WVU IACUC Model Guidance Sheet: Experimental Autoimmune Encephalitis (EAE)

Purpose

EAE is a commonly used animal model to study Multiple Sclerosis. This document is meant to provide guidance on common induction methods used for this model and welfare considerations that should be addressed when proposing to work with this animal model.

Definitions

EAE- Demyelinating disease of the central nervous system which is induced by administering a combination of central nervous system components (cells and/or peptides) and Complete Freund's Adjuvant with or without pertussis toxin or viral/pathogen inoculation.

Acute Phase: The first clinical episode of disease.

Remission: Phase of clinical improvement following clinical episode of paralysis. There is generally a reduction in clinical score for at least 2 days after peak score.

Relapse: Increase of at least one grade in clinical score for at least 2 days after remission.

Complete Freund's Adjuvant (CFA)- Adjuvant commonly used in research which consists of an oil-in-water emulsion containing killed *Mycobacterium tuberculosis*.

Guidance

1. Introduction
    a. EAE is a common model of multiple sclerosis which results in a progressive ascending paralysis in mice.
    b. The degree of paralysis and progression of disease (acute/chronic/relapsing-remitting) varies based on strain and combination of compounds administered.
    c. The disease progression generally follows a pattern starting with decreased tail tone > hindlimb paresis > hindlimb paraplegia > urinary incontinence > quadriparesis > atonic bladder > quadriplegia > dyspnea > moribund.
    d. All procedures related to the model ***must*** be described in the animal use protocol. This includes:
        i. Model induction
        ii. Timeline expected for model, expected disease progression for the model and planned study endpoint
        iii. Frequency of monitoring and scoring system used
        iv. Supportive care provided at various disease stages
        v. Humane endpoints
        vi. Potential adverse outcomes and how they are managed

2. Common Model Induction Procedures
    a. Two Common Methods
        i. Active induction by immunization
        ii. Passive induction through adoptive transfer
    b. Commercially prepared kits are available for induction of EAE models in mice.
        i. Hooke Laboratories has kits for a variety of EAE models. This is a convenient source of both information and reagents for the models.
    c. SJL mouse model (active induction)
        i. Common relapsing/remitting model induced with proteolipid protein (PLP) and CFA +/- pertussis toxin
    d. C57BL/6 mouse model (active induction)
        i. Chronic EAE model induced with myelin oligodendrocyte glycoprotein (MOG) and CFA + pertussis toxin
    e. If using pertussis toxin, animals will require ABSL2 housing.

3. EAE Animal Care Recommendations
    a. Animals should be observed daily and records maintained starting on the day which symptoms should begin (this will vary based on the model used). A scoring system should be used to evaluate each mouse daily. Records of the scores should be kept by the laboratory for review if concerns arise.
    b. There are a variety of scoring systems available for use. Please ensure the chosen scoring system is in the animal use protocol.
    c. The protocol should clearly state the score which will be designated as the study endpoint. Depending on the degree of advanced disease required for the project, the animals may require category E designation.
        i. Scoring systems are typically on a 0 to 5 scale.
    d. Weight/Body Condition Scoring
        i. Weight should be obtained prior to induction of disease.
            – Animals should be weighed weekly once clinical signs are first observed.
            – Weigh animals twice weekly once they are observed to have hindlimb paralysis.
            – Weigh animals daily when forelimb paresis is observed.
    e. Nutritional Support
        i. Supplements can be initiated as soon as ascending weakness is observed.
        ii. Recommended supplementation: Food on cage floor, soft chow, diet gel, bacon softies.
        iii. Hydration should be checked during weighing and veterinary staff contacted if supplemental fluids are required.
    f. Bladder should be checked regularly and expressed twice daily once an enlarged bladder is noted (atonic bladder).
    g. Monitor for signs of dermatitis, urine scald, penile prolapse and tail lesions. Contact veterinary staff if observed.
    h. Animals can be placed on paper bedding once ascending paralysis is observed. Submit special care form to Office of Laboratory Animal Resources (OLAR) staff to initiate this change in care.

4. Model Considerations
    a. Potential adverse outcomes
        i. All mice receiving CFA will develop obvious bumps in the area of injection ~2-4 days after injection. These bumps may remain for the experiment's duration.
        ii. Some animals will develop ulcerations at the injection site. A description of management should be in the animal use protocol. If deep lesions are present, veterinary staff should be contacted for care.
    b. Factors impacting model
        i. Stress before EAE onset may reduce disease severity.
        Recommend:
            – Acclimation to facility/lab for at least 7 days
            – Minimize noise and vibration stress
            – Avoid excessive handling and low stress handling techniques should be implemented.
            – Avoid moving animals on carts
        ii. Age of the animal can impact disease, with older animals having more severe disease.
        iii. Females show more consistent disease.
        iv. Strain/sub-strain can affect disease progression.
        v. Pertussis dose and potency (if used). Higher doses increase disease severity.

References

https://hookelabs.com/protocols/

https://www.taconic.com/taconic-insights/neuroscience/eae-mouse-models-of-multiple-sclerosis.html

Miller SD, Karpus WJ. Experimental autoimmune encephalomyelitis in the mouse. Curr Protoc Immunol. 2007 May; Chapter 15:15.1.1-15.1.18. doi: 10.1002/0471142735.im1501s77. PMID: 18432984; PMCID: PMC2915550. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2915550/