THE PATHOGENESIS AND AGE RELATED SUSCEPTIBILITY OF OC43 VIRUS IN MICE

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Coronavirus OC43 is a human respiratory virus which was isolated in organ culture. It has since been adapted to grow in suckling mouse brain but no further work on the pathogenesis of this virus has been described.

CD1 mice infected intracerebrally or extraneurally with OC43 virus develop a lethal neurotropic infection. Organs and tissues were removed from infected mice and tested for the presence of viral antigen and/or infectious virus. Replication of OC43 is confined solely to the nervous system, neither infectious virus nor viral antigen could be detected in any extraneural tissue tested including heart, liver, lungs, spleen, thymus and adrenals.

Examination of the brains of infected mice by FAT revealed that by 48 hours post infection there was extensive infection of the brain and particularly of the cerebral cortex. Infection of the cerebellum, however, was restricted to Purkinje cells. Spinal cord; ganglia and retina were also positive by FAT.

Histological examination of extensively infected brain by H&E stain revealed very little necrosis and luxol fast blue staining did not demonstrate any demyelination.

Infected mice develop an age related susceptibility to the virus becoming resistant to infection by ic inoculation by 20 days of age and by ip inoculation by 15 days of age.

We have carried out experiments to investigate which of the following possible mechanisms were responsible for the resistance to OC43 infection in adult mice.

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A) Injected virus does not reach the brain - this could not be responsible as the mice remain resistant even when inoculated with large doses of virus ic.

B) Differences in interferon production of sensitivity - 12 adult (resistant) mice were inoculated intravenously with Anti-interferon globulin (AIG) followed 1 hour later by ic inoculation with 10^6SMic LD_{50} OC43. At 3 days pi the animals were given a second dose of AIG. Eleven of the mice treated with AIG remained well and examination of their brains by FA at 7 dpi did not reveal any viral antigen. We conclude therefore that interferon is not responsible for the resistance in adult mice.

C) Inability of macrophages to support infection - Cultures of peritoneal macrophages from 2 day old and 12 week old mice were infected with $10^5 TCID_{50}$ OC43 per ring culture. The cultures were examined by FA for the presence of viral antigen at 48, 72 hours and 7 days after infection and were negative at all times.

Likewise peritoneal MØ removed from 2 day old and 12 week old mice infected with OC43 were negative for viral antigen. There is no difference in the ability of macrophages from mice of different ages to support infection.

D) Maturation of the cell mediated immune system - Experiments were carried out to investigate what effect immunosuppression of adult mice and the transfer of adult spleen cells to suckling mice would have on the outcome in infection with OC43.

Immunosuppression of adult mice with cyclophosphamide does not increase their susceptibility to OC43, a proportion of 15 day old mice given a previously sub-lethal dose died. The brains of the dead mice were positive for viral antigen.

The immune system, whilst being partially protective in 15 day old mice, was not the sole factor in this resistance. Neither immune or non-immune spleen cells were capable of protecting the suckling mice.

E) Inability of the virus to grow in adult brain cells - as mechanisms A-D are not responsible for the resistance the ability or otherwise of the virus to grow in brain cells must play an important role.

In order to better understand the interaction between OC43 and neural cells - cultures of neural cells have been established and the effect of the virus on the different cell types is being investigated.