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LRA by ELISA/ACT®

CLINICAL PEARLS UPDATE#26

Multiple Sclerosis

May 21, 2004

Dear Colleague,

Multiple Sclerosis (MS) is characterized by multiple sites of autoimmune engagement that can be seen as repair deficits. Particular regard has been paid to myelin basic protein becoming foreign to the body in people with MS.

This may exacerbate or be causative of MS. **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

Viglietta V, Baecher-Allan C, Weiner HL, Hafler DA. Loss of Functional Suppression by CD4+CD25+ Regulatory T Cells in Patients with Multiple Sclerosis. *J Exp Med* 2004;199(7):971-979.

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CD4(+)CD25(+) regulatory T cells contribute to the maintenance of peripheral tolerance by active suppression because their deletion causes spontaneous autoimmune diseases in mice. Human CD4(+) regulatory T cells expressing high levels of CD25 are suppressive in vitro and mimic the activity of murine CD4(+)CD25(+) regulatory T cells. Multiple sclerosis (MS) is an inflammatory disease thought to be mediated by T cells recognizing myelin protein peptides. We hypothesized that altered functions of CD4(+)CD25(hi) regulatory T cells play a role in the breakdown of immunologic self-tolerance in patients with MS. Here, we report a significant decrease in the effector function of CD4(+)CD25(hi) regulatory T cells from peripheral blood of patients with MS as compared with healthy donors. Differences were also apparent in single cell cloning experiments in which the cloning frequency of CD4(+)CD25(hi) T cells was significantly reduced in patients as compared with normal controls. These data are the first to demonstrate alterations of CD4(+)CD25(hi) regulatory T cell function in patients with MS.

Waldner H, Collins M, Kuchroo VK. Activation of antigen-presenting cells by microbial products breaks self-tolerance and induces autoimmune disease. *J Clin Invest* 2004;113(7):990-997.

Center for Neurologic Diseases, Brigham and Women's Hospital and Harvard Medical School, Cambridge, Massachusetts, USA.

We describe the generation of mice that express a transgenic T cell receptor (TCR) (5B6) specific for the encephalitogenic myelin proteolipid protein (PLP) peptide 139-151, on the experimental autoimmune encephalomyelitis-resistant (EAE-resistant) B10.S background. Despite harboring a high frequency of self-reactive T cells, 5B6 transgenic mice on the B10.S background rarely develop spontaneous EAE, which is in striking contrast to 5B6 transgenic mice on the EAE-susceptible SJL background. The relative resistance to spontaneous EAE in transgenic B10.S mice is not due to deletion or anergy of T cells, but appears to be controlled by APCs. Analysis of APCs revealed a lower activation state and a lower T cell-activating capacity for APCs from B10.S mice than for those from EAE-susceptible SJL mice. When APCs in 5B6 transgenic B10.S mice were activated, for example, via TLR9 or TLR4, T cell tolerance was broken, resulting in EAE. Our findings demonstrate that activation of APCs via innate immune receptors can break self-tolerance and trigger the development of autoimmunity even in a genetically resistant strain. These findings suggest that the

development of autoimmune diseases such as multiple sclerosis is determined at least partly by the endogenous activation state of APCs.