

GENE EXPRESSION ANALYSIS OF HUMAN IGA AND LUPUS NEPHRITIS: SIMILARITIES AND DIFFERENCES

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IgA nephropathy (IgAN) and lupus nephritis (LN) are both heterogeneous diseases characterized by glomerular immune complex deposition. Their diagnosis and treatment are mainly based on clinical symptoms and histological description, not necessarily reflecting underlying pathophysiology or giving information on prognosis.

Renal biopsies from living donors (LD, n=21) and patients with IgAN (n=27) and LN (n=32) were collected from an international multi-center cohort (ERCB). Affymetrix microarrays were processed separately for the glomeruli and the tubulointerstitium (TI) compartments.

The mRNAs and associated transcriptional regulatory networks differentially regulated compared to LD were identified for each disease. Hierarchical cluster showed that gene expression profiles grouped patients independent of histological diagnoses. The molecular signatures segregated 2 distinct subgroups inside IgAN and LN. About 3.2-fold more genes were regulated in the glomeruli of patients with LN vs. LD than in IgAN patients. In the glomeruli of IgAN and LN, 874 common genes were regulated in the same direction. A group of 234 common transcripts was able to predict GFR in both diseases. Evaluating infiltrating cell specific transcripts in the renal tissue, a circulating B-cell specific signature of 239 and 236 transcripts was found in LN and IgAN glomeruli and confirmed the segregation of two molecular subgroups as defined by the genome wide expression profiling analysis. 21 common B-cell genes were significantly differentially regulated ($q < 0.05$) between the LN and IgAN subgroups.

In summary, the common transcriptional mechanisms between both diseases and their subgroups reflect active immune infiltrating cell signatures. The shared key nodes between IgAN and LN will lead to common and disease specific pathways and thereby help to identify therapeutic networks.