

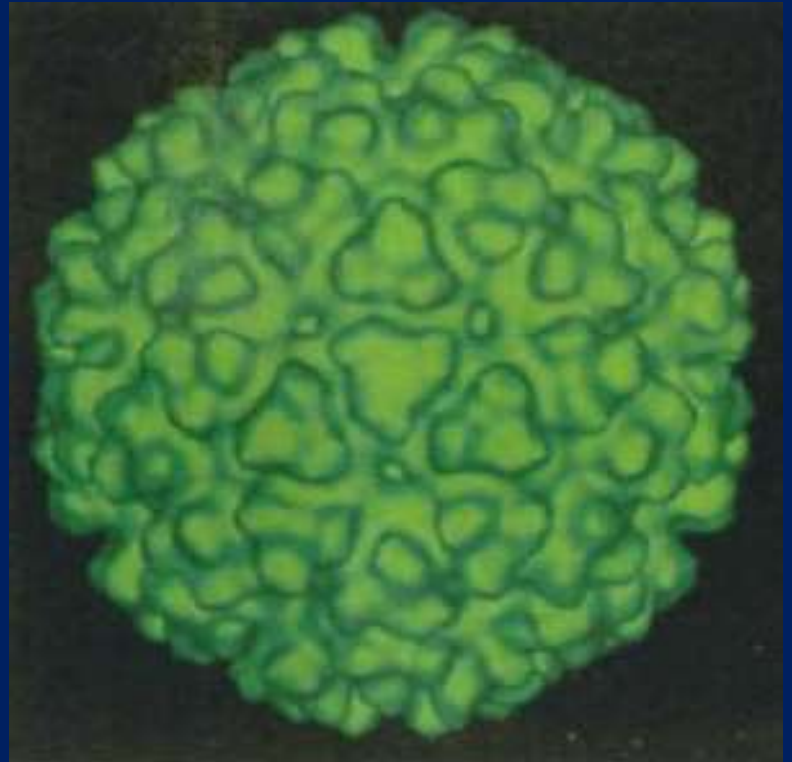
Alphaviruses

Friends and Foes

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Alphaviruses (Togaviridae)*

- > 30 alphaviruses identified
- Infect both vertebrates and arthropodes
- ssRNA genome
- Enveloped viruses
- Broad host range
- Neurotropism
- Pathogens causing epidemics



*Togaviridae family: Alphaviruses
Rubiviruses

TABLE 1. The alphaviruses

Complex	Abbreviation ^a	Virus name ^b	Strains	Distribution	Sequence reference(s)
VEE/EEE group	→ EEE	EASTERN EQUINE ENCEPHALITIS	North American	North America	68, 569, 592
	→ VEE	VENEZUELAN EQUINE ENCEPHALITIS	South American Trinidad donkey TC-83	South America South America Central America	258
	EVE	Everglades		Florida	589
	MUC	Mucambo		Brazil, Peru	589
	PIX	Pixuna		Brazil	589
SF group	→ SF	SEMLIKI FOREST		Africa, Eurasia	137, 138, 540
	MID	Middelburg		Africa	516
	→ CHIK	Chikungunya		Africa	85
	ONN	O'NYONG-NYONG		Africa	292
	RR	ROSS RIVER	Nelson Bay, T48	Australia, Oceania	116
	BF	Barmah Forest		Australia	10
	GET	Getah		Australia, Asia	
	SAG	Sagiyama		Japan	
	BEB	Bebaru		Malaysia	
	MAY	Mayaro		South America	85
SIN group	→ SIN	SINDBIS	AR86, AR339, Girdwood, Karelian fever OCKELBO (OCK)	Africa, Asia, Europe, Australia	517
	AURA	AURA		Scandinavia	485
	WHA	WHATAROA		Brazil, Argentina	434
	BAB	Babanki		New Zealand	484
	KYZ	Kyzylagach		West Africa USSR	
Recombinant or uncertain	→ WEE	Western equine encephalitis		North America, South America	177, 592
	HJ	Highlands J		Eastern U.S.A.	484, 587
	FM	Fort Morgan		Western U.S.A.	
Ungrouped	NDU	Ndumu		Africa	
	??	Buggy Creek		Western U.S.A.	

Strauss & Strauss (1994) The Alphaviruses: Gene Expression, Replication, and Evolution. *Microbiol. Rev.* 58, 491-562.

Pathogens – Epidemics*

Symptoms: headache, fever, rash, arthralgia, encephalitis

VEE (Venezuelan equine encephalitis virus)

- Human, equine encephalitis (fatal outcome)
- Outbreaks in North and South America
- Vaccination (TC-83): outbreaks subsided in 1972

CHIKV (Chikungunya virus)

- Epidemics in Kenya, Madagascar, La Reunion, Thailand, China
- La Reunion: 244'000 cases, 203 deaths in 2005-2006
- Brazil, Mexico in 2016-2017
- High chance of new outbreaks

*Azar et al. (2020) Epidemic Alphaviruses: Ecology, Emergence and Outbreaks. *Microorganisms* 8, 1167

Pathogens – Epidemics*

SIN (Sindbis virus)

- Northern Europe and South Africa
- Self-limited or subclinical, largely undiagnosed
- Regular outbreaks in Sweden and Finland 1995-2012 with postulated 7-year-cycle

MAYV (Mayaro virus)

- Outbreaks in Brazil in 1981, 1991, 2015
- Potentially the next arbovirus to cause a large epidemic
- Cross-reaction of attenuated CHIKV might prevent MAYV infection

*Azar et al. (2020) Epidemic Alphaviruses: Ecology, Emergence and Outbreaks. *Microorganisms* 8, 1167

Pathogens – Epidemics*

EEEV (Eastern equine encephalitis virus) /MADV (Madariaga virus)

- Asymptomatic infections, low number of cases (North America)
- Recent local outbreaks/epizootics in Massachusetts

WEEV (Western equine encephalitis virus)

- More severe in horses than in humans (North America)
- Submergence/emergence of WEEV isolates unclear

RRV (Ross River virus)

- 55-75% of human RRV infections asymptomatic (Australia)
- Continuous threat of new outbreaks in Australia

SFV (Semliki Forest virus)

- Minor outbreaks in Africa

*Azar et al. (2020) Epidemic Alphaviruses: Ecology, Emergence and Outbreaks. *Microorganisms* 8, 1167

Examples of Alphavirus Vaccines

Target	Vaccine	Findings
VEEV	VEEV TC-83 strain	IND vaccination showed 80% vaccine efficacy
VEEV	EHV-1 vector VEEV envelope	Protection against VEEV in mice
VEEV	VSV vector VEEV envelope	Protection against VEEV in mice
CHIKV	Measles virus vector CHIKV capsid and envelope	Good safety Strong immune response in Phase II
RRV	Inactivated RRV	Phase III trial concluded
MAYV	Attenuated CHIKV	Some protection against MAYV in mice
EEEV	Eilat virus vector EEEV envelope	Protection against EEEV in mice
EEEV	Eilat virus vector CHIKV envelope	80% protection against EEEV in mice
WEEV	Adenovirus vector WEEV envelope	Protection against WEEV in mice
WEEV	SINV vector WEEV envelope	40-100% protection against WEEV in mice
EEEV	CMV DNA vector EEEV envelope	High levels of neutralizing antibodies
VEEV	CMV DNA VEEV envelope	Protection against VEEV in mice
VEEV, EEEV and WEEV	Trivalent DNA vaccine	Protection against VEEV, EEEV and WEEV in mice

Self-amplifying Alphavirus Vectors

- 200,000-fold RNA amplification in the cytoplasm of host cells
- Transient expression of antigens
- Alternative application of viral particles, RNA replicons or plasmid DNA
- Ideal for vaccine development against infectious diseases

