A DEMYELINATING CORONAVIRUS MHV-A59 CAUSES UPREGULATION OF INTERFERON BETA GENE EXPRESSION IN ASTROCYTES. E. Lavi* O. Wang, and J.A. Halatsky. Dep. of Pathology, University of Pennsylvania, Philadelphia PA 19104.

Infection of mice with coronavirus mouse hepatitis virus strain MHV-A59 causes focal acute encephalitis, hepatitis and chronic demyelinating disease. To investigate host interferon (IFN) response to viral infection within the brain, RNA was extracted from A59-injected and mock-injected mice, RT-PCR amplified with primers specific for the various IFNs, transferred to nylon membranes and hybridized with IFN specific digoxigenin-labeled probes. A59 infection caused upregulation of IFN-beta and IFN-gamma RNA (but not IFN-alpha) within the brain 1-4 days after inoculation and returned to normal at day 7 post inoculation. Infection of primary astrocyte cultures from newborn mice with A59 caused upregulation of IFN-beta RNA, but not IFN-gamma or IFN-alpha. Polyclonal rabbit-anti mouse IFN alpha/beta or anti IFN beta was given to groups of 4-week-old C57BL/6 mice at a dose of 10,000 U per 1000 g body weight i.p. treatment, 24 hours prior to i.c. inoculation of 1LD50 of MHV-2 (a non-neurotropic strain), or MHV-A59. At various intervals post inoculation virus titers from brains and livers were determined by plaque assay, and the histopathology was analyzed by H&E staining. Treatment with pre-immune rabbit serum had no effect on disease outcome in either one of the viruses. While IFN antibodies had little or no effect on the outcome of disease in MHV-A59 infection, mice treated with either anti IFN alpha/beta or anti IFN beta prior to MHV-2 infection had higher titers of virus recovered from the brain and histopathological enhancement of acute meningoencephalitis. Thus, while IFN-gama may be produced by inflammatory cells during acute encephalitis, IFN-beta upregulation is probably due to a local effect of astrocytes. IFN-beta may also have a protective role against brain invasion of the non neurotropic MHV-2 virus.

THE INTERACTION BETWEEN APOLIPOPROTEIN E AND ALZHEIMER'S AMYLOID B-PEPTIDE IS DEPENDENT ON B-PEPTIDE CONFORMATION. Adam A Golabek, Claudio Soto and Thomas Wisniewski. NYU Medical Center, Department of Neurology, 550 First Avenue, New York, NY 10016

Alzheimer disease (AD) is neuropathologically characterized by the cerebral deposition of amyloid in the form of senile plaques and amyloid angiopathy, accompanied by neurofibrillary tangles formation and neuronal loss. The major component of the amyloid is a 39 to 44 amino acid residue protein termed amyloid B (Aβ). The Aβ peptide also exists as a normal protein in biological fluids, called soluble Aβ. sAβ is thought to have a more random coil and/or a-helical structure, while Aβ in the amyloid possesses a crossed β-sheet structure. The major risk factor for late-onset AD is the inheritance of the apolipoprotein (apo) E4 isotype of apo E. We and others have shown the immunohistochemical and biochemical presence of apo E within senile plaques, where it is complexed with Aβ. It has also been shown that apo E binds to Aβ and that apo E4 in particular, promotes a β-sheet structure in vitro. Currently, we have investigated the sequential and conformational aspects of the apo E/Aβ interaction. We show, that apo E preferentially binds to Aβ peptides with a high content of β-sheet conformation. This can in part explain the formation of complexes between Aβ and apo E within the senile plaque in vivo.