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

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Bioinformatics Analyst & Outreach Coordinator

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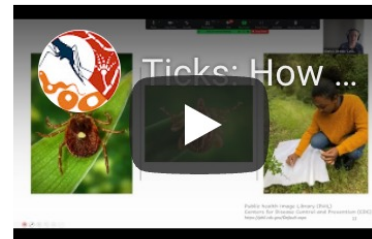
Date	Time (US Eastern)	Webinar Topic	Presenter	Registration Link/Recording
March 8, 2022	11AM	Ticks: How to analyze omics and field population data sets in VectorBase	VEuPathDB	
March 22, 2022	11AM	Bunyavirales in Ticks	BV-BRC	**Registration link**
April 5, 2022	11AM	Tick Endosymbionts	BV-BRC	**Registration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

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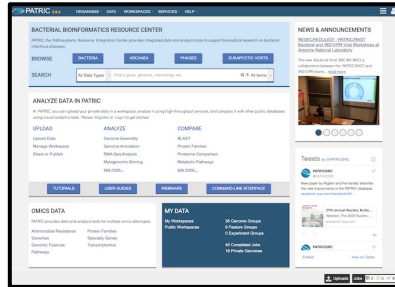
AGENDA

- BV-BRC and *Bunyavirales* Overview

- BV-BRC Website Demo: 2 viral use cases
  - Comparative genomics
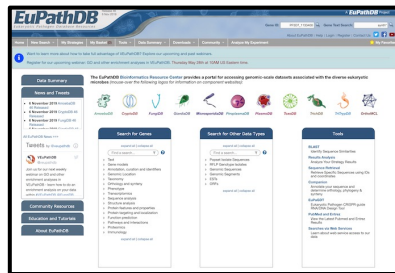 - Viral isolation and characterization

- Q&A / Discussion

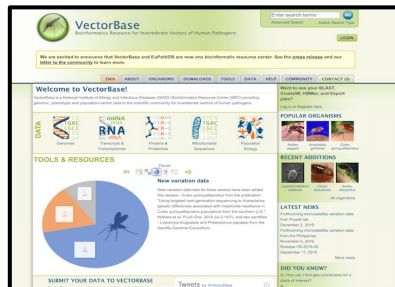# Bioinformatic Resource Centers (2019-2024)
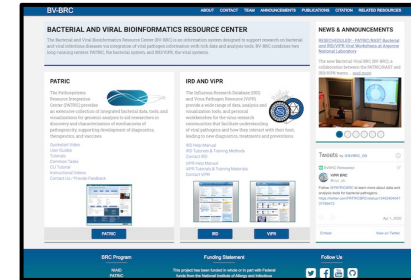

Viruses:
IRD/ViPR
Northrop, JCVI
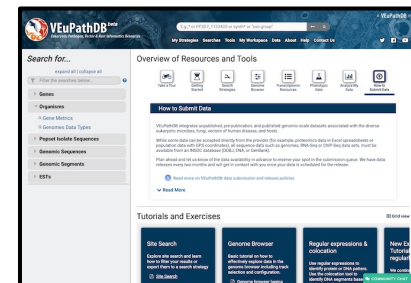
Bacteria:
PATRIC
UChicago, VT

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

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
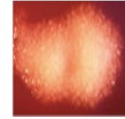
Tick transmitted bacterial genera

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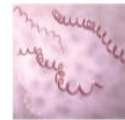- *Rickettsia* = 197 genomes

Bacteria Genera
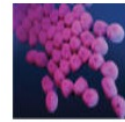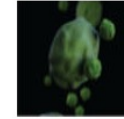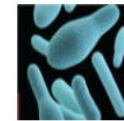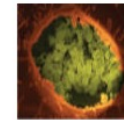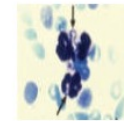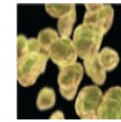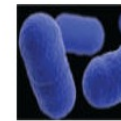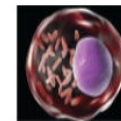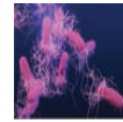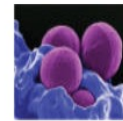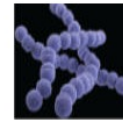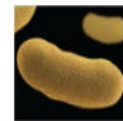
Acinetobacter	Campylobacter	Francisella	Salmonella
Bacillus	Chlamydia	Helicobacter	Shigella
Bartonella	Clostridium	Listeria	Staphylococcus
Borreliella	Coxiella	Mycobacterium	Streptococcus
Brucella	Ehrlichia	Pseudomonas	Vibrio
Burkholderia	Escherichia	Rickettsia	Yersinia

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

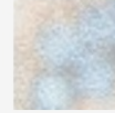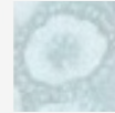**Single-Stranded Positive-Sense RNA**
- Caliciviridae
- Coronaviridae
- *Flaviviridae*
- Hepeviridae
- Picornaviridae
- *Togaviridae*
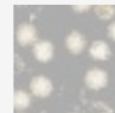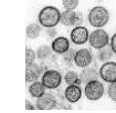
Single-Stranded Negative-Sense RNA
- *Bunyavirales*
- Filoviridae
- Paramyxoviridae
- Orthomyxoviridae
- Pneumoviridae
- *Rhabdoviridae*
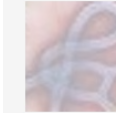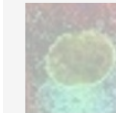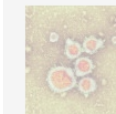
Double-Stranded RNA
- *Reoviridae*
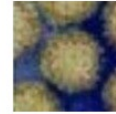
Single-Stranded DNA
- *Parvoviridae*
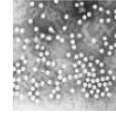
Partially Double-Stranded DNA
- Hepadnaviridae
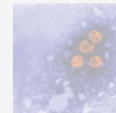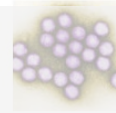
Double-Stranded DNA
- Adenoviridae
- *Asfarviridae*
- Herpesviridae
- Polyomaviridae
- *Poxviridae*
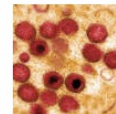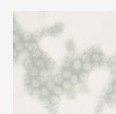
Bunyavirales order: Tick borne virus families

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
Saphire 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:
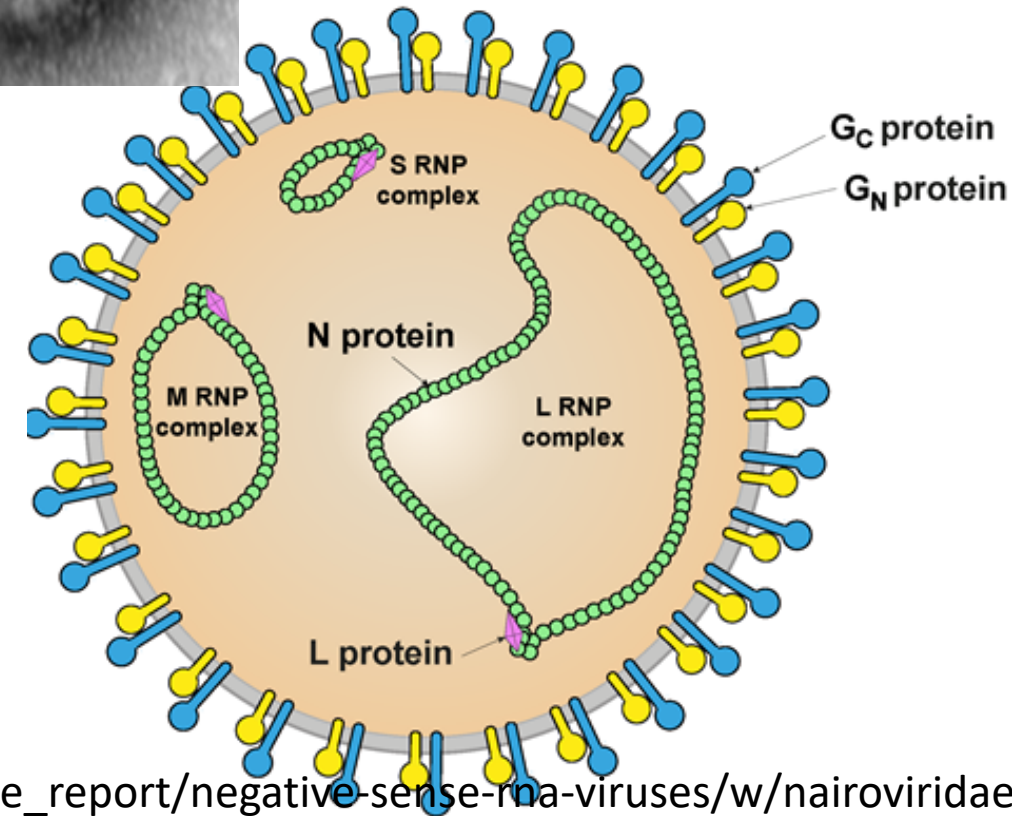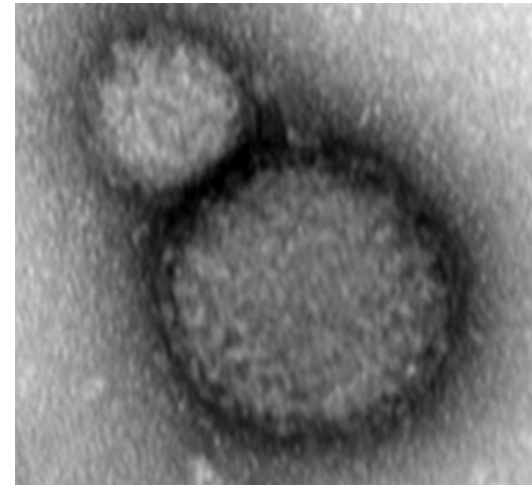 | | |
  |---|---|
  | S | ~ 2 kb |
  | M | ~ 5 kb |
  | L | ~ 12 kb |

- 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.
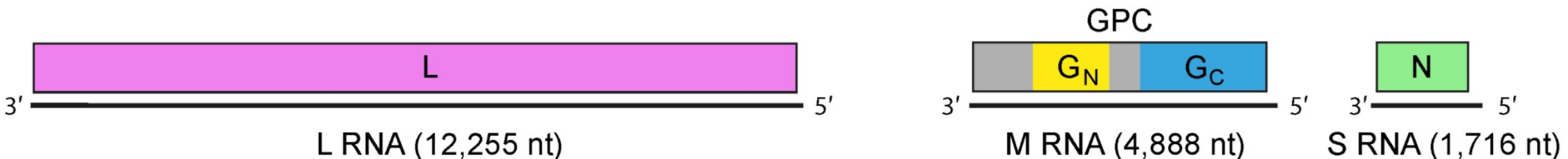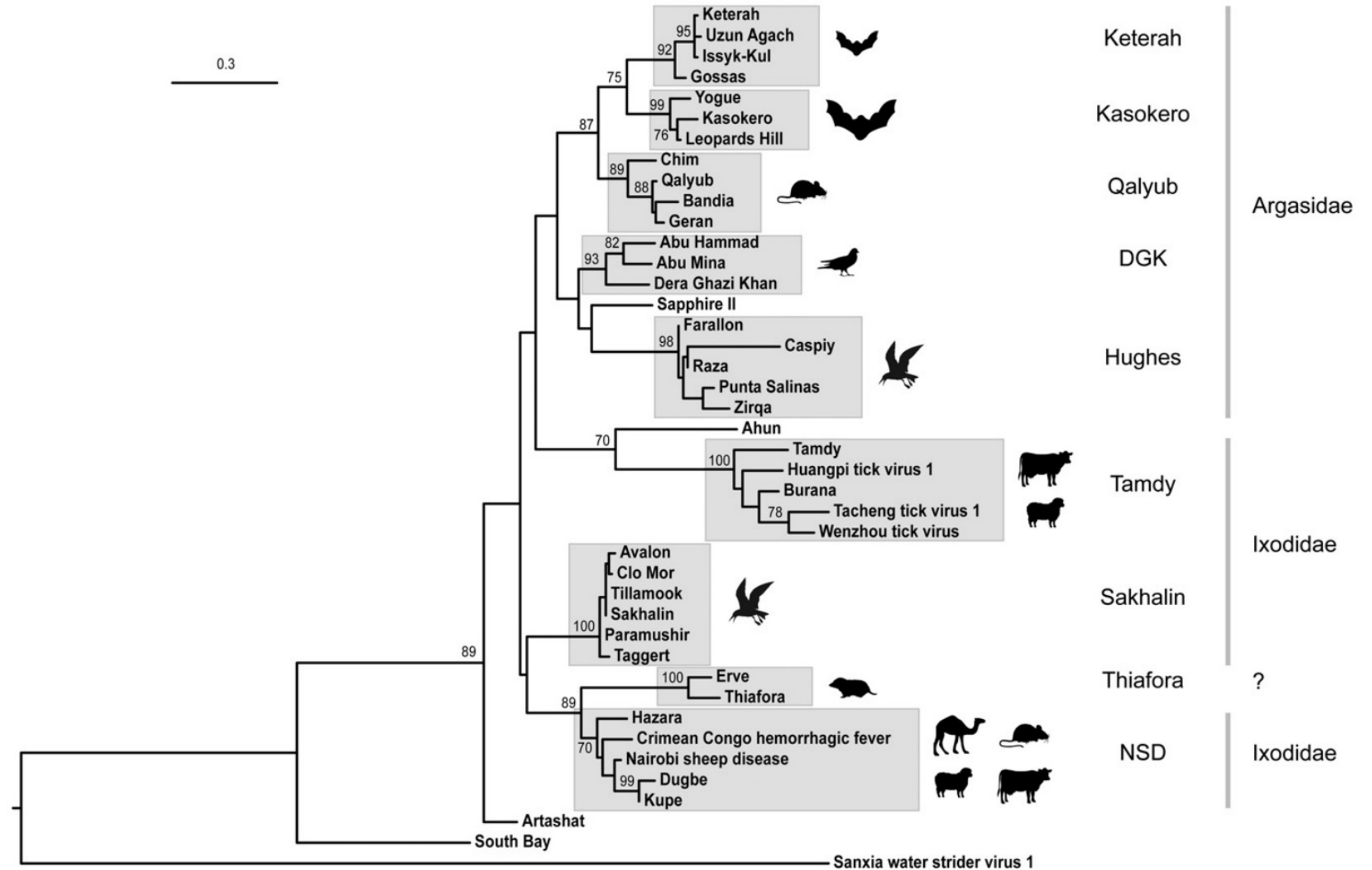
Phylogeny

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 ≥ 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 [1], Florine Em Scholte [1], Valerie Ohlendorf [2][3], Anne Kopp [2][3], Marco Marklewitz [2][3], Christian Drosten [2][3], Stuart T Nichol [1], Christina Spiropoulou [#][1], Sandra Junglen [#][2][3], Éric Bergeron [#][1]

- 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
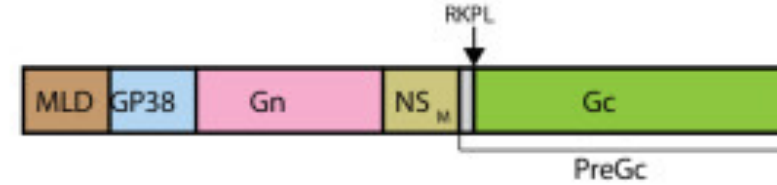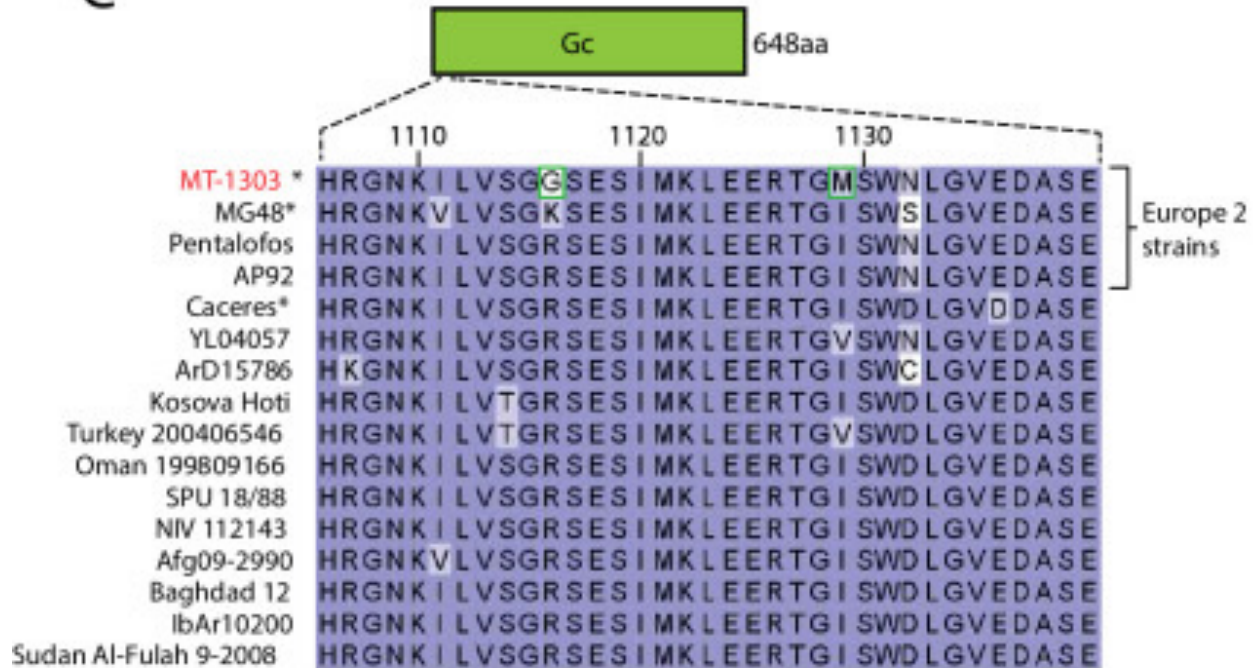
Strain names:
  ref seq: IbAr10200
  mutant: MT-1303
Mutation:
  R1116G

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

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