shows a peripheral disposition and may protrude from the surface, possibly interacting with other cellular components or with neighbouring neurofilaments. The results presented here indicate that the function performed by the 200K protein is not rigidly required by every neurofilament, and is not needed at all stages of development. It should be possible to correlate the presence and absence of this protein with morphological and physiological attributes of particular neurones, and so elucidate the role of this protein in neuronal dynamics.

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Virus persistence and recurring demyelination produced by a temperature-sensitive mutant of MHV-4

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Mouse hepatitis virus type 4 (MHV-4, the JHM strain), a positive-strand RNA virus of the coronavirus family, is well documented as an inducer of acute and chronic demyelination in mice, as well as subacute demyelination in rats, due to a cytopathic effect on oligodendrocytes. However, experiments to explore the role of virus and host factors in the production of chronic or recurrent demyelinating disease have been limited because MHV-4 usually produces demyelination in conditions that frequently induce a fatal necrotizing encephalomylitis. To circumvent this problem, we have made and selected mutant viruses that caused both a high incidence of demyelination and a low incidence of encephalitis-induced mortality. One such mutant, designated ts8, consistently caused acute demyelination in over 90% of intracerebrally injected 4–5-week-old mice from several susceptible strains within 6–10 days. In addition, ts8 typically did not cause fatal necrotizing encephalitis, showing a low mortality (<5%) when infected with a single dose of the virus. This unique tropism of ts8 for oligodendrocytes, but a limited one for neuronal cells, indicated that ts8 is also useful for delineating specific processes of primary infection and replication in oligodendrocytes, and so elucidate the role of this protein in neuronal dynamics.

Recurrent demyelination, usually occurring in small foci, was evident 365 days after inoculation. This reflected a tendency of this model now allows a detailed study of virus, and physiological attributes of particular neurones, and so elucidate the role of this protein in neuronal dynamics.

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Fig. 2  a, Remyelinated axons were evident at 28 days after infection. They are characterized by thin myelin sheaths around large axonal profiles (see arrows). ×5,760. b, Recurrent demyelination is evident on an axon previously remyelinated (thin myelin sheath around a large axonal profile) shown at 57 days after infection. ×14,400. c, A small focus of demyelination surrounded by intact myelinated axons is shown in a portion of the lateral column of the spinal cord at 365 days after infection. ×576. d, An example of a completely demyelinated axon at 365 days after infection. ×14,400. e, An MHV virion, with its characteristic corona, is demonstrated within a cytoplasmic vacuole, in an oligodendrocyte located near demyelinated axons at 365 days after infection. ×108,000.

The aetiology and pathogenic mechanism(s) of injury in multiple sclerosis, the most common demyelinating disease of man, is unknown. A large body of epidemiological and experimental evidence suggests that this disorder is due to an autoimmune and/or viral disorder. The availability of the ts8 model should help to further our understanding of the pathogenic mechanism and genetic control of virus-induced acute and recurrent demyelination.

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