Evaluating the transcriptome of iMCD-TAFRO

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Background: Idiopathic Multicentric Castleman disease (iMCD) patients show severe symptoms and involve multiple regions of enlarged lymph nodes that demonstrate "Castleman-like" features under the microscope. These characteristic features may include a constellation of regressed or hyperplastic germinal centers, follicular dendritic cell prominence, hypervascularization, and polytypic plasmacytosis. Patients must undergo excisional lymph node biopsy to be diagnosed with CD as they all share specific changes to the lymph nodes. Therefore, to better understand these changes we decided to study the most severe subset, iMCD-TAFRO, by using an unbiased gene expression profiling method to study the transcriptome of the lymph node.

Methods: This study used previously preserved formalin-fixed, paraffin-embedded (FFPE) lymph node tissue from a cohort of 11 iMCD-TAFRO and 8 sentinel control groups. After RNA extraction, we used Nanostring nCounter, a novel digital read-out technology with fluorescent color-coded barcode probes. For an unbiased approach, various analytical methods such as Gene Set Enrichment Analysis (GSEA), Ingenuity pathway analysis (IPA), and GO enrichment analysis were used to interpret our gene expression data.

Results and Discussion: After identifying differentially expressed (DE) genes of iMCD-TAFRO compared to sentinel, we identified genes that were previously shown to be highly elevated in circulation such as PLA2GS2A and CCL23. Through GSEA, we found an enriched signature for the coagulation cascade. IPA and GO analysis were consistent with upregulation of transcripts related to the complement cascade. Future work is needed to better understand the roles that these DE genes and pathways play in the transcriptome of iMCD-TAFRO lymph nodes.