Conclusion The raised levels of VEGF in SLE might be related to the process of endothelial repair present in different organs of lupus patients.

OP0009 SLE-RELATED T CELL AUTOIMMUNITY TO HISTONES AND NUCLEOSOMES IS AN INHERENT PROPERTY OF THE NORMAL IMMUNE SYSTEM

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Background Systemic lupus erythematosus (SLE) is characterised by the generation of pathogenic B cell and T cell autoimmunity to DNA and nucleosomes. Human polyomavirus T-antigen may play a central role in initiating B cell and T cell autoimmunity to nucleosomes. Recent data demonstrate that nucleosome-T-antigen complexes stimulate nucleosome-specific B cells and T-antigen specific T cells through a hapten-carrier-like process, also indirectly resulting in termination of non-responsiveness of histone-specific T cells. This process is relevant to both SLE and normal individuals.

Objectives This work focuses on whether immune (T-antigen specific) and autoimmune (histone-specific) T cells from normal individuals share functional, structural and genetic characteristics with those deriving from SLE.

Methods Histone-specific T cell clones were generated by stimulation of peripheral blood mononuclear cells with nucleosome-T-antigen complexes and subsequently maintained by pure histones. T-antigen specific T cell clones were initiated and maintained by polyomavirus T-antigen. The frequencies of circulating T cells specific for these antigens were determined in healthy individuals and SLE patients by limiting dilution of blood mononuclear cells. T cell receptor gene usage and structure of their variable regions were determined by cDNA sequencing. The sequences were compared between the T cell populations, and between normal and SLE subjects for both T-antigen and histone specificity.

Results The frequencies of circulating T-antigen- or histone-specific T cells in normal individuals were similar to those of SLE patients. Some of the histone-specific T cells, derived from normal individuals, were clonally expanded, indicating that these cells are functionally activated *in vivo* in healthy individuals. Although heterogeneous for variable region structure and gene usage, histone specific T cells from healthy individuals and SLE patients selected glutamic and/or aspartic acids at position 99 and 100 of the Vb-CDR3.

Conclusion Autoimmune T cells induced among peripheral blood mononuclear cells from normal individuals were highly similar to those from SLE, demonstrating that T cell autoimmunity to nucleosomes is an inherent property of the normal immune system.

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OP0071 A PATHOGENIC ANTI-DNA ANTIBODY BINDS TO ALPHA-ACTININ IN RENAL MESANGIAL CELLS

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Background Anti-DNA antibodies have been demonstrated to play an important role in the pathogenesis of nephritis in systemic lupus erythematosus. One mechanism by which anti-DNA antibodies may contribute to nephritis is by cross-reactivity with renal antigens. However, the identity of this renal antigen remains elusive.

Objectives To identify the target antigen bound by a pathogenic anti-DNA antibody in renal tissue.

Methods Western blotting and immunoprecipitations of total cell lysate from mesangial cell lines derived from the autoimmune MRL-lpr/lpr mouse (lpr-mc) and a non-autoimmune BALB/c mouse (mc), with R4A, a pathogenic murine IgG2b anti-DNA antibody, and with 95, a non-pathogenic antibody derived from R4A by site-directed mutagenesis. The immunoprecipitated protein was identified by matrix assisted laser desorption ionisation mass spectrometry (MALDI-MS) of tryptic digests.

Results The pathogenic anti-DNA antibody R4A, but not control isotype-matched antibodies, bound to and immunoprecipitated a 100 kD protein from mesangial cell lysates. Binding was more pronounced using lpr-mc rather than non-autoimmune mc lysate. Little effect on binding was seen after treatment of the cell lysate or R4A with DNase, while proteinase K treatment abolished binding. Preliminary MALDI-MS analysis revealed that alpha-actinin, an actin bundling protein that plays a role in experimental nephritis models, is present in the protein band immunoprecipitated by R4A. R4A, but not 95, binds to immobilised alpha-actinin by ELISA; Furthermore, double stranded DNA significantly inhibited the binding of R4A to the 100 kD mesangial cell protein, as well as to purified alpha-actinin. Serum of MRL-lpr/lpr lupus mice with active disease contain high-titer antibodies to alpha-actinin.

Conclusion The nephritogenicity of some anti-DNA antibodies may be mediated via cross-reactivity with a glomerular antigen. Variations in the display of the cross-reactive antigen in the target organ between individuals may underlie differential susceptibility to anti-DNA antibody induced renal disease.

OP0072 INCREASED CALRETICULIN EXPRESSION ON SURFACE MEMBRANES OF MONOCYTES AND NEUTROPHILS IN SYSTEMIC LUPUS ERYTHEMATOSUS: RELEVANCE TO APOPTOTIC CELL CLEARANCE

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Background Increased numbers of apoptotic leukocytes¹ and impaired clearance of apoptotic cells² have been demonstrated in SLE. Patients with C1q deficiency almost invariably develop SLE, probably because C1q is important in the clearance of apoptotic cells by monocyte/macrophages.³ Calreticulin has been shown to bind to the early complement component C1q, and