

IMMUNE EXHAUSTION AND SENESCENCE IN RECURRENT PROSTHETIC JOINT INFECTION: A IMMUNOPHENOTYPIC LANDSCAPE STUDY

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1 INTRODUCTION & AIM

2 METHODS

Despite advances in surgical techniques, the causes of recurrent prosthetic joint infection (PJI) remain unclear. While T-cells are critical for infection control, the specific immunophenotypic landscape of patients suffering from recurrent PJI remains poorly defined. This study aimed to characterize the CD3+ T-cell compartments in a cohort of recurrent PJI patients to identify distinct immune signatures and senescence patterns associated with chronic infection.

CD3+ T-cells were isolated from 15 patients: recurrent PJI, uneventful PJI and uneventful prosthetic replacement. A 18-marker spectral flow cytometry panel was utilized to assess markers of activation, differentiation, and exhaustion (including CD57, PD-1, TIM-3, and $\gamma\delta$ -TCR subsets). Data were analysed using Self-Organizing Map (FlowSOM) unsupervised clustering on a 10x10 grid, resulting in 20 distinct metaclusters (MC). Patients were subsequently grouped via hierarchical clustering (Ward linkage, Euclidean distance) based on their metacluster frequency profiles.

3 RESULTS

The mean age of the cohort was 77 years-old. There were 4 total hip arthroplasties and 11 total knee arthroplasties. The analysis identified three distinct immunophenotypic patient clusters (Figure 1). Cluster 1 characteristics specially differ from clusters 2 and 3. There were no differences in terms of age between clusters ($p>0.05$). Cluster 1 corresponds to 5 cases of recurrent PJI. This group was dominated by CD8+ terminally differentiated effector memory cells (TemRA), with MC10 (CD57^{dim}) constituting 54.8% of T-cells (vs 25.86% in cluster 2; $p=0.03$) which is consistent with exhaustion and immunosenescence. Cluster 2 and 3 corresponds to 9 patients with uneventful PJI or joint replacement. They showed a CD4+ predominance of 62.1% (vs 16.96% in cluster 1; $p<0.001$), characterized by lower expression of activation markers. There was one outlier characterized by profound T-cell exhaustion, where 75.3% of cells expressed high levels of PD-1 and TIM-3 (MC12). In this patient, a hematoproliferative condition was observed.

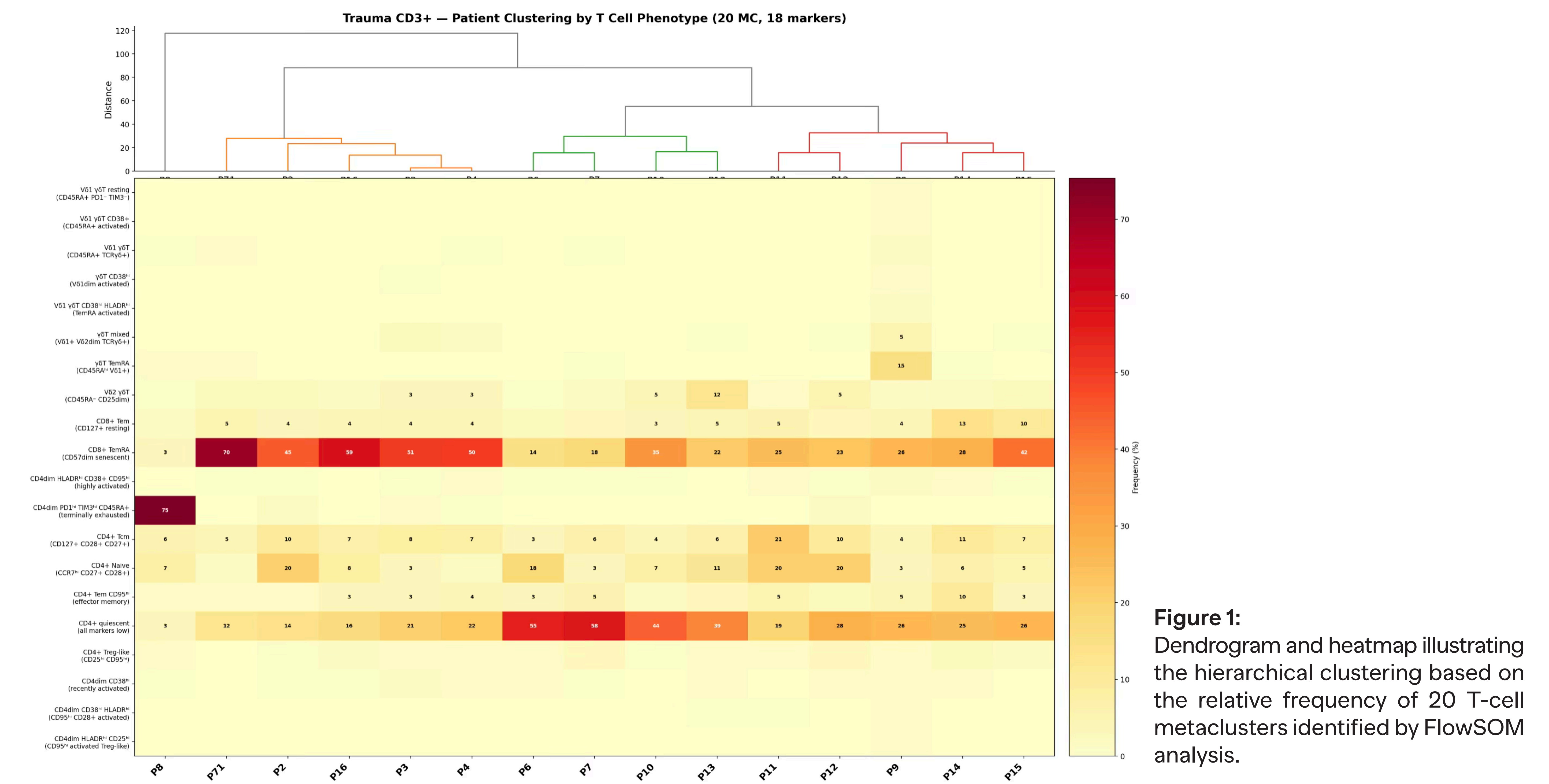


Figure 1: Dendrogram and heatmap illustrating the hierarchical clustering based on the relative frequency of 20 T-cell metaclusters identified by FlowSOM analysis.

4 CONCLUSIONS

Patients with recurrent PJI exhibit highly senescent immune response regardless patient age when CD8+ TemRA was analysed. To the best of our knowledge, this is the first study to evaluate the relationship between immune senescence and PJI.