

Emerging Vector Borne Pathogens

**Mammalian Reservoirs of Zoonotic Agents:
From the Field to the Lab**



There are more than 4,600 species of mammals

About 1,800 of those are rodents (Rodentia)

About 1,200 of those are bats (Chiroptera)

65% of mammalian species

Hantaviruses and Their Rodent Reservoirs

Why don't reservoir rodents have pathology when infected with their hantaviruses?

Why are they unable to clear the virus?

Sin Nombre virus and the deer mouse (*Peromyscus maniculatus*)



Sin Nombre Virus Infection: Human vs. Deer Mouse

Characteristic	Human (HCPS)	Deer Mice (no disease)
Virus in lungs	Yes	Yes
Infected cells	Capillary endothelial cells	Capillary endothelial cells
Endothelial damage	No	No
Cardiopulmonary disease	Yes	No
Pulmonary inflammation	Yes	No
Pulmonary T cell infiltrates	Yes	No
Cytokines	Pro-inflammatory	Anti-inflammatory
T cells	CD4 ⁺ and CD8 ⁺ CTL (PBL)	CD4 ⁺ Treg
Neutralizing antibody	Yes	Yes
Mortality	36% (immunopathology)	None
Fate of virus	Clearance in survivors	Lifelong infection

And rats infected with Seoul hantavirus
Easterbrook et al., PNAS 2007

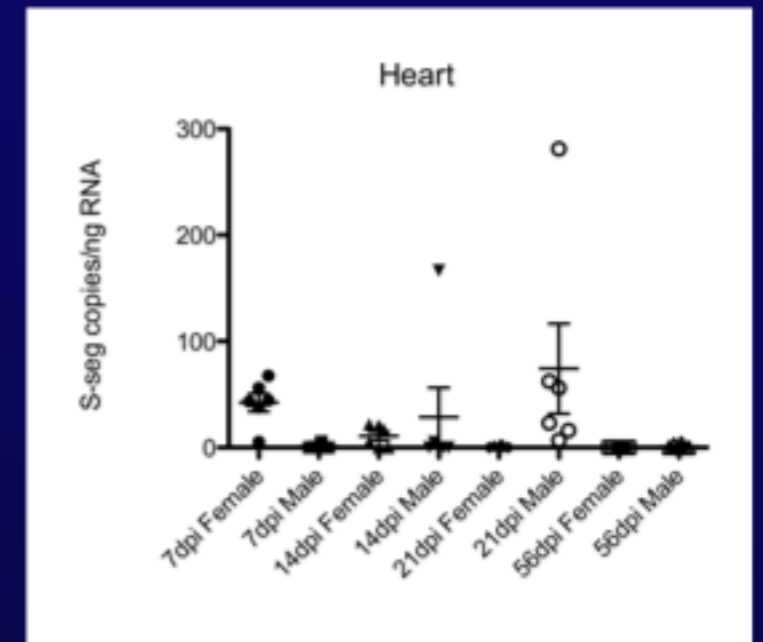
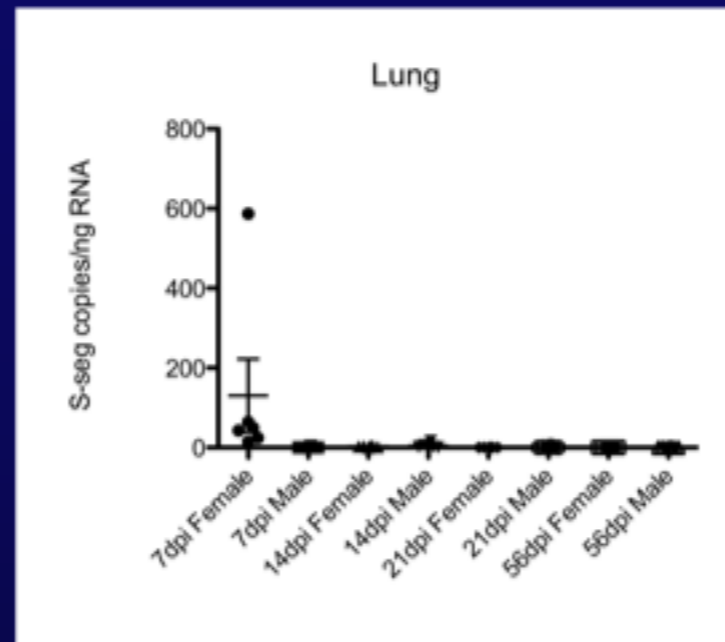
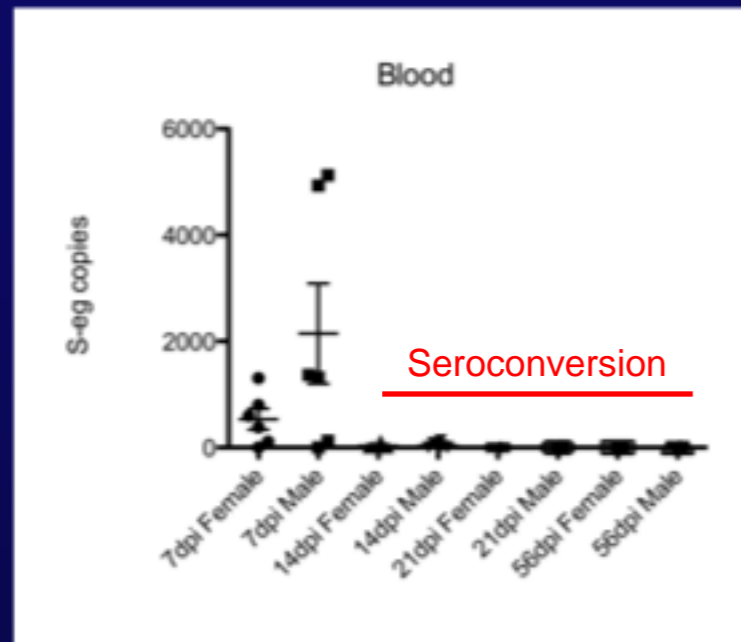
Schountz et al., PNAS 2007
Schountz et al., JVI 2012

New World Hantaviruses



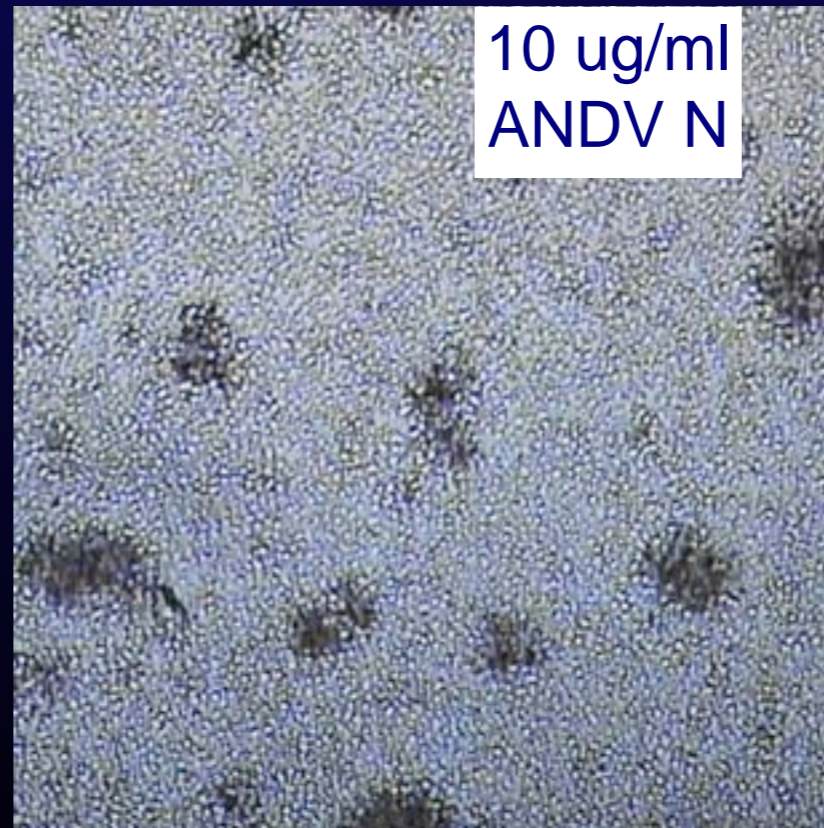
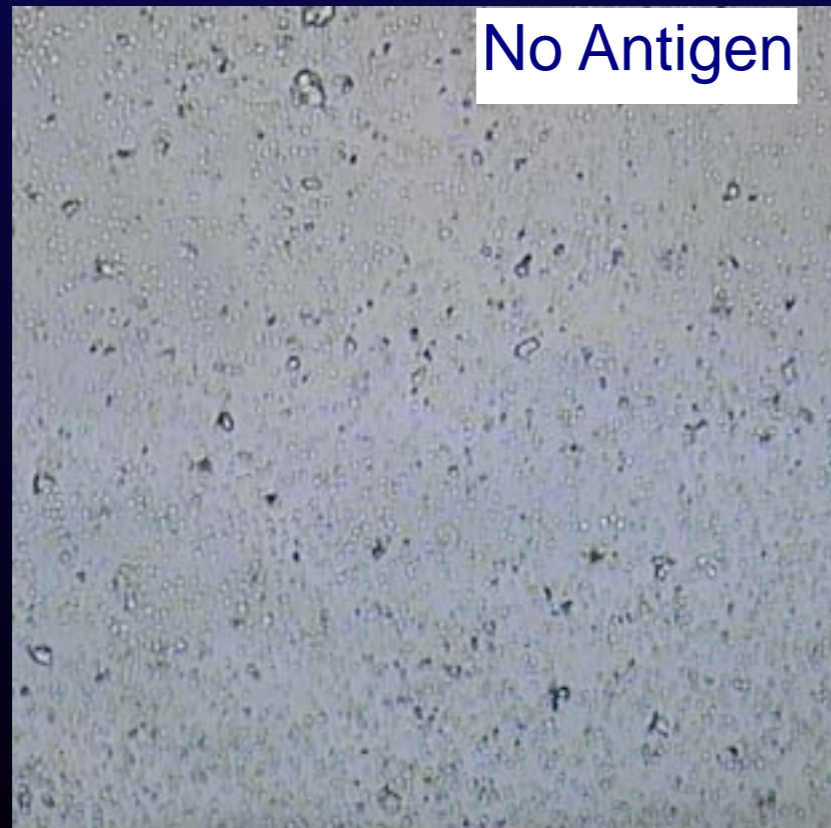
Andes Virus Infects Deer Mice

But they appear to clear it without disease



Viral RNA Copy Number (Taq-Man)

Spengler et al., PLOS One 2013



72 hour lymph node cultures from a deer mouse infected with ANDV 14 days before

Schountz et al., submitted

Experimental Infection

16 Deer Mice

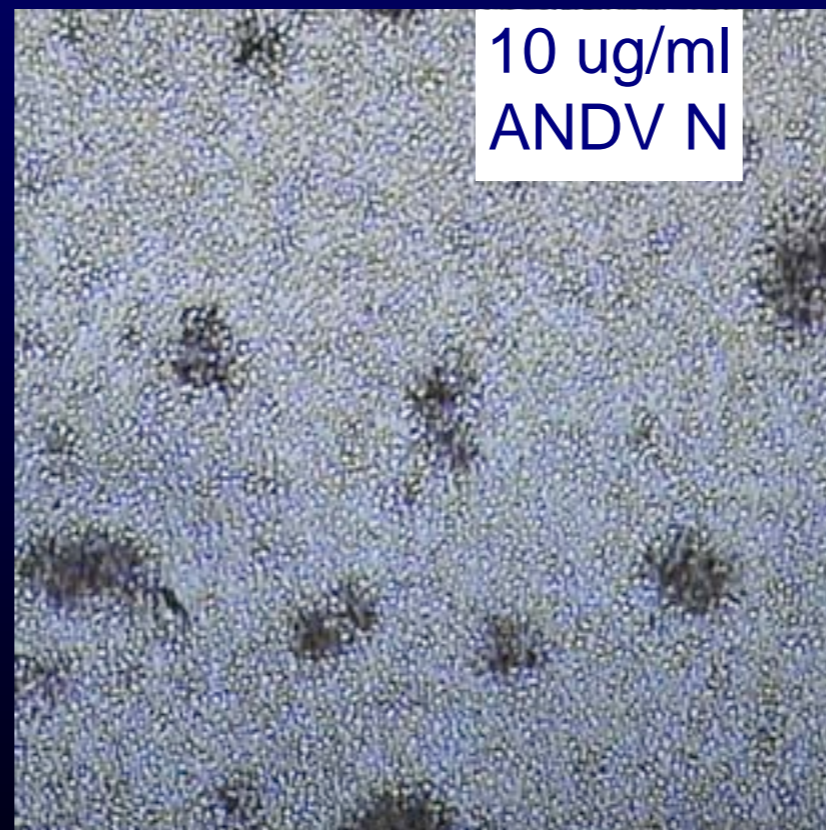
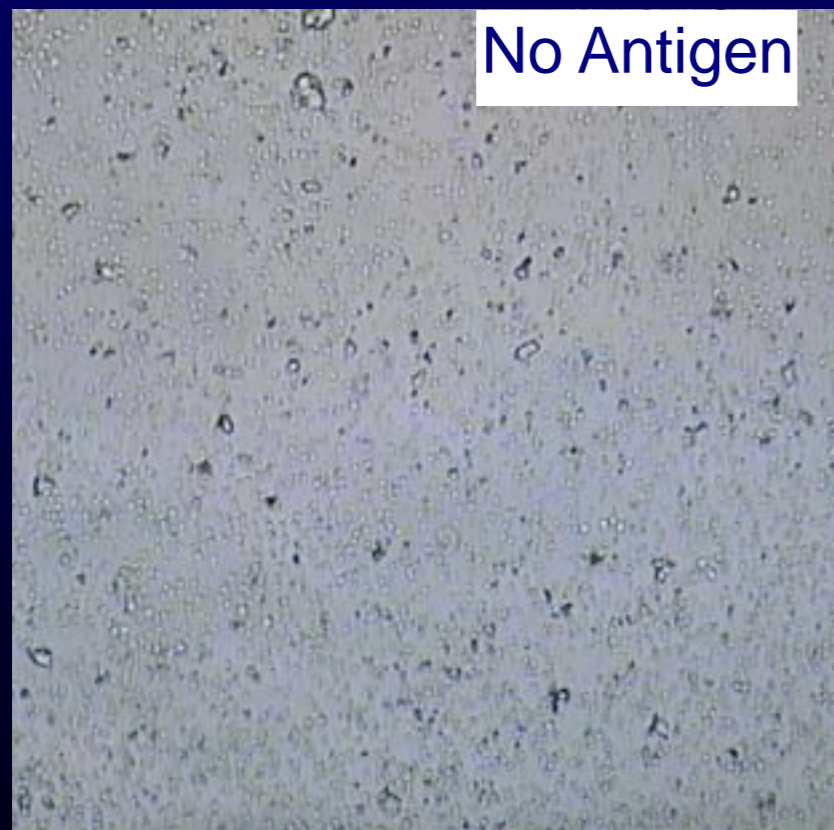
5 infected with SNV < Reservoir

8 infected with ANDV < Nonreservoir

3 uninfected controls

Harvest lymph nodes

14 days post infection



72 hour lymph node
cultures from a deer
mouse infected with ANDV
14 days before

94 Gene PCR
Immunoarray
(GAPDH normalized
 $\Delta\Delta Ct$)

BSL-4, Rocky Mountain Laboratories
Hamilton, MT, USA

Antibody Titers to Nucleocapsid

ELISA day 14

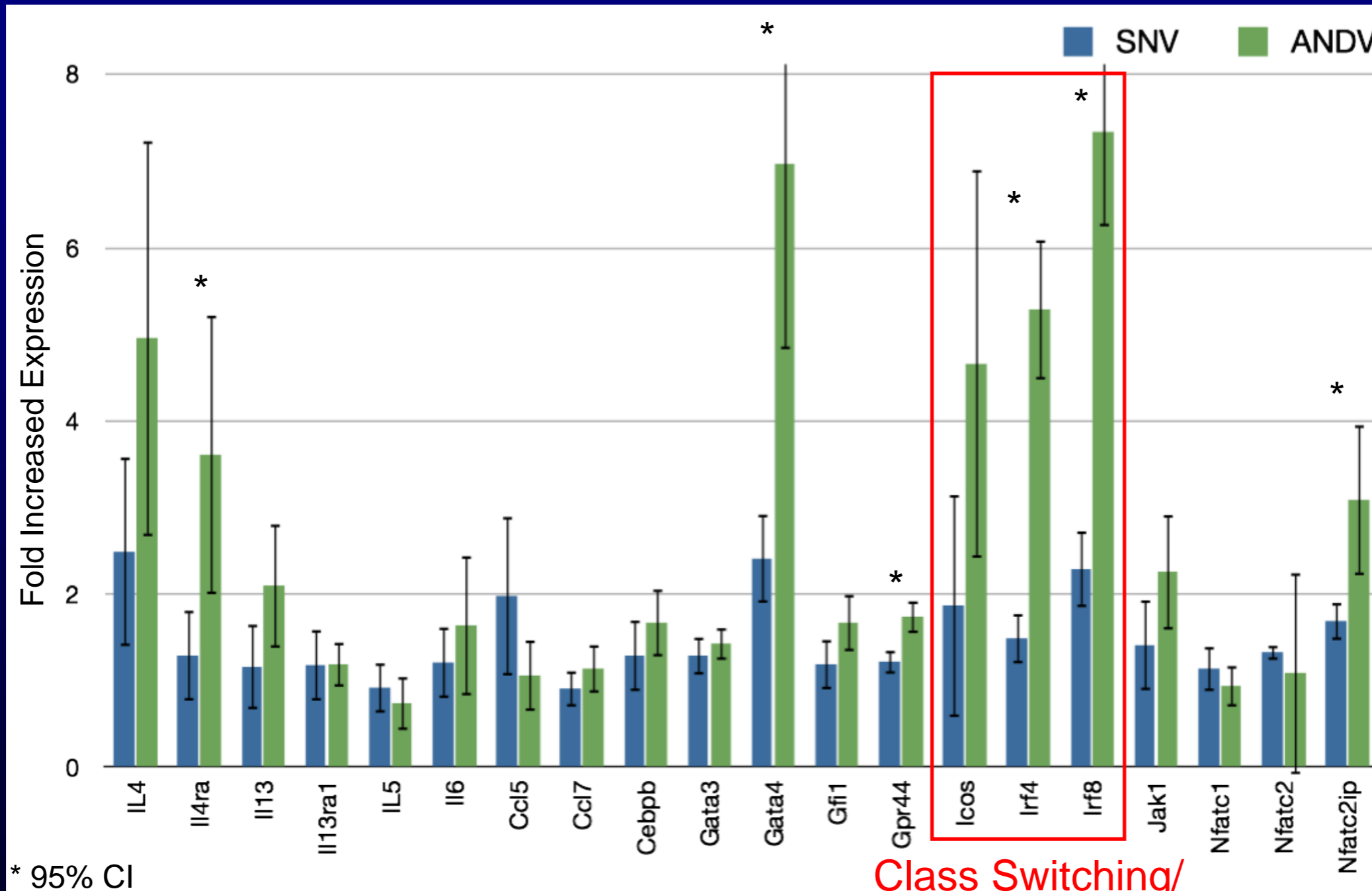
SNV: 0/5 (<100)

ANDV: 7/8 (titers of 100 or 200)

Uninfected: 0/3 (<100)

Th2/B Cell Gene Expression

94-gene real-time PCR array



Class Switching/
Affinity Maturation

Conclusions

- Deer mice infected with ANDV appear healthy
- No behavioral or hematological differences
- Most of the 94 immune genes on the array were not modulated
- Of expressed genes, most were at similar levels
- However, Th2 expression levels higher in ANDV-infected deer mice
- Class switching and affinity maturation

Hantaviruses and Their Rodent Reservoirs

Why don't reservoir rodents have pathology when infected with their hantaviruses?

Subtle immune response?

Why are they unable to clear the virus?

Failure to seroconvert quickly?

New World Hantavirus Biosafety

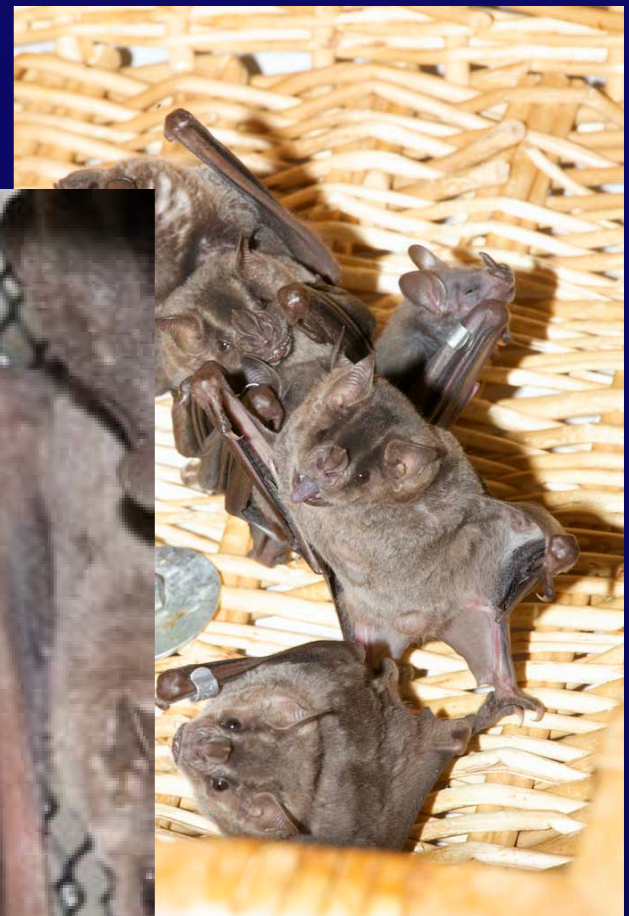
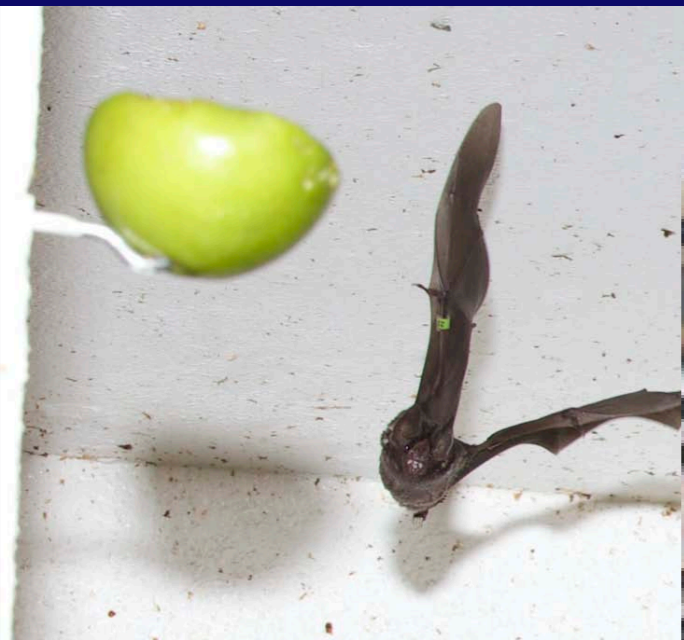
Hantavirus Cardiopulmonary Syndrome

- **BSL-2**: Laboratory manipulation of viruses **not known** to cause human disease
- **BSL-2 with BSL-3 precautions**: Manipulating tissues from euthanized animals infected with **HCPS-causing hantaviruses**
- **BSL-3**
- Laboratory manipulation and propagation of viruses **that cause HCPS**
- Animal infections with viruses **not known** to cause human disease *Can transition live cells to BSL-2*
- **BSL-4**: Animal infections with viruses **that cause HCPS** *Cannot transition live cells to BSL-3 or -2*

Maporal Virus

- Hantavirus isolated from fulvous pygmy rice rat (*Oligoryzomys fulvescens*) in western Venezuela
- Principal reservoir host is delicate pygmy rice rat (*Oligoryzomys delicatus*)
- No known cases of human disease
- Causes an HCPS-like disease in Syrian golden hamsters (*Mesocricetus auratus*)
- Animal BSL-3
 - Deer mouse susceptibility?

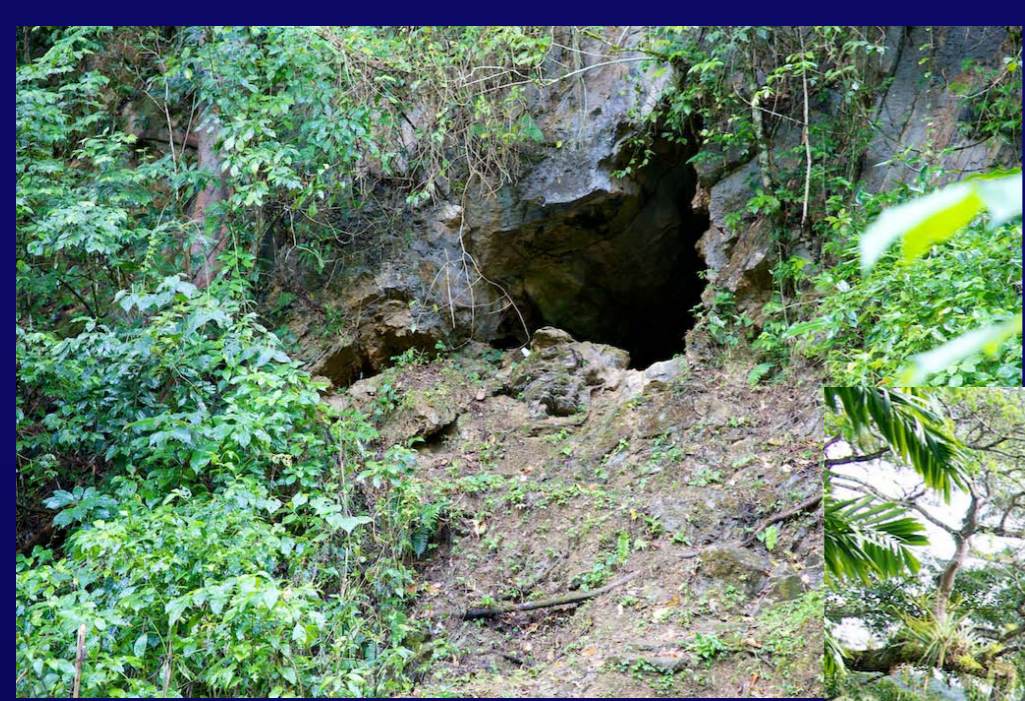
UNC Bat Colony



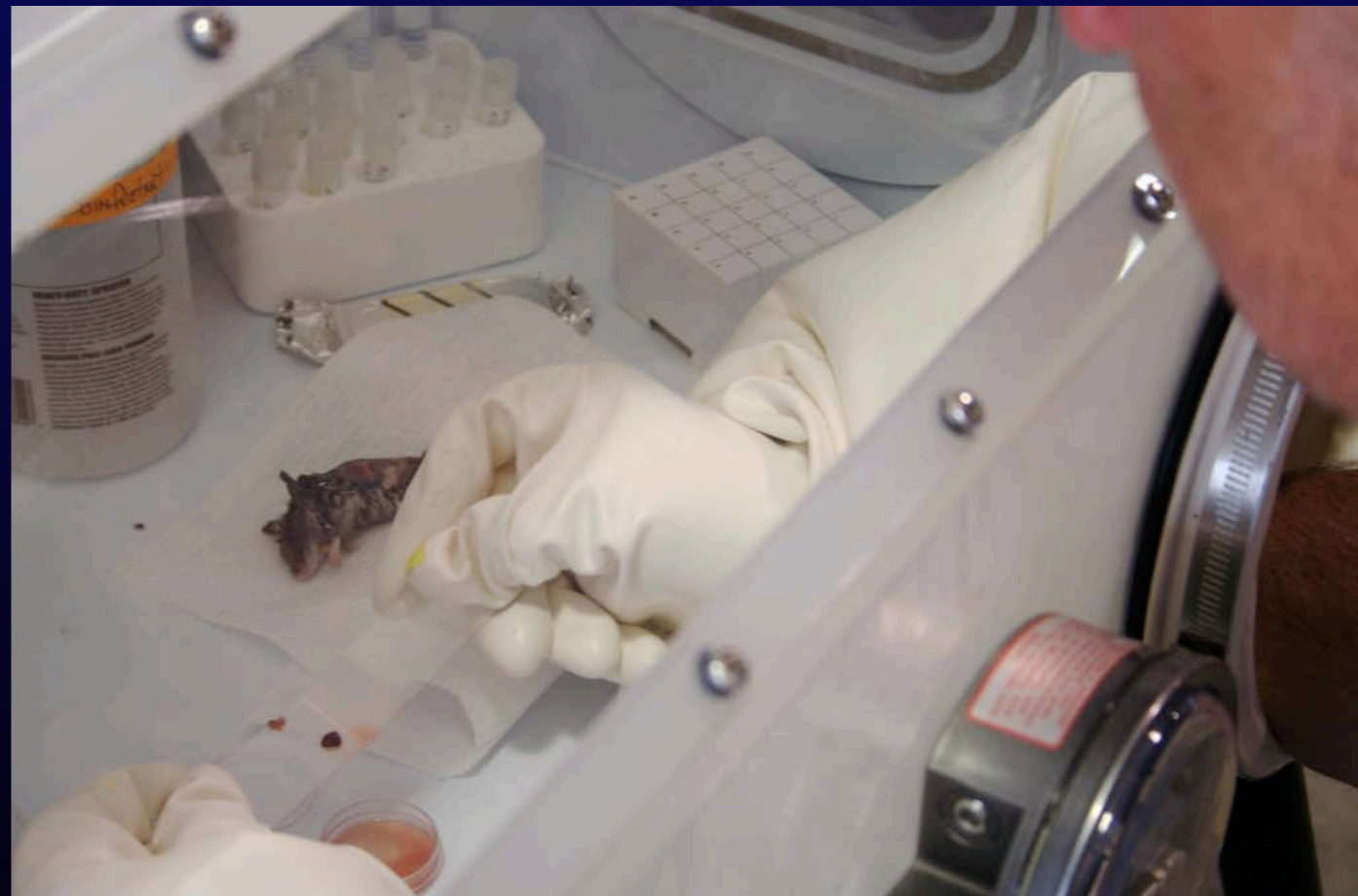
Two species of
Caribbean fruit bat
Artibeus jamaicensis
Carollia perspicillata



Trinidad and Tobago



Field Work with Reservoirs



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