Experimental autoimmune encephalomyelitis, a model of multiple sclerosis

Experimental autoimmune encephalomyelitis (EAE) is an inflammatory disease of the central nervous system that is widely used as a model of Multiple Sclerosis. The disease presents in a series of exacerbations and remissions and is characterized by loss of nerve conduction and chronic progression of disability. Macrophages and T lymphocytes mediate the destruction of the myelin sheath surrounding the nerves leading to improper nerve conduction. Research into the pathogenesis of EAE has indicated that it has many similarities with other autoimmune and chronic inflammatory diseases.

Model description
Models are available in mice and rats. In general, EAE is induced by immunization with a well-defined synthetic peptide with encephalitogenic properties. The most frequently used model is induced in SJL mice where the first clinical symptoms appear about 10 days after immunization. The first phase of clinical activity is followed by a relapse in a majority of the sensitized animals. This EAE model in SJL mice has been successfully used at TNO to demonstrate immunosuppressive effects of IL-10¹, anti-CD40L², dexamethasone (Figure 1), glatiramer-acetate (Copaxone) and many proprietary compounds. The model is also sensitive to novel therapeutic strategies aimed at tolerance induction⁴⁻⁶.

Typically, mice are immunized with a myelin-derived peptide (PLP₁₃₉₋₁₅₁ for SJL, MOG₃₅₋₅₅ for C57BL/6) and clinical parameters of disease (weight-loss and paralysis/paresis) are monitored daily. The duration of the monitoring period depends on whether the client is primarily interested in interference with the first phase of disease or with the chronic relapsing phase. An optional read-out is the evaluation of inflammation and/or demyelination of the CNS (Figures 2 and 3).

Advantages
- Various models available in mice and rats
- Evaluation of effects on inflammation and demyelination
- Validated with a wide range of compounds
- Various optional read-out parameters
- Various routes of drug administration
- Customized study design

Applications
- Identification of anti-inflammatory compounds
- Identification of drugs with the potential to treat (auto)immune disorders
- Evaluation of protocols and strategies that induce immunological tolerance
Experimental autoimmune encephalomyelitis, a model of multiple sclerosis established in mice and rats

Alternatively, EAE can be monitored in DA rats (MOG\textsubscript{1-125}). This model shows two relapses, and histopathological examination reveals both inflammatory cells and demyelination.

Modulation of disease activity usually requires the analysis of immunological parameters to gain insight into the mechanism of action of the test substance. Optional analyses include assessment of cellular composition of infiltrates in central nervous tissue, production of cytokines, expression of receptors and other cell surface molecules, production of specific antibodies.

Read-out systems
- Monitoring of clinical symptoms
- Delayed-type-hypersensitivity
- Immunohistochemical evaluation of cellular infiltration and demyelination of the central nervous system
- Antigen-specific T cell responses (proliferation and cytokines)
- Flowcytometry
- Antibodies

References