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INAUGURAL ONE HEALTH CONFERENCE

1 - 3 November 2021

Characterization of Bunyamwera, Batai, and Ngari viruses: Unrecognized Arboviruses of One Health Importance in Rwanda

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OUTLINE

- Background and Rationale
- Comparison of *in vitro* infection kinetics and *ex vivo* stability of Bunyamwera, Batai, and Ngari viruses
- *In vivo* Investigation
- Identification of Orthobunyaviruses during Rift Valley Fever outbreak in Rwanda in 2018
- General conclusions

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Background and rationale

Bunyavirales order

- More than 350 viruses
- Families:

  Hantaviridae, Fimoviridae, Nairoviridae, Phasmaviridae, **Peribunyaviridae**, Mypoviridae, Phenuiviridae**,** Wupedeviridae, Cruliviridae, Arenaviridae

- Prototype/ study model : Bunyamwera virus (BUNV)
- Vectors: mosquitoes, ticks, flies, midges & rodents
- Cause diseases in humans, animals, and plants
- Distribution: worldwide

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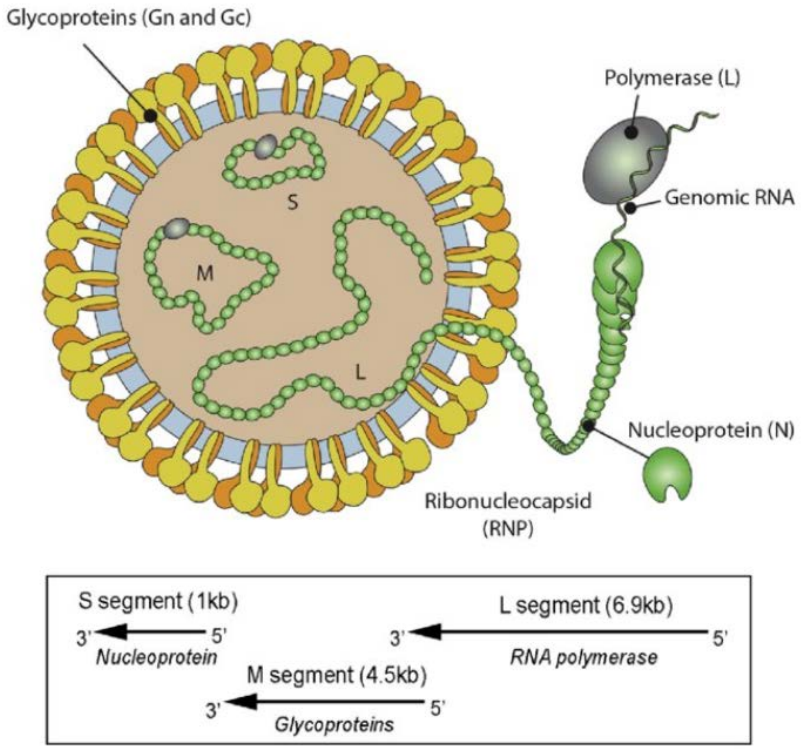
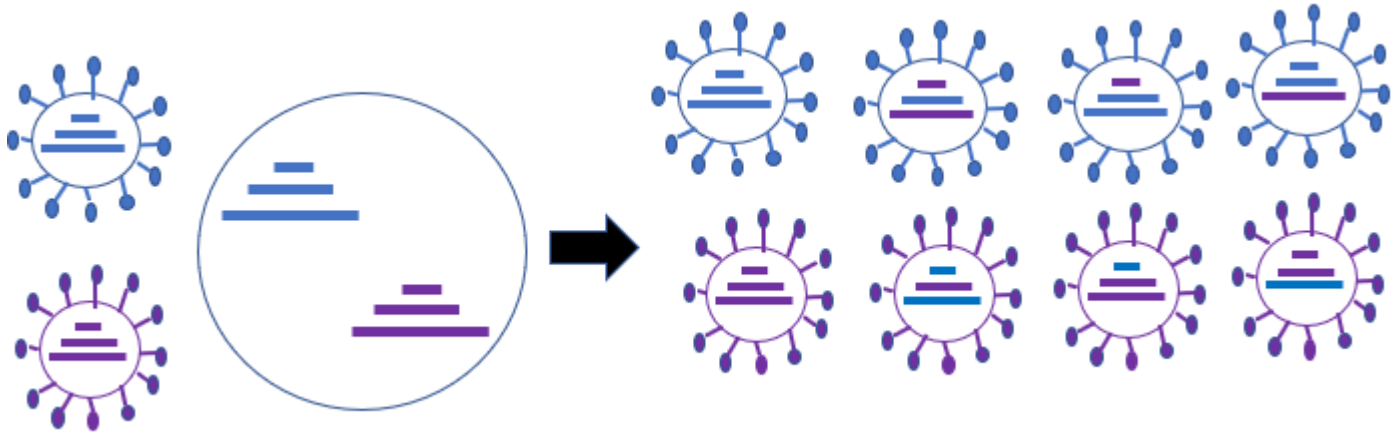


Bunyamwera virus genome
(prototype of Bunyavirales order)

Reassortment

co-infections→ novel segment combinations



- Change in host range
- Change in vector range
- Change in pathogenesis

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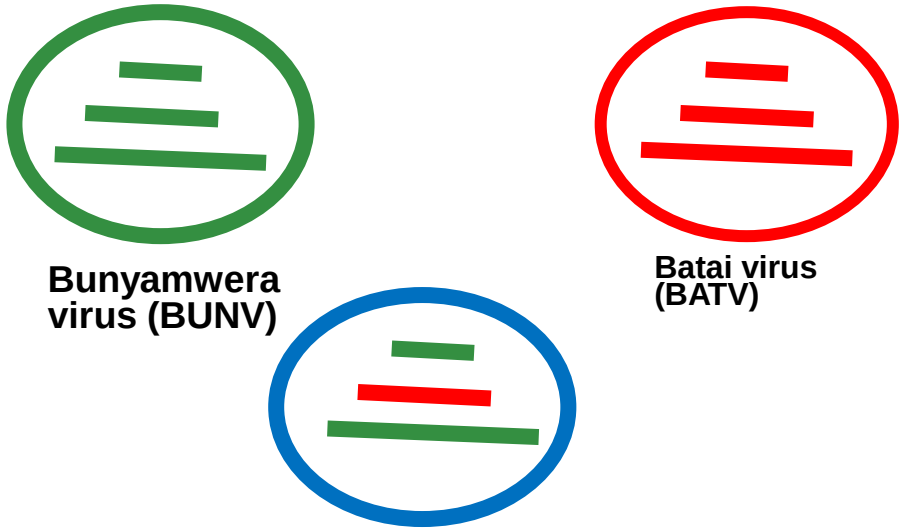
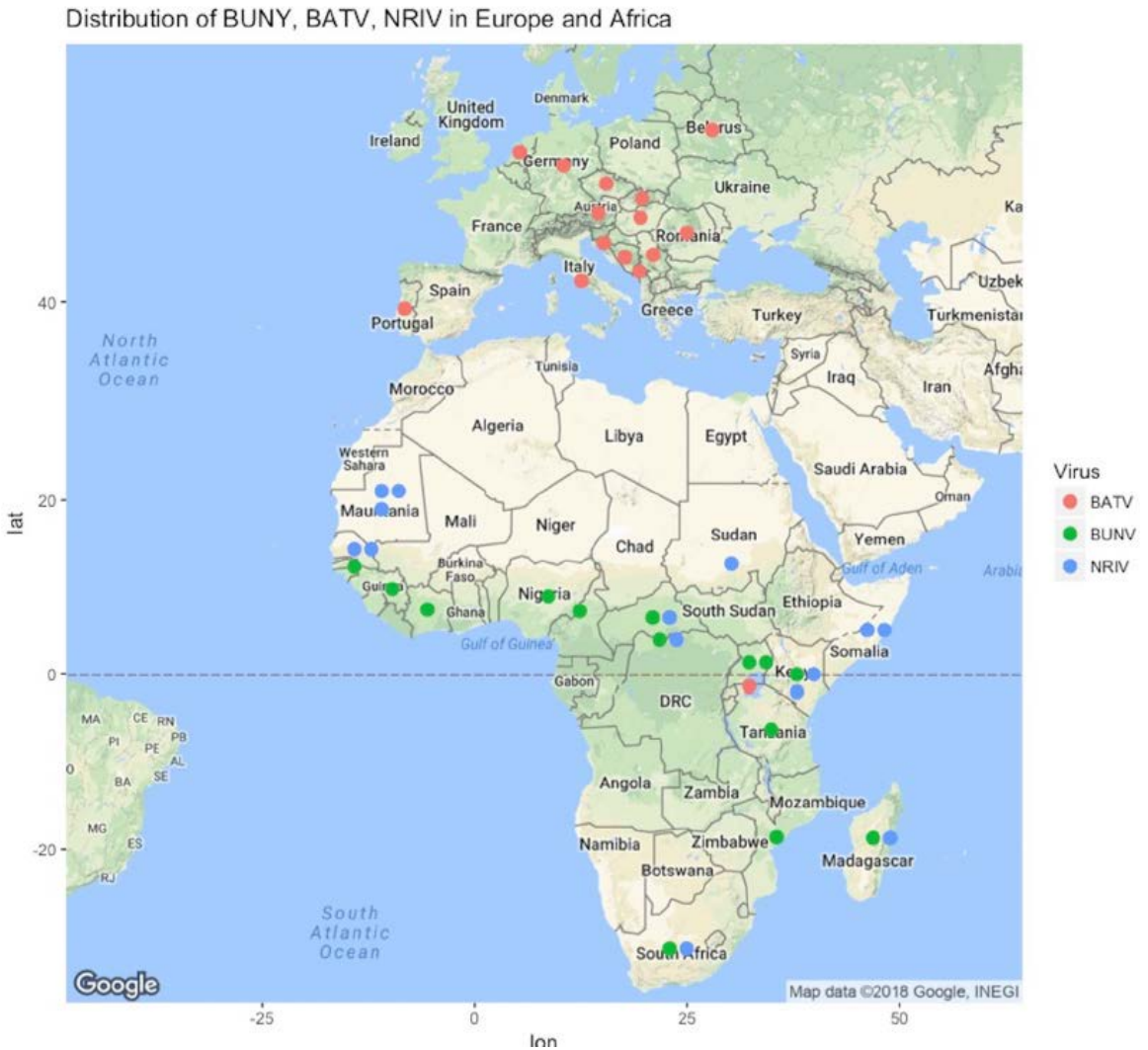
Ngari virus (NRIV): the only well confirmed NATURAL reassortant





BUNV, BATV, NRIV:

- Similarity with **Rift Valley Fever Virus (RVFV)** - ecological niche, host range, and clinical manifestation

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	RVFV	BUNV	BATV	NRIV
Classification	Family: Phenuiviridae Genus: ***Phlebovirus***	Family: Peribunyaviridae Genus: ***Orthobunyavirus***	Family: Peribunyaviridae Genus: ***Orthobunyavirus***	Family: Peribunyaviridae Genus: ***Orthobunyavirus***
Vectors	Mosquitoes, ticks, flies	Mosquitoes	Mosquitoes, midges	Mosquitoes, ticks
Hosts	Ruminants (domestic and wild), humans	Humans, ruminants	Cattle, humans, pigs, birds	Humans, antibodies were found in goats
Main symptoms	Ruminants: abortions Humans: Febrile illness, hemorrhagic fever, neurological complications	Animals: abortions, teratogenic effects Humans: febrile illness, neurological complications	Animals: abortions, premature births, congenital defects Humans: febrile illness	Animals: abortions in goats Humans: very severe hemorrhagic fever
Virulence	+++	++	+	++++

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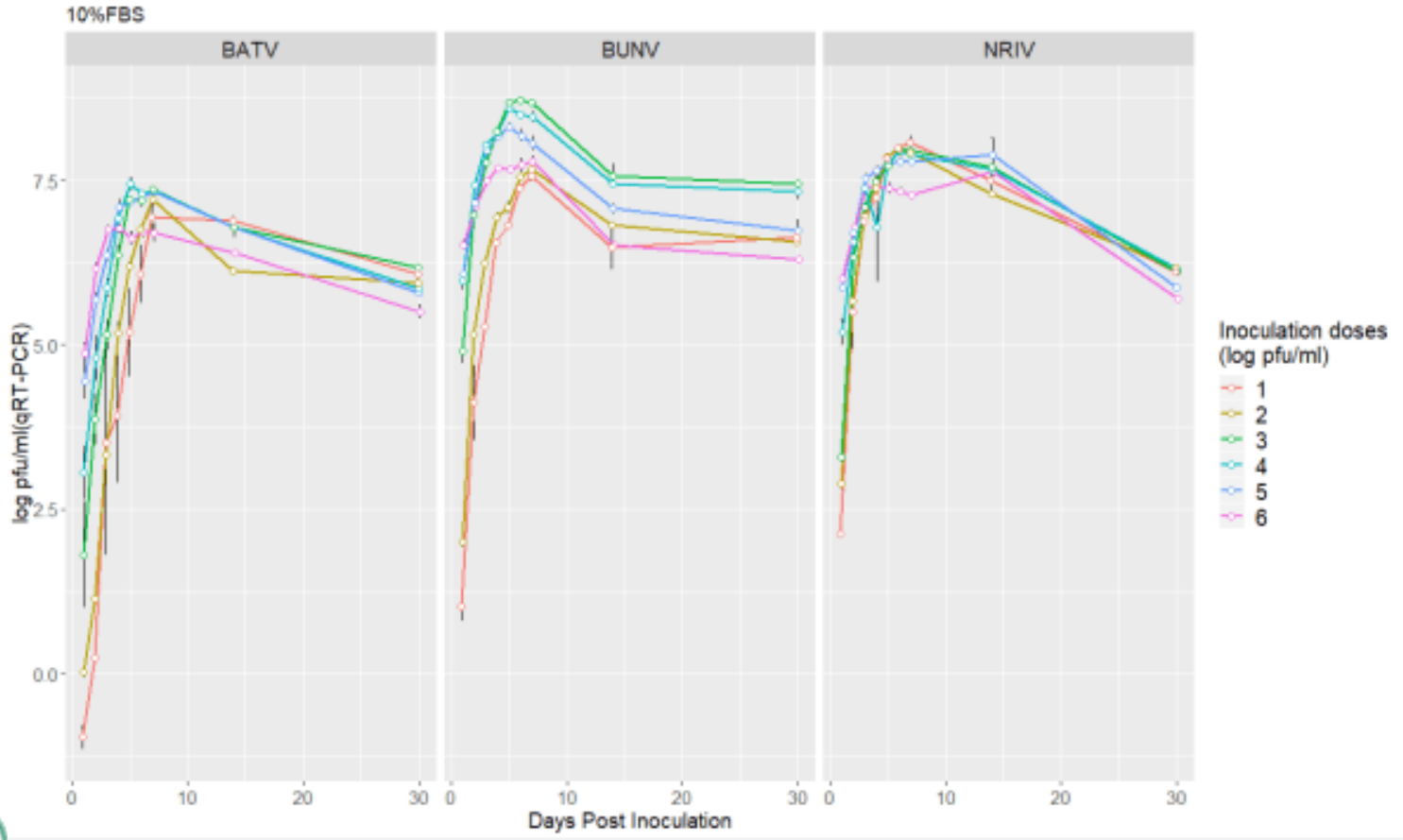
1. In vitro investigation

Hypothesis 1

Given their genetic relationship, *in vitro* infection kinetics of BUNV, BATV, and NRIV will be similar

>>>Vero cells



10% FBS: Optimal growth conditions

No difference in infection kinetics

Viral detection while cells are dead

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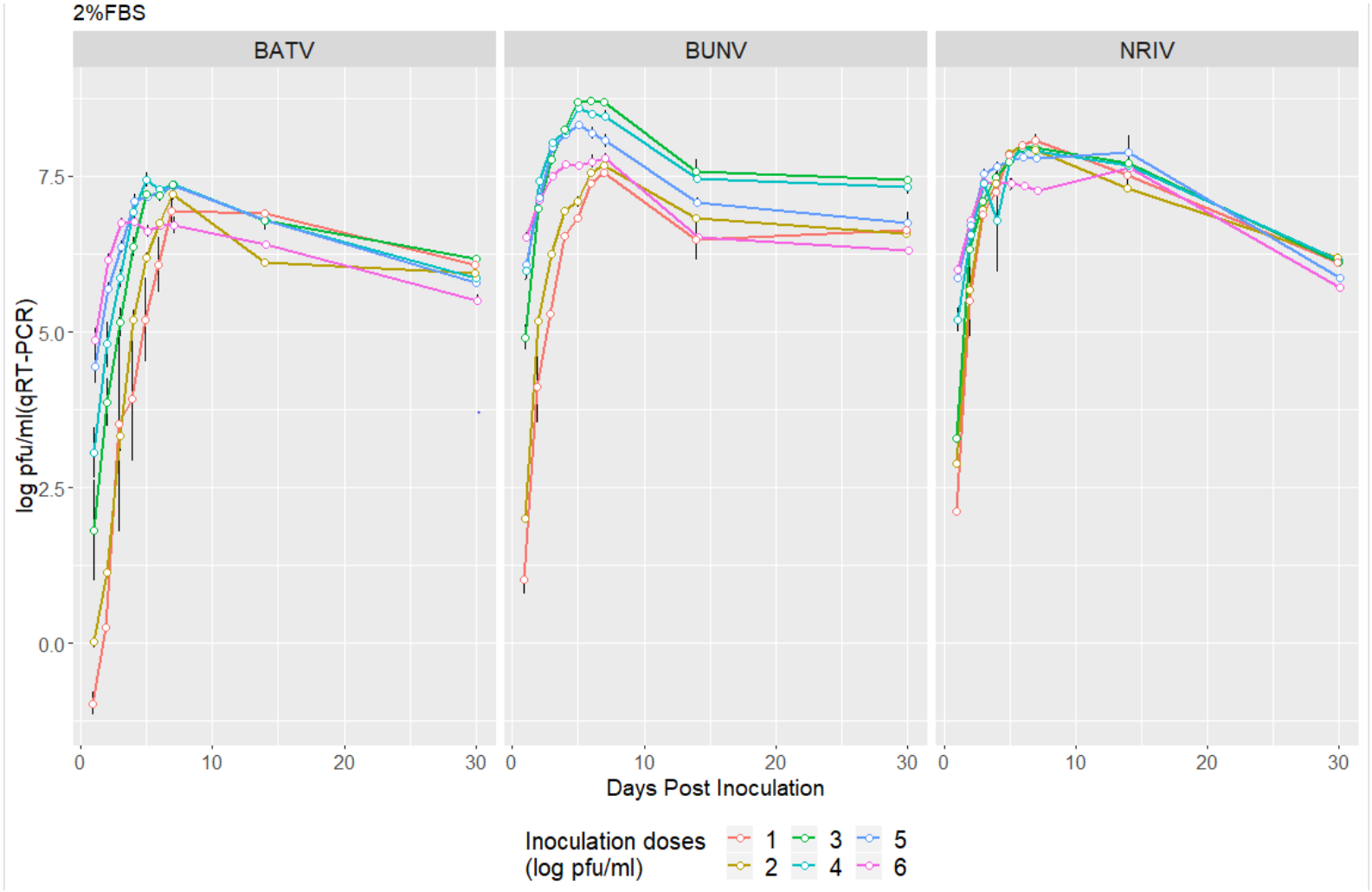

2% FBS: sub-standard conditions

Still viral detection while cells are dead

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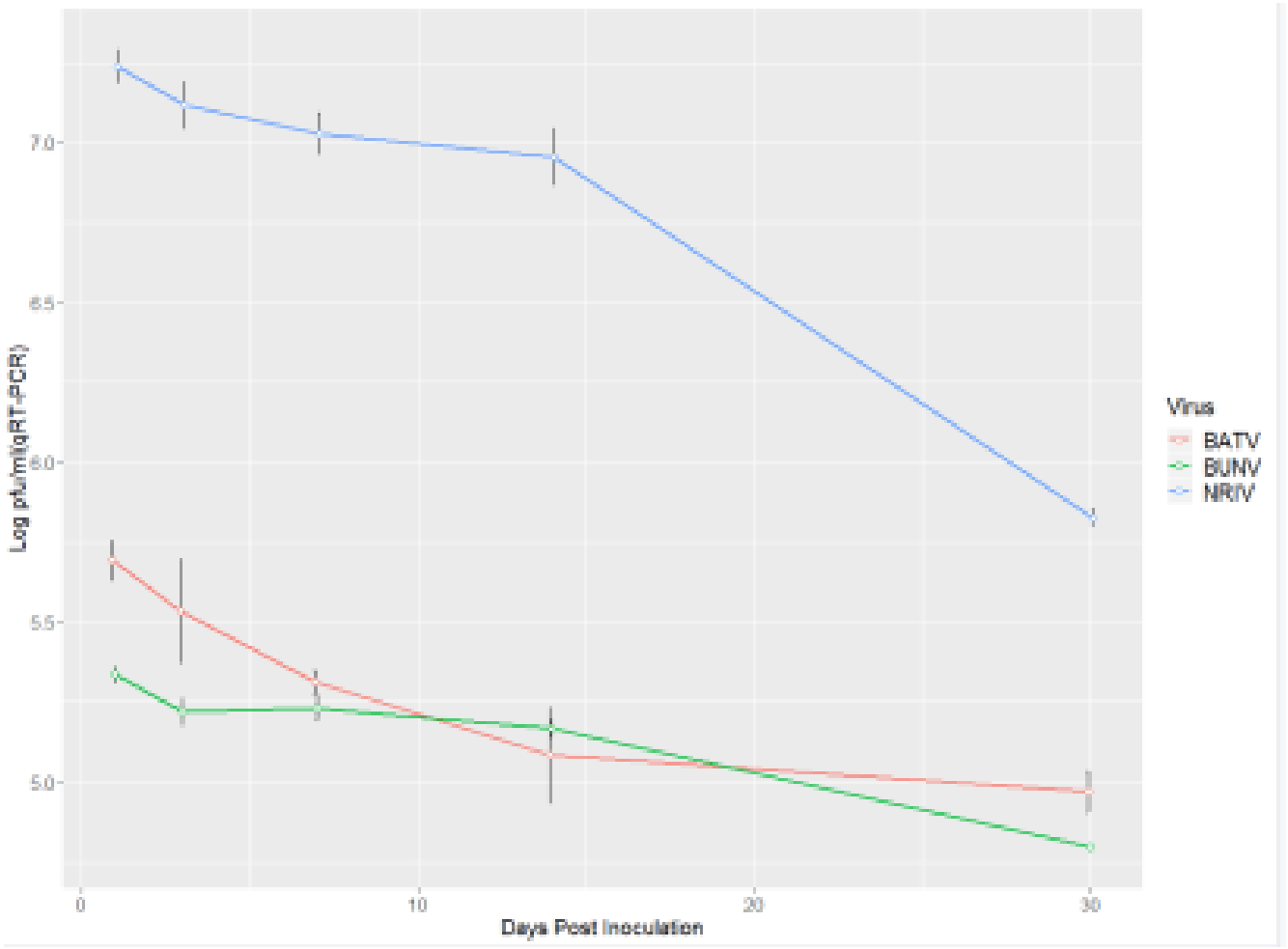
Stability in cell-free media



BUNV, BATV, and NRIV are stable in cell free media

Infectivity test

Vero cells – 10 % FBS
Vero cells – 2 % FBS
Cell free media

BUNV, BATV, and NRIV remained infectious

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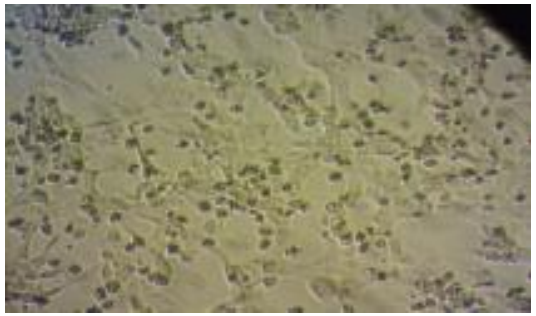
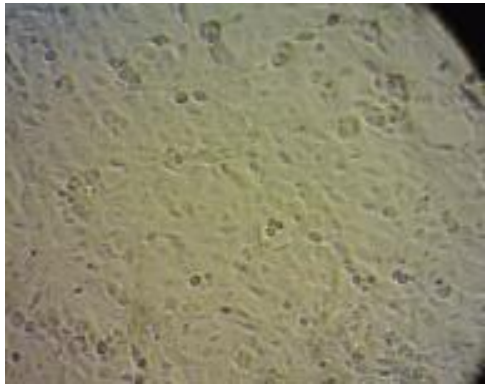
1%Triton-X-100 (detergent) inactivation, 1hr incubation



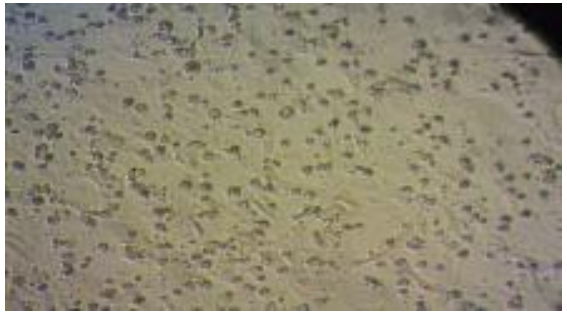
Non-inactivated BUNV

Triton-X-100 inactivated BUNV

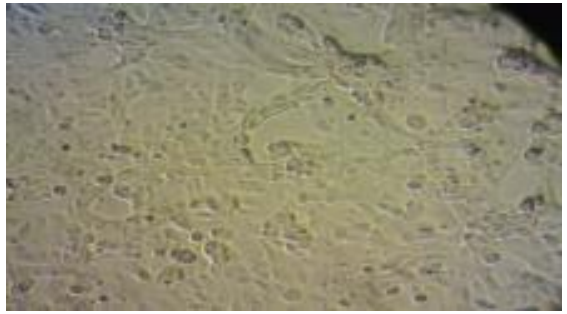
RNA detected:
1-7dpi but no growth



Negative control



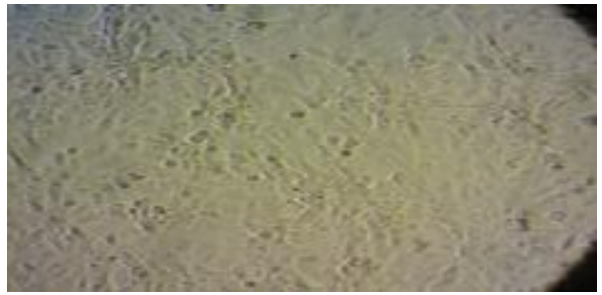
Non-inactivated BATV



Triton-X-100 inactivated BATV

1%Triton – X-100 inactivates BUNV, BATV, NRIV

Non-inactivated NRIV



Triton-X-100 inactivated NRIV

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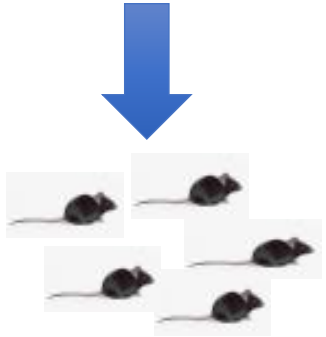
2. *In vivo* investigation

Hypothesis 2

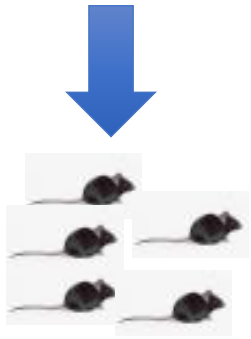
Given their genetic relationship, *in vivo* infection kinetics of BUNV, BATV, and NRIV will be similar

a. C57BL/6 mice
10-week-old

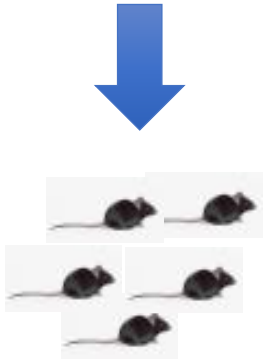
BUNV



BATV



NRIV



Sub-cutaneous injection:
100 µl of 10^6 pfu/ml

Bled

- 30 dpi: antibodies

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Antibodies	Virus neutralized					
	BUNV		BATV		NRIV	
	PRNT50	PRNT80	PRNT50	PRNT80	PRNT50	PRNT80
BUNV	4736	272	384	128	320	20
BATV	<20	<20	656	<20	<20	<20
NRIV	944	40	2816	1280	>10240	3456

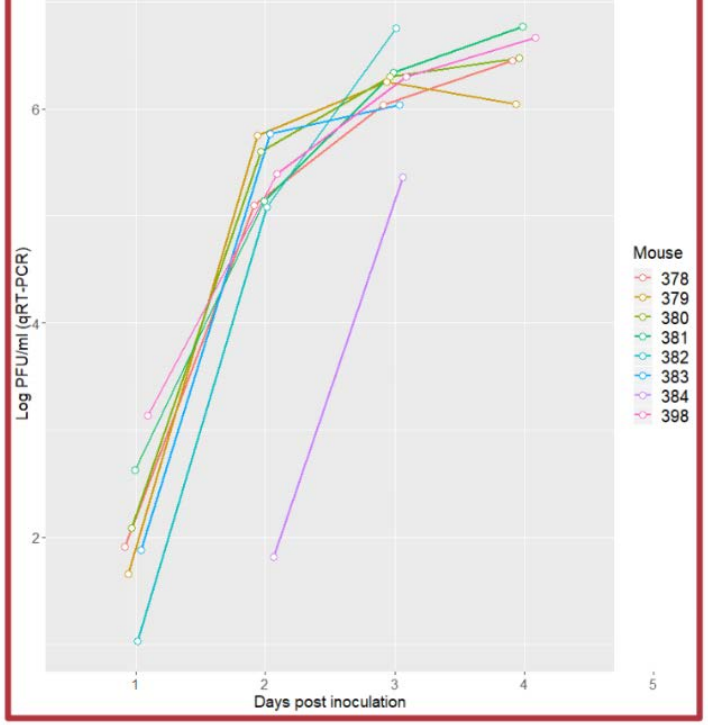
b. IRF 3/7 DKO

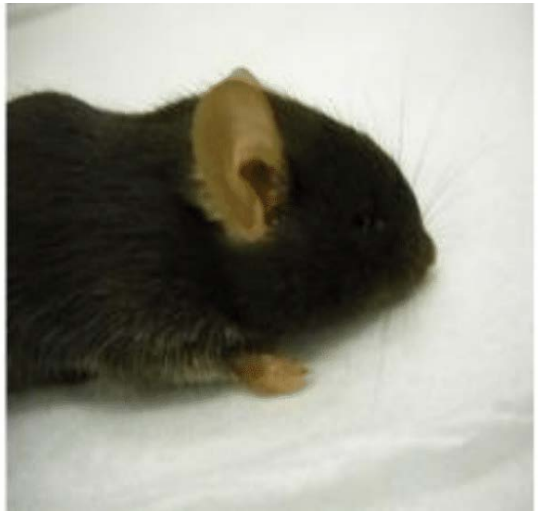
8-9 female mice

Sub-cutaneous injection of 100 µl of 10^6 pfu/ml of BUNV

Clinically:

- Hunched puncture and lethargy (100%)
- Facial swelling (62.5%)





Novel model ?

Facial edema is seen in another Bunyavirus infections in humans: Lassa virus

BUNV: BSL2

Lassa Virus: BSL3

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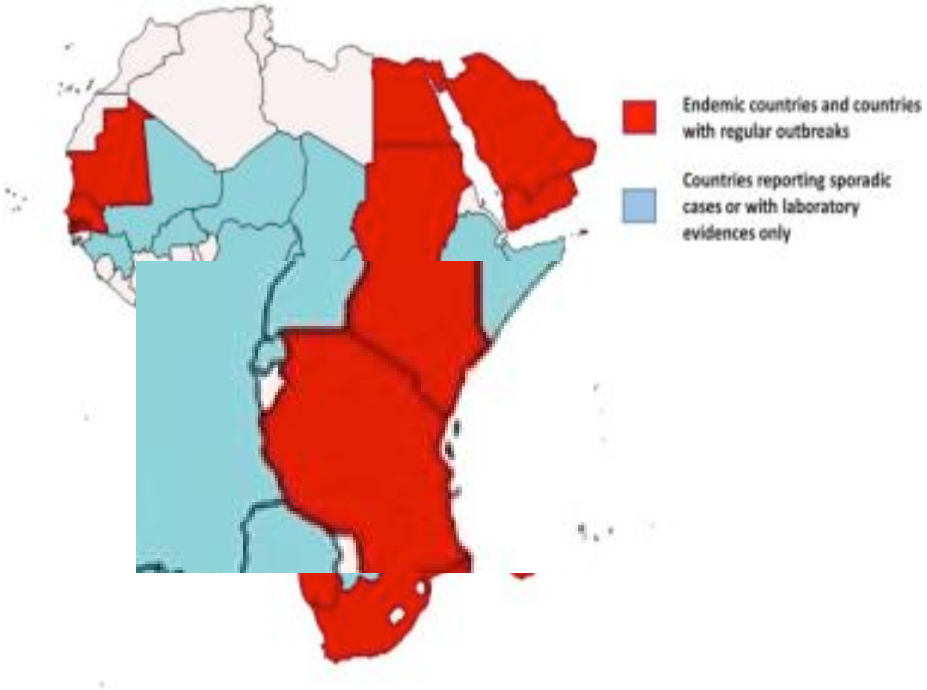
3. Identification of Orthobunyaviruses in RVF outbreak in Rwanda in 2018

Hypothesis 3

BUNV, BATV, and/or NRIV co-circulate in Rwanda and contribute to the burden of RVFV-like disease

>>>Investigate the presence of BUNV, BATV, and NRIV in Rwanda during ongoing RVFV outbreak



ELSEVIER

Preventive Veterinary Medicine

Volume 134, 1 November 2016, Pages 197-210

Rift Valley fever transmission dynamics described by compartmental models

Maria Luisa Danzetta, Rossana Bruno, Francesca Sauro, Lara Savini, Paolo Calistri

frontiers in Veterinary Science

A Review of Bunyamwera, Batai, and Ngari Viruses: Understudied *Orthobunyaviruses* With Potential One Health Implications

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- 2 times/year: **May- June** and Dec-Jan
  Rainy seasons: March-April and Oct-Nov

- May-July 2018: largest outbreak


Home » Africa » Rift Valley fever outbreak confirmed in Rwanda

Rift Valley fever outbreak confirmed in Rwanda

by ROBERT

June 16, 2018 Africa, Animal diseases, Headlines No Comments

- Diagnosis: **mostly clinical** after few cases of molecular confirmation

BUNV and NRIV (maybe BATV) are underreported Bunyaviruses co-circulating with RVFV in Rwanda and may contribute to the burden of disease

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- 185 blood samples (157 cattle & 28 goats), all over the country, May-July 18
- Inclusion criteria:
  - **Abortion within 5 days**
  - **Hemorrhagic fever**
  - Sharing farms with death cases (RVF suspicion) within 5 days

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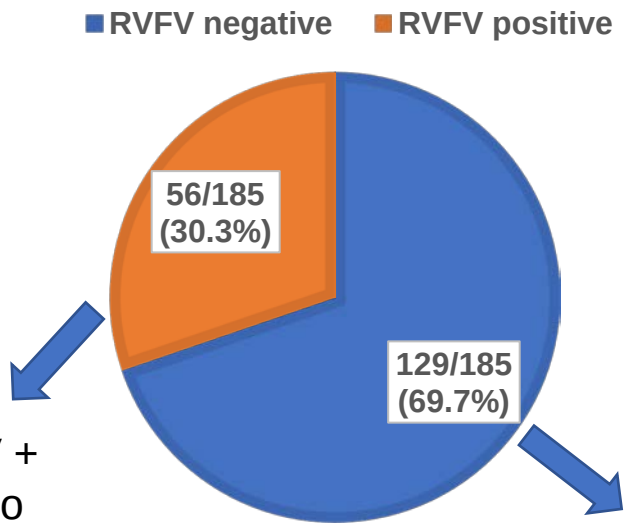
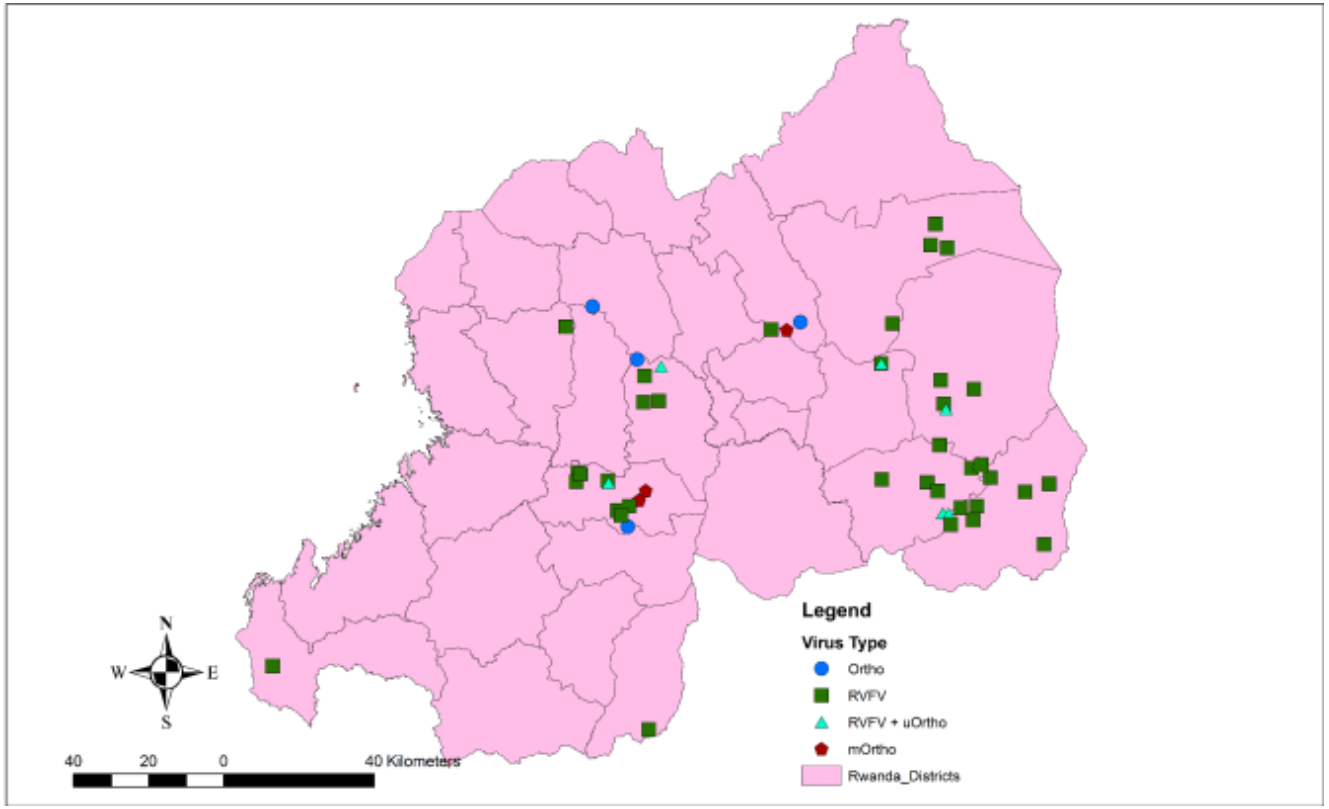


10 RVFV + with Ortho segments

- 5 BUNV confirmed
  - 3 additional segment +
- 4 BATV suggested (RT- PCR)
  - 10 segment +



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General conclusions

In vitro studies of BUNV, BATV, and NRIV in Vero cells

- NRIV is not significantly different from parental viruses *in vitro*
- **BUNV, BATV, and NRIV are stable and remain infectious in extracellular conditions up to 30 dpi**
- 1%Triton-X-100 after 1hr incubation can be used to inactivate BUNV, BATV, and NRIV

In vivo studies

- **NRIV strongly neutralize BATV**
- **BUNV in IRF 3/7 DKO: possible model for diffuse hemorrhagic fever (for BSL 3 viruses)**

Investigation of RVF outbreak in Rwanda

- **2nd time BATV is molecularly detected in Africa**
- **1st time co-infection BUNV and BATV is reported (in cattle)**
- **1st time Bunyavirus other than RVFV is reported in Rwanda**
- Potential other bunyaviruses or reassortment events
- Clinical diagnosis might mask presence of pathogens

Future perspectives

Rwanda

- Deeper epidemiological investigation of BUNV, BATV, and NRIV: identification of competent vectors, hosts, and suitable ecological niche
- Assessment of levels of co-circulation of RVFV and these three viruses
- Assessment of zoonotic transmission of BUNV, BATV, and NRIV
- Surveillance efforts for pathogen discovery whenever possible

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THANK YOU

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