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

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MODEL DESCRIPTION

EAE is a useful model for multiple sclerosis (MS), a human inflammatory demyelinating disease of the central nervous system (CNS), and resembles disease in many aspects. In both MS and EAE, demyelinating lesions in the white matter of CNS, caused by infiltrating T cells , macrophages and B cells, can be found. EAE is an antigen driven autoimmune model in which immunization against myelin antigens elicits strong T cell responses. Different immunization protocols result in varying disease characteristics.

CELLULAR IMMUNOLOGY

EAE is a CD4+ T cell-mediated disease affecting CNS. Mononuclear cell infiltration results in a demyelinating autoimmune disease. Activated Th1 and Th17 cells are thought to be the main culprit in EAE and MS. Different immunization protocols decides the response type and also 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 inititiated, driven by IL-23. T cell infiltration into CNS occures 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 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 myeling directly. In contrast to MS, EAE models are dependent on neutrophils but CD8+T cells are not essential.
Most EAE models are well reflecting the immunological component of MS pathophysiology but are limited in adressing the neurodegerantive mechanisms of autoimmune inflammation.

EAE MODELS

EAE resembles the human disase 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 strains, immunogens and adjuvants is very valuable since it allows fpr inducing different types of disease and pathologies. For more detailed information on our models, see disease specific information sheets.

Read more:

T cell Mediated Pathogenesis in EAE: Molecular Mechanisms. Kurschus. *Biomed J.* (2015)
Myelin Oligodendrocyte Glycoprotein (MOG35-55) Induced Experimental Autoimmune Encephalomyelitis (EAE) in C57BL/6 mice. Bittner et al. *J. Vis. Exp.* (2014)
Mouse Models of Multiple Sclerosis: Experimental Autoimmune Encephalomyelitis and Theiler´s Virus-Induced Demyelinating Disease. McCarthy et al. *Methods Mol. Biol.* (2012)
Experimental Autoimmune Encephalomyelitis (EAE) as a Model for Multiple Sclerosis. Constantinescu et al. *Br. J. Pharmacol.* (2011)

Myelin Oligodendrocyte glycoprotein (MOG)$_{35-55}$ - Induced EAE in mouse

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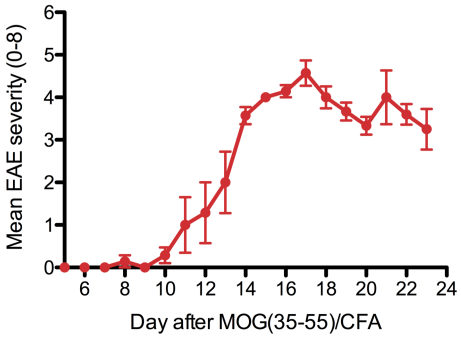
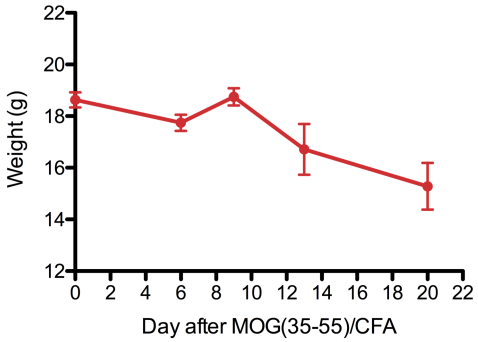
MODEL DESCRIPTION

EAE is the most common animal model for MS sharing many clinical and pathophysiological features. EAE induced with MOG peptide (35-55) in C57BL/6 mice are the most frequently used model and is a reliable, reproducable and well characterized model. The immunogenic epitope MOG35-55 is emulsified in CFA and injected s.c. followed by two pertussis toxin injections i.p. (d0 and day 2). Mice develop a monophasic EAE with ascending flaccid paralysis around 1-2 weeks after immunization. Myelin-specific T cells are activated in the periphery and migrate into the CNS across the blood-brain-barrier. Upon entry into the CNS, T cells are re-actviated by antigen-presenting cells, ultimately resulting in demyelination and axonal cell death. Pertussis toxin has been suggested to modulate the blood-brain barrier.





CHARACTERISTICS

MOG35-55 induced EAE is a severe monophasic, demyelinating encephalomyelitis with onset after around 1-2 weeks and reaches maximum score a few days later. 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).

In this model, disease is accompanied by demyelination of the CNS, which can be assessed by histology at termination. In additon, recall IL-17 and IFN-g responses from LNs cells can be assayed ex vivo either as a measurement of drug efficacy or prediction of efficacy for selection of lead compounds before in vivo experiment.

EXERIMENTAL OUTLINE

Disease induction protocol:	S.c. injection of MOG35-55 in CFA day 0
Pertussis toxin:	I.p. day 0 and day 2
Strain:	C57BL.6
Suggested group size:	12 mice/group
Duration:	25 days (+)
Onset:	Day 10-14
Max disease:	Day 15-20
Positive controls:	Cyclosporine A,

EVALUATION AND ENDPOINTS

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

Read more:

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

Myelin Oligodendrocyte Glycoprotein (MOG35-55) Induced Experimental Autoimmune Encephalomyelitis (EAE) in C57BL/6 mice. Bittner et al. *J. Vis. Exp.* (2014)

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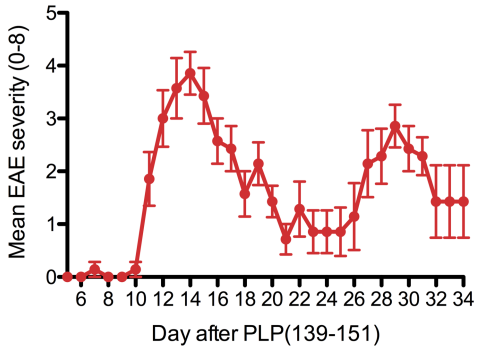
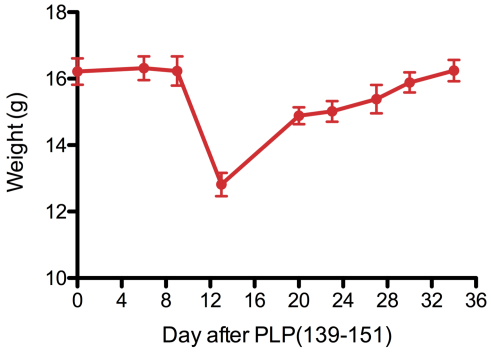
PLP139-151
Induced EAE in mouse

MODEL DESCRIPTION

Myelin proteolipid protein (PLP) induced EAE in SJL mice results in a relapsing-remitting disease, suitable for studies of efficacy. The encephalogenic peptide aa 139-151 is emulsified in adjuvant and and injected s.c. Disease can be boosted with injection of pertussis toxin injections. Mice develop a relapsing EAE with ascending flaccid paralysis around 1-2 weeks after immunization. Autoreactive T cells are activated in the periphery and migrate into the CNS across the blood-brain-barrier. Upon entry into the CNS, T cells are re-actviated by antigen-presenting cells, ultimately resulting in demyelination and axonal cell death.





CHARACTERISTICS

PLP-induced EAE is a severe and demyelinating encephalomyelitis with a relapsing-remitting 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-g responses from LNs 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 experiment.

EXERIMENTAL OUTLINE

Disease induction protocol:	S.c. injection of PLP139-151 in CFA day 0
Strain:	SJL
Suggested group size:	10-12/group
Duration:	20-25 days (+)
Onset:	Day 10-14
Max disease:	Day 15-20
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)

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