Emerging Zoonoses: Preparedness and Response

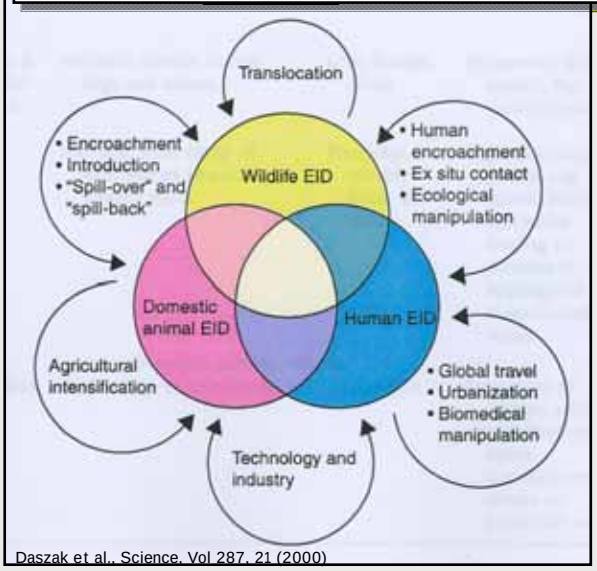
Chesapeake Area Biological Safety Association

- 2011 Annual Scientific Symposium -

Frederick, MD

June 15, 2011

Nearly 60% of all human infectious diseases and 75% of all emerging diseases are of zoonotic origin.



Daszak et al., Science, Vol 287, 21 (2000)

Examples:

1. **Domestic animals to wildlife** – Canine Distemper
2. **Wildlife to humans** – Ebola, Monkeypox,
3. **Domestic animals to humans** – Rift Valley Fever, Crimean-Congo Hemorrhagic Fever, Nipah

High containment (BSL-4) facilities

Class III biosafety cabinet will be helpful in cases of uncertain biocontainment level

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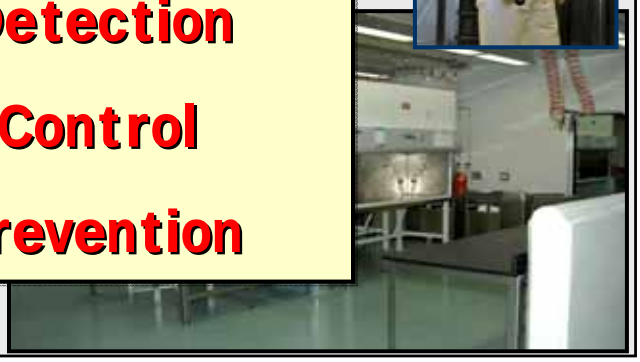
Key elements
- preparedness & response -

Surveillance

Detection

Control

Prevention



Microbiological Emergency Response Team (MERT)

Easily transportable and reliable … PCR capability

… for the detection of:

Filoviruses

…s

…, H5N1)

…RS)

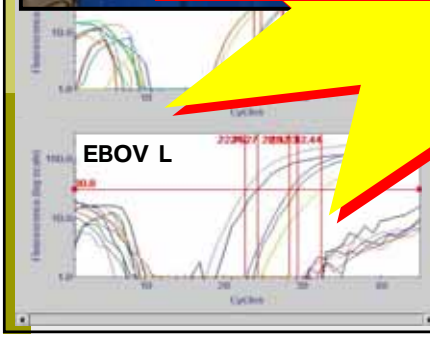
…es (Nipah, Hendra)

…s A & E

…ssp.

Neisseria spp.
Vibrio cholera
Shigella spp.
Salmonella spp.
…acillus anthracis
…ncisella tularensis
…Yersinia pestis
Brucella sp.
Burkholderia pseudomallei & mallei
Ricin

Differential diagnosis
Continuing platform development



Problems with deployment, transport and on-site support

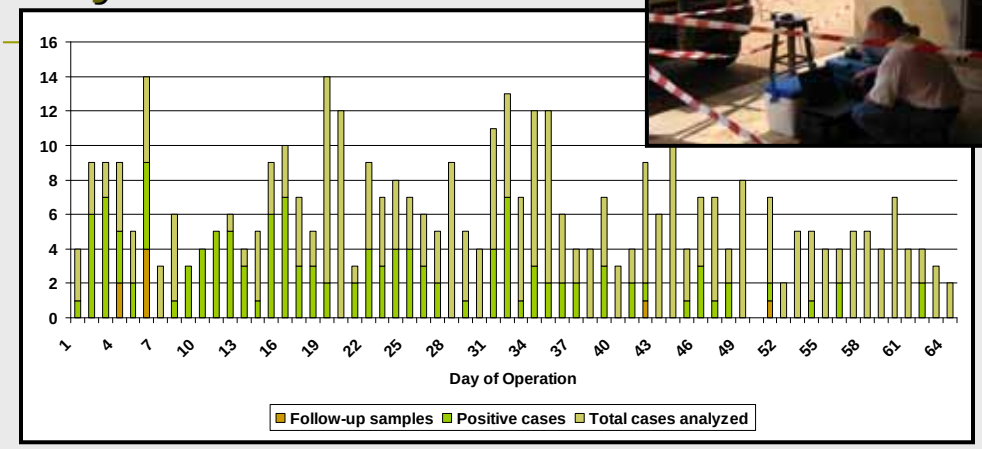
- simple, small, reliable & robust -

Mbomo, Republic of the Congo (Ebola – 2003)

- testing only -

Laboratory floor plan

Daily work load



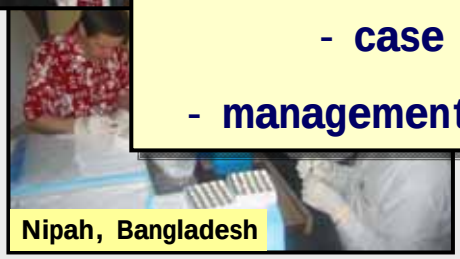
Sample receiving to diagnosis ~4 hours

Concurrence with ref. lab (CDC, Luanda) 97.5%

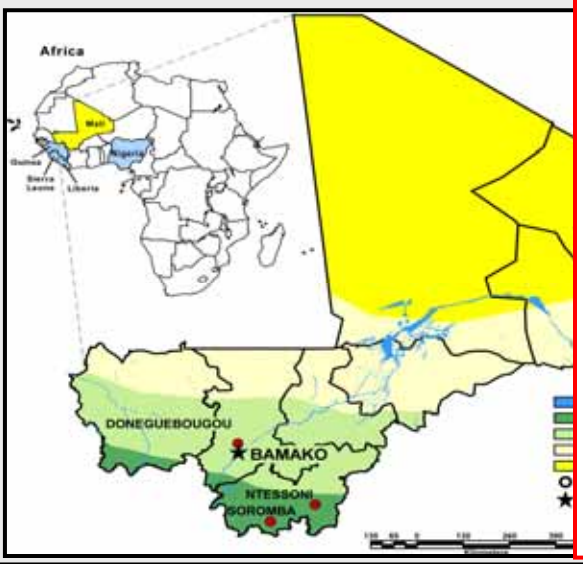
Outbreak Investigation
- gaining international reputation -

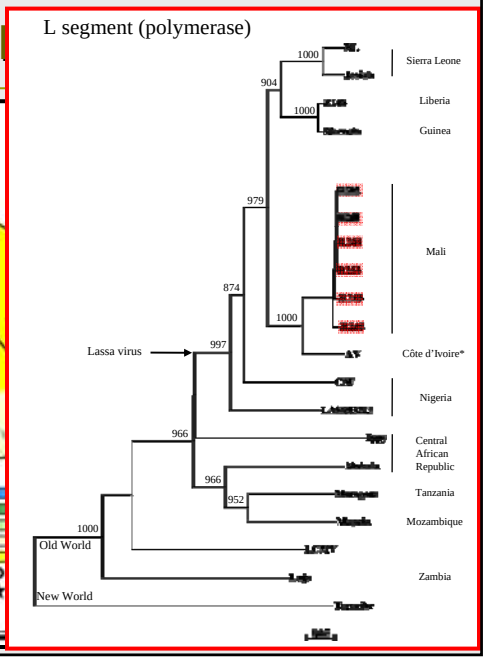
Benefit of field lab

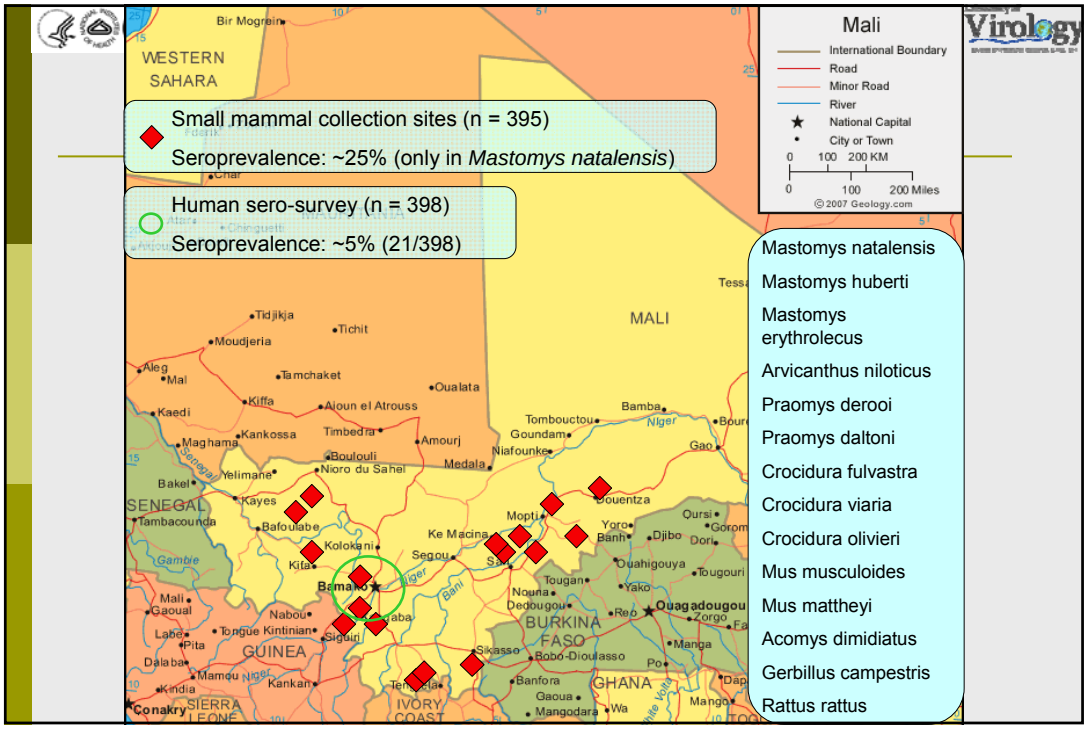
- case patient management
- safe burial in the community
- case finding
- management of survivors



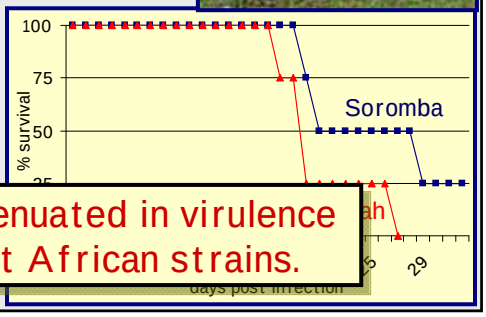
Lassa in


Africa
DONEGUEBOUGOU
BAMAKO
NTESSONI
SOROMBA


L segment (polymerase)
1000
Sierra Leone
904
1000
Liberia
Guinea
979
Mali
874
1000
Lassa virus
997
Côte d'Ivoire*
Nigeria
966
Central African Republic
966
952
Tanzania
Mozambique
1000
Old World
Zambia
New World

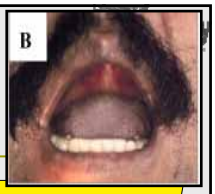

Small mammal collection sites (n = 395)
Seroprevalence: ~25% (only in Mastomys natalensis)
Human sero-survey (n = 398)
Seroprevalence: ~5% (21/398)
Mali
International Boundary
Road
Minor Road
River
National Capital
City or Town
0 100 200 KM
0 100 200 Miles
©2007 Geology.com
Mastomys natalensis
Mastomys huberti
Mastomys erythrolecus
Arvicanthus niloticus
Praomys derooi
Praomys daltoni
Crocidura fulvastra
Crocidura viaria
Crocidura olivieri
Mus musculoides
Mus mattheyi
Acomys dimidiatus
Gerbillus campestris
Rattus rattus
WESTERN SAHARA
MALI
SENEGAL
GUINEA
BURKINA FASO
GHANA
IVORY COAST
SIERRA LEONE
Bir Mogrein
Tidjikja
Tichit
Moudjeria
Aleg
Mal
Tamchaket
Kiffa
Ajoun el Atrouss
Oualata
Kaedi
Kankossa
Timbedra
Amourj
Maghama
Boulouli
Nioro du Sahel
Yelimane
Bakel
Kayes
Tambacounda
Bafoulabe
Kolokani
Kita
Bamako
Mali
Gaoual
Nabou
Tongue Kintinian
Siguiri
Labe
Pita
Dalaba
Mamou
Kindia
Kankan
Conakry
Tombouctou
Goundam
Niafounke
Medala
Bamba
Gao
Mopti
Douentza
Ke Macina
Segou
Sikasso
Bobo-Dioulasso
Banfora
Gaoua
Mangodara
Wa
Tougan
Nouna
Dedougou
Reo
Ouagadougou
Yako
Ouahigouya
Tougouri
Zorgo
Manga
Djibo
Dori
Yoro
Banh
Oursi
Po
Mango

Virulence of Lassa strains

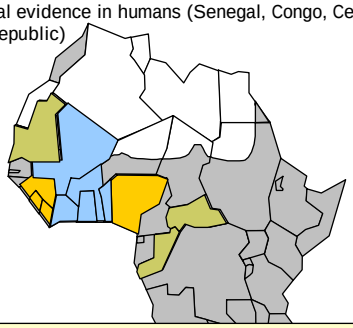


Soromba strain seems attenuated in virulence compared to other West African strains.

Lassa fever

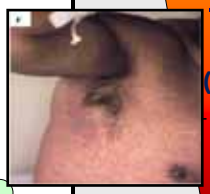


Mastomys distribution
Endemic zone (Guinea, Sierra Leone, Liberia, Nigeria)
Sporadic cases (Cote d'Ivoire, Ghana, Benin, Burkina Faso, Mali)
Serological evidence in humans (Senegal, Congo, Central African Republic)



At risk population ~ 60-120 million

Imported cases reported in USA, Britain, Germany, the Netherlands, Canada



80% subclinical

- fever, headache, malaise
- profuse weakness
- pain, tenderness (chest, abdominal)
- pharyngitis, cough
- vomiting, GI symptoms

20% severe

(life-threatening)

- conjunctivitis, mucosal bleeding
- petechial rash
- neck/fascial swelling
- shock

Hendra virus

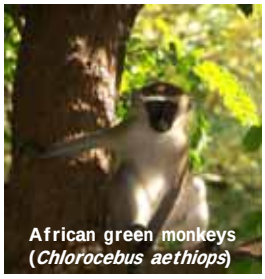
Challenge
(5 x 10^5 pfu intratracheal)

Rhesus macaque
(*Macaca mulatta*)

No clinical symptoms

Cynomolgus macaque
(*Macaca fascicularis*)

No clinical symptoms

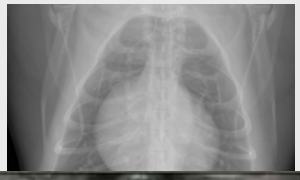


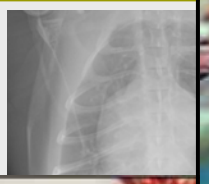
African green monkeys
(*Chlorocebus aethiops*)

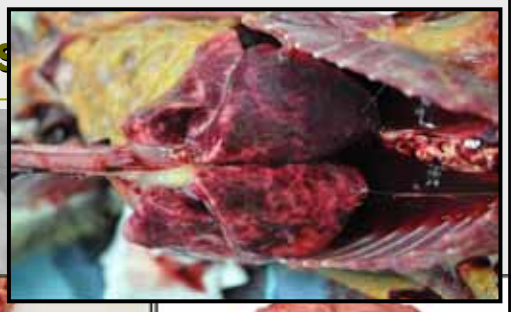
Acute respiratory distress
encephalitis

- Zoonotic transmission only

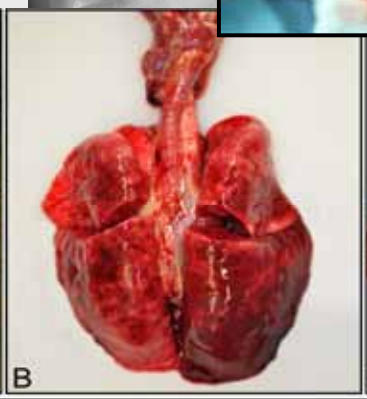
ARDS-like s



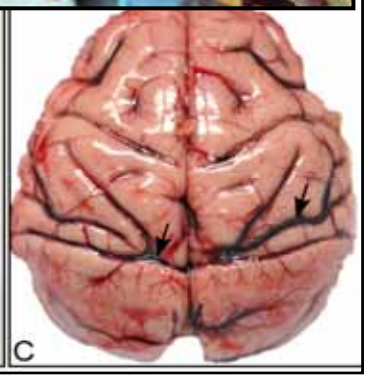




A

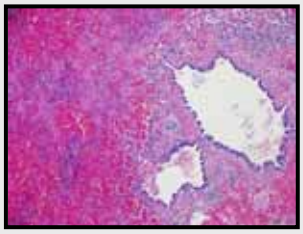


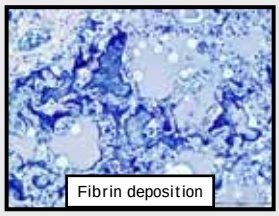
B



C

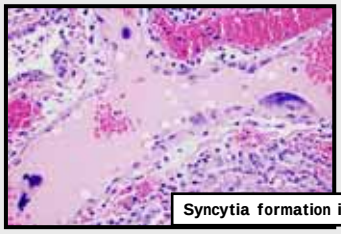
Histopathology

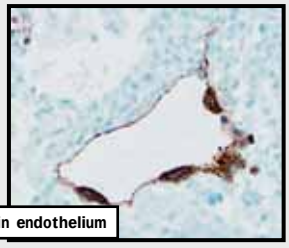


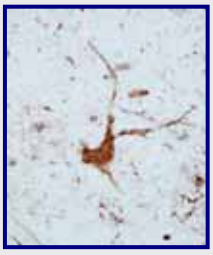


Lung

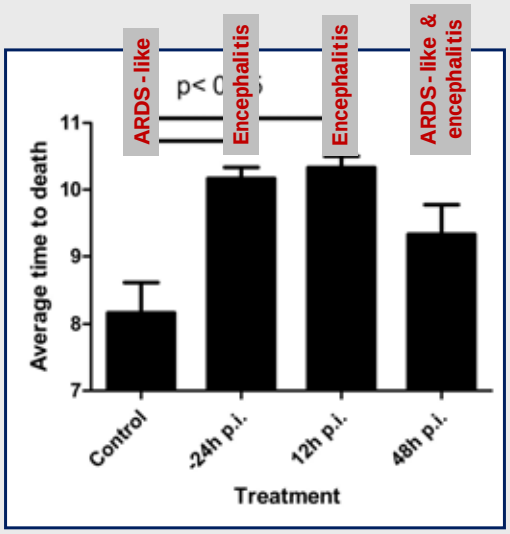
Brain







Ribavarin efficacy



Treatment scheme
- loading dose: 50 mg/kg s.c.
- maintenance dose: 10 mg/kg s.c.
- scheme: 3 times daily for 14 days

Henipah conclusion

Mother, daughter offered experimental hendra virus treatment

ABC

Andree Withey and Nikole Jacobi, ABC
May 27, 2010, 10:49 am

Buzz up! | Send | Share | Print

An experimental drug for hendra virus has been offered to a mother and daughter on Queensland's Sunshine Coast who have been exposed to the deadly disease.

Related Links

virus at a Tewantin property on the Sunshine Coast 10 days ago.

Humoral immune response seems main mechanism of protection

- Neutralizing antibodies seem effective in treatment
- Vaccines should be possible !!!!!

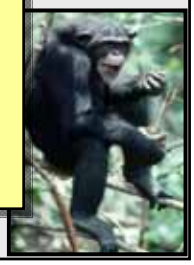
Hendra problem could be tackled with horse vaccination
Nipah problem ???

Intentional Release

Vaccines strategies/requirements for rare but high impact infectious diseases

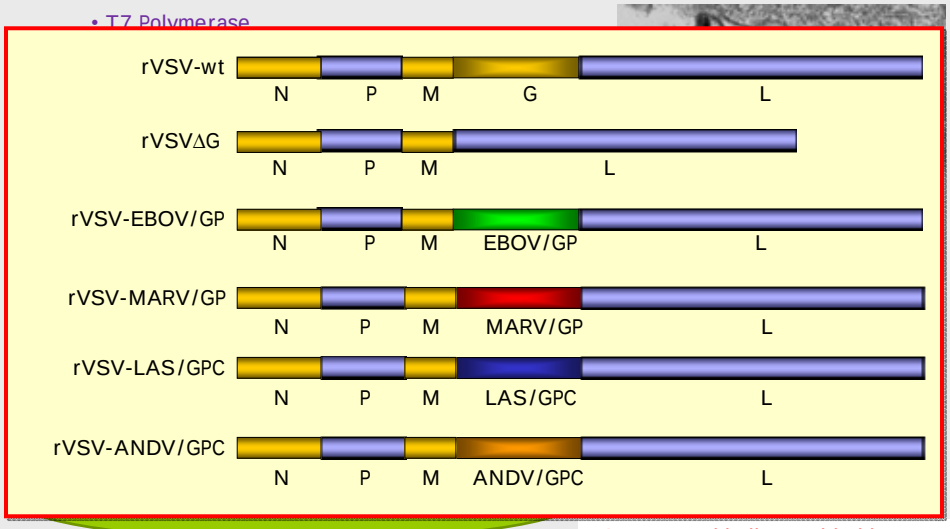
(e.g. EBOV HF, MARV HF, Lassa F)

- targeted rather than a population-based approach
- single rather than boost immunization approach
- safe and efficacious
- short time to immunity
- widely cross-protective
- little interference and reusable
- potential for post-exposure treatment



Vesicular stomatitis virus (VSV) reverse genetics system

- T7 Polymerase

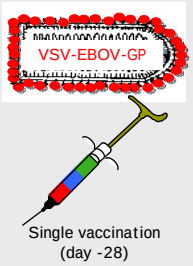


VSV system kindly provided by J. Rose

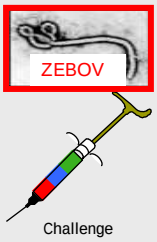
'The magic bullet'

- Emergency vaccine for Ebola, Marburg, Lassa & other VHFs -

Pre-exposure



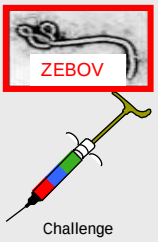
Single vaccination (day -28)



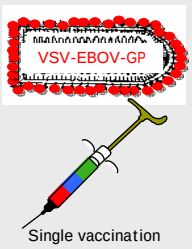
Challenge (day 0)

Complete (often 'sterile') protection

Post-exposure



Challenge (day 0)



Single vaccination (day +1-+2)

No, partial or complete protection

Special Pathogens, NML, PHAC

Ebihara H, Jones SM, Ströher U, Safronetz D, Kobinger G, Marzi A, Gren J, Feldmann F, Grolla A, Jones S, Leung A

LV, DIR, NIAID, NIH

T. Geisbert, UTMB, Galveston, USA
C. Broder, Uniformed Services, Bethesda, USA
M. Jarvis, Oregon Health and Science University, Portland, USA
G. Kobinger, J. Strong, A. Grolla, Public Health Agency of Canada, Winnipeg

Public Health Agency of Canada (PHAC)
National Institutes of Health (NIH)

Ebola and 'Great Apes'

Common chimpanzee (*Pan troglodytes*)

Western gorilla (*Gorilla gorilla*)

'Disseminating' vaccine strategy

(Michael Jarvis, VGTI, Oregon Health and Science University, Portland, Oregon, USA)

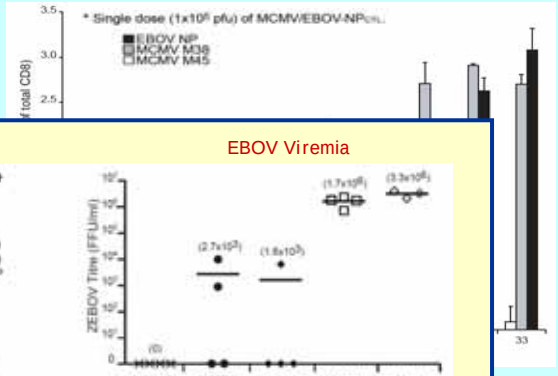
- CMV is highly immunogenic
- CMV is host specific, with each species infected by its own CMV
- CMV is ubiquitous and benign
- CMV immunity does not prevent reinfection
- CMV has evolved to spread e

Protot

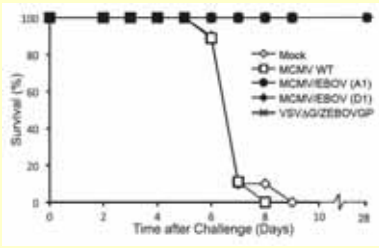
MCM

MCM

*Single Vaccination Gives Long-lasting EBOV-specific T cell Response



Survival



EBOV Viremia