Abstract 37. Antibody modulation of coronavirus encephalitis
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The JHM strain of murine hepatitis virus (MHV-4) is used as an animal model of virus-induced diseases of the central nervous system (CNS). Demyelination results from viral infection of the oligodendrocytes but this disease is usually masked by a fulminant lethal encephalomyelitis due to neuronal infection. Passive transfer of monoclonal antibody (MAb) to two of three neutralization sites on the viral attachment and fusion glycoprotein E2 modulated disease from fatal encephalitis to demyelination. An essential role for antibody alone was demonstrated by protection of nude mice from lethal viral encephalitis after passive transfer of MAb or serum from MHV-4 immune animals. Quantitation of antibody response at the epitope level emphasized the importance of neutralizing antibody levels. Passive transfer of immune serum containing 0.52 μg/ml antibodies against epitope A (E2), one of the three neutralization sites on the E2 glycoprotein, was sufficient to confer protection, whereas an immune serum containing 0.28 μg/ml of such antibodies failed to protect mice. Upon peripheral inoculation, nude mice generated a limited antibody response to MHV-4, both IgG and IgM. We are currently investigating whether such a level of antibodies is sufficient to confer protection against a subsequent normally lethal intracerebral challenge.

Thus, appropriate antibody response to MHV-4 is important in determining the outcome of virus infection of the CNS.

Abstract 38. Molecular characterization of murine retroviruses inducing spongiform lower motor neuron disease
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Some ecotropic retroviruses isolated from wild mice were shown to be able to induce hind limb paralysis in their natural environment or when inoculated to newborn mice. We have recently cloned the DNA genome of one of these viruses in a prokariotic vector and shown that the virus recovered from this cloned DNA could induce paralysis. This result indicated unambiguously that a retrovirus, and not another passenger virus, was the etiologic agent. To identify the viral sequences responsible for inducing paralysis, we constructed chimeric viral genomes with parental DNA from this neurotropic virus and from the non-neurotropic amphotropic 4070-A MuLV. Chimeric MuLVs, recovered after microinjection of viral DNA into NIH/3T3 cells, were inoculated into susceptible mice. We found that the chimeric MuLVs harboring the LTR region or the gag-pol region of the neurotropic genome could not induce paralysis. However, the chimeric MuLV with the pol-env region of the neurotropic genome could induce paralysis, indicating that this region harbors the primary determinant of paralysis. DNA probes specific for the genome of this neurotropic virus have been constructed. With these DNA probes, we were able to detect specific provirus integrated in genomic DNA of infected cells. DNA sequencing data of the LTR and the env region will also be presented.

Abstract 39. Pathogenic mechanisms in murine leukemia virus induced neurologic disease
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We have previously shown that host genes and immunity both play a role in determining the expression of neurologic disease following Cas-Br-M MuLV infection of neonatal mice by affecting the rate at which MuLV p30 accumulates in brain. However, the mechanism by which replicating MuLV, MuLV p30 or other viral proteins produces the spongiform encephalomyelopathy associated with this paralytic syndrome is unclear. Temperature sensitive mutants of Moloney (Mol) MuLV are capable of inducing neurologic disease in susceptible mice. An early ts mutant of Mol MuLV induced neurologic disease clinically and pathologically