

**Systemic Transcriptomic Dissection and Network Biology of Antiphospholipid Syndrome:
Unveiling Hub Drivers, Functional Clusters, and Transcriptional Motifs in Vascular and
Obstetric Pathology**

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Abstract

Background and Objectives: Antiphospholipid syndrome (APS) is an autoimmune thrombophilia associated with vascular thrombosis and adverse obstetric outcomes, including recurrent pregnancy loss and placental insufficiency. Neutrophil activation and thrombo-inflammatory responses are key contributors to APS pathogenesis. This study aimed to identify key hub genes, functional modules, and regulatory motifs associated with neutrophil dysfunction in primary APS using an integrated bioinformatics approach.

Methods: Transcriptomic dataset GSE102215 from peripheral neutrophils of primary APS patients and healthy controls was re-analyzed using GEO2R. A protein-protein interaction network was constructed via Cytoscape. Hub genes were identified using the CytoHubba plugin across four algorithms: Maximal Clique Centrality, Density of Maximum Neighborhood Component, Maximum Neighborhood Component, and Degree. Functional network modules were detected using ClusterONE, while promoter and motif analyses were performed using Tomtom and GOMo.

Results: Transcriptomic profiling revealed significant inflammatory and innate immune pathway activation. Integrated CytoHubba analysis identified 18 hub genes: AHNK, IL7R, TRAFD1, RAB8A, LTB, ARHGEF12, COTL1, RABGAP1, PTP4A1, DOCK8, RAC2, STAT1, IRF7, MYD88, CXCL8, ITGAM, MPO, and TLR4. ClusterONE revealed densely connected modules related to leukocyte activation and cytoskeletal organization. Promoter analysis indicated enrichment of NF-kappa B, IRF, and AP-1 regulatory motifs.

Conclusion: This integrated network analysis identified an 18-gene hub signature driving neutrophil activation and thrombo-inflammatory responses in primary APS, providing candidate targets for biomarker discovery and therapeutic exploration in obstetric antiphospholipid syndrome.

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