Arterivirus[‡]

Arteriviridae

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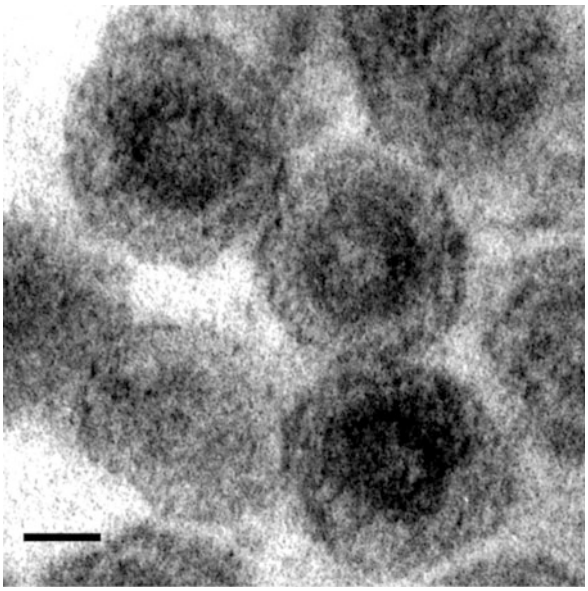

Porcine respiratory and reproductive syndrome virus. Fig. 1
Negative staining of extracellular PRRSV particles. Length of bar [nm]: 20.[courtesy of J. Pol, ID-DLO, Lelystad, the Netherlands; reprinted with permission from Snijder EJ, Meulenberg JJM (1998) J Gen Virol 79:961–979]

Virion

Morphology:	icosahedral
Envelope:	yes
Diameter [nm]:	50–60
Length [nm]:	-
Structural components:	capsid, envelope
Buoyant density [g/mL]:	1.13–1.17
Additional information:	envelope lacks prominent surface projections; the above density is in sucrose

[‡]This chapter was reprinted from the first edition of the Springer Index of Viruses. Taxonomy and classification of the virus species described in this chapter may have changed.

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Genome

Nucleic acid:	RNA
Strandedness:	single-stranded
Polarity:	positive-sense
Configuration:	linear
Segments:	1
Size [kb]:	12.7–15.7
G + C content [%]:	48–53
Transcription units:	7–9
Additional information:	mRNAs form a nested set with common 5′ and 3′ sequences

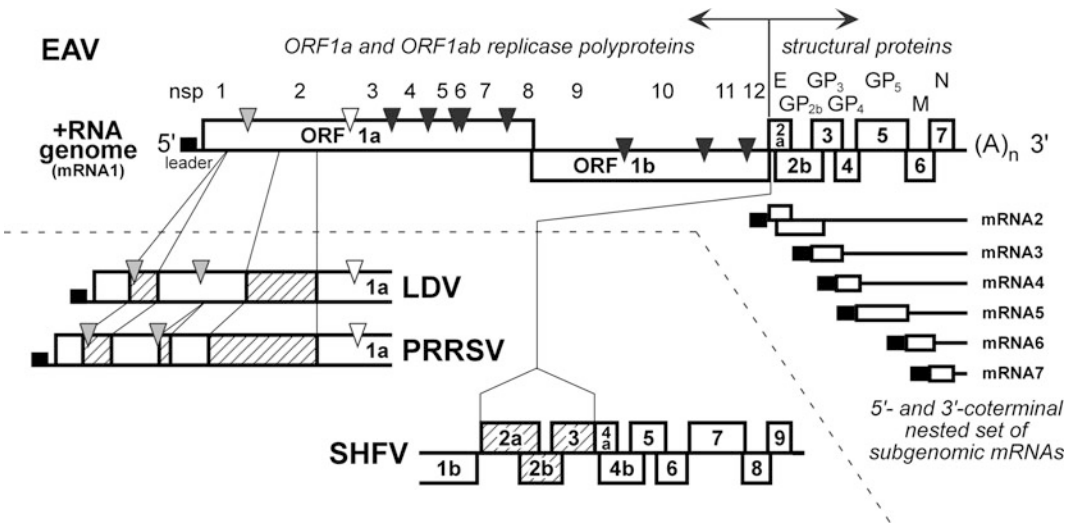
Replication Strategy

Entry mechanism:	receptor-mediated endocytosis
Site of transcription:	cytoplasm
Transcriptase:	viral RNA-dependent RNA polymerase
Site of genome replication:	cytoplasm
Replicase:	viral RNA-dependent RNA polymerase
Replication intermediate:	genome-length minus strand RNA
Site of virion assembly:	smooth intracellular membranes
Egress mechanism:	budding into smooth intracellular membranes, transport to cell membrane, exocytosis
Additional information:	structural proteins are translated from a nested set of subgenomic mRNAs; replication-complex is associated with virus-induced double membrane structures

History

Year	Event/Discovery	Reference
1953	First documented outbreak of equine arteritis in Bucyrus, USA; isolation of equine arteritis virus (EAV)	Doll ER, et al. (1957) Cornell Vet 47:3–41
1960	Isolation of lactate dehydrogenase-elevating virus (LDV) from laboratory mice	Riley V, et al. (1960) Science 132:545–547
1964	First outbreaks of simian hemorrhagic fever virus (SHFV) in macaques in USA and Russian research centers	Tauraso NM, et al. (1968) Am J Trop Med Hyg 17:422–431
1975	Characterization of the EAV genome as a single RNA molecule of positive polarity	van der Zeijst BAM, Horzinek MC (1975) Virology 68:418–425
1987	Emergence of porcine reproductive and respiratory syndrome (PRRS) in North America	Keffaber, KK (1989) Am Ass Swine Pract Newsletter 2:1–10
1990	All EAV mRNAs are shown to contain a common 5′ leader sequence, which is derived from the 5′ end of the genome	de Vries AAF, et al. (1990) Nucleic Acids Res 18:3241–3247

Year	Event/Discovery	Reference
1991	Emergence of PRRS in Europe and isolation of the Lelystad strain of PRRSV	Wensvoort G, et al. (1991) Vet Quarterly 13:121–130
1991	Publication of the EAV genomic sequence; arteri- and coronaviruses are proposed to be evolutionarily related	den Boon JA, et al. (1991) J Virol 65:2910–2920
1992	Identification of the products of EAV ORFs 2b, 5, 6, and 7 as structural proteins	de Vries AAF, et al. (1992) J Virol 66:6294–6306
1993	Publication of the complete genomic sequence of a European PRRSV strain (Lelystad virus)	Meulenberg JJM, et al. (1993) Virology 192:62–72
1993	Publication of the genomic sequence of LDV (LDV-C strain)	Godeny EK, et al. (1993) Virology 194:585–596
1996	Classification of the families Arteriviridae and Coronaviridae in the novel order Nidovirales	Cavanagh D (1997) Arch Virol 142:629–633
1996	Identification of the products of PRRSV ORFs 3 and 4 as structural glycoproteins	van Nieuwstadt AP, et al. (1996) J Virol 70:4767–4772
1997	Description of an infectious cDNA clone for EAV	van Dinten LC, et al. (1997) Proc Natl Acad Sci USA 94:991–996
1997	Publication of the sequence of the 3′-terminal region (6.3 kb) of the SHFV genome	Smith SL, et al. (1997) Gene 191:205–210
1998	Description of an infectious cDNA clone for PRRSV (Lelystad strain)	Meulenberg JJM, et al. (1998) J Virol 72:380–387
1998	The glycosylation state of LDV GP5 is reported to determine virus neutralization and neuropathogenicity	Li K, et al. (1998) Virology 242:239–245
1999	Publication of the complete genomic sequence of the North American PRRSV prototype strain VR2332	Nelsen CJ, et al. (1999) J Gen Virol 80:307–315
1999	Completion of the EAV replicase processing analysis	van Dinten LC, et al. (1999) J Virol 73:2027–2037
1999	Identification of the E protein as an additional envelope protein of EAV	Snijder EJ, et al. (1999) J Virol 73:6335–6345



Genome organization and expression of EAV and major differences (hatched) with other arteriviruses. Fig. 2 Names of EAV gene products, replicase cleavage sites, and subgenomic mRNAs are shown. [modified with permission from Snijder EJ, Meulenberg JJM (1998) J Gen Virol 79:961–979]

Genus Members

Species	Abbr.	Synonym(s)	Wild-type isolates	Host range	Membership status
Equine arteritis virus	EAV		EAV-Bucyrus	horses, donkeys	type species
Lactate dehydrogenase-elevating virus	LDV		C, P	mice	approved member
Porcine respiratory and reproductive syndrome virus	PRRSV	Swine infertility and respiratory syndrome virus	Lelystad virus, VR2332	pigs	approved member
Simian hemorrhagic fever virus	SHFV		LVR	monkeys (specific species)	approved member

Nucleotide Sequences

Genomic region	Virus species	Strain	Nucleotides	Accession number	Reference
complete genome	EAV	Bucyrus	12704	Y07862	den Boon JA, et al. (1991) J Virol 65:2910–2920
complete genome	LDV	C	14171	L13298	Godeny, EK (1993) Virology 194:585–596
complete genome	LDV	P	14104	U15146	Palmer GA, et al. (1995) Virology 209:637–642
complete genome	PRRSV	Lelystad virus	15098	M96262	Meulenberg JJM, et al. (1993) Virology 192:62–72
complete genome	PRRSV	VR2332	15409	PRU87392	Nelsen CJ, et al. (1999) J Virol 73:270–280
complete genome	PRRSV	16244B	15428	AF046869	Allende R, et al. (1999) J Gen Virol 80:307–315
3′-terminal region of genome	PRRSV	isolate 10	4920	L04493	Conzelmann KK, et al. (1993) Virology 193:329–339
3′-terminal region of genome	SHFV	LVR	6314	U63121	Smith SL, et al. (1997) Gene 191:205–210

Proteins

Protein	Abbr.	MW [kDa]	Time of expression	Accession numbers	Additional information
EAV non-structural protein 1	EAV nsp1	29	early	P89939	papainlike cysteine protease (PCP) in C-terminus; essential for subgenomic RNA synthesis
LDV/PRRSV non-structural protein 1 α	nsp1-α	18–20	early	Q83017, Q04561	homologous to N-terminus of EAV nsp1; contains additional PCP
LDV/PRRSV non-structural protein 1 β	nsp1-β	26–27	early	Q83017, Q04561	homologous to C-terminal half of EAV nsp1
non-structural protein 2	nsp2	61–131	early	P89939, Q83017, Q04561	membrane-associated, cysteine protease in N-terminus

Protein	Abbr.	MW [kDa]	Time of expression	Accession numbers	Additional information
non-structural protein 3	nsp3	23–25	early	P89939, Q83017, Q04561	hydrophobic, membrane-associated
non-structural protein 4	nsp4	21–22	early	P89939, Q83017, Q04561	chymotrypsin-like serine protease (main protease)
non-structural protein 5	nsp5	18–19	early	P89939, Q83017, Q04561	hydrophobic, membrane-associated
non-structural protein 6	nsp6	2	early	P89939, Q83017, Q04561	
non-structural protein 7	nsp7	23–30	early	P89939, Q83017, Q04561	
non-structural protein 8	nsp8	5–6	early	P89939, Q83017, Q04561	nsp8 is identical to the N-terminal domain of nsp9
non-structural protein 9	nsp9	75–76	early	P89939, Q06503, Q04561	RNA-dependent RNA polymerase
non-structural protein 10	nsp10	47–51	early	P89939, Q06503, Q04561	contains putative Zn finger and ATPase/helicase
non-structural protein 11	nsp11	24–26	early	P89939, Q06503, Q04561	contains conserved nidovirus-specific domain
non-structural protein 12	nsp12	12–19	early	P89939, Q06503, Q04561	
envelope protein	E	8–9	late		encoded by ORF2a (EAV, LDV), 2b (PRRSV), or 4a (SHFV)
glycoprotein 2b/2a/4b	GP2b, GP2a, GP4b	24–27	late	P28992, Q04566, Q83019, P89136	encoded by ORF2b (EAV, LDV), 2a (PRRSV), or 4b (SHFV)
glycoprotein 3/5	GP3, GP5	18–29	late	P28993, Q04567, Q83020, P89137	encoded by ORF3 (EAV, LDV, PRRSV) or ORF5 (SHFV)
glycoprotein 4/6	GP4, GP6	17–20	late	P28994, Q83021, 04568, P89138	encoded by ORF4 (EAV, LDV, PRRSV) or ORF6 (SHFV)
glycoprotein 5/7	GP5, GP7	22–31	late	P28995, Q83022, Q04569, P89139	encoded by ORF5 (EAV, LDV, PRRSV) or ORF7
membrane protein	M	18–19	late	P28991, Q04565, Q83023, Q87062	triple-spanning membrane protein
nucleocapsid protein	N	12–14	late	P19810, Q04558, Q89680, Q87063	basic, phosphorylated protein

Biology

Virus species	Permissive cell lines	Tissue tropism	Cytopathic effects	Additional information
EAV	BHK-21, RK-13, Vero, MA-104	macrophages	rounding of cells, detachment from surface	CPE develops in 16–20 hours
LDV	none; primary macrophages only	macrophages	too few cells infected to detect CPE	LDV is usually grown in mice

Virus species	Permissive cell lines	Tissue tropism	Cytopathic effects	Additional information
PRRSV	MA-104, MARC-145, CL2621, PAM	macrophages	rounding of cells, detachment from surface	PRRSV induces apoptosis
SHFV	MA-104	macrophages	rounding of cells, detachment from surface	

Diseases

Disease	Causative agent	Affected organism	Characteristics	Route of transmission	Geographic distribution
equine arteritis	EAV	horses, donkeys	vascular lesions, anorexia, fever, edema, abortion	aerosols, sexual	world-wide
age-dependent poliomyelitis	LDV	specific (MuLV-positive) mice	paralysis due to destruction of motor neurons	trans-placental, contact	unclear
porcine reproductive and respiratory syndrome	PRRSV	pigs	respiratory distress, reproductive failure	aerosols; sexual	world-wide
simian hemorrhagic fever	SHFV	macaques	fever, anorexia, dehydration, hemorrhagic lesions, death	aerosols; contact	occurs in primate centers

Vaccine Strains

Strain	Attenuation procedure	Additional information	Reference
EAV Arvac	266 serial passages on different cell lines	live attenuated vaccine	McCollum WH (1986) Am J Vet Res 47:1931–1934
EAV Artervac (based on EAV-Bucyrus)	formalin-inactivated vaccine		Fukunaga Y, et al. (1990) J Vet Med SerB 37:135–141
PRRSV RespPRRS (based on PRRSV VR2332)	serial passages on CL2621 cells	live attenuated vaccine	Gorcyca D, et al. (1995) Proc Am Ass Swine Pract, Omaha, NE, USA, pp 1–22
PRRSV PrimePacPRRS	serial passages in cell culture	live attenuated vaccine	Schering-Plough Animal Health, Elkhorn, NE, USA
PRRSV Suipravac	formalin-inactivated vaccine		Laboratorios Hipra, Amer (Girona), Spain

Vector Constructs

Vector	Backbone strain	Application	Insertion capacity [kb]	Additional information	Reference
pEAV030	EAV-Bucyrus	expression	unknown	infectious cDNA clone of the EAV RNA genome	van Dinten LC, et al. (1997) Proc Natl Acad Sci USA USA 94:991–996
pABV414	PRRSV-Lelystad virus	expression	unknown	infectious cDNA clone of the PRRSV RNA genome	Meulenberg JJM, et al. (1998) J Virol 72:380–387

References

1. Plagemann PGW, Moennig V (1992) Adv Vir Res 41:99–192
2. Plagemann PGW (1996) In: Fields Virology, 3rd edn. Lippincott-Raven Publishers, Philadelphia, pp 1105–1120
3. de Vries AAF, Horzinek MC, Rottier PJM, de Groot RJ (1997) Semin Virol 8:33–47
4. Snijder EJ, Meulenberg JJM (1998) J Gen Virol 79:961–979
5. Brinton MA (1999) In: Encyclopedia of Virology, 2nd edn. Academic Press, San Diego, pp 89–97
6. Snijder EJ, Meulenberg JJM (2001) In: Fields Virology, 4th edition. Lippincott, Williams and Wilkins, Philadelphia (in press)