Poster D-10

Gene Expression Profiling in Autoimmunity: Molecular Signatures of Systemic Lupus Erithematosus, Rheumatoid Arthritis and Type 1 Diabetes Mellitus

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Short Abstract: Gene expression profiling can allow new insights on molecular pathogenesis of autoimmune diseases. Based on this assumption, we are using the cDNA microarray technology to trace hybridization signatures of systemic lupus erithematosus, rheumatoid arthritis and type 1 diabetes mellitus patients.

Long Abstract:
Autoimmune diseases are the result from the imbalance of self-non-self discrimination, in which the self body constituents are dangerously recognized by the immune system. Systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and type 1 diabetes mellitus (DM1) are prototypes of autoimmune diseases, which touch 3-5% of world-wide population. While clinically established, the etiology of these diseases is still unknown. There are important genetic predisposition associated to MHC allele polymorphism and many environmental factors seems to be involved, such as sun light exposure, hormonal imbalance and drugs. In this context, gene expression profiling can allow new insights on their molecular pathogenesis. Based on this assumption, we are using the cDNA microarray technology to trace hybridization signatures of RA, SLE and DM1 patients. In this study, total RNA samples were prepared from peripheral blood lymphocytes of patients and control individuals and converted to Cy5-labeled cDNA probes. A pool of total RNA from several human cell lines was converted to Cy3-labeled cDNA probes, which served as reference. These probes were then hybridized with microarrays containing 4,500 sequences from the human cDNA IMAGE Consortium. Normalization was performed within and across the data set by means of Printtip Lowess (linear regression method) and reassignment of M values through median absolute deviation values. We used ANOVA, SAM and other statistic mathematical algorithms, which allowed pointing out the significantly expressed genes. Unsupervised hierarchical clustering allowed separation of the three autoimmune diseases

studied according to their expression profiling. >From the 4,500 sequences analyzed, we found a set of ~ 2,000 sequences containing those that share the same expression pattern among diseases and other that are exclusive. The respective genes were associated to several important biological processes implicated in the autoimmune reaction, such as inflammation, cellular metabolism and communication. The hybridization signatures obtained strongly suggest that the three autoimmune diseases studied share common transcriptional (dis)regulation, which can be associated to their genetic pathogenesis. (Supported by Fapesp 99/12135-9; 01/09519-1, GLS is fellow from CNPq).