

Background

- PJI is estimated to cost over \$1.85 billion in the US by 2030
- Treatment focuses on the microbe but does not consider host immune status, which is the first line of defense against foreign pathogens
- Limited protein biomarker or gene expression studies
 - Focused on inflammatory products (neutrophil, cytokines, secreted molecules)
- Protein/gene expression analysis can reveal –
 - Pathogen-associated signatures
 - PJI signatures
 - Novel biomarkers that are not inflammatory products

Purpose

To characterize the host transcriptional response during active joint infection, with the goal of identifying novel pathways for further investigation.

Methods

- Samples collected from TKA patients between August 2023 and September 2024
- Single academic medical center
- Tissue was homogenized using Qiagen TissueLyser Bead Mill Homogenizer
- RNA isolation – Trizol and RNAeasy cleanup
- Library prep – KAPA mRNA Hyperprep kit
- Sequencing – Illumina NovaSeq S1, pair-end read, 100 cycles
- Analysis – Alignment to human genome (GRCh38) using STAR, statistical analysis using R, pathway analysis using g:Profiler
- Cohorts: TKA (n=9), Aseptic Revision (n=10), Septic Revision (n=14) *one septic case was from the same individual with repeat DAIR (**Figure 1**)

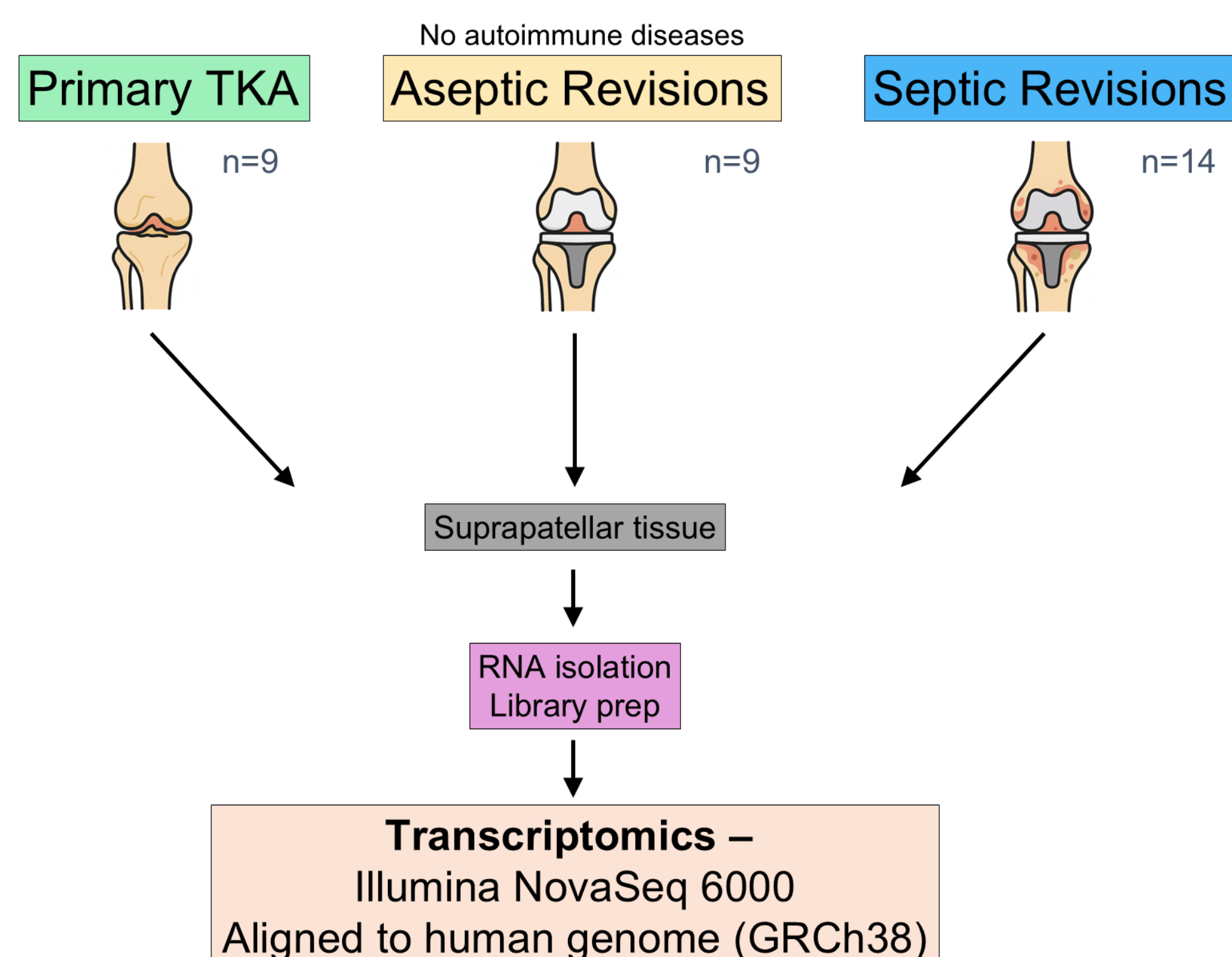


Figure 1. Study cohorts and workflow

Table 1. Patient Demographics

Variable	TKA (n=9)	Aseptic (n=9)	Septic (n=13)	p-value
Age, years (range)	64.8 ± 8.5 (54.0 – 76.0)	65.9 ± 11.1 (51.0 – 85.0)	64.0 ± 8.6 (46.0 – 80.0)	0.706
Sex (%)				
Male	5 (56)	7 (78)	8 (62)	0.589
Female	4 (44)	2 (22)	5 (38)	
Race				
Caucasian	7 (70)	8 (69)	11 (85)	0.438
African American or Black	3 (30)	1 (31)	2 (15)	
Charlson Comorbidity Index	2.7 ± 1.7 (1 – 5)	2.9 ± 1.9 (1 – 7)	3.0 ± 2.0 (0 – 6)	0.749
BMI, kg/m ² (range)	35.10 ± 5.05 (28.67 – 43.95)	29.87 ± 3.92 (23.57 – 35.15)	36.36 ± 7.79 (27.50 – 52.92)	0.051

References

- Premkumar A, Kolin D, Farley K, Wilson J, McLawhorn A, Cross M, Sculco P. "Projected Economic Burden of Periprosthetic Joint Infection of the Hip and Knee in the United States. *J Arthroplasty*. 2021; 36(5): 1484-1489.e3.
- Patel R. "Periprosthetic Joint Infection" *N Engl J Med*. 2023; 388(3):251-262.
- Piuizzi NS, Klika AK, Lu Q, Higuera-Rueda CA, Stappenbeck T, Visperas A. "Periprosthetic joint infection and immunity: Current understanding of the host-microbe interplay" *J Orthop Res*. 2024; 42(1):7-20.

Results

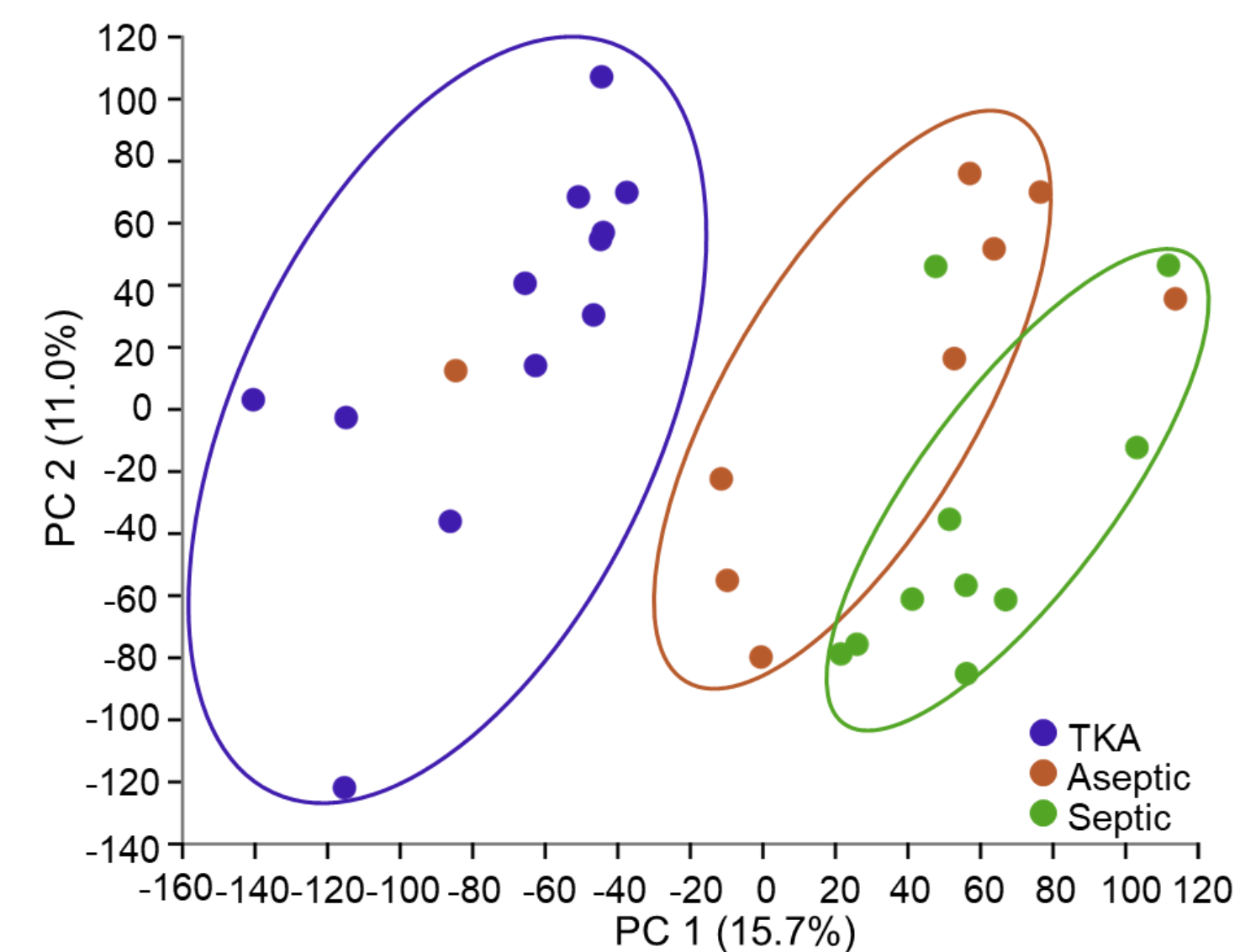


Figure 2. PCA plot depicting overall sample clustering based on transcriptomics

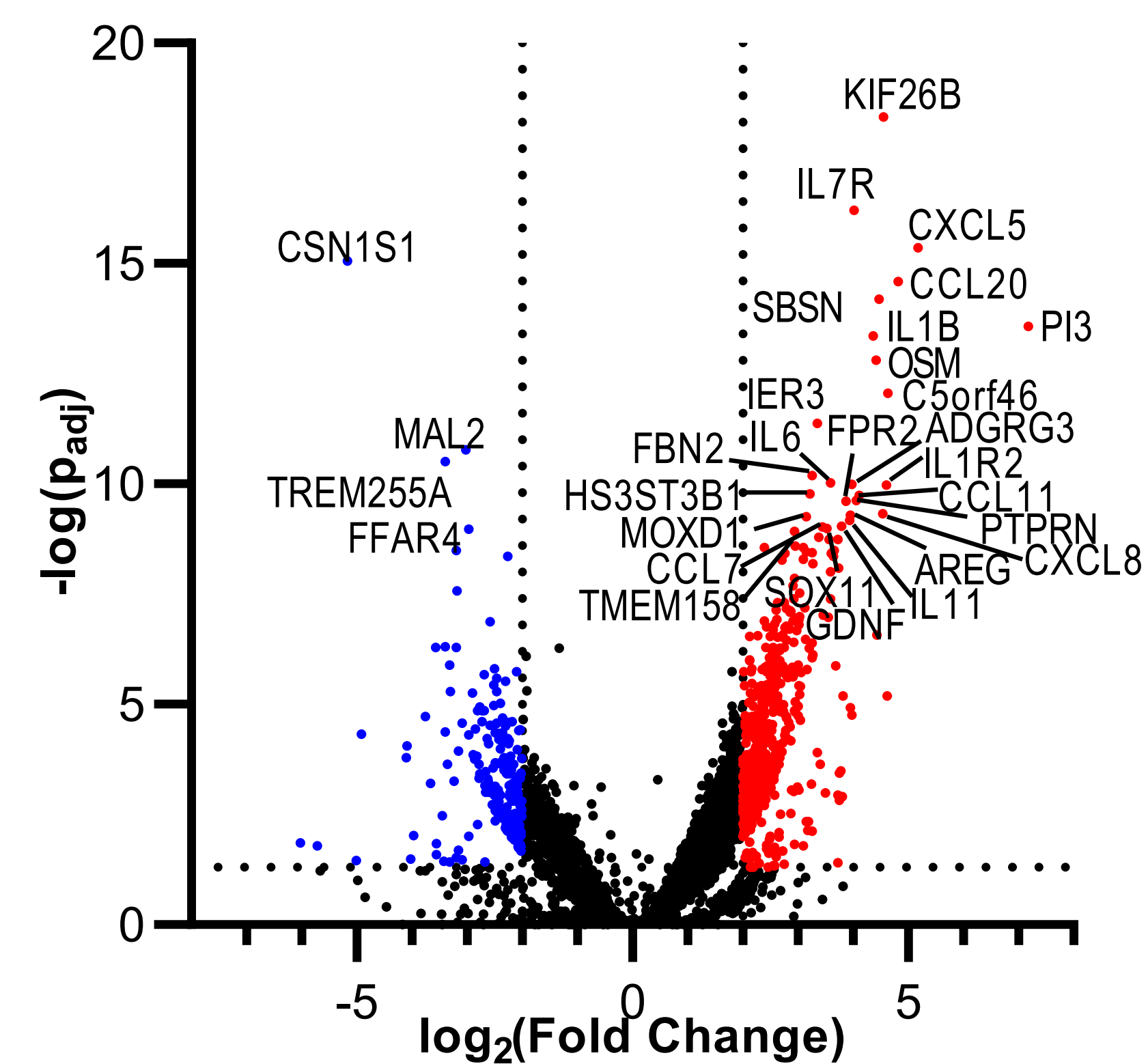


Figure 3. Differential protein expression between groups. Volcano plot comparing septic vs. aseptic (control)

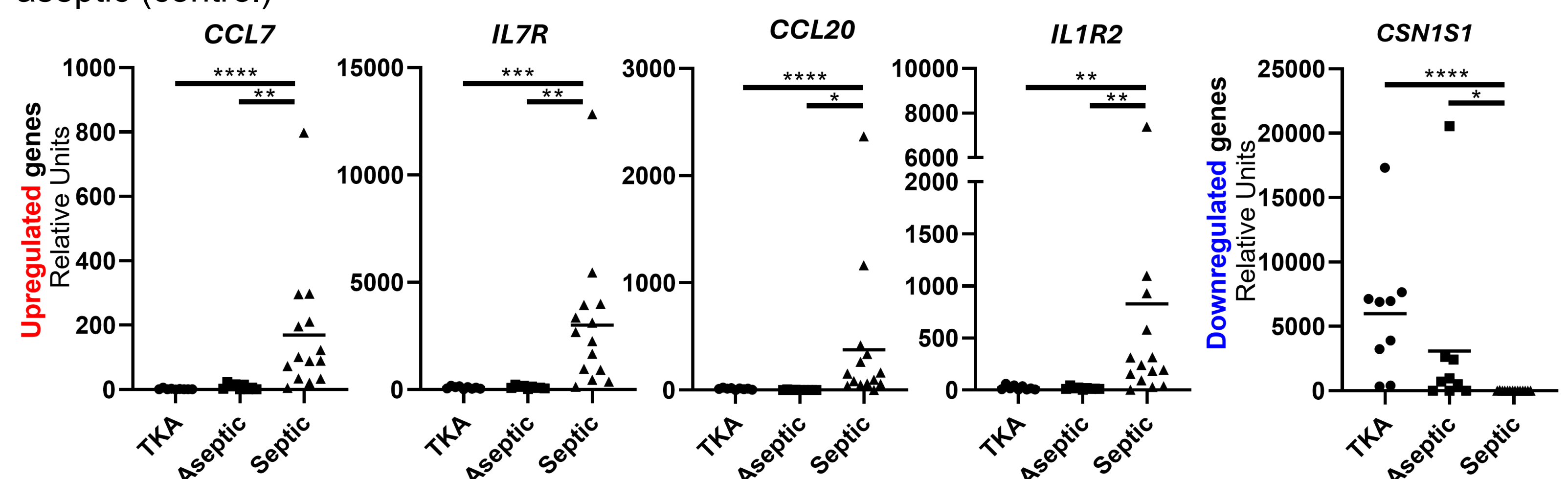


Figure 4. Differential gene expression between groups related to immune regulation.

* $p < 0.05$ is considered significant; ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$

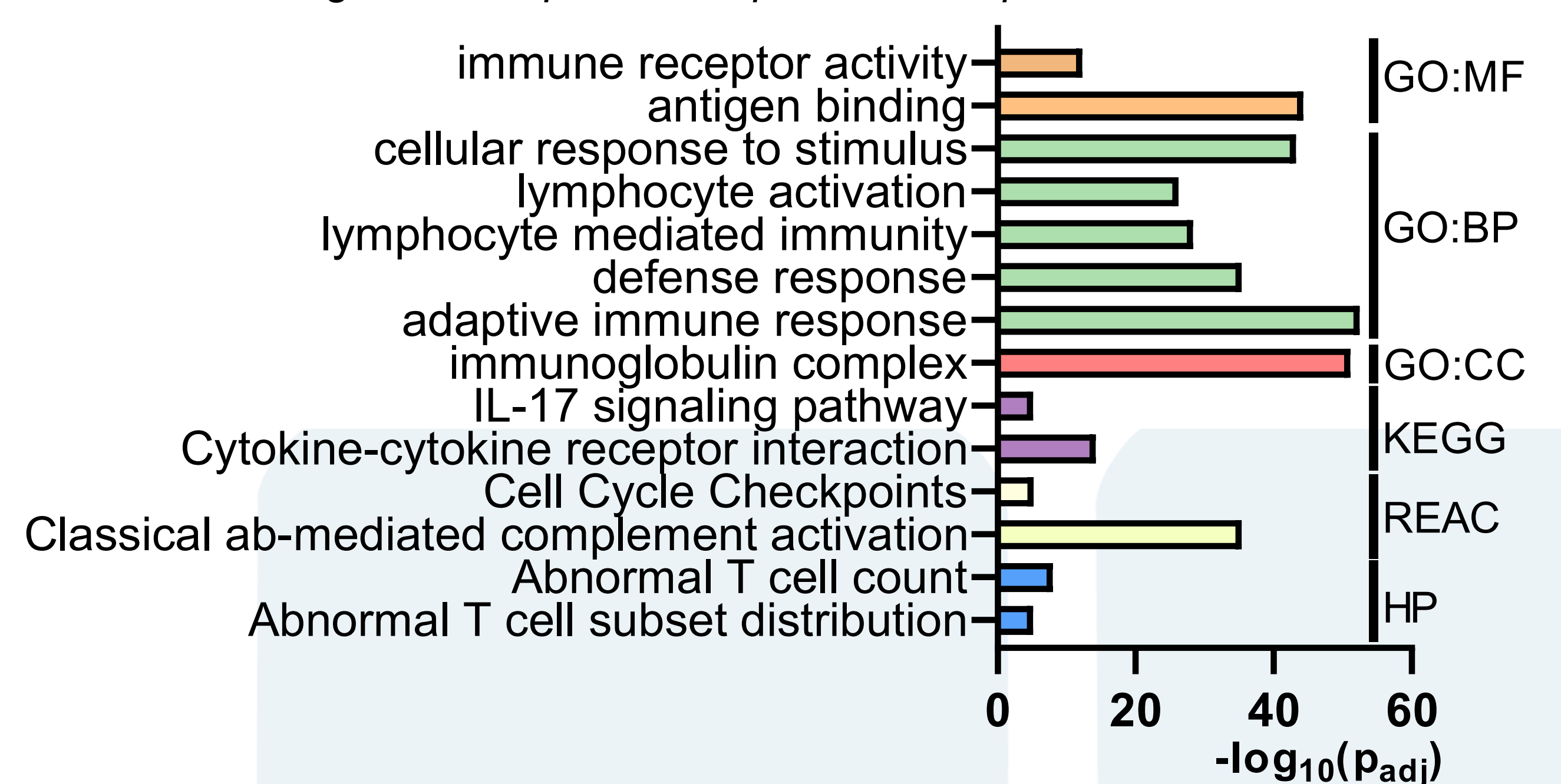


Figure 5. Pathway Analysis. Overrepresented pathways in upregulated gene expression in septic compared to aseptic.

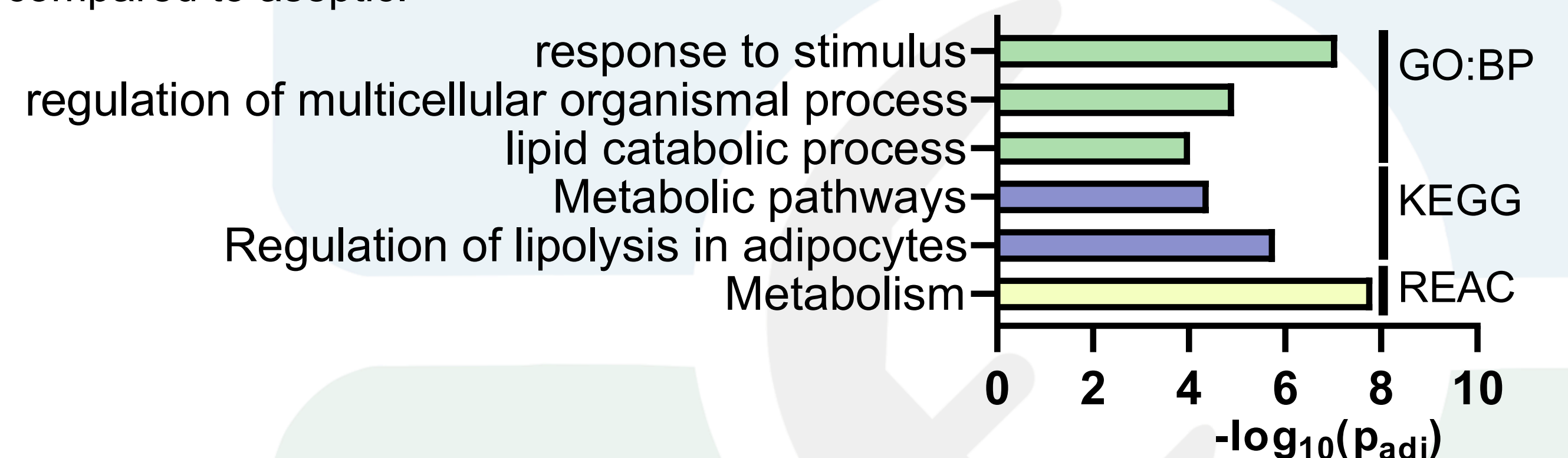


Figure 6. Pathway Analysis. Overrepresented pathways in downregulated gene expression in septic compared to aseptic.

Conclusion

- Differential expression of immune genes are seen in periprosthetic tissue. This hints at an underappreciated role/dysregulation of the immune system at the site of infection.
- Warrants further cellular analysis into the presence and function of immune cells at the infection site.