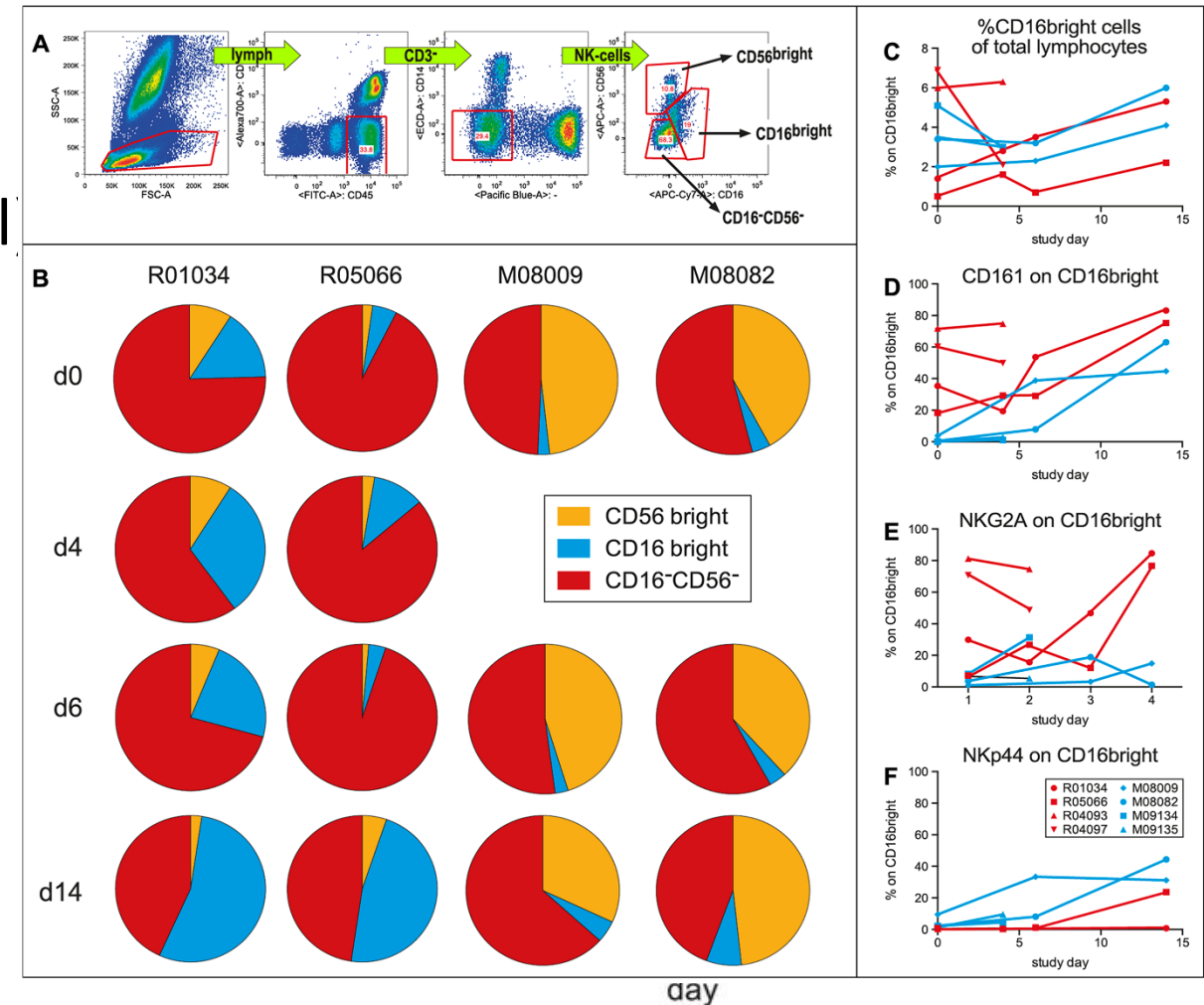


Marmoset-based infectious disease research under biocontainment conditions

Jean Patterson, PhD
Texas Biomedical Research Institute
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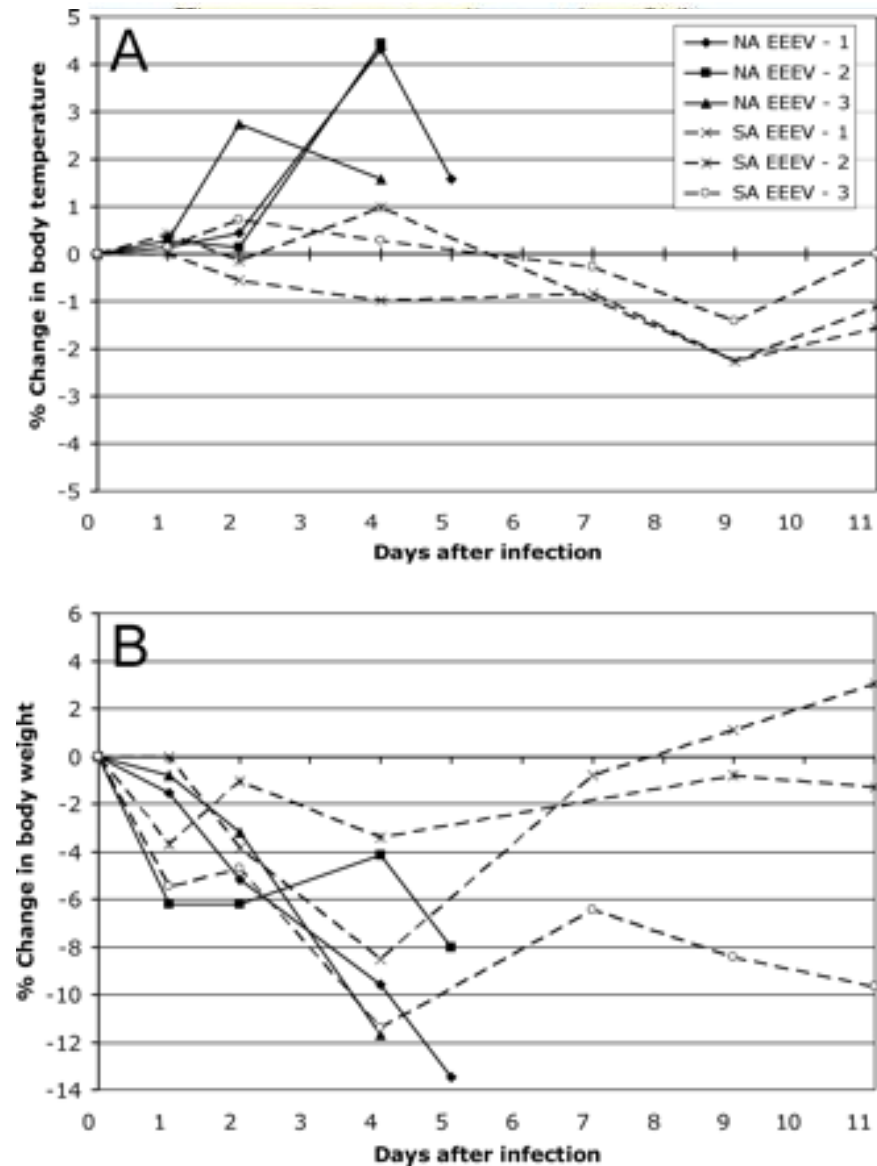
West Nile virus

- Common marmoset found to be equivalently susceptible to infection with WNV as macaques, (the traditional model
- Did not develop clinical signs of WNV disease.
- Virus induced a rapid $CD56^{dim}CD16^{bright}$ natural killer response, followed by IgM and IgG antibody responses.



Eastern Equine Encephalitis

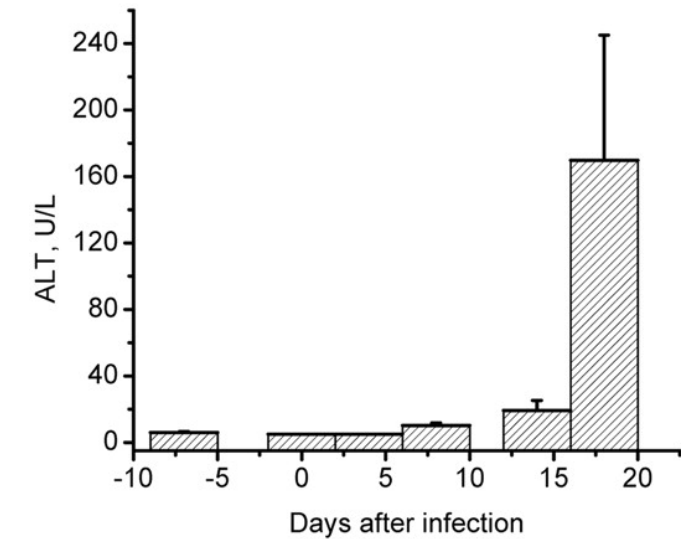
- Eastern equine encephalitis virus (EEEV) produces the most severe human arboviral disease in North America- potential biological weapon.
- South American strains are genetically and antigenically distinct strains from South America (SA) have seldom been associated with human disease.
- EEEV produces neurologic disease that resembles human and equine infections in lab mice however, both NA and SA strains of EEEV are highly virulent in mice.
- When inoculated, the NA EEEV-infected animals either died or were euthanized on day 4 or 5 after infection due to anorexia and neurologic signs, but the SA EEEV-infected animals remained healthy and survived
- Common marmoset can be a useful model of human EEE for testing antiviral drugs and vaccine candidates.



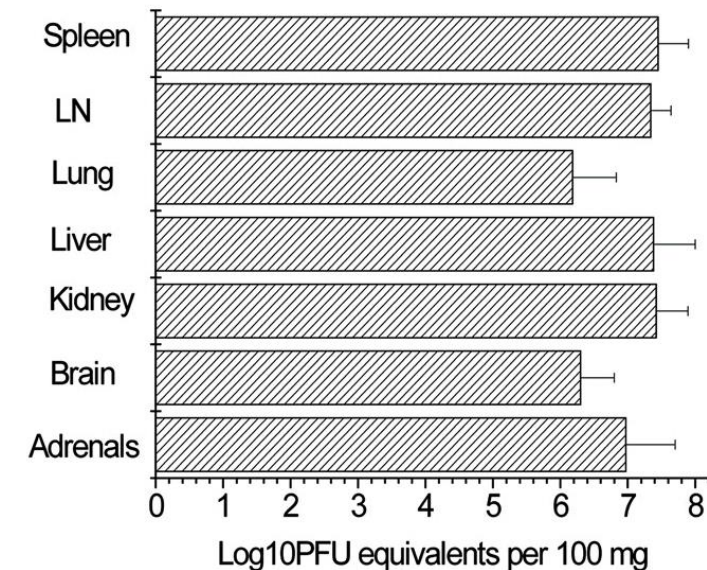
Lassa Virus

- Infection resulted in a systemic disease with clinical and morphological features mirroring those in fatal human Lassa infection:
 - fever, weight loss,
 - high viremia and viral RNA load in tissues,
 - elevated liver enzymes,
 - severe morbidity between days 15 and 20.
- Histopathology findings included
 - multifocal hepatic necrosis with mild inflammation and hepatocyte proliferation,
 - lymphoid depletion,
 - interstitial nephritis.
- Marmoset model showed the similar immunosuppression seen in human disease.

A ALT in plasma

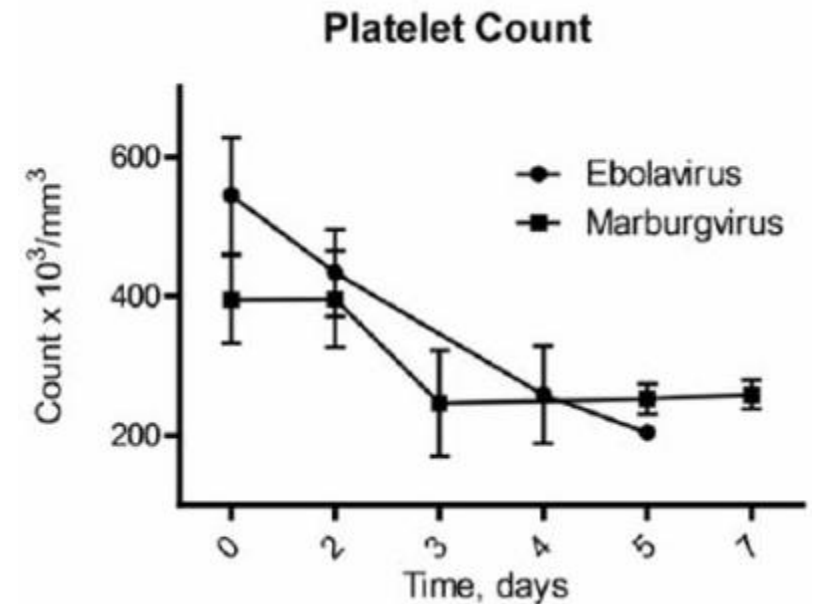
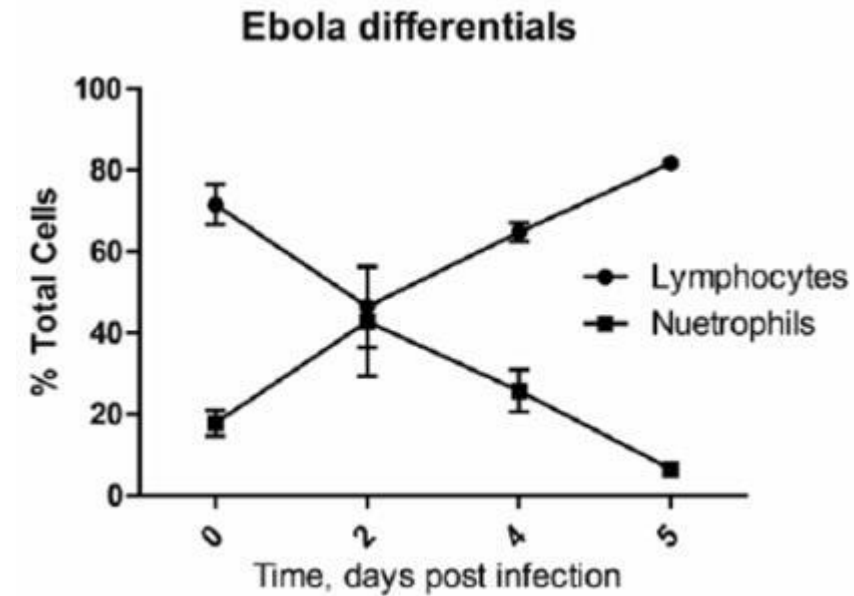


D Viral Load in Tissues



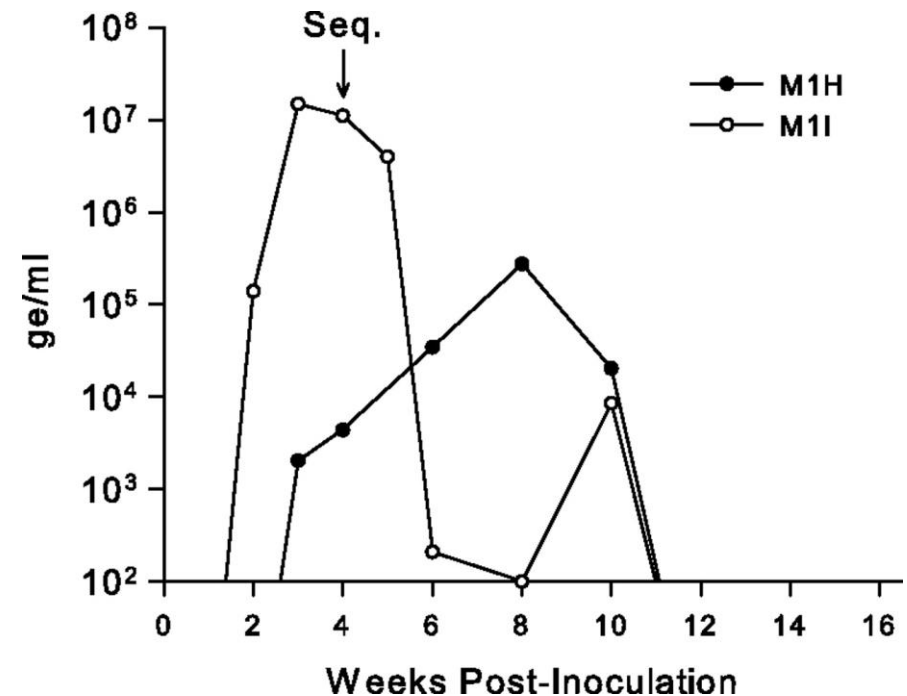
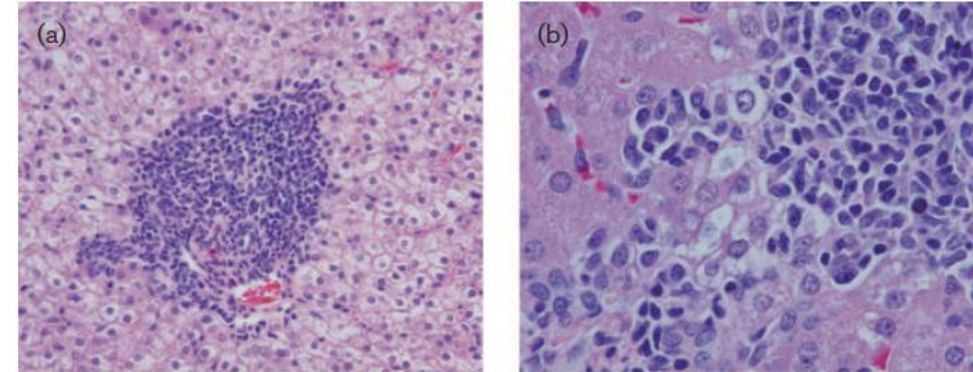
Ebola virus

- The infection resulted in a systemic fatal disease with clinical and morphological features closely resembling human infection.
- Symptoms include
 - weight loss, fever,
 - high virus titers in tissue,
 - thrombocytopenia, neutrophilia,
 - high liver transaminases and phosphatases and disseminated intravascular coagulation.
- Evidence of multifocal to coalescing hepatic necrosis was seen in EBOV animals



GB virus B

- Animals were susceptible to infectious serum as well as GBV-B transcripts.
- Hepatic pathology persisted for periods of up to 6 months in some animals.
- Hepatitis was characterized influx of both B cells and T cells within the first 2 months of primary infection.
- Marmosets exhibit two phenotypes upon infection
 - susceptible phenotype
 - the partially resistant phenotype.
- We speculate that the marmoset partially resistant phenotype may be due to a polymorphism in the marmoset population that affects critical virus-host interactions and that wild-type GBV-B is capable of rapidly adapting to this altered host.



MERS- CoV – two reports

Lethal pneumonia (Falzarno et al)

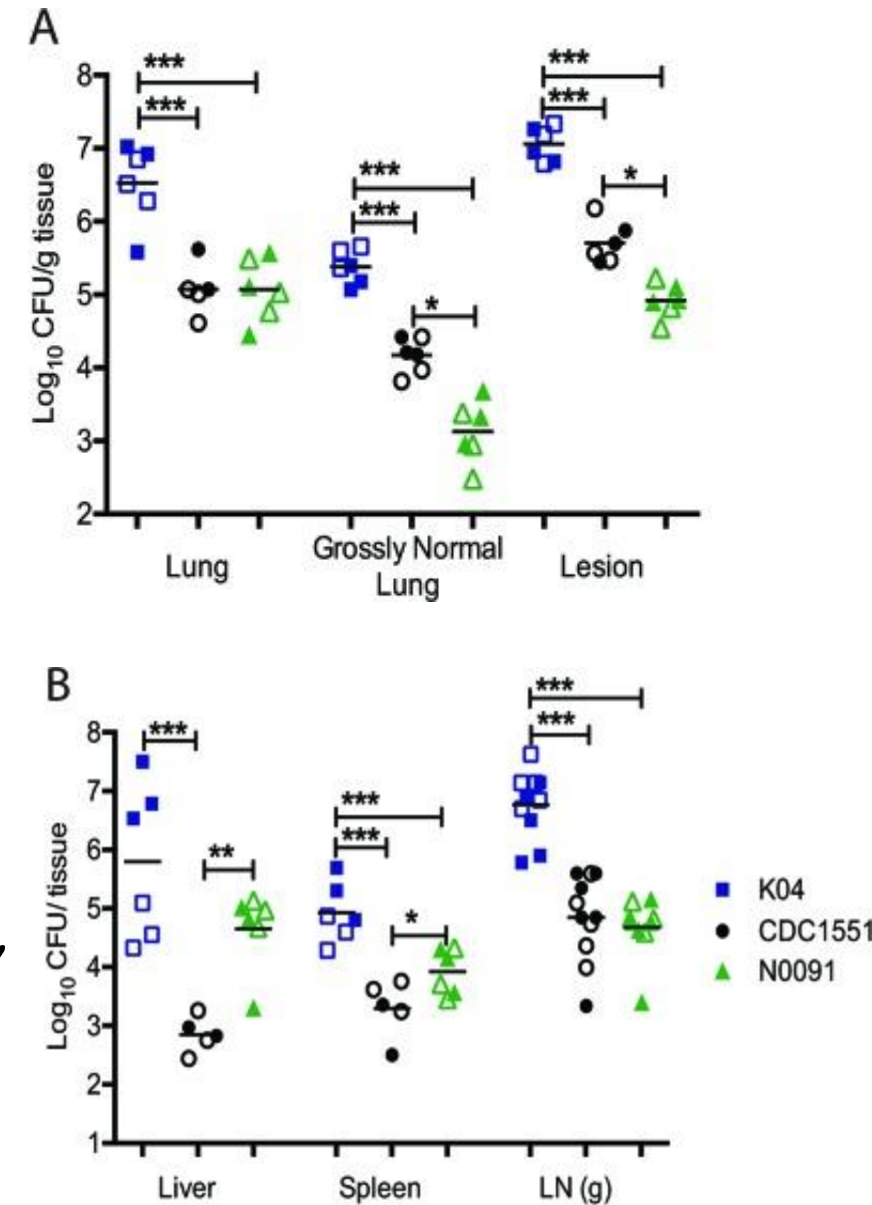
- Marmosets developed a progressive severe pneumonia leading to euthanasia of some animals.
- Extensive lesions were evident in the lungs of all animals
- Some animals were viremic; high viral loads detected in the lungs
- Total RNAseq demonstrated the induction of immune and inflammatory pathways.

No lethal pneumonia (Johnson et al)

- Marmosets developed a mild to moderate non-lethal respiratory disease with limited other clinical signs.
- Mild to moderate clinical signs of disease that are likely due to manipulations of the marmoset rather than as a result of robust viral replication.

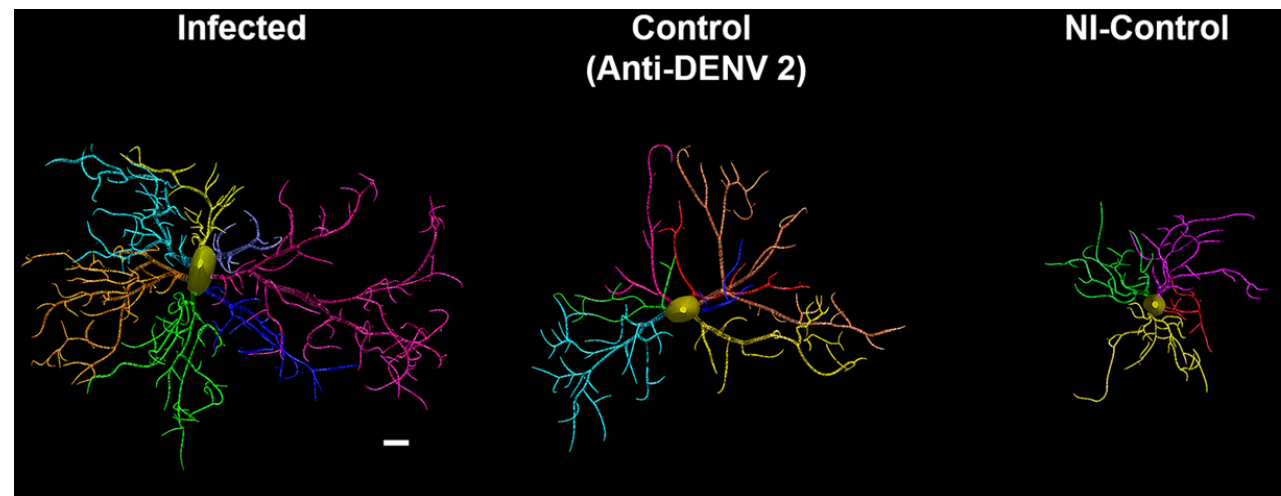
Mycobacterium tuberculosis

- Common marmosets were experimentally infected with diverse strains of *M. tb.* of various pathogenic potentials-
 - isolates of the modern Beijing lineage, (K04)
 - the Euro-American X lineage (CDC 1551)
 - *M. africanum.* (N0091)
- All strains produced fulminant disease with a spectrum of progression rates and clinical sequelae.
- Lesion pathology revealed the entire spectrum of lesions observed in human TB patients. The three strains produced different rates of progression to disease, various extents of extrapulmonary dissemination, and various degrees of cavitation.
- Attractive small animal model of human disease that recapitulates both the complex pathology and spectrum of disease observed in humans.



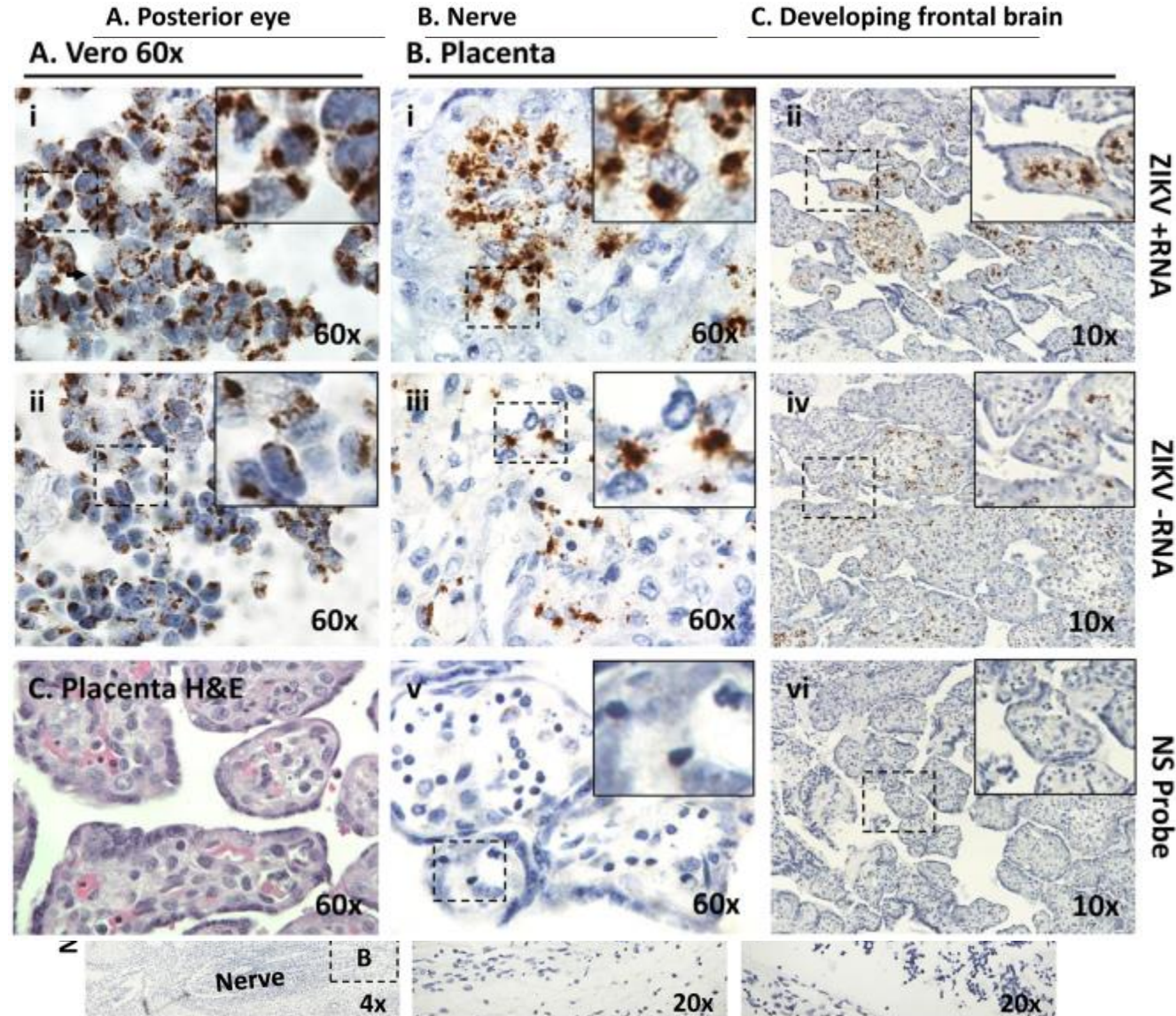
Dengue virus

- Three animals received weekly subcutaneous injections of DENV3 (genotype III)-infected supernatant of C6/36 cell cultures, followed 24 h later by anti-DENV2 antibody for 12 weeks.
- There were marked morphological changes in the microglial population of ADE monkeys characterized by more highly ramified microglial processes, higher numbers of trees and larger surface areas.



Zika Virus

- Spontaneous pregnancy loss was observed 16–18 days post-infection, with extensive active placental viral replication and fetal neurocellular disorganization similar to that seen in humans.
- These findings underscore the key role of the placenta as a conduit for fetal infection, and demonstrate the utility of marmosets as a highly relevant model for studying congenital ZIKV disease and pregnancy loss.



Koch's postulates

- Titi monkey adenovirus (TMAdV), caused a fulminant pneumonia outbreak in a colony of titi monkeys (*Callicebus cupreus*) at a national primate center in 2009.
- Common marmosets (*Callithrix jacchus*) was used to test cross-species TMAdV infection.
- Although no virus was re-isolated-
 - nasal cultures were positive for TMAdV by real-time qRT-PCR for up to 15 days post-inoculation,
 - TMAdV inoculation produced both clinically apparent disease and antibody responses
- Thus, River's modifications to Koch's postulates, which recognize the additional serological evidence of antibody production in response to a viral infection, have been fulfilled.
- These findings further establish the potential for adenovirus cross species transmission and provide the basis for development of a monkey model useful for assessing the zoonotic potential of adenoviruses.

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