ABSTRACT #16

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Title: Transcriptomic sequencing of pediatric patients with Kikuchi-Fujimoto Disease reveals abnormal upregulation of Type 1 Interferon Signaling Response

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Introduction: Kikuchi-Fujimoto disease (KFD) is a self-limited lymphadenitis of unclear etiology that typically occurs after a viral infection. Though presence of immune cell infiltrates on histology suggests an autoimmune origin, the pathogenesis is unknown and can be difficult to differentiate from other autoimmune disorders based on symptomology and histology alone.

Methods: To understand the pathogenesis of KFD, we performed targeted RNA sequencing of 15 KFD and 9 non-KFD reactive controls using the HTG EdgeSeq platform, a probe-based RNA-sequencing technology from HTG Molecular Diagnostics. Two thousand and three autoimmunity-related genes were evaluated from archived formalin fixed paraffin embedded lymph node tissue and analyzed using a modified bulk-RNA-seq workflow. Differential expression (DE) gene analysis of KFD cases compared to controls was performed using limma. Cell proportions of patient samples were estimated by CibersortX deconvolution using the LM22 signature matrix.

Results: DE gene analysis revealed 60 significantly DE and upregulated genes, 68% of which were associated with the type I interferon (IFN) response pathway. Gene expression pathway analysis revealed enrichment of IFN signaling, anti-viral and autoimmune pathways. Protein-protein interaction analysis and molecular complex detection algorithm identified a 15 gene module composed of genes RSAD2, OAS3, OAS2, OASL, IFIT3, IFIT1, ISG20, STAT2, XAF1, MX1, IRF7, IFITM1, MX2 and IFI27. IFI6, an apoptosis regulator, was identified as a seed gene within that module. Additionally, transcription factor target analysis identified enrichment of IFN response elements and IFN response factors. Finally, estimated proportion of M1 macrophage population was increased in KFD in comparison to control.

Conclusion: Our study is the first to apply transcriptomic sequencing to a series of KFD patients and discover a novel association between type I IFN signaling and KFD. Our preliminary data suggest that the source of IFN signaling is from type 1 immune cells, such as M1 macrophages or plasmacytoid dendritic cells. Follow up studies will further investigate the source and mechanism of IFN activation.

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