MULTICOHORT TRANSCRIPTOME ANALYSIS REVEALS KEY GENES FOR SYSTEMIC LUPUS ERYTHEMATOSUS

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INTRODUCTION:

Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease with complex pathophysiology and limited therapeutic options. The absence of reliable patient stratification and robust biomarkers hinders precision medicine approaches in SLE.

AIM:

Therefore, this study aimed to identify consistently differentially expressed genes (DEGs) across independent transcriptome datasets from whole blood of SLE patients using a multicohort integrative strategy.

METHODS:

Public RNA-seq datasets (GSE72509, GSE112087, GSE122459, and GSE80183) were retrieved from the Gene Expression Omnibus. Batch effects were corrected using the ComBat_seq function from the sva package. DEG analysis was performed using both the limma+edgeR and DESeq2 frameworks, and only genes identified as significant in both approaches were retained. DEGs were selected based on a false discovery rate (FDR) < 0.01 and absolute log2 fold-change > 1. Gene Ontology (GO) enrichment analysis was conducted separately for upregulated and downregulated genes passing these criteria to characterize the biological processes most affected in SLE.

RESULTS:

First, the integrated transcriptomic analysis of multiple cohorts was corrected as described (Fig. 1). The corrected dataset revealed a robust set of differentially expressed genes between systemic lupus erythematosus (SLE) patients and healthy controls. The volcano plot (Fig. 1A) highlighted a prominent inflammatory signature strongly associated with innate immune activation, with upregulated genes such as IFI27, OTOF, IFI44L, SIGLEC1, RSAD2 (log2FC > 3, FDR < 0.01). These genes are primarily involved in the type I interferon signaling pathway. Functional enrichment analysis (Fig. 2B) showed that the differentially expressed genes were significantly associated with biological processes such as defense response to viruses, response to viruses, and negative regulation of viral genome replication, all GO related to interferon-signaling pathways.

CONCLUSION:

Our multicohort transcriptomic analysis highlights the pivotal role of type I interferon signaling and innate immune activation in the pathogenesis of systemic lupus erythematosus (SLE). The consistent upregulation of interferon-stimulated genes across independent datasets underscores their potential as robust biomarkers of disease activity and promising therapeutic targets. These findings deepen our understanding of SLE's molecular landscape and support the rationale for developing targeted therapies, including CAR-T cell strategies that aim to modulate aberrant immune responses.

KEYWORDS:

systemic lupus erythematosus, transcriptome, genes.