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### Inflammatory profiling and immune cell infiltration in dysthyroid optic neuropathy: insights from bulk RNA sequencing

**Abstract:**

Dysthyroid optic neuropathy (DON), the most severe complication of thyroid eye disease (TED), lacks clear mechanisms and effective treatments. This study aimed to identify key pathways and inflammation-related genes driving DON progression. Retro-orbital tissues from DON, non-DON TED, and healthy controls were analyzed using bulk RNA sequencing. Differentially expressed genes (DEGs) were identified and subjected to GO enrichment and weighted gene co-expression network analysis (WGCNA). Immune cell infiltration was evaluated using single-sample Gene Set Enrichment Analysis (ssGSEA), and core inflammatory genes were validated by qPCR. Analysis revealed significant upregulation of inflammation- and fibrosis-related genes in DON, including CXCL14, CCL21, HP, MGP, and FN1. GO and WGCNA analyses highlighted immune activation and extracellular matrix remodeling. Key inflammatory-related DEGs (IRDGs) such as CCL21, HP, and SLCO2A1 were strongly associated with immune pathways. ssGSEA showed increased infiltration of activated B cells, CD4 T cells, mast cells, and Th1 cells in DON tissues. Correlation analysis linked IRDGs with various immune cells, notably activated B and regulatory T cells. qPCR confirmed upregulation of HP, TPSAB1, and PLA2G2A in DON. This is the first study to identify the key molecular and immune drivers of DON through bulk transcriptomic analysis, emphasizing the central role of inflammation-related molecules and immune cell infiltration in its pathogenesis. The identified IRDGs and their associated pathways provide novel insights for innovative diagnostic and therapeutic strategies.

### Biography

**Yuanping Hai** obtained his PhD degree in June 2022 from Johannes Gutenberg University Mainz, Germany, with a research focus on Thyroid Eye Disease. He is currently a postdoctoral fellow at Southern Medical University, China. He was awarded a Youth Project grant by the National Natural Science Foundation of China (NSFC) in 2023. Dr. Hai has published over 20 scientific papers, including 6 studies related to Thyroid Eye Disease as first author, co-first author, or co-corresponding author.