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DEFINING T HELPER (CD4) CELL-SPECIFIC DISEASE SIGNATURES IN ACTIVE, INACTIVE AND AUTOLOGOUS STEM CELL TRANSPLANTED LUPUS PATIENTS BY GLOBAL GENE EXPRESSION PROFILING

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Background Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that affects multiple organs, whose pathology is mainly caused by the augmented interferon (IFN) signaling pathway. The objective of this study was to analyse the particular role of peripheral CD4+T cells in the pathogenesis of SLE by global gene expression profiling.

The major focus was set on the comparison of disease-active and -inactive patients either by standard drug treatment or by autologous stem cell transplantation (ASCT) that is assumed to completely reset the autoreactive immunologic memory.

Materials and methods Affymetrix HG U133 Plus 2.0 gene expression arrays were made from purified peripheral CD4+T cells from six active SLE, two inactive SLE by standard drug treatment and three inactive SLE who underwent ASCT as well as three healthy donors. The list of IFN pathway-related genes was obtained from Ramos PS *et al*¹ (Arthritis Rheum 2011). In total, 2220 genes were chosen as targeted IFN signatures in this analysis. The data were analysed using BioRetis database and GENESIS clustering software.

Results Comparing IFN-imprints in active, inactive and ASCT-treated inactive SLE patients, it was obvious that inactive patients treated by low-dose cortisone showed only a marginal IFN-signature (233 probe sets) as compared to active patients (573). Unexpectedly, 562 differentially expressed probe sets were identified in ASCT-treated patients who are under long-term remission for 8–13 years. Considering the expression magnitude of IFN-regulated transcripts, it was quite obvious that a clear quantitative difference was observed in the strength of the IFN imprints detected in CD4+T cells from active patients and ASCT-treated patients. Although 322 IFN pathway-related probe sets were detected in common for active patients and ASCT-treated patients, about two-third of them (202) had much higher expression levels in active patients.

Conclusion The authors could show for the first time leucocyte-specific IFN signatures for peripheral monocytes and CD4+T cells. Comparing IFN responses in active, inactive and ASCT-treated inactive SLE patients, the striking IFN signature of active SLE patients was dramatically attenuated in the successfully treated patients, although an IFN-imprint was still detectable in all SLE patients including ASCT-treated and inactive SLE. Further analyses using monocytes data from ASCT-treated patients are under way in order to clarify the role of IFN signatures on the disease phenotype of SLE. This knowledge may help to improve and to expand diagnostic applications regarding disease activity and therapy stratification of SLE patients.

REFERENCE

1. **Ramos PS**, Williams AH, Ziegler JT, *et al*. Genetic analyses of interferon pathway-related genes reveal multiple new loci associated with systemic lupus erythematosus. *Arthritis Rheum* 2011;**63**:2049–57.