A TRANSCRIPTOMIC APPROACH FOR LUPUS NEPHRITIS CLASSIFICATION

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Progression of lupus nephritis (LN) is driven by intra-renal molecular mechanisms, currently only partially understood. Defining transcriptional activity might reflect the distinct functional status in LN.

Renal biopsy tissues were obtained from the ERCB cohort: 32 patients with LN and 16 controls (living donors, LD). Affymetrix HG-U133A microarrays were processed from glomeruli and tubulo-interstitium (TI) mRNAs and analyzed individually using a customized data processing pipeline (www.GenePattern.org).

The Bayesian network approach represents a powerful method for identifying molecular markers of disease. In the TI, the top-scoring network predicting of GFR employed mRNA levels of EGR-1, VCAM-1 and FAS in the entire LN cohort. In LN, the immune response system was highly activated, with over-representation of the IFN signaling, as well as interleukins signaling pathways (IL-2,-4,-6,-10), complement and coagulation cascades. Genome wide expression profiling and principle component analysis segregated two subgroups of patients (LN1 and 2) indistinguishable by histopathology or renal function characteristics. LN1 and 2 were compared to define the molecular mechanisms responsible for LN segregation. In the TI, the leukocyte extravasation pathway was one of the top canonical pathways significantly regulated in LN2 vs. LN1, implicating this pathway among others in LN disease course. In glomeruli, significant regulated signaling pathways between LN1 and 2 included: protein ubiquitination, oxidative phosphorylation, IGF-1 and VEGF signaling pathways.

Renal gene expression signatures in LN identified unique subgroups with distinct glomerular and TI fingerprints. Further analysis could provide a molecular based categorization of disease progression and prediction of therapeutic responses.