

■ ELISA/ACT Biotechnologies LLC ■

# LRA by ELISA/ACT®

## CLINICAL PEARLS UPDATE#25

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### *Polyendocrinopathy syndrome*

May 14, 2004

Dear Colleague,

In health, we have homeostatic tolerance in our immune defense and repair component of the body's control system. This means we neutralize and recycle foreign invaders without persisting immune defense reactivity. Deletion of circulating reactive lymphocytes is part of this 'resetting, forgiving and forgetting' mechanism. However, the body must be in a repair rather than reactive defense mode for this to take place. This is elegantly confirmed by Venanzi and his group from Joslin Diabetes Center/Brigham and Women's Hospital elegantly point out in the first abstract below. Soderbergh and colleagues report, in the 2<sup>nd</sup> abstract, the prevalence of autoantibodies (including 9 intracellular markers) in polyendocrinopathy syndrome type 1 (APECED1, more types to come). This suggests to us that healthy intracellular components become distorted by accumulated toxins [primarily xenoestrogen chemicals and toxic minerals], amplified by shifts in intracellular pH balance, to become 'foreign' to the individual (self). When altered, these intracellular components can be recognized as 'foreign' by our immune defense and repair system.

Our first line comprehensive care program is designed to determine which items keep an individual 'stuck' in reactive defense; our treatment guide is designed to restore repair resilience, tolerance, and homeostatic equilibrium so that sustained good health emerges. A common repair deficit in distressed individuals may play a causative role.

**LRA by ELISA/ACT tests and plans** are designed to address the causes of these and other autoimmune conditions. **The program includes substitution for reactive items as determined by this functional, *ex vivo*, comprehensive procedure, an alkaline way repair diet, targeted supplementation to replete**

**antioxidants and enhance detoxification systems, and healing actions to engage the mind and body in a common direction.**

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***

**Venanzi ES, Benoist C, Mathis D. Good riddance: Thymocyte clonal deletion prevents autoimmunity. *Curr Opin Immunol* 2004; 16(2): 197-202.**

**Section on Immunology and Immunogenetics, Joslin Diabetes Center, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, 1 Joslin Place, Boston, MA 02215, USA.**

Clonal deletion is arguably the most important mechanism of eliminating self-reactive thymocytes from the T-cell repertoire. Recent work has identified new players in this process. On the thymocyte side, several molecules have been newly implicated in the pathway from initial T-cell receptor signaling through to the final result: gene transcription and thymocyte apoptosis. In addition, several proapoptotic molecules have been found to be necessary for the death of self-reactive thymocytes. On the antigen-presenting cell side, the expression of peripheral self-antigens, regulated at least in part by the autoimmune regulator (AIRE) protein, is crucial for complete elimination of autoreactive thymocytes. The importance of thymic peripheral antigen expression and clonal deletion to self-tolerance is demonstrated in the autoimmune diseases autoimmune-polyendocrinopathy-candidiasis-ectodermal dystrophy and type-1 diabetes mellitus (APECED1).

**Soderbergh A, Myhre AG, Ekwall O, Gebre-Medhin G, Hedstrand H, Landgren E, Miettinen A, Eskelin P, Halonen M, Tuomi T, Gustafsson J, Husebye ES, Perheentupa J, Gylling M, Manns MP, Rorsman F, Kampe O, Nilsson T. Prevalence and clinical associations of 10 defined autoantibodies in autoimmune polyendocrine syndrome type I. *J Clin Endocrinol Metab* 2004;89(2):557-562 and 544-547.**

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The prevalence of autoantibodies against nine intracellular enzyme autoantigens, namely 21-hydroxylase, side-chain cleavage enzyme (SCC), 17 alpha-hydroxylase, glutamic acid decarboxylase 65, aromatic L-amino acid decarboxylase, tyrosine phosphatase-like protein IA-2, tryptophan hydroxylase (TPH), tyrosine hydroxylase, cytochrome P450 1A2, and against the extracellular calcium-sensing receptor, was assessed in 90 patients with autoimmune polyendocrine syndrome type I. A multivariate logistic regression analysis was performed for the presence of autoantibodies as independent predictors for different disease manifestations. Reactivities against 21-hydroxylase and SCC were associated with Addison's disease with odds ratios (ORs) of 7.8 and 6.8, respectively. Hypogonadism was exclusively associated with autoantibodies against SCC with an OR of 12.5. Autoantibodies against tyrosine phosphatase-like protein IA-2 were associated with insulin-dependent diabetes mellitus with an OR of 14.9, but with low sensitivity. Reactivities against TPH and, surprisingly, glutamic acid decarboxylase 65, were associated with intestinal

dysfunction, with ORs of 3.9 and 6.7, respectively. TPH reactivity was the best predictor for autoimmune hepatitis, with an OR of 27.0. Hypoparathyroidism was not associated with reactivity against any of the autoantigens tested. No reactivity against the calcium-sensing receptor was found. Analysis of autoantibodies in autoimmune polyendocrine syndrome type I patients is a useful tool for establishing autoimmune manifestations of the disease as well as providing diagnosis in patients with suspected disease.