COMMON PATHWAYS AND MOLECULAR SIGNATURES IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: A SYSTEMS BIOLOGY PERSPECTIVE

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INTRODUCTION

Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are seronegative spondyloarthropathies (SpA) that share an association with HLA-B27 and enthesitis (McGonagle *et al*., 2019). PsA, linked to psoriasis, affects peripheral (asymmetric) and axial joints (Mease, 2011), using the CASPAR criteria (Taylor *et al.*, 2006). AS focuses on the axial skeleton (Taurog *et al*., 2016), with a strong link to HLA-B27 (Reveille *et al.*, 2009) and diagnosis using the ASAS criteria (Sieper *et al.*, 2009). Both use the IL-17/IL-23 pathway (Bie *et al.,* 2023) and respond to anti-TNF and anti-IL-17. However, PsA responds well to conventional DMARDs (cDMARDs) (Gossec *et al.*, 2020), unlike axial SpA (Van der Heijde *et al.*, 2017). Crucially, axial AS responds poorly to IL-23 inhibition (Liu *et al.,* 2022), a key therapeutic difference.

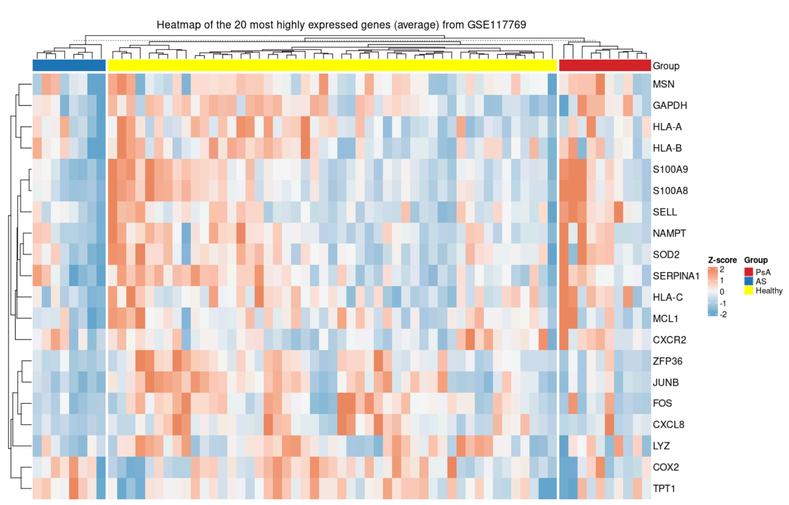
OBJECTIVE

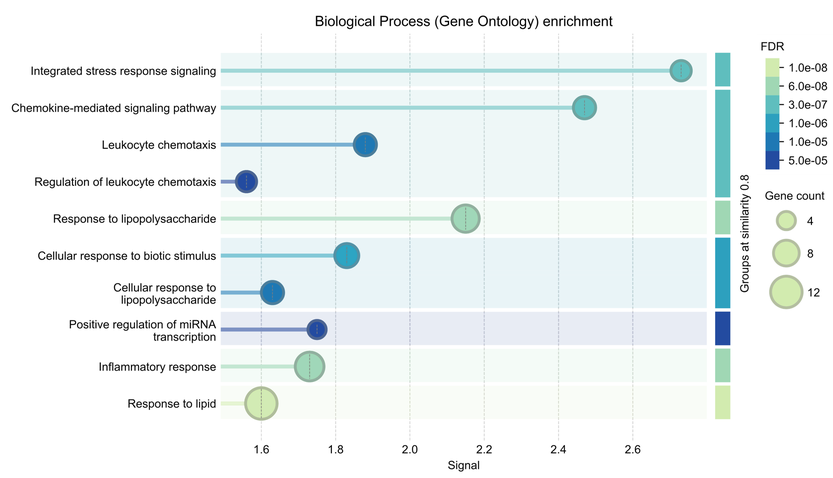
The objective of this study, based on transcriptomic analysis of RNA-Seq data, was to verify the deregulation of molecular pathways and the differential expression of key genes in ankylosing spondylitis and psoriatic arthritis, aiming to identify genetic factors, biological processes, and pathways that are shared and specific to each syndrome.

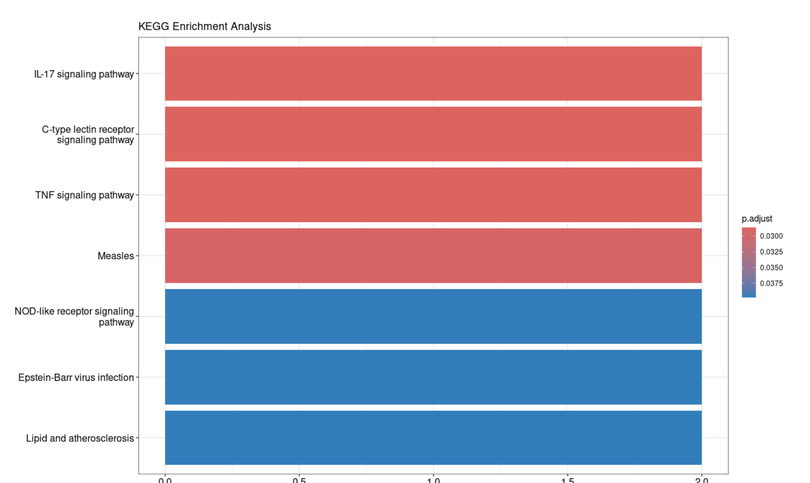
METHODOLOGY

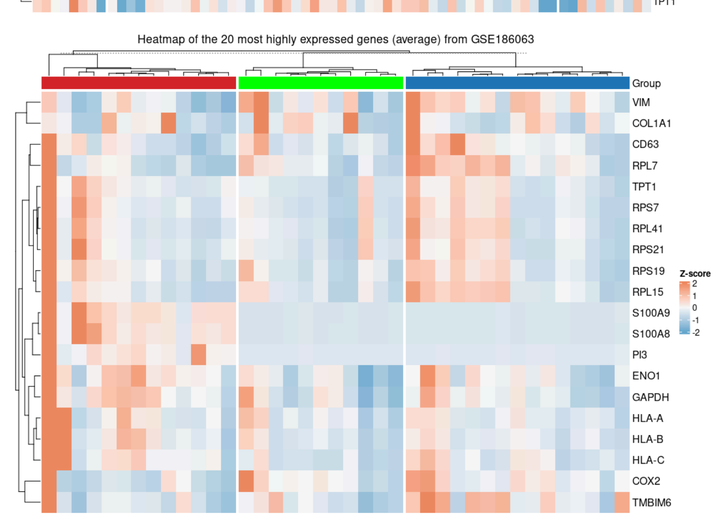
This study used comparative genomics to investigate PsA and AS. The workflow began with text mining (PubMed 2014-2024) and platforms (Enrichr-KG, DisGeNET) to select 433 relevant shared genes. Next, transcriptomic data (RNA-Seq) were selected from GEO (GSE186063, GSE117769, GSE205748, GSE221786), including skin and PBMC samples (patients/controls), some with IL-17 pathway stimulation (CytoStim). Analyses were performed in R (v. 4.4.1). Differentially expressed genes (DEGs) were identified (DESeq2, edgeR) with strict statistical thresholds (p-adj < 0.05, Log2FC > 1). Functional enrichment analysis (GO/KEGG) was performed (clusterProfiler). Protein-protein interaction (PPI) networks were constructed (STRING, score > 400) to identify “hub genes” via centrality metrics (visNetwork). Gene regulatory networks (GRNs) (TRRUST, ENCODE) were used to identify “Master Regulators” (MRs) that control DEGs. Finally, the profiles of DEGs, pathways, hubs, and MRs of PsA and AS were integrated and compared (ggplot2) to identify common and distinct molecular mechanisms.

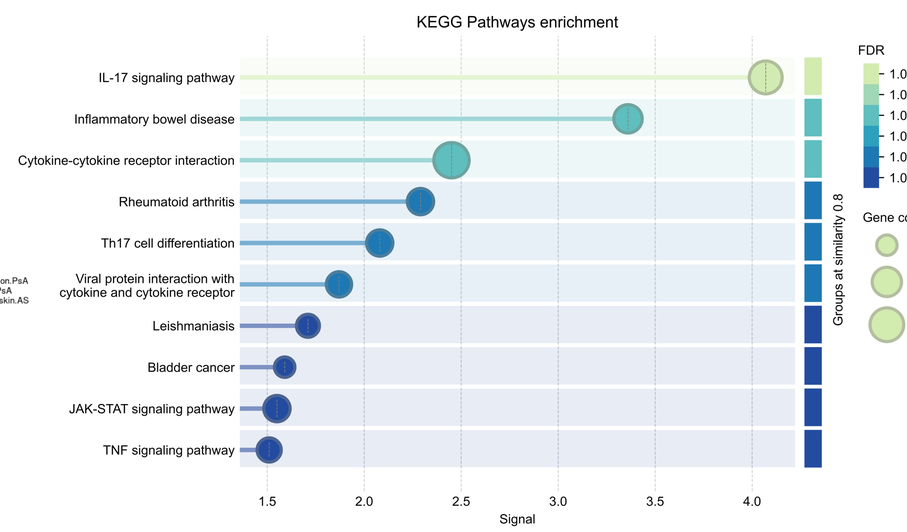
RESULTS

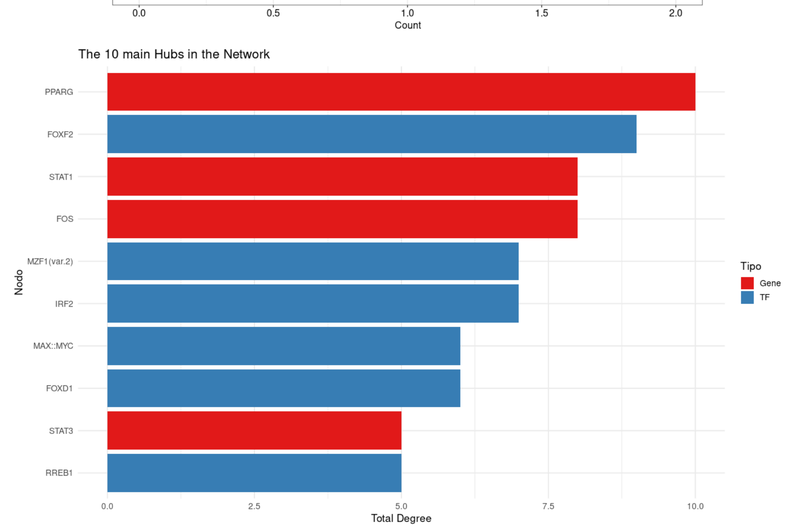












CONCLUSION

The analysis of the 433 genes confirmed findings in the literature and revealed new elements with biomarker potential. The integration of transcriptomic data, PPI networks, functional enrichment, and master regulators highlighted both common inflammatory mechanisms and immunopathological particularities between PsA and AS. Similarities: IL-17 signaling pathway, TNF signaling pathway, and lipid metabolism. The identification of central genes (PPARG, STAT1, FOS, STAT3) and less explored regulators (FOXF2, MZF1, MAX::MYC) points to new regulatory pathways and potential therapeutic targets.

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