

# Multiple Sclerosis

## Introduction

Multiple sclerosis (MS), also known as disseminated sclerosis, is an autoimmune condition with demyelination of central nerves often resulting in physical and cognitive disabilities in many patients. It has a prevalence of 2 to 150 per 100,000 in the population, usually occurring in young adults and females.

Several disease-modifying treatments are currently available in different countries, including: Avonex and Rebif (interferon beta-1a), Betaseron or Betaferon (interferon beta-1b), Copaxone (polypeptide Glatiramer acetate), Mitoxantrone (immunosuppressant) and Natalizumab (humanized monoclonal antibody).

For several decades, rodent experimental autoimmune encephalomyelitis (EAE) has been broadly used as an important pharmacology model in new drug discovery and evaluation for MS. Mechanistic investigations on the immunopathogenesis of the demyelinating process, in different EAE models, have greatly elucidated the responsible mechanisms for autoimmune-caused neurological tissue damage and concepts of different therapeutic strategies.



## PharmaLegacy Models and Research Tools

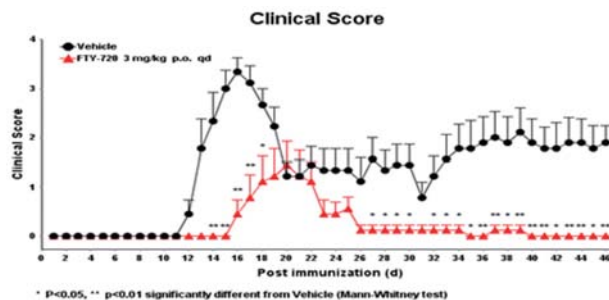
EAE Models	SJL mice	C57BL/6 mice	Lewis rats
<b>Antigen Specificity</b>	PLP 139-151	MOG 35-55	MBP
<b>Disease Onset and Recovery</b>	Day 12-14, no recovery	Day 12-14, no recovery	Day 10-12, recover within 6-8 days
<b>Disease Type</b>	Relapsing-remitting	Chronic progression	Monophase progression
<b>Similarities to Human Disease</b>	Relapsing-remitting disease course with demyelination and axonal damage	Chronic-progressive disease course with demyelination and axonal damage	T cell inflammation and weak antibody response
<b>Utility</b>	Two-episode diseases. Ideal for studying the effects of immunotherapeutic agents and various treatment regimens.	Variable disease incidence and course with cytotoxic demyelination. Ideal for studying T cell, macrophage mediated demyelination, axonal injury in demyelinated plaques and demyelinating anti-MOG autoantibody response.	High reproducibility. The acute onset and spontaneous recovery resemble the exacerbation and remission seen in MS.
<b>Primary Endpoints</b>	EAE disease score, incidence, mortality, mean maximum disease score, group mean score, EAE onset and duration, body weight		
<b>Additional Endpoints</b>	Histopathology, immunohistochemistry, hematology, cytokines / chemokine analysis, T cell proliferation, permeability of BBB		

## Related Capabilities

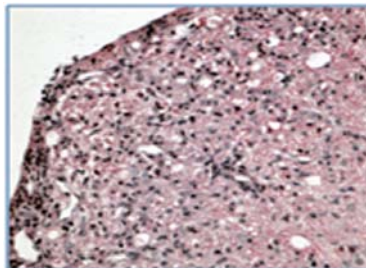
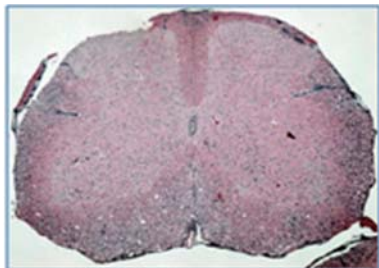
- \* Disease transfer model: T-cell adoptive transfer in mice
- \* Assays for antigen-specific T-cell responses
- \* Flow cytometry analysis of cell functions including intracellular staining of cytokines
- \* Western blotting detection of signal transduction

## Case Study - PLP Induced EAE Model

### Effects of FTY-720 on PLP induced chronic relapse EAE in SJL mice:



Mice were subcutaneously immunized with PLP peptide emulsion. The symptom of EAE development (black) represents the disease progression of human relapsing-remitting MS. Daily oral administration of the reference drug, FTY-720 (a widely documented immunosuppressant for EAE) (red), demonstrates its effectiveness in reduction of disease score, postponement of disease onset and amelioration of disease relapse.



The section of spinal cord from a MOG35-55 EAE C57BL/6 mouse showed significant infiltrations in the White matter (H&E, 40x left, and 200x right)

PharmaLegacy's fully validated EAE models are backed by many years' experience in MS research and animal modeling and produce a very reproducible disease induction and results. These models have been providing clients with the options of various treatment strategies / regimens at different stages of relapsing-remitting progression, closely simulating the therapeutic options for patients.

#### About PharmaLegacy Services

- World-class quality with increased speed and output at competitive cost.
- International GLP and QA-based operation.
- Electronic data management system (BioBook) for quality execution and maximum IP protection.
- AAALAC accredited large capacity to house over 10,000 animals under SPF and conventional conditions.
- Availability of 4,000 non-human primates for research use.