Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that can virtually involve any organ system of the body. Many efforts have been made to elucidate the pathology, but the molecular mechanisms are still not understood. Lymphocytes are considered to play an important role in SLE pathogenesis. Aberrantly activated T cells mediate inflammatory responses and activate B cells to differentiate and produce autoantibodies, resulting in multisystem manifestations [1, 2]. With the wide use of gene technique, more genetic studies on SLE were performed and differentially expressed genes (DEGs) were identified. Integrating and re-analyzing these data can help us understand the molecular mechanisms and identify diagnostic and therapeutic targets of SLE.

Methods: In our study, we downloaded the microarray datasets GSE45888 and GSE10325 from Gene Expression Omnibus (GEO) database to identify the candidate genes in T and B cells respectively. Methods: Datasets GSE45888 and GSE10325 were downloaded from GEO (http://www.ncbi.nlm.nih.gov/geo). The DEGs between T or B cells and control samples were screened using GEO2R (http://www.ncbi.nlm.nih.gov/geo/geo2r). Log2FC (fold change) >1 and P-value <0.05 were considered statistically significant. To analyze the function of DEGs, biological analyses were performed using DAVID database (http://david.ncifcrf.gov). P<0.05 was considered statistically significant. The PPI networks of DEGs were constructed using STRING database, and an interaction with a combined score >0.4 was considered statistically significant. The PPI networks were drawn using Cytoscape and the most significant module was identified using MCODE. The criteria for selection were: MCODE scores >5, degree cut-off=2, node score >0.5 and k-score >10. The hub genes were selected with degrees ≥10.

Results: After standardization of the microarray results, DEGs in T and B cells were identified respectively (Fig. 1).

Changes in biological processes in T and B cells were both mainly enriched in type I interferon signalling pathway, defense response to virus, and negative regulation of viral genome replication. Changes in cell component in T cells was enriched in the cytosol while in B cells it was in cytoplasm. KEGG pathway analysis revealed that the DEGs of T cells were mainly enriched in influenza A, measles, herpes simplex infection and hepatitis C, while DEGs of B cells were mainly enriched in measles. Changes in molecular function were not listed because the p values were >0.05. 4 genes were identified as hub genes (2 in each cell population). In T cells, the hub genes are PLSCR1 and GINS2. PLSCR1 may contribute to the prothrombotic tendency in SLE. GINS2 is involved in the initiation of DNA replication and cell cycle progression. In B cells, the hub genes are ISG15 and TOP2A. Increased ISG15 is correlated with lymphoproliferation in SLE patients. TOP2A encodes a DNA topoisomerase and anti-topoisomerase II antibody could be found in SLE.

Conclusion: In our study, 2 mRNA microarray datasets were analyzed to obtain DEGs between SLE T and B cells versus healthy controls. A total of 56 DEGs were identified in T cells and 83 in B cells. Most of the DEGs were upregulated. Changes in biological processes in T and B cells were mainly related to type I interferon signalling pathway and anti-virus function. KEGG also showed the same. PLSCR1 and GINS2 were hub genes in T cells while ISG15 and TOP2A were hub genes in B cells. Overexpression of these genes might play an important role in the pathogenesis of SLE.

References: