RNA sequencing reveals specific modulation in gene signatures from patients with IgG4-related diseases

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Objectives:

We aimed to characterize the molecular differences and the effects from prednisone treatment among multi-organ involved IgG4-related disease (RD), Mikulicz's disease (MD) and IgG4-related retroperitoneal fibrosis (RF).

Method:

RNA sequencing was conducted on blood from 17 MD (ages 32-81; 8 Males), 19 RD (ages 48-80; 13 Males), 3 RF (ages 48-65; 3 Males) and 10 control subjects (ages 30-57; 7 Males). In which, 10 MD and 8 RD patients were subjected to treatment with prednisone (__60 mg) and glucocorticoid-sparing agents. Others received only prednisone or with no treatment. Six RD patients had a longitudinal time point.

Results:

The mRNA levels of IgG4 and IgE, the gene signatures of Th2, eosinophil, and neutrophil were over-expressed in MD and RD, compared to that in control samples. B-cell signature was suppressed in RD, MD, and RF versus controls. While Th1, Th2, Treg, and eosinophil signatures were increased, whereas Tfh genes and a B cell signature were decreased at flare disease state in RD. Nuclear division/mitosis-associated genes correlated most with IgG4 expression. Prednisone treatment in MD or RD led to increased neutrophil, but decreased eosinophil and Treg signatures. A similar pattern was observed with IgG4 and IgE in MD patients after prednisone treatment.

Conclusions:

IgG4, IgE, B-cell, T-cell subpopulations, eosinophil, and neutrophil cell-specific genes/gene signatures are regulated in MD, RD, and RF diseases. Prednisone selectively modulates Treg, eosinophil, and neutrophil signatures. Molecular signatures are varied at different disease states. Further functional studies may help to elucidate role of the molecular signatures involved the pathogenesis of IgG4-related diseases.