

Rat models of Multiple Sclerosis (MS) - Experimental Autoimmune Encephalomyelitis (EAE)



MODEL DESCRIPTION

EAE is the most commonly used model for MS, a human inflammatory demyelinating disease of the central nervous system (CNS), and resembles disease in many aspects. EAE is an antigen driven autoimmune model in which immunization against myelin antigens elicits strong T cell responses which initiates its pathology with CNS myelin destruction. EAE is induced by immunization with CNS tissue or myelin peptides. Different immunization protocols result in varying disease characteristics.

CELLULAR IMMUNOLOGY

Activated Th1 and Th17 cells are thought to be the main culprit in EAE and MS. Different immunization protocols decides response type and disease pattern in EAE. Injected antigens emulsified in immune stimulating adjuvant is presented on MHCII and stimulate autoantigen-specific T cells that escaped thymic negative selection. The CD4⁺ effector cells, commonly induced in EAE, start with expression of IL-17 in LNs and some days later, a multi-cytokine program is initiated, driven by IL-23. T cell infiltration into CNS occurs around day 8-9 after immunization and these cells mostly express IL-17. Finally, in the CNS effector T cells are found to express either IL-17, IFN-g or GM-CSF or a combination of all three. T cells in the CNS are reactivated by macrophages, DCs and B cells presenting myelin autoantigens and secreting cytokines.

Macrophages play several roles in the pathogenesis of EAE by destroying the BBB by secretion of metalloproteases allowing leucocytes to infiltrate the CNS. Secondly, macrophages also damage myelin directly. In contrast to MS, EAE models are dependent on neutrophils but CD8⁺T cells are not essential.

EAE MODELS

EAE resembles the human disease in many ways. However, based on the heterogeneity of disease course and lesion pathology in MS it is difficult to model all aspects of MS in one animal model. Thus, the availability of different rat strains, immunogens and adjuvants is very valuable since it allows inducing different types of disease and pathologies. In addition to the actively induced models, the CD4⁺ T cell dependency of the rat EAE models allows for adoptive T cell transfer of autoimmune T cells after ex vivo re-stimulation. For more detailed information on our models, see disease specific information sheets.

	SCH/IFA	MOG1-125/IFA	MOG1-125/CFA	MBP/CFA
Strain	DA	DA	Lewis	Lewis
Disease course	Chronic relapsing	Chronic progressive	Chronic progressive	Acute
Demyelination	Yes	Yes	Yes	No
Experiment duration	25 days (+)	20 days (+)	25 days (+)	20 days

Read more:

T cell Mediated Pathogenesis in EAE: Molecular Mechanisms. Kurschus. *Biomed J.* (2015)

Actively Induced Experimental Autoimmune Encephalomyelitis in Rats. Weissert. *Methods in Molecular Biology* (2015)

Experimental Autoimmune Encephalomyelitis (EAE) as a Model for Multiple Sclerosis. Constantinescu et al. *Br. J. Pharmacol.* (2011)

Spinal Cord Homogenate (SCH)-Induced EAE in rat

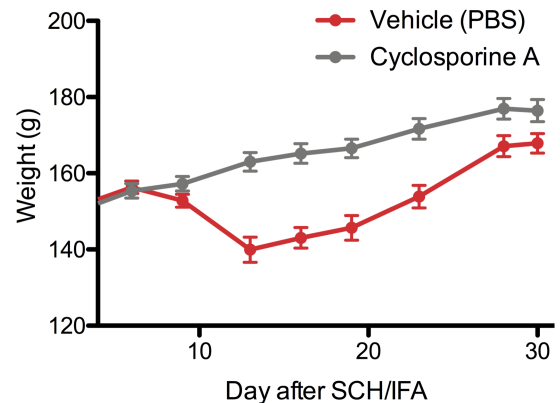
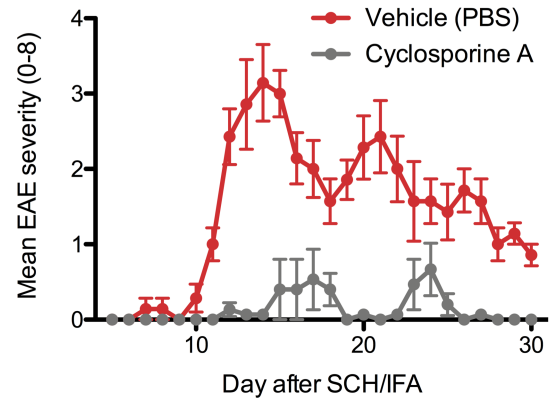
MODEL DESCRIPTION

EAE is an antigen driven autoimmune model of Multiple Sclerosis (MS), in which immunization against myelin antigens elicits strong T cell responses which initiates its pathology with CNS myelin destruction. EAE is induced by immunization with CNS tissue or myelin peptides. Different immunization protocols result in varying disease characteristics. SCH-induced EAE is induced in DA rats with a homogenate of spinal cord from naive animals emulsified in Incomplete Freund's Adjuvant (IFA).

CHARACTERISTICS

SCH-induced EAE is a severe, relapsing and demyelinating encephalomyelitis. Animals with EAE develop ascending flaccid paralysis that initially affects the tail (score 1-2), later involves hind limbs (score 3-6), forelimbs (score 7) and ultimately result in quadriplegia and death (score 8). The disease is CD4+ T cell mediated and dependent on both Th1 and Th17 cells.

In this model, disease is accompanied by demyelination of the CNS as can be assessed by histology at termination. In addition, IL-17 and IFN- γ responses from LN cells can be assayed ex vivo either as estimation on drug efficacy in vitro or prediction of efficacy for selection of lead compounds before in vivo experiments. The CD4+ T cell dependency of this model allows for adoptive T cell transfer following ex vivo stimulation of autoreactive T cells.



EXPERIMENTAL OUTLINE

Disease induction protocol:	S.c. injection of SCH in IFA day 0
Strain:	DA
Suggested group size:	12 rats/group
Duration:	25 days (+)
Onset:	Day 8-12
Max disease:	Day 13-16
Positive controls:	Cyclosporine A,

EVALUATION AND ENDPOINTS

Clinical signs:	Macroscopic scoring (0-8)
General health:	Weight
Follow up analyses:	Antibodies to CNS antigens, cytokines
Histology	Demyelination and cell infiltration in CNS



Read more:

T cell Mediated Pathogenesis in EAE: Molecular Mechanisms. Kurschus. *Biomed J.* (2015)
 Actively Induced Experimental Autoimmune Encephalomyelitis in Rats. Weissert. *Methods in Molecular Biology* (2015)
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MOG₁₋₁₂₅-

Induced EAE in rat

MODEL DESCRIPTION

EAE is an antigen driven autoimmune model of Multiple Sclerosis (MS), in which immunization against myelin antigens elicits strong T cell responses which initiates its pathology with CNS myelin destruction. EAE is induced by immunization with CNS tissue or myelin peptides. Different immunization protocols result in varying disease characteristics.

MOG-induced EAE is induced in DA or Lewis rats with protein emulsified in Incomplete Freund's Adjuvant (IFA) or Complete Freund's Adjuvant (CFA) respectively, and are models well suited for studies of immune mechanisms relevant to MS.

CHARACTERISTICS

MOG-induced EAE is a severe and demyelinating encephalomyelitis with a chronic progressive disease course. Animals with EAE develop ascending flaccid paralysis that initially affects the tail (score 1-2), later involves hind limbs (score 3-6), forelimbs (score 7) and ultimately result in quadriplegia and death (score 8).

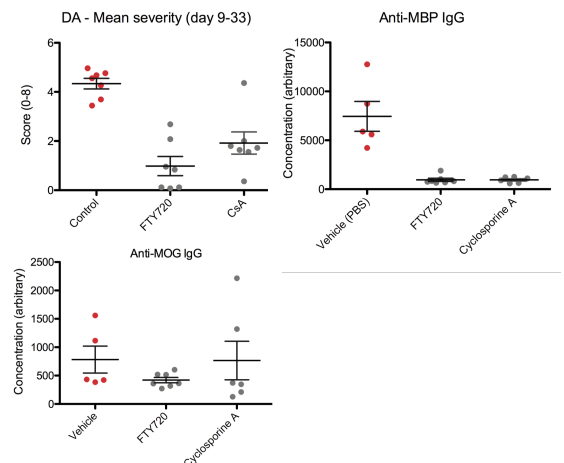
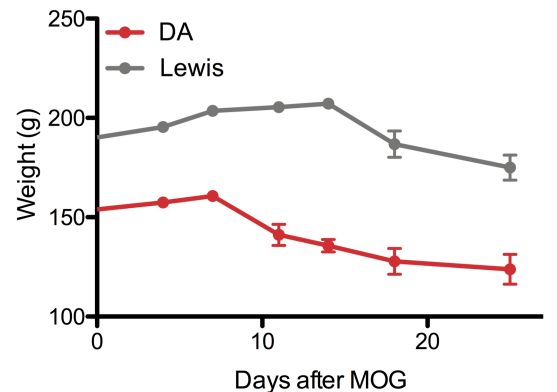
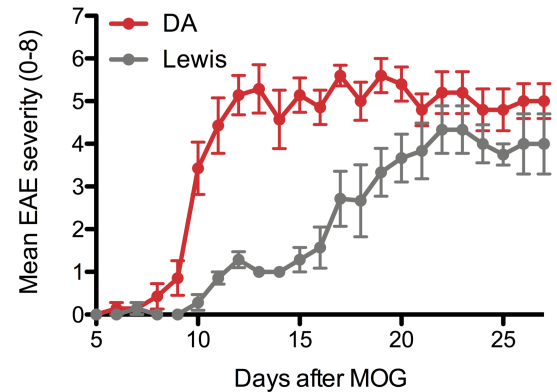
The disease is CD4+ T cell mediated and dependent on both Th1 and Th17 cells. T cells, B cells and macrophages are recruited to the inflammatory site resulting in demyelination and axonal loss. IL-17 and IFN- γ responses from LN cells can be assayed ex vivo as estimation on drug efficacy in vivo or prediction of efficacy for selection of lead compounds before in vivo experiments. The CD4+ T cell dependency of this model allows for adoptive T cell transfer following ex vivo stimulation of autoreactive T cells.

EXPERIMENTAL OUTLINE

Disease induction protocol:	S.c. injection of MOG in IFA or CFA day 0
Strain:	DA or Lewis
Suggested group size:	10 rats/group
Duration:	20-25 days (+)
Onset:	Day 8-10
Max disease:	Day 12-20
Positive controls:	Cyclosporine A

EVALUATION AND ENDPOINTS

Clinical signs:	Macroscopic scoring (0-8)
General health:	Weight
Follow up analyses:	Antibodies to CNS antigens, cytokines
Histology:	Demyelination and cell infiltration in CNS



Read more:

- T cell Mediated Pathogenesis in EAE: Molecular Mechanisms. Kurschus. *Biomed J.* (2015)
- Actively Induced Experimental Autoimmune Encephalomyelitis in Rats. Weissert. *Methods in Molecular Biology* (2015)
- Experimental Autoimmune Encephalomyelitis (EAE) as a Model for Multiple Sclerosis. Constantinescu et al. *Br. J. Pharmacol.* (2011)

Myelin Basic Protein - Induced EAE in rat

MODEL DESCRIPTION

EAE is an antigen driven autoimmune model of Multiple Sclerosis (MS), in which immunization against myelin antigens elicits strong T cell responses which initiates its pathology with CNS myelin destruction. EAE is induced by immunization with CNS tissue or myelin peptides. Different immunization protocols result in varying disease characteristics. MBP-induced EAE is induced in Lewis rats with MBP protein emulsified in Complete Freund's Adjuvant (CFA).

CHARACTERISTICS

MBP-induced EAE is a severe encephalomyelitis with a acute monophasic disease course. Animals with EAE develop ascending flaccid paralysis that initially affects the tail (score 1-2), later involves hind limbs (score 3-6), forelimbs (score 7) and ultimately result in quadriplegia and death (score 8). Disease has an onset around day 8-10 after immunization and experiment can normally be terminated around day 20.

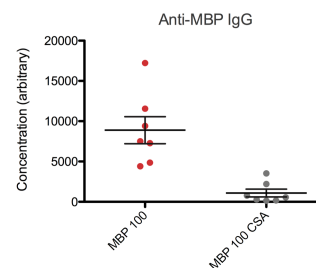
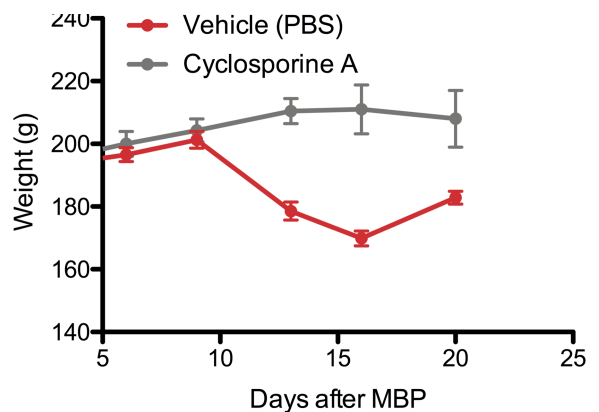
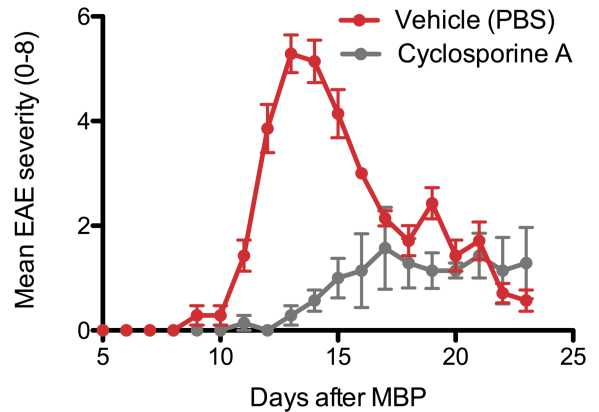
In this model, disease is not accompanied by demyelination of the CNS and there is mainly infiltration of T cells in the CNS. The model is thus suitable for studies to assess basic immunological mechanisms in regard to T cell function in autoimmune disease.

EXPERIMENTAL OUTLINE

Disease induction protocol:	S.c. injection of MBP in CFA day 0
Strain:	Lewis
Suggested group size:	10 rats/group
Duration:	20 days
Onset:	Day 8-10
Max disease:	Day 12-14
Positive controls:	Cyclosporine A

EVALUATION AND ENDPOINTS

Clinical signs:	Macroscopic scoring (0-8)
General health:	Weight
Follow up analyses:	Antibodies to CNS antigens, cytokines
Histology	Cell infiltration in CNS



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