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Animal Models for the Study of Human Disease: Chapter 42. Animal Models for the Study of Multiple Sclerosis

Robert H. Miller, Sharyl Fyffe-Maricich, Andrew V. Caprariello

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The most common demyelinating disease of the central nervous system (CNS) in the young adult population is multiple sclerosis (MS). MS is characterized by the focal loss of myelin sheaths in the brain and in the spinal cord of patients that is correlated with elevated activity of the immune system directed toward CNS antigens including myelin. The progression of MS is highly variable, but in many cases, it is characterized by a series of relapsing and remitting attacks that slowly increase residual functional deficit. Often, after several years, the disease transitions to a more progressive phenotype. Much of what is known about the pathology of MS is derived from a number of animal models. The most common animal model for the study of MS is experimental allergic encephalitis (EAE), which depending upon the host animal can present as relapsing/remitting or progressive disease. Although EAE has provided mechanistic insights implicating T-cell activation in the onset and progression of disease, understanding the mechanisms of pathology onset and myelin repair in the CNS require alternative models. One emerging hypothesis is that activation of T cells is secondary to pathogenesis of oligodendrocytes and animals models in which targeted loss of oligodendrocytes are beginning to reveal an understanding of the initiation of CNS demyelination. Myelin repair is difficult to study in the setting of EAE or oligodendrocyte pathogenesis; however, toxin models that result in localized demyelination as a consequence of direct injection or oral delivery have provided critical insights into cells of origin, timing, and molecular mechanisms guiding remyelination. Taken together, these three distinct model systems provide a strong basis for dissecting cell and molecular mechanism of demyelination as well as characterizing the efficacy of targeted therapeutics.

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