G: profiler Results:

Functional Enrichment Analysis

To elucidate the biological roles of the 55 sepsis-related genes, a functional enrichment analysis was performed using **g:Profiler**, which integrates multiple functional annotation databases, including Gene Ontology (GO), KEGG pathways, and Reactome. The analysis identified significant Gene Ontology terms, pathways, and cellular components that provide insights into the molecular and cellular mechanisms underlying sepsis. These findings highlight the critical roles of these genes in immune regulation, inflammatory processes, and pathogen recognition, all of which are central to the pathophysiology of sepsis.

ID	Source	Term ID	Term Name	p_{adj} (query_1)
1	GO:MF	GO:0005102	signaling receptor binding	1.008×10^{-22}
2	GO:MF	GO:0001530	lipopolysaccharide binding	3.965×10^{-7}
3	GO:MF	GO:0140375	immune receptor activity	2.166×10^{-6}
4	GO:MF	GO:0019955	cytokine binding	5.379×10^{-5}
5	GO:MF	GO:0001875	lipopolysaccharide immune receptor activity	1.707×10^{-4}
6	GO:BP	GO:0006954	inflammatory response	1.729×10^{-45}
7	GO:BP	GO:0007159	leukocyte cell-cell adhesion	1.154×10^{-25}
8	GO:BP	GO:0060559	positive regulation of calcidiol 1-monooxygena...	3.334×10^{-5}
9	GO:BP	GO:0043388	positive regulation of DNA binding	1.182×10^{-4}
10	GO:BP	GO:0043281	regulation of cysteine-type endopeptidase acti...	2.171×10^{-4}
11	GO:BP	GO:0032963	collagen metabolic process	4.714×10^{-4}
12	GO:BP	GO:0045944	positive regulation of transcription by RNA pol...	7.756×10^{-4}
13	GO:BP	GO:0003158	endothelium development	2.503×10^{-3}
14	GO:BP	GO:0019233	sensory perception of pain	4.517×10^{-3}
15	GO:BP	GO:0061844	antimicrobial humoral immune response media...	4.797×10^{-3}
16	GO:CC	GO:0030141	secretory granule	1.024×10^{-14}
17	GO:CC	GO:0009986	cell surface	1.206×10^{-14}
18	GO:CC	GO:0005576	extracellular region	7.713×10^{-14}

1. Biological Processes (GO:BP)

The analysis revealed a strong enrichment in biological processes associated with immune response and inflammation, which are hallmark features of sepsis. The top terms include:

- **Inflammatory response** (*padj* = 1.79e-45): This process plays a central role in sepsis pathology, where dysregulated immune activation leads to widespread inflammation, tissue injury, and multi-organ dysfunction.

- **Leukocyte cell-cell adhesion** (*padj* = 1.15e-25): This term highlights the importance of immune cell interactions in mediating cellular migration, adhesion, and communication during the immune response. Leukocyte adhesion is essential for directing immune cells to infection sites.
- **Endothelium development** (*padj* = 2.50e-03): Vascular integrity is crucial in sepsis, as endothelial dysfunction often leads to increased vascular permeability and circulatory collapse.
- **Positive regulation of DNA binding** (*padj* = 1.18e-04): This term reflects transcriptional regulatory mechanisms necessary for activating immune-related genes during sepsis progression.

These enriched processes align with known mechanisms of sepsis, where excessive and dysregulated inflammatory responses contribute to disease severity.

2. Molecular Functions (GO:MF)

The molecular functions enriched in this gene set provide insights into the mechanisms through which these genes mediate immune responses. Key terms include:

- **Signaling receptor binding** (*padj* = 1.00e-22): This term indicates that many genes encode proteins that interact with cellular receptors, driving intracellular signaling cascades crucial for immune activation.
- **Lipopolysaccharide binding** (*padj* = 3.96e-07): This term is particularly relevant in sepsis caused by Gram-negative bacteria. It reflects the recognition of bacterial endotoxins (LPS), which are potent activators of the inflammatory response via Toll-like receptors.
- **Immune receptor activity** (*padj* = 2.16e-06): Genes involved in this function are integral to the activation of immune signaling pathways, such as cytokine and chemokine signaling, which orchestrate the immune response to infection.

These molecular functions emphasize the critical roles of pathogen recognition and immune receptor signaling in initiating and regulating the host response to sepsis.

3. Cellular Components (GO:CC)

The enrichment of cellular component terms sheds light on the subcellular localization and functional context of the proteins encoded by the genes:

- **Secretory granule** (*padj* = 1.02e-14): Secretory granules store and release inflammatory mediators such as cytokines, which are central to the immune response in sepsis.
- **Extracellular region** (*padj* = 7.71e-13): Many of the proteins encoded by these genes are secreted into the extracellular space, where they function as signaling molecules, antimicrobial peptides, or cytokines.
- **Cell surface** (*padj* = 1.20e-14): Proteins localized to the cell surface, such as receptors and adhesion molecules, are crucial for cellular interactions during immune responses.

These enriched components highlight the extracellular and membrane-associated activities of the sepsis-related proteins, consistent with their roles in immune signaling and pathogen recognition.

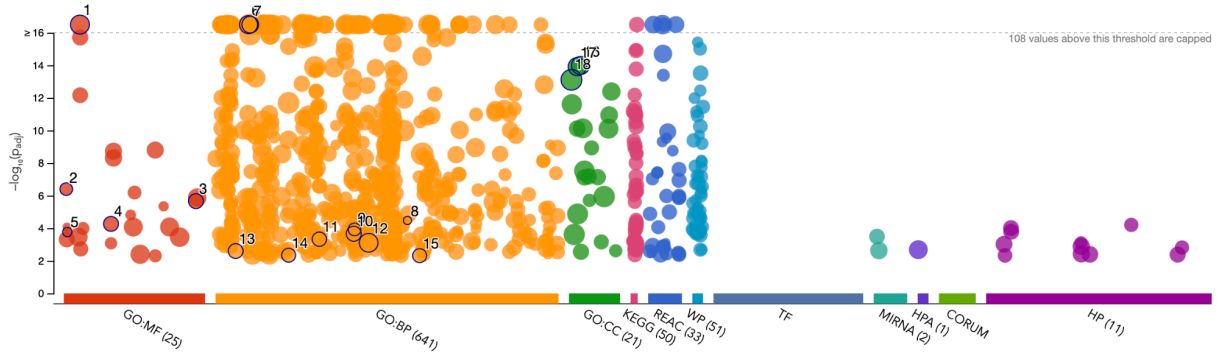
4. Pathophysiological Relevance to Sepsis

The results strongly suggest that the selected genes are deeply involved in key processes that drive sepsis pathogenesis. Terms such as **inflammatory response**, **lipopolysaccharide binding**, and **leukocyte cell-cell adhesion** are directly related to immune dysregulation, endothelial dysfunction, and systemic inflammation—hallmarks of sepsis. These findings underscore the biological relevance of these genes as potential biomarkers or therapeutic targets.

Additionally, terms associated with transcriptional regulation and protein secretion reflect the broader cellular responses to infection, including cytokine release and immune cell activation. For example, the enrichment of **endothelium development** provides insights into vascular changes that contribute to sepsis-induced organ damage.

5. Visualization of Results

The functional enrichment results are visualized in a scatterplot, where each dot represents an enriched term. The terms are grouped by categories such as **GO:MF**, **GO:BP**, and **GO:CC**, and their significance is represented by the y-axis (`-log10(p-value)`). The most significant terms, such as **inflammatory response** and **signaling receptor binding**, are highlighted with the highest y-axis values, reflecting their strong statistical significance.



6. Implications for Diagnostic Gene Discovery

The functional enrichment analysis provides a strong foundation for further exploration of these genes as sepsis biomarkers. Genes associated with highly enriched terms, such as **lipopolysaccharide binding** or **inflammatory response**, are particularly promising for diagnostic applications. Their involvement in pathogen recognition and immune regulation suggests that these genes could help distinguish sepsis from other inflammatory conditions, potentially enabling earlier and more precise diagnoses.