


# Tick Borne Pathogens: Bunyavirales and the BV-BRC Mar 22, 2022

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# Tick-Borne Pathogens Webinar Series




**VEuPathDB** Release 56  
15 Feb 2022


Site search, e.g. PF3D7\_1133400 or \*reductase or "binding protein"

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Date	Time (US Eastern)	Webinar Topic	Presenter	Registration Link/Recording
March 8, 2022	11AM	Ticks: How to analyze omics and field population data sets in VectorBase	VEuPathDB	
March 22, 2022	11AM	Bunyavirales in Ticks	BV-BRC	<a href="#">Registration link</a>
April 5, 2022	11AM	Tick Endosymbionts	BV-BRC	<a href="#">Registration link</a>
April 19, 2022	11AM	Metagenomic analysis of tick samples	BV-BRC	<a href="#">Registration link</a>
May 3, 2022	11AM	Resources for Eukaryotic Pathogens Transmitted by Ticks	VEuPathDB	<a href="#">Registration link</a>
May 17, 2022	11AM	Comparative Genomics of Tick-Transmitted Bacteria	BV-BRC	<a href="#">Registration link</a>
May 31, 2022	11AM	Flaviviridae in Ticks	BV-BRC	<a href="#">Registration link</a>
June 14, 2022	11AM	RNA-Seq and SNP analysis of bacteria transmitted by ticks	BV-BRC	<a href="#">Registration link</a>

<https://veupathdb.org/veupathdb/app/static-content/tickwebinars.html>

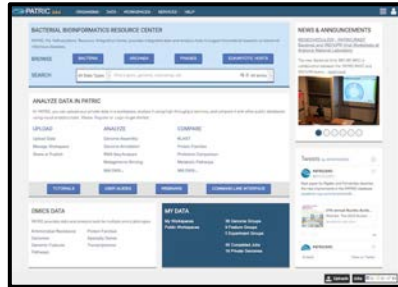
# AGENDA

- BV-BRC and *Bunyavirales* Overview
- BV-BRC Website Demo: 2 viral use cases
  - Comparative genomics
  - Viral isolation and characterization
- Q&A / Discussion

# Bioinformatic Resource Centers (2019-2024)



Viruses:  
IRD/ViPR  
Northrop, JCVI



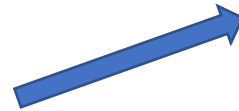
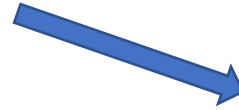
Bacteria:  
PATRIC  
UChicago, VT



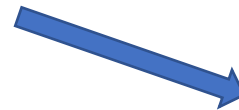
Eukaryotes:  
EuPathDB  
UPenn, UGA



Vectors:  
Notre Dame  
EBI/EMBL



Bacteria and Viruses:  
BV-BRC  
UChicago, JCVI, UVA



Eukaryotes and Vectors:  
VEuPathDB  
UPenn, UGA  
Notre Dame, EBI/EMBL

# Introduction to BV-BRC Webinar Series

**Friday, February 25 - Introduction to BV-BRC**

<https://youtu.be/sPh9syjXpuA>

**Friday, March 4 - Information for PATRIC users and bacterial researchers**

<https://youtu.be/efNsqDFFCi0>

**Friday, March 11 - Information for IRD and ViPR users and viral researchers**

<https://www.youtube.com/watch?v=nyH7YdX5pPc>

**Friday, March 18 - BV-BRC Private Workspace (Workbench)**

[https://www.youtube.com/watch?v=\\_kyo2uZ6g2c](https://www.youtube.com/watch?v=_kyo2uZ6g2c)

**Friday, March 25 - Finding and working with data**

<https://virginia.zoom.us/j/98150773227?pwd=V2FqRVJEBTNiSXRhN1pUeUNpMjRsQT09>

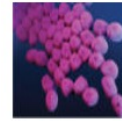
**Friday, April 1 - Tools and Services**

<https://virginia.zoom.us/j/98150773227?pwd=V2FqRVJEBTNiSXRhN1pUeUNpMjRsQT09>

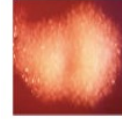
# Tick transmitted bacterial genera

- *Anaplasma* = 84 genomes
- *Borrelia* = 868 genomes
- *Coxiella* = 122 genomes
- *Francisella* = 1082 genomes
- *Rickettsia* = 197 genomes

## Bacteria Genera



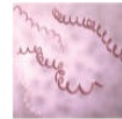
*Acinetobacter*



*Bacillus*



*Bartonella*



*Borrelia*



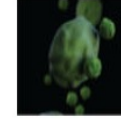
*Brucella*



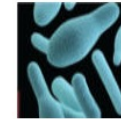
*Burkholderia*



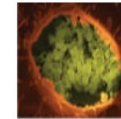
*Campylobacter*



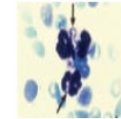
*Chlamydia*



*Clostridium*



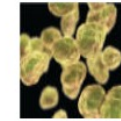
*Coxiella*



*Ehrlichia*



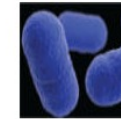
*Escherichia*



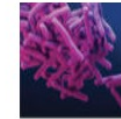
*Francisella*



*Helicobacter*



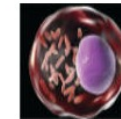
*Listeria*



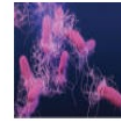
*Mycobacterium*



*Pseudomonas*



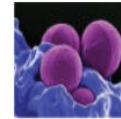
*Rickettsia*



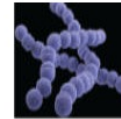
*Salmonella*



*Shigella*



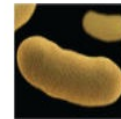
*Staphylococcus*



*Streptococcus*



*Vibrio*



*Yersinia*

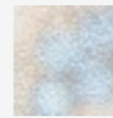


# Tick-borne viral families

- *Asfarviridae*: 6,967 genomes  
African Swine Fever Virus
- *Bunyavirales* = 47,564 genome segments  
LCMV  
CCHFV  
Rift Valley fever virus  
SFWTV
- *Flaviridae* = 370,713 genome segments  
Jingmen tick virus  
Kyasanur Forest disease virus  
Powassan virus  
Tick-borne encephalitis virus
- *Reoviridae* = 132370 genome segments  
Colorado tick fever virus

## Virus Families

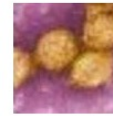
### Single-Stranded Positive-Sense RNA



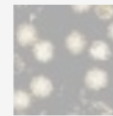
*Caliciviridae*



*Coronaviridae*



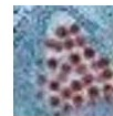
*Flaviviridae*



*Hepeviridae*

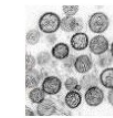


*Picornaviridae*

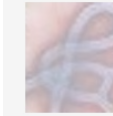


*Togaviridae*

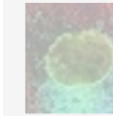
### Single-Stranded Negative-Sense RNA



*Bunyavirales*



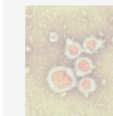
*Filoviridae*



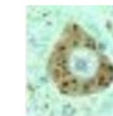
*Paramyxoviridae*



*Orthomyxoviridae*

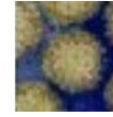


*Pneumoviridae*



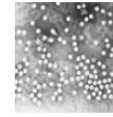
*Rhabdoviridae*

### Double-Stranded RNA



*Reoviridae*

### Single-Stranded DNA



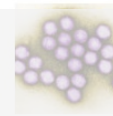
*Parvoviridae*

### Partially Double-Stranded DNA

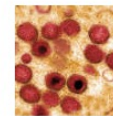


*Hepadnaviridae*

### Double-Stranded DNA



*Adenoviridae*



*Asfarviridae*



*Herpesviridae*



*Polyomaviridae*



*Poxviridae*

# *Bunyavirales* order: Tick borne virus families

## **Arenaviridae\***

Cruliviridae

Fimoviridae

Hantaviridae

Leishbuviridae

Mypoviridae

## **Nairoviridae\***

## **Peribunyaviridae\***

Phasmaviridae

## **Phenuiviridae\***

Tospoviridae

Wupedeviridae

unclassified Bunyavirales

Black = can infect humans

\* Tick borne



# *Nairoviridae* species that infect humans

Abu Hammad virus

Artashat orthonairovirus

Bandia virus

**Beiji nairovirus**

Burana virus

Chim orthonairovirus

Clo Mor viru

**Crimean-Congo hemorrhagic fever orthonairovirus**

Dera Ghazi Khan orthonairovirus

**Dugbe orthonairovirus**

Estero Real virus

Farallon virus

Geran virus

Grotenhout virus

Hazara virus

Hughes orthonairovirus

Kasokero orthonairovirus

Kupe virus

**Nairobi sheep disease virus**

Nairovirus sp. Hc652

Nayun tick nairovirus

Norway nairovirus 1

Pacific coast tick nairovirus

Paramushir virus

Punta Salinas virus

Pustyn virus

Qalyub orthonairovirus

Rondonia orthonairovirus

Sakhalin orthonairovirus

Sapphire II virus

Soldado virus

**Songling virus**

South Bay virus

**Tacheng Tick Virus**

Taggert virus

**Tamdy orthonairovirus**

Tillamook virus

Tofla virus

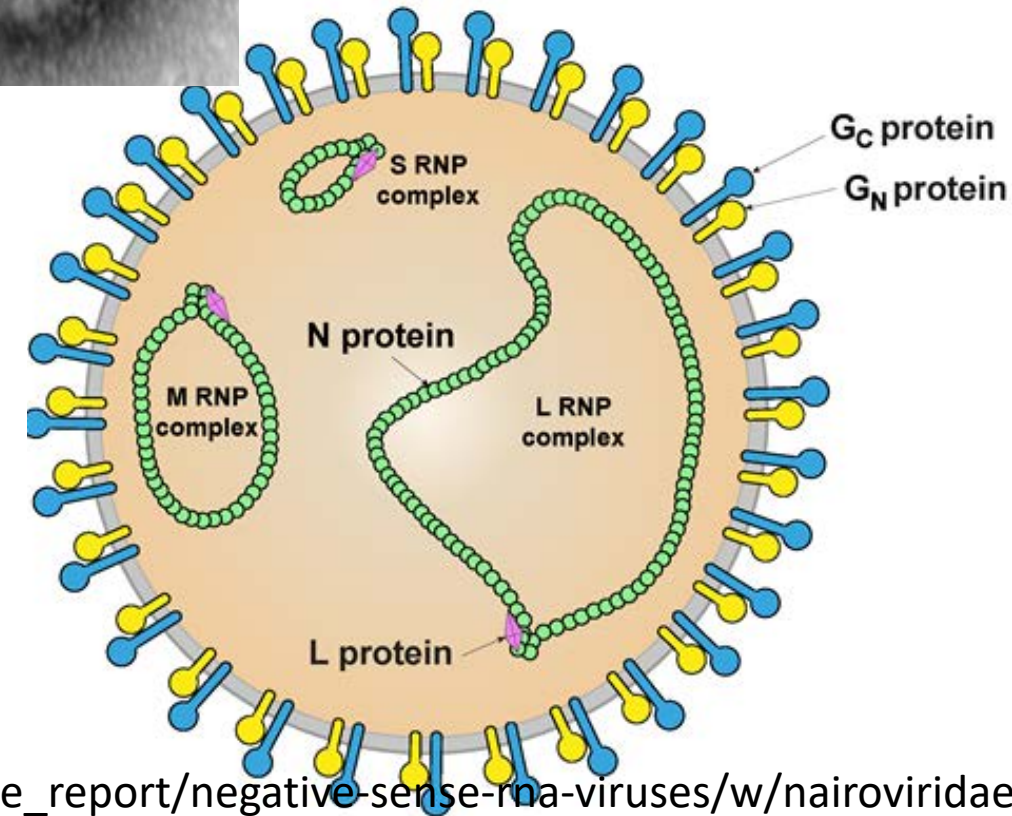
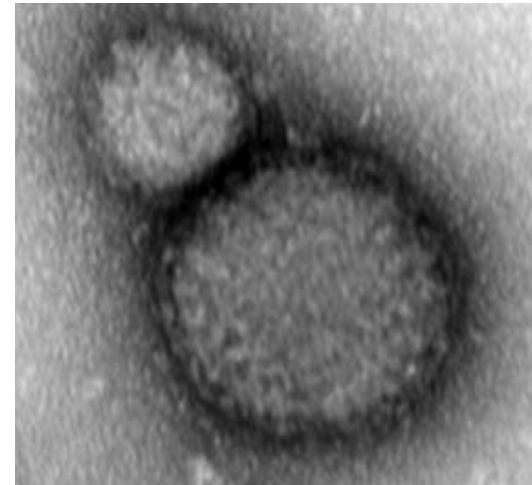
Vinegar Hill virus

**Yezo virus**

# Viral Characteristics

- 80–120 nanometers (nm) in diameter
- Pleomorphic, enveloped viruses.
- Genome: 3 single-stranded, negative-sense RNA molecules:

S	~ 2 kb
M	~ 5 kb
L	~ 12 kb
- Replication: Cytoplasmic.
- Translation: cap-snatching; mRNAs lack poly(A).

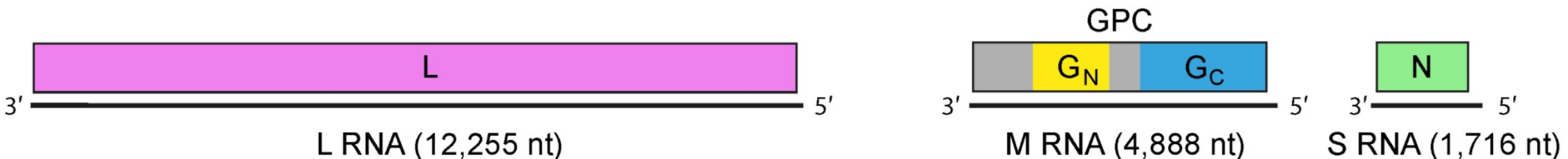


# Genome & Proteome

**Nucleoprotein (N):** Structural virion protein (60–68 kD). Component of the RNP inside virions. Oligomerizes and encapsidates orthonairoviral genomic segments. Functions as an exoribonuclease.

**Glycoprotein (GP):** Structural virion protein consisting of two subunits (GN 30–45 kD, GC 72–84 kD). Produced via proteolytic cleavage from the orthonairoviral genome-encoded precursor GPC. Cleavage produces GN, GC, and non-structural glycoproteins. Inserts into virion membranes as GP spikes composed of GN and GC. As a putative class I fusion protein, GP mediates cell-surface and internal receptor binding, virion-cell membrane fusion and, thereby cell entry.

**Large protein (L):** Structural virion protein (250–450 kD) with RdRP, helicase, and endoribonuclease domains. Component of the RNP inside virions. Oligomerizes and mediates transcription and replication of orthonairoviral RNA segments. Contains an ovarian tumor family-like domain (OTU) that is conserved among all orthonairoviruses. Mediates cap-snatching for viral mRNA capping.



**B**

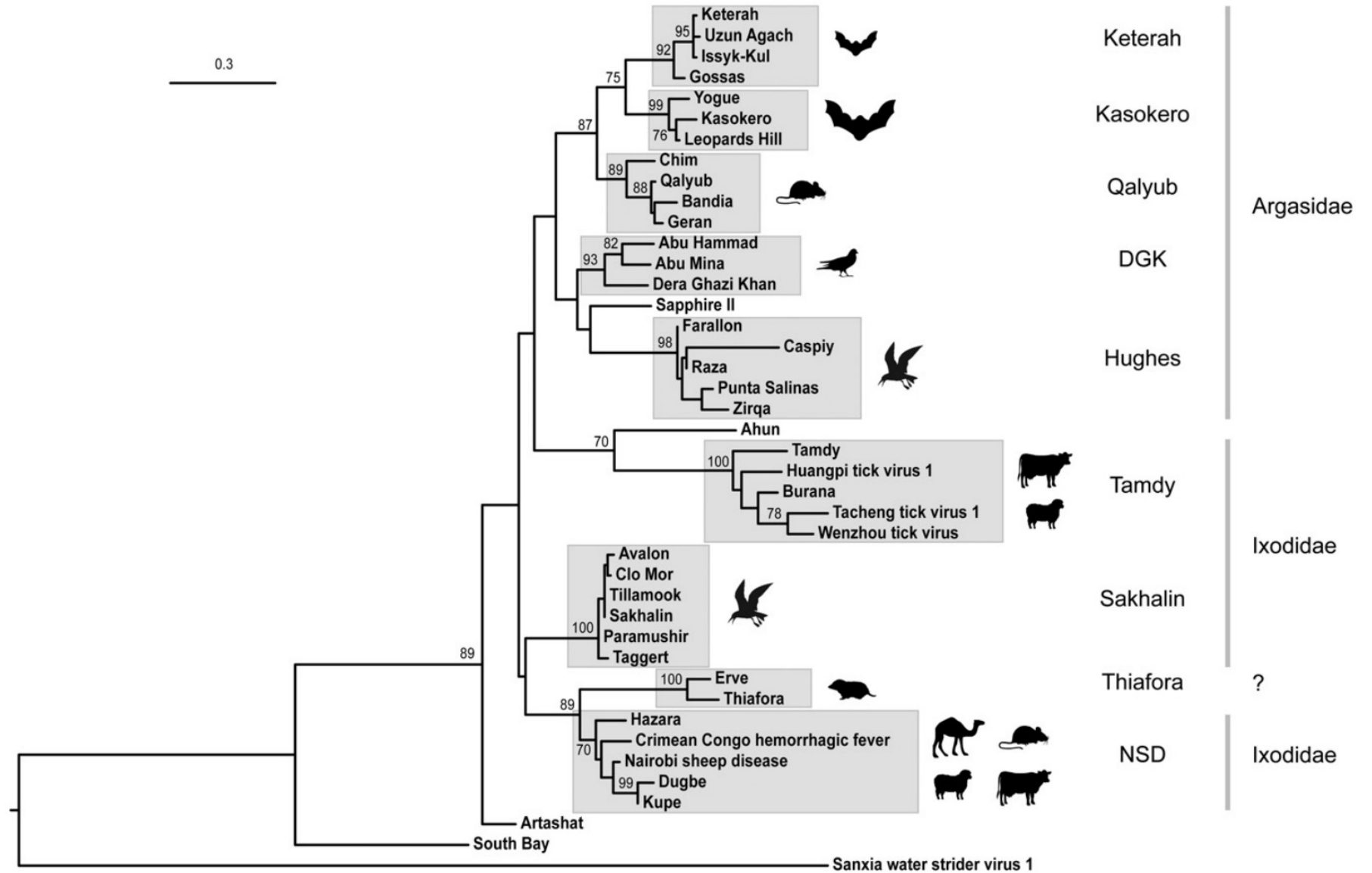


FIGURE 1. Maximum-likelihood phylogenetic trees inferred from Clustal X alignments of amino acid sequences of proteins encoded in nairovirus L RNA segments. **(A)** Tree inferred from full-length L protein sequences. **(B)** Tree inferred from partial sequence (154 amino acids) of L proteins indicating the sources of isolation of the viruses from vertebrate hosts and hard or soft tick vectors. Genogroup assignments of clades in each tree are shown. The description of virus isolates and GenBank accession numbers of sequences used in the alignments are provided in Table 1. Horizontal branch lengths are drawn to a scale of amino acid substitutions/site and all bootstrap proportion values  $\geq 70\%$  are shown.

# Focus on Two Use Cases

- 1) Point mutation analysis of dataset in Crimean Congo Hemorrhagic Fever virus.
  - Search and Assemble dataset
  - Create [MSA](#) to verify and look for other genomes
  - Use [MetaCats](#) to search for other tick specific sites.
- 2) Isolation and characterization of an “unknown” Nairovirus.
  - SRA file analysis ([taxonomic classifier](#))
  - Read QC and mapping ([fastq utils](#))
  - *de novo* sequence assembly ([assembly](#))
  - Blast against viral database ([blast](#))
  - Annotate my genome ([Annotation](#))

# A single mutation in Crimean-Congo hemorrhagic fever virus discovered in ticks impairs infectivity in human cells

Brian L Hua<sup>1</sup>, Florine Em Scholte<sup>1</sup>, Valerie Ohlendorf<sup>2 3</sup>, Anne Kopp<sup>2 3</sup>,  
Marco Marklewitz<sup>2 3</sup>, Christian Drosten<sup>2 3</sup>, Stuart T Nichol<sup>1</sup>, Christina Spiropoulou<sup># 1</sup>,  
Sandra Junglen<sup># 2 3</sup>, Éric Bergeron<sup># 1</sup>

- single amino acid change appears to make the virus less able to infect human cells
- mutation prevents viral-cell (human) fusion step
- may explain why this strain and others in the Europe 2 group do not cause severe human disease

## Strain names:

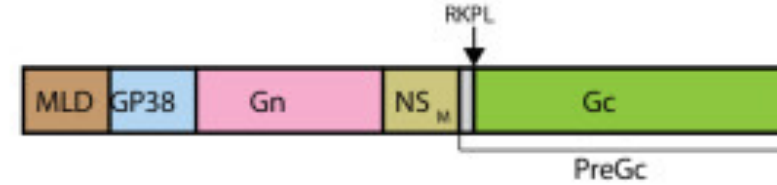
ref seq: [IbAr10200](#)

mutant: [MT-1303](#)

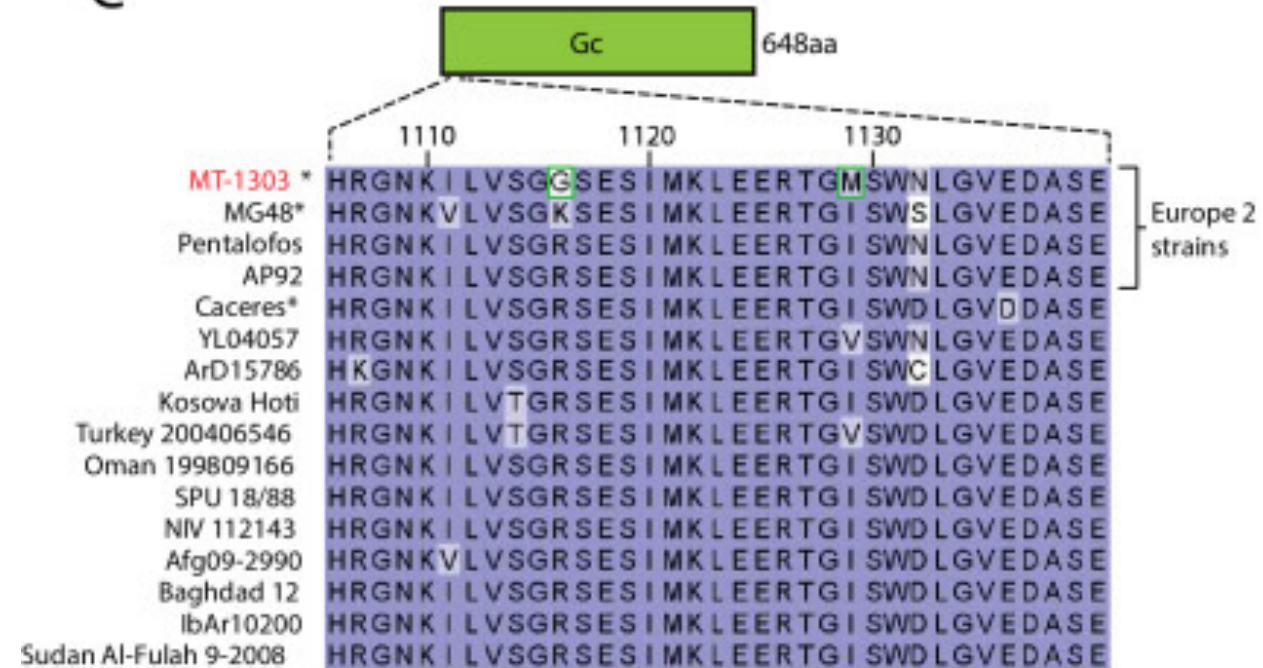
## Mutation:

[R1116G](#)

A



C





# Where can I find out more?

- Instructional videos on YouTube
- Tutorials and user guides
- Helpdesk
- Social media
  - Twitter @BVBRC\_DB
  - Facebook @BVBRC19
  - Reddit r/BRC\_users

