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LRA by ELISA/ACT[®]

CLINICAL PEARLS UPDATE#18

Lupus

January 26, 2004

Dear Colleague:

Lupus (SLE, Systemic lupus erythematosis) is characterized by multiple sites of autoimmune engagement that can be seen as repair deficits. Anti-DNA antibodies and anti-DNA T lymphocytes play important roles in this aspect of autoimmunity. Free radical (antioxidant deficit) and cytotoxic environmental chemicals may predispose cells to self-destruct faster than the individual can recycle their DNA. This may exacerbate or be causative of lupus. **LRA by ELISA/ACT[®] tests and plans are designed to enhance host immune repair functions by reducing defense work and stimulating repair abilities. Sustainable remissions are the expected result.**

We encourage you to share this valuable clinical update newsletter with your colleagues and staff so they can learn more about how our comprehensive approach can be applied to their practice with beneficial results. Please also let us know if any of your colleagues or staff would like to be added to our email distribution list.

We are grateful for the opportunities to be of service to you and your patients.

Sincerely,

Russ Jaffe, MD, Ph.D., CCN, NACB
Lab Director

Herkel J, Mimran A, Erez N, Kam N, Lohse AW, Marker-Hermann E, Rotter V, Cohen IR. **Autoimmunity to the p53 protein is a feature of systemic lupus erythematosus (SLE) related to anti-DNA antibodies.** *J Autoimmun* 2001;17(1):63-69.

The induction of anti-DNA autoantibodies in systemic lupus erythematosus (SLE) patients is problematic because mammalian DNA is poorly immunogenic at best. Here we demonstrate a chain of connected antibodies in SLE patient sera that could account for the induction of anti-DNA antibody, and possibly for some of the pathogenic features of SLE. We now report that SLE patients, in addition to anti-DNA, produce antibodies to the carboxy-terminal domain of the tumour suppressor molecule p53; this p53 domain recognizes damaged DNA. Hence, these anti-p53 antibodies could mimic damaged DNA immunologically. Indeed, SLE sera do contain anti-idiotypic antibodies to a prototypic anti-p53 antibody. Moreover, SLE anti-DNA antibodies also recognize this type of anti-p53 antibody. Indeed, binding of affinity-purified anti-DNA both to DNA and to the anti-p53 antibody could be blocked by a p53 peptide derived from the DNA-binding domain. This mimicry of the p53 DNA-binding domain by the SLE anti-DNA antibodies is functional: activation of the p53 molecule could be inhibited by such anti-DNA antibodies. Thus, anti-DNA antibodies may arise in SLE patients by a chain of idiotypic autoimmunity centered around p53 autoimmunity. The SLE anti-DNA and anti-p53 antibodies can functionally block p53 activation, and so could affect apoptosis.

Cohen IR. **Antigenic mimicry, clonal selection and autoimmunity.** *J Autoimmun* 2001;16(3):337-340.

The triggering of autoimmunity by infection or immunization is often blamed on antigenic mimicry. But the concept of antigen mimicry impinges on our understanding of adaptive immunity in general, and not only on autoimmunity. Here are some thoughts about the consequences of immune mimicry.

Cohen IR. **Discrimination and dialogue in the immune system.** *Semin Immunol* 2000;12(3):215-9; discussion 257-344.

This paper presents reasons for concluding that the immune system maintains the individual body throughout the vicissitudes of life without the need to make an absolute distinction between self and nonself. Self-maintenance and defence against parasites both require measured inflammation, and the immune system, in both its innate and adaptive arms, regulates inflammation. The intensity, dynamics and orchestration of inflammation emerge from an ongoing dialogue.

Schwartz M, Cohen IR. **Autoimmunity can benefit self-maintenance.** *Immunol Today* 2000 Jun;21(6):265-268.

Autoimmunity is usually considered only as a cause of disease; nevertheless, human T-cell repertoires are filled naturally with autoimmune lymphocytes. Here, we review evidence that autoimmune T cells can help heal damaged tissues, indicating that natural autoimmunity could also be a cause of health.



Cohen IR, Schwartz M. **Autoimmune maintenance and neuroprotection of the central nervous system.** *J Neuroimmunol* 1999;100(1-2):111-114.

The genesis of immune privilege high in the evolutionary tree suggests that immune privilege is necessary, if not advantageous for the progressive development of the CNS. Upon reaching a certain degree of complexity, it seems as if the CNS was obliged to restrain the immune system from penetrating the blood-brain barrier. CNS autoimmunity against myelin proteins is known to be a contributory factor in the pathophysiology of multiple sclerosis and in the animal model of experimental autoimmune encephalomyelitis (EAE) (Wekerle, 1993). Such autoimmunity has therefore been regarded as detrimental and hence obviously undesirable. However, recent findings in our laboratory suggest that T-cell autoimmunity to CNS self-antigens (Moalem et al., 1999), if expressed at the right time and the right place, can do much good in the CNS. We shall review the experiments briefly, and then discuss their implications for our understanding of immune privilege and CNS maintenance after injury.

