**ADRENOCORTICOTROPIC HORMONE: MODULATION OF ANTIGEN-PRESENTING CELL PHENOTYPE AND FUNCTION**

M. Jensen, B. Arnason

*N*eurology, *University of Chicago, Chicago, IL*

**Background:** During relapses of relapsing-remitting multiple sclerosis (RRMS), T-cell reactivity to numerous myelin antigens increases. Severity of attacks is linked to T-cell migration into the central nervous system (CNS). Autoreactive T cells recognize peptides derived from self-proteins (ie, proteins of the myelin sheath) when bound to major histocompatibility complex (MHC) II molecules expressed on the surface of antigen-presenting cells (APCs; ie, monocytes, macrophages, dendritic cells). APCs also express several co-signaling molecules that are either inhibitory or stimulatory toward T-cell activation. Relative expression of these co-signaling molecules by APCs dictates whether an APC will activate or anergize T cells encountered. APCs that express high levels of CD86 but low levels of immunoglobulin-like transcript 3 (ILT3) activate T cells, while APCs with high ILT3 but low CD86 levels anergize T cells (ie, tolerogenic APCs).

**Objectives:** To measure levels of ILT3 (inhibitory) and CD86 (activatory) on APCs from RRMS patients in relapse and during stable disease, and on APCs of healthy controls, and to determine the effect of adrenocorticotropic hormone (ACTH) on APC-expressed ILT3 and CD86 and on APC-mediated activation of T cells.

**Methods:** Levels of ILT3 and CD86 on freshly isolated APCs of active RRMS patients, stable RRMS patients, and controls were measured by flow cytometry. ILT3 and CD86 were also measured on APCs after culture with and without ACTH.

**Results:** ILT3 levels on APCs of RRMS patients in relapse are significantly decreased compared with levels seen in stable RRMS and in healthy controls. Levels of CD86 are comparable in patients with active RRMS, patients with stable RRMS, and controls. The ILT3 to CD86 ratio on APCs of RRMS during relapse appears to favor T-cell activation. ACTH dampens CD86 up-regulation on APCs of RRMS and controls and favors the formation of tolerogenic APCs.

**Conclusions:** ACTH may exert a beneficial effect in RRMS through modulation of APC phenotype and function.

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