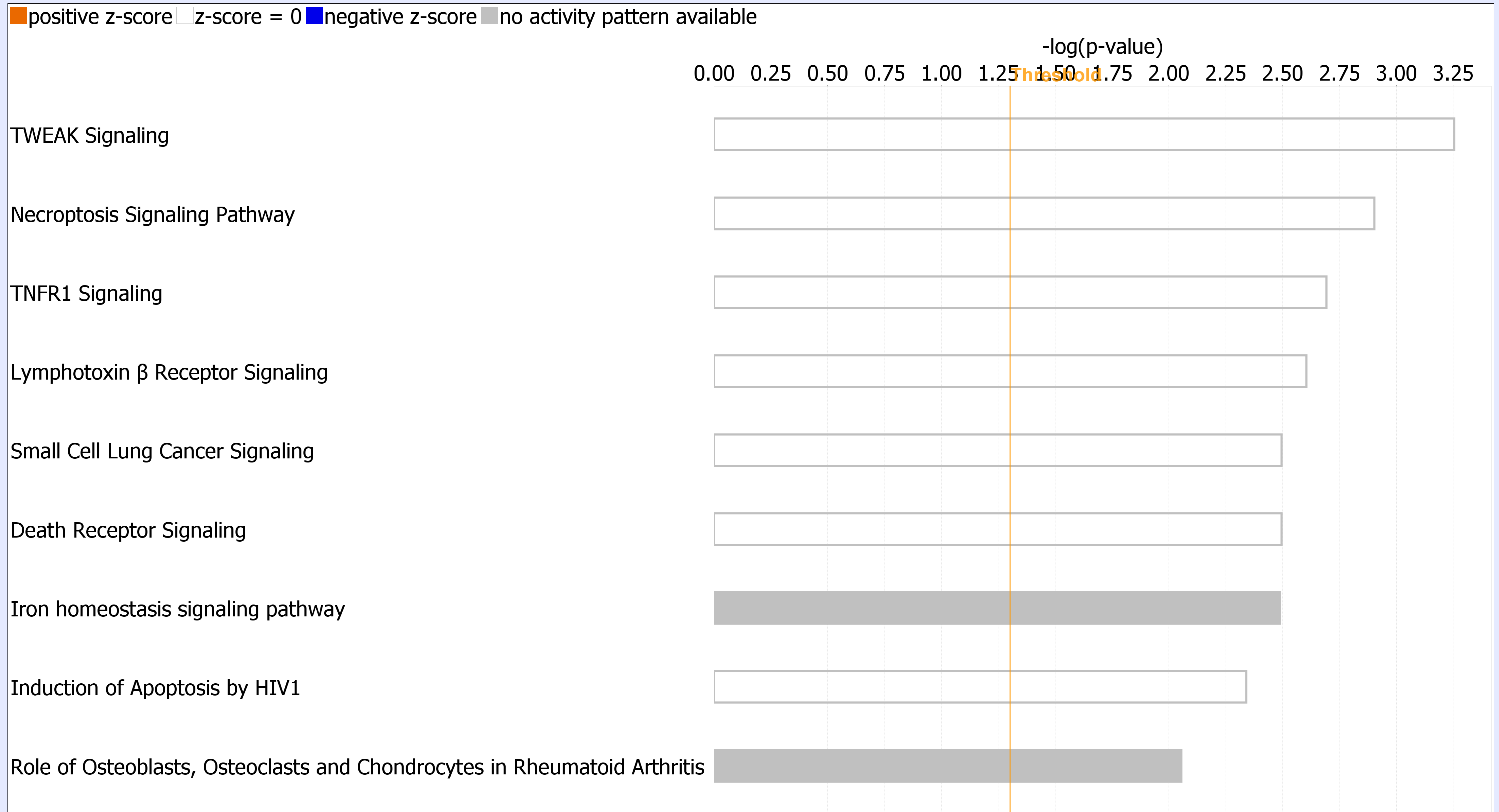


Figure 5: Signaling pathways [$-\log(P\text{-value}) > 2.00$] associated with the two diseases. The x-axis shows the $-\log(P\text{ values})$ and the y-axis shows the pathway names. The yellow line indicates the threshold P-value for significance.

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