

## CONTROL OF MEASLES ENCEPHALITIS IN THE RAT BY CD4+ T-CELLS

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Measles virus (MV) is a neurotropic virus causing acute encephalitis as well as persistent infections in subacute sclerosing panencephalitis or measles inclusion body encephalitis. Clinical studies have shown that both, humoral and cellular immune reactions are essential for overcoming acute measles. It is well documented that neutralising antibodies directed against the MV hemagglutinin (H) and fusion (F) glycoproteins block the adsorption and fusion steps of the viral life cycle and hence restrict viral spread in tissue. Detailed knowledge about the role of the cellular immune response (CMI) to MV is still lacking. In our rat model of MV-induced fatal encephalitis we show by clinical, histopathological and virological studies that the immunisation of rats with recombinant vaccinia viruses (VVR) expressing MV nucleocapsid (N), F and H proteins induces protective immunity against challenge infection with neurotropic MV, but phospho (P) and matrix (M) protein are ineffective. In vivo depletion of CD8+ T cells does not influence the protective effect of VVR immunisation. MV neutralising antibodies were shown to occur too late to account for the observed protection. Furthermore, by adoptive transfer of CD4+ T cells with specificity for individual MV proteins within 24 hours after infection, the occurrence of encephalitis and the spread of MV in the CNS was prevented in weanling rats. These observations indicate that a MV-specific CD4+ T cell response in the absence of CD8+ T cells and neutralising antibodies is sufficient to overcome viral CNS disease and clear the infection.

## CHARACTERIZATION OF THE INFLAMMATORY RESPONSE IN THE CENTRAL NERVOUS SYSTEM OF RATS WITH DIFFERENT SUSCEPTABILITY TO CORONAVIRUS MHV4-INDUCED ENCEPHALITIS

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The inflammatory response in the central nervous system (CNS) of Lewis and Brown Norway rats was evaluated after intracerebral infection with the murine coronavirus MHV4. Distribution of infiltrating lymphocyte subsets and viral antigens was identified by immunohistological staining. Colour maps showing the spatial arrangement of lymphocytes and viral antigens in pathologically altered CNS areas were created by digital image processing of stained CNS sections and dynamic changes in the infiltrating cell population were monitored by flow-cytometry on lymphocytes isolated from the CNS. In clinically susceptible Lewis rats, viral antigens were detected throughout the central nervous system including spinal cord. Onset as well as recovery from neurological disease was associated with high numbers of infiltrating CD8+ T-cells which localized close to virus-infected cells expressing high levels of class I major histocompatibility antigens. Convalescence was accompanied by a slight increase in numbers of B(OX33+)-cells in the CNS and the accumulation of immunoglobulin-containing cells in the centre of virus-infected areas. In clinically resistant Brown Norway rats, virus-infected cells were few in number and never detected in the spinal cord. In contrast to Lewis rats CD8+ T-cells were identified in virus-affected areas of Brown Norway rats only early after infection and flow cytometry revealed considerably lower numbers of cells with this phenotype than was found in the CNS of susceptible Lewis rats. Although the infiltration profile of B(OX33+)-lymphocytes was comparable in Brown Norway and Lewis rats as determined by flow-cytometry, less immunoglobulin-containing B-cells were detected in virus-infected areas of Brown Norway rats.