

## **Dysregulation of apoptosis pathways in lupus patients revealed by network analysis of dynamic gene expression data.**

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A central role for B cells in the SLE pathogenesis has been established by work performed at multiple laboratories in both mice and humans [Wakeland et al, 01; Harley, J.B. and Kelly, 02; Wu et al, 07]. B cell defects including abnormal function of key signaling molecules, B-cell receptor signaling defects, and perturbations in B cell developmental subsets certainly play a central role in the breakdown of B cell tolerance and subsequently in the pathogenesis of SLE.

Further progress in this area could be associated with microarray technology. In this report we applied standard and original methods of analysis of microarray data for delineating the main events in BCR signaling in Epstein-Barr Virus transformed B cells from SLE patients and normal controls. The experimental design of this research is based on duplication of each step of the experimental and analytical procedures. These steps include -Selection of genes with significant variability of expression levels; -Verification of the expression profile reproducibility for these genes; - Gene partition into clusters using clustering procedure; - Networking of HV genes based on partial correlation.

The analysis produced network of gene regulatory interactions working in course of B-cell activation. Some of them are common for patients/controls groups, and others are different. All details of the network were reproduced in two independent experiments, making them reliable information about gene functional interconnections in course of B cell activation.

Here are obtained evidences for significant the differences in the apoptotic signaling in the activated B lymphocytes from normal donors compared with lupus patients. These evidences include preferred expression of anti-apoptotic genes together with down-regulated pro-apoptotic genes in patient's samples and also several examples of differences in functional associations in the signaling pathways regulating apoptosis