Experimental Autoimmune Encephalomyelitis

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This issue of Biomedical Journal includes three review articles on experimental autoimmune encephalomyelitis (EAE), an animal model of multiple sclerosis (MS). EAE shares several pathological aspects with MS: Inflammation, demyelination, and neuronal death, even though EAE is not the same disease. In addition, EAE proved to be an excellent model to characterize pathogenic T lymphocytes and to test drugs with therapeutic potential in MS. The first review article is written by Dr. Florian C. Kurschus on "T cell-mediated pathogenesis in EAE: Molecular mechanisms".[1] The second review is from Dr. Jean–Charles Guery and colleagues on "Estrogen-mediated protection of EAE: Lessons from the dissection of estrogen receptor (ER)-signaling *in vivo*".[2] The third one is by Dr. Stephen Anderton: "Peptide immunotherapy (PIT) in EAE".[3]

Dr. Kurschus's review article describes the different populations of CD4 + T lymphocytes capable of triggering and maintaining EAE. The complex role of Th17 lymphocytes is discussed and the major role of IL-23 and granulocyte-macrophage colony-stimulating factor (GM-CSF) is presented, even though the exact mechanism of action of GM-CSF is still unknown. Finally, several models of EAE induced by CD8 + T cells are analyzed and discussed. Overall, this very interesting article reviews the different encephalitogenic T lymphocytes and the effector mechanisms leading to demyelination and inflammation in the central nervous system (CNS).

The second article, by Dr. Guery and colleagues, presents and analyzes the studies showing that estrogens are the hormones mediating the protective effect of pregnancy on MS. Furthermore, the authors analyze the experimental evidence demonstrating the anti-inflammatory effects of estrogens on EAE. The potential cellular targets of estrogens are presented and their role is thoroughly discussed. Finally, the authors present their data in which several lines of ER alpha conditional knockout mice were used to identify the primary cellular target of estrogen. Using the mouse line in which ER alpha was eliminated from T lymphocytes, they established that estrogen-induced EAE protection required the expression of ER alpha in T lymphocytes. They also discuss evidence showing that estrogens are able to act on CNS-resident cells through ER alpha or ER beta. This excellent review shows that the identification of biochemical pathways involved in the protective effects of estrogens in MS is of major importance.

The third article, by Dr. Anderton, analyses the potential of PIT in EAE. Most PIT studies have been performed on naive T lymphocytes and three mechanisms of tolerance have been identified: Apoptotic death of specific T cells, unresponsiveness of T lymphocytes unable to produce IL-2 or effector cytokines and regulatory T cells. Repetitive or prolonged administration of peptide generated two types of regulatory T lymphocytes, those expressing Foxp3 and those which produce IL-10. The author discusses the problem occurring during PIT treatment of EAE. Indeed, PIT is complicated by anaphylactic reactions due to soluble peptide injected in mice immunized with the same peptide and producing anaphylactic anti-peptide antibodies. The author describes an experiment from his laboratory that shows the protective efficacy of PIT in EAE. They used an altered peptide ligand which is recognized as a T cell receptor ligand but does not bind to antibodies. This altered peptide was able to inhibit an ongoing EAE triggered by the wild-type peptide. Finally, the author presents and discusses transcriptional and epigenetic changes in

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PIT-responsive T cells. This first rate review summarizes our knowledge on PIT and analyses the remaining questions concerning its mode of action on committed T lymphocytes.

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