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# Journal club

## NEUROENDROCRINE EFFECTS ON AUTOIMMUNITY

The work of Don Mason and colleagues in the rat contributed enormously to our understanding of cellular immunity and autoimmunity. Of all their studies of immune regulation, the work that surprised me most was a 1989 paper that described a role for adrenal corticosteroids in modulating autoimmune pathology.

By generating antibodies to rat cell surface markers, Mason, Alan Williams and colleagues generated a library of reagents with which to dissect cellular interactions and analyse the functions of some of these molecules. Their discoveries included the subdivision of rat $CD4^+$ T cells on the basis of CD45 isoform expression into those cells that mediated autoimmune pathology and those that could regulate it. This information was used to characterize the cellular events that occur during the induction of autoimmunity by thymectomy and low-dose irradiation.

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Mason's group noticed that when experimental allergic encephalomyelitis (EAE) was induced in Lewis rats, transient lymphopenia developed in association with the developing paralysis, and that cell counts normalized during recovery of the animal. Given an older body of literature documenting the effects of corticosterone on cell numbers and lymphocyte traffic, Mason and colleagues further explored the influence of corticosterone levels on EAE. They showed that following adrenalectomy, Lewis rats were unable to recover from EAE.

This observation enabled the group to explain why Lewis rats were susceptible to the induction of EAE whereas PVG rats, congenic for Lewis MHC, were resistant. PVG rats were rendered susceptible to EAE by adrenalectomy and their disease could be controlled by the administration of corticosteroids. On examining basal corticosteroid levels in Lewis and PVG rats, it became evident that PVG rats had higher levels of serum corticosteroid both at rest and in response to stress. This increased stress response protected PVG rats from the induction of autoimmunity.

This study highlighted the potential for genetically determined variations in the neuroendocrine system and its response to cytokines or environmental stress to impact on the predisposition to autoimmunity. Many of us working in the field of autoimmunity at the time were focused on regulatory T cells and tolerance-inducing protocols. We had failed to look at the bigger picture as Don Mason had done.

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**ORIGINAL ARTICLE** MacPhee, I. A. *et al.* Spontaneous recovery of rats from experimental allergic encephalomyelitis is dependent on regulation of the immune system by adrenal corticosteroids. *J. Exp. Med.* **169**, 431–445 (1989)
**FURTHER READING** Mason, D. *et al.* The role of the neuroendocrine system in determining genetic susceptibility to experimental allergic encephalomyelitis in the rat. *Immunology* **70**, 1–5 (1990)