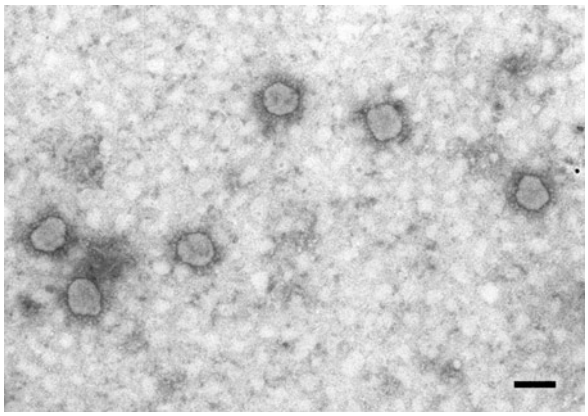
Alphacoronavirus[‡]

Coronaviridae

Nicola Decaro



Alphacoronavirus-1 (TGEV). Fig. 1
Transmission electron micrograph, negative staining of purified virus. Length of bar (nm): 100(Courtesy of Dr. A. Lavazza, Istituto Zooprofilattico di Lombardia ed Emilia Romagna, Italy)

Virion

Morphology:	Spherical
Envelope:	Yes
Diameter (nm):	120–160
Length (nm):	
Structural components:	Core, capsid, envelope
Buoyant density (g/mL):	1.23–1.24
Buoyant density method:	CsCl
Lipid composition:	Envelope lipids are derived from cytoplasma membrane of host cell
Additional information:	Surface projections made by the spike (S) protein

Genome

Nucleic acid:	RNA
Strandedness:	

[‡]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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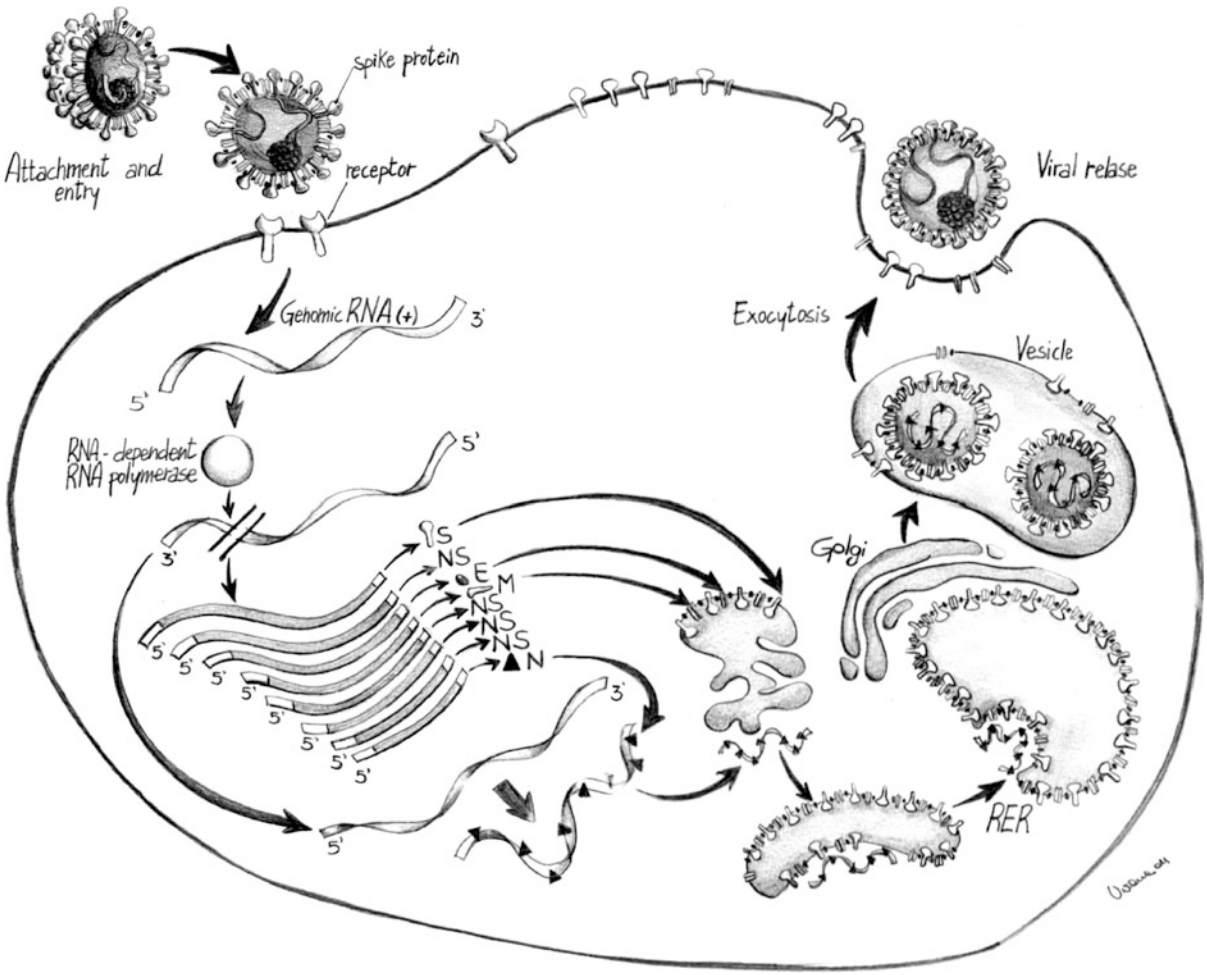
Polarity:		
Configuration:		
Segment organization:	Segment no. 1 (kb):	27.1–29.4
	One segment(s):	27.1–29.4 (kb) total (calculated)
G + C content (%):	37.6–41.8	
mRNA transcripts:	7–10	
Open reading frames:	7–10	
Additional information:	The genome contains a leader at the 5′ end and a poly(A) tail; genes are arranged in the order 5′-replicase-S-E-M-N-3′, with a variable number of other genes that are believed to be non-structural	

Replication

Entry mechanism:	Receptor-mediated endocytosis
Site of transcription:	Cytoplasm
Transcriptase:	Virus-encoded RNA-dependent RNA polymerase
Site of genome replication:	Cytoplasm
Replicase:	Virus-encoded RNA-dependent RNA polymerase
Replication intermediate:	Negative-strand RNA intermediate
Site of virion assembly:	Cytoplasm, the intermediate compartment
Egress mechanism:	Budding through the pre-Golgi and Golgi to the apical surfaces (TGEV)
Additional information:	Only the membrane (M) and envelope (E) proteins are required for the production of virus-like particles (VLPs)

History

Year of event	Event	References
1946	Transmissible gastroenteritis virus (TGEV) associated with enteritis in swine	Doyle and Hutchings (1946)
1965	Coronaviruses associated with common colds in humans	Tyrrell and Bynoe (1965)
1975	Radiolabeling (TGEV) clarifies fundamental coronavirus protein composition (S, N, M proteins)	Garwes and Pocock (1975)
1975	ICTV approves Coronaviridae family with one genus, Coronavirus	Tyrrell et al (1975)
1980	Demonstration that antibodies to feline enteric coronavirus enhance feline infectious peritonitis	Pedersen and Boyle (1980)
1989	Alternative model for transcription (TGEV): discontinuous transcription during negative strand synthesis	Sethna et al (1989)
1982	Amino peptidase N receptor for TGEV and HCoV-229E	Delmas et al (1992)
1996	ICTV recognises Coronaviridae as containing 2 genera: Coronavirus and Torovirus	Cavanagh et al (1997)



Alpha-, Beta-, and Gamma coronavirus replication cycle. Fig. 2
HE protein is present only in some Betacoronaviruses (Courtesy of Dr Viviana Tarallo, Department of Veterinary Public Health, Valenzano, Italy)

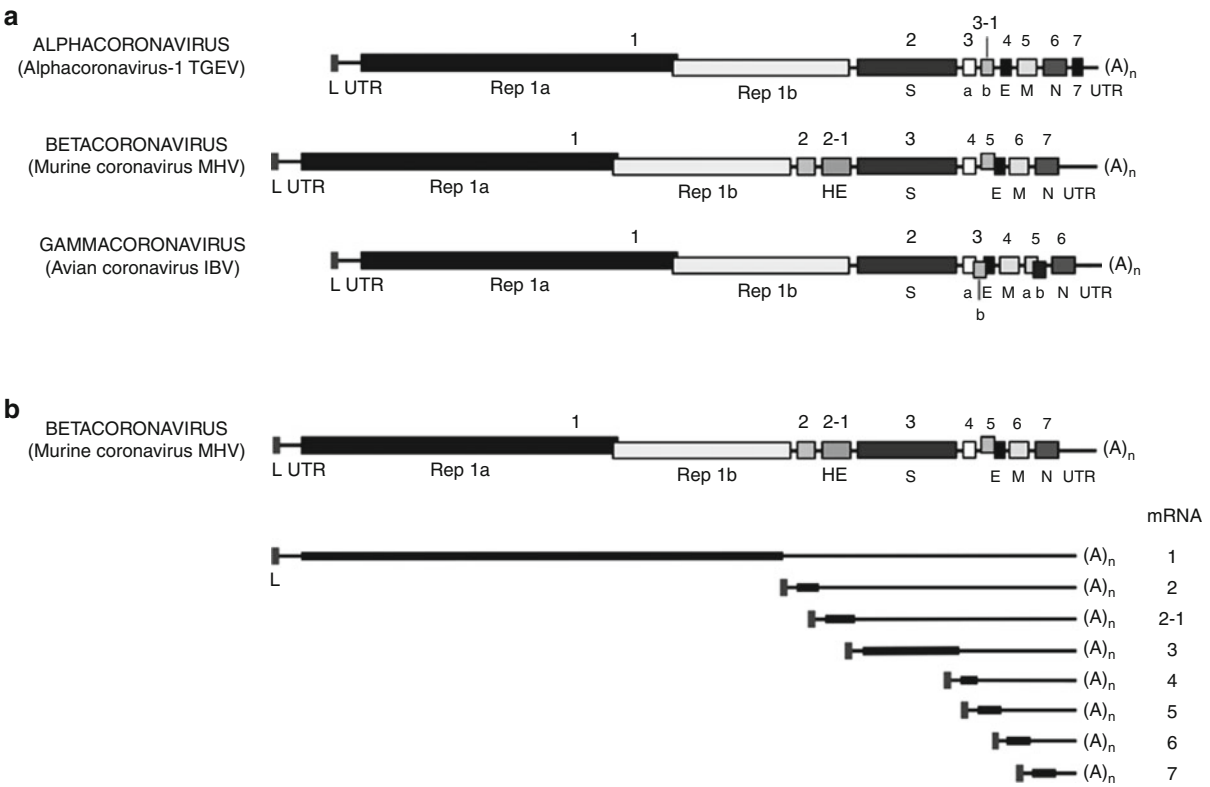
Year of event	Event	References
1996	ICTV recognises the order Nidovirales containing families Coronaviridae and Arteriviridae	Cavanagh et al (1997)
1999	Recombinant TGEV shows that S protein determines enteropathogenicity and virulence	Sanchez et al (1999)
2000	Engineering the largest RNA virus genome (TGEV) as an infectious bacterial artificial chromosome	Almazan et al (2000)
2001	Full-length c-DNA of HCoV-229E amplified in a vaccinia virus eukaryotic vector	Thiel et al (2001)
2002	First crystal structure of a coronaviral (TGEV) protein (main protease)	Anand et al (2002)
2002	Human coronavirus NL63 isolated in the Netherlands	van der Hoek et al (2004)
2005	Design of wide-spectrum inhibitors of coronavirus main protease	Yang et al (2005)

Year of event	Event	References
2008	CCoV recognised as most likely ancestor of TGEV	Lorusso et al (2008)
2009	ICTV recognises the family Coronaviridae as containing two subfamilies, Coronavirinae and Torovirinae, with the former including three genera	Carstens (2010)
2009	According to the new taxonomy, genus Coronavirus is replaced by genera Alpha-, Beta- and Gammacoronavirus, corresponding to the old antigenic groups	Carstens (2010)
2009	TGEV, CCoV, FCoV and related viruses are recognised as host variants of a unique species, Alphacoronavirus-1, prototype of the genus Alphacoronavirus	Carstens (2010)

Genus Members

Species name	Synonyms	Wild-type strains/ isolates	Natural host range	Experimental host range	Membership status
Alphacoronavirus-1	Transmissible gastroenteritis virus/Porcine respiratory (TGEV/PRCoV); Canine coronavirus type I/type II (CCoV-I/CCoV-II); Feline coronavirus type I/type II (FCoV-I/FCoV-II); Flying squirrel coronavirus (FSCoV); Chinese bamboo rat coronavirus (CBRCoV); Lesser Indian civet coronavirus (LICCoV); Masked palm civet coronavirus (MPCCoV); Siberian weasel coronavirus (SWCoV); Yellow-bellied weasel coronavirus (YBWCoV); Raccoon dog coronavirus (RDCoV); Chinese ferret badger coronavirus DM95/ 2003 (CFBCoV-DM95/2003); Spotted hyena coronavirus	TGEV:Purdue, Miller; CCoV-I:Elmo/02; CCoV-II:I-71, CB/05, 341/05; FCoV-I:TN-446; FCoV-II: 79-1146	Swine (TGEV); dogs (CCoV); cats (FCoV); carnivores		Type species
Human coronavirus 229E (HCoV-229E)		VR- 740	Humans		Approved member
Human coronavirus NL63 (HCoV-NL63)		SWE 10614/2004; Amsterdam 057; KR05-28; GRE 109/03	Humans		Approved member
Miniopterus bat coronavirus 1 (Mi-BatCoV-1)		61	Bats (Miniopterus spp.)		Approved member
Miniopterus bat coronavirus HKU8 (Mi-BatCoV-HKU8)		AFCD77	Bats (Miniopterus spp.)		Approved member
Porcine epidemic diarrea virus (PEDV)		CV777	Swine (Sus scrofa)		approved member

Species name	Synonyms	Wild-type strains/ isolates	Natural host range	Experimental host range	Membership status
Rhinolophus bat coronavirus HKU2 (Rh-BatCoV-HKU2)		GD/430/2006	Bats		app'roved member
Scotophilus bat coronavirus 512 (Sc-BatCoV-512)		BtCoV/512/2005	Bats (Scotophilus spp.)		Approved member
Ferret coronavirus (FrCoV)	Ferret enteric coronavirus ; Ferret systemic coronavirus (FrECoV; FrSCoV)	enteric strain MSU-2; systemic strain MSU-1	Ferrets (Mustela putorius furo)		Tentative member
Harbor seal coronavirus 1		HS1	Pacific harbor seals (Phoca vitulina richardsii)		Tentative member
Mink coronavirus (MiCoV)		WD1127	Mink (Mustela vison)		Tentative member



Genome organization of Alpha-, Beta-, and Gammacoronavirus prototypes (A) and transcription map of Murine coronavirus MHV (B). Fig. 3

Numbers above *bars* ORFs, *L* leader, *UTR* untranslated region, *Rep* = replicase; *(A)n* poly A (Modified from Springer Index of Viruses, 1st edn. with permission)

Nucleotide Sequences

Genomic region	Species	Strain	Nucleotides	Access number	References
Complete genome	Alphacoronavirus-1 (TGEV)	Purdue-Madrid	28,580	AJ271965	Almazan et al (2000)
Complete genome	HCoV-229E		20,580	AF304460	Thiel et al (2001)
Complete genome	HCoV-NL63	Amsterdam 057	27,550	DQ445911	Pyrc et al (2006)
Complete genome	Sc-BatCoV-512	BtCoV/512/2005	28,203	NC_009657	Tang et al (2006)
Complete genome	PEDV	LZC	28,042	EF185992	Cheng et al (2007), direct submission
Complete genome	Mi-BatCoV-HKU8	AFCD77	28,773	EU420139	Chu et al (2008)
Complete genome	Alphacoronavirus-1 (FCoV-I)	FCoV-I Black	29,256	EU186072	Tekes et al (2008)
Complete genome	Alphacoronavirus-1 (FCoV-II)	FCoV-II DF-2	28,632	DQ286389	Taboni et al (2007), direct submission
Complete genome	Alphacoronavirus-1 (CCoV-II)	CCoVII NTU336/F/2008	29,363	GQ477367	Chuang et al (2008), direct submission
genomic 3′ end	Alphacoronavirus-1 (CCoV-II)	CCoV-II CB/05	8,745	DQ112226	Buonavoglia et al (2006)
Replicase (partial)	Mi-BatCoV-1	61	591	AY864198	Poon et al (2005)
Replicase (partial)	Alphacoronavirus-1 (CBRCoV)	Guangxi/B305/2005	275	EF584902	Dong et al (2007)
Replicase (partial)	Alphacoronavirus-1 (LICCoV)	Guangxi/D690/2005	486	EF584903	Dong et al (2007)
Replicase (partial)	Alphacoronavirus-1 (YBVCoV)	Guangxi/D726/2005	343	EF584904	Dong et al (2007)
Replicase (partial)	Alphacoronavirus-1 (MPCCoV)	Guangxi/D728/2005	486	EF584905	Dong et al (2007)
Replicase (partial)	Alphacoronavirus-1 (SWCoV)	Guangxi/D1000	486	EF584906	Dong et al (2007)
Replicase (partial)	FSCoV	Guangxi/E001/2006	486	EF584907	Dong et al (2007)
Complete genome	Rh-BatCoV-HKU2	GD/430/2006	27,165	EF203064	Lau et al (2007)
Replicase (partial)	Alphacoronavirus-1 (RDCoV)	GZ43/2003	5,274	EF192159	Vijaykrishna et al (2007)
from ORF3 to E gene	Alphacoronavirus-1 (CCoV-I)	CCoV-I Elmo/02	2,145	AY426983	Lorusso et al (2008)
Complete genome	MiCoV	WD1127	28,941	HM245925	Spiro et al (2010), direct submission
genomic 3′ end	FrCoV	enteric strain MSU-2	8,618	GU338457	Wise et al (2010)
Replicase (partial)	Alphacoronavirus-1 (CFBCoV-DM95/2003)	DM95/2003	5,274	EF192160	Vijaykrishna et al (2007)
Replicase (partial)	Harbor seal coronavirus 1	HS1	208	FJ766501	Nollens et al (2010), direct submission
spike protein gene (partial)	Spotted hyena coronavirus	Es450a	429	DQ317972	East et al (2004)

Proteins

Protein name	Protein name abbreviation	Number of amino acids	Molecular weight (kDa)	Time of expression	Accession numbers	Additional information
Polyprotein 1ab (Replicase complex)	pp1ab	6632–6896	740–800	Throughout	NP_073549; YP_003766; ABQ57215; NP_598309; ABG47077; ACA52170; ADB28906; YP_003038530; CAB91143	Encoded by two ORFs, 1a and 1b; pseudoknot involved in frameshifting; cleaved to several products, including an RNA-dependent RNA polymerase
Spike glycoprotein	S	1222–1470	180–220	Throughout	ABG89317; CAA80971; AAR11077; ABG89335; YP_003038553; YP_001552234	Highly glycosylated; forms homotrimers; likely cleaved to S1 and S2 subunits in CCoV-I
Membrane protein	M	221–267	23–35	Throughout	ACN23167; ABU49663; ABQ57227; YP_001552239; ABG47081; YP_001718615; ABE97133; NP_073555; ADB28912; YP_003029902; ADD49352	N-linked or O-linked glycans; triple-spanning
Envelope protein	E	75–82	9–12	Throughout	ABU49662; ABG89314; ACJ63235; ACS44221; ACJ64179; ADI80524; ADD49351; ABQ57210; AAK38658; ABQ57234; YP_001351686; ABE97139; AAG48595	Essential for virion assembly; E plus M forms virus-like particles
Nucleocapsid protein	N	374–441	50–60	Throughout	ABQ57236; ACA52175; ABG47082; ABE97141; ADI80526; ACK77286; ABB90485; ACJ64190; ABO88144; ADC53234; ADD49353; ADC34660	Highly basic phosphoprotein; forms a helical nucleocapsid
Non-structural protein 3	ns3 (gp3)	207	28	Throughout	AY426983	Unique to CCoV-I (Geselavirus); gene located between S and 3a genes; N-glycosilated
Non-structural protein 3a	ns3a	60–94	7.8	Throughout	ACN79570; ABD97836; AAL89749; AAF02715; YP_003429311; ACJ64176; ABK79897	Unique to Geselavirus; located between S and E genes; non essential for replication; may be truncated in some strains

Protein name	Protein name abbreviation	Number of amino acids	Molecular weight (kDa)	Time of expression	Accession numbers	Additional information
Non-structural protein 3b	ns3b	108–251	27.7–31	Throughout	ACN79567; ABG89332; ABG89311; ABQ57225; ADC67067; ADI80514; ABE97131; ABM64812; ADD26775; ACT10973; AAR88621; YP_001718606	ns3c in CCoV/FCoV; ns3 in HCoV-NL63/PEDV/bat Alphacoronaviruses; ns4 in HCoV-229E; non essential; may be truncated in some strains
CCoV/FCoV non-structural protein 3b	CCoV/FCoV ns3b	71–73	7.8	Throughout	ACT10972; YP_003029910; ACJ63244; AAR88614	Unique to CCoV/FCoV (also known as ns3x); Non essential for replication; may be truncated in some strains
Non-structural protein 7 (7a)	ns7 (7a)	78–105	9.1	Throughout	ACJ63238; CAA62202; ABG89313; ABG89307	Unique to Geselavirus; ns7a in FCoV/CCoV; non essential for replication; may be truncated in some strains
Non-structural protein 7b	ns7b	162–213	14	Throughout	ACJ63239; ACJ64183; CAA47250; CAA62193	Unique to FCoV/CCoV (Geselavirus); non essential for replication; may be truncated in some strains
BatCoV-HKU8 non-structural protein 7	BatCoV-HKU8 nsp7	248	28.5	Throughout	ACA52176; YP_001718617	Unique to Miniopterus bat coronavirus HKU8
BatCoV-HKU2 non-structural protein 7	BatCoV-HKU2 nsp7	99	11.8	Throughout	ABQ57213; ABQ57221; ABQ57229; YP_001552241	Unique to Rhinolophus bat coronavirus HKU2

Biology

Species	Permissive cell lines	Tissue tropism	Cytopathic effects	Additional information
Alphacoronavirus-1 (TGEV)	ST, PK15, LLC-PK1	Epithelium of enteric and respiratory tract	Cell lysis with little syncytia formation	Respiratory variants replicate poorly in gut
PEDV	Vero	Epithelium of the enteric and respiratory tract	Formation of large syncytia	High mortality produced by virulent strains
Alphacoronavirus-1 (FCoV)	NLFK, A72, fcwf-D, CRFK	Intestinal epithelium and lymph nodes	Cell rounding, focal detachment and lysis	Some strains of FCoV are more virulent; FCoV-I replicates at low efficiency in vitro
Alphacoronavirus-1 (FIPV)	NLFK, A72, fcwf-D, CRFK	Peritoneum, liver, lymphoid organs	Cell rounding, focal detachment and lysis	Antibody-dependent enhancement of infectivity
Alphacoronavirus-1 (CCoV)	CRFK, A72, ST	Epithelium of the intestines	Cell rounding, focal detachment and lysis	CCoV-I does not replicate in vitro; pantropic CCoV CB/05 infects internal organs

Species	Permissive cell lines	Tissue tropism	Cytopathic effects	Additional information
HCoV-229E	L132, MRC-5, IMHP	Upper respiratory tract		Some HCoV infect oligodendrocytes and neural cell
HCoV-NL63	LLC-MK2; Vero-B4; primary cultures of HAE	Upper and lower respiratory tract	Diffuse CPE with cell detachemnt and deterioration	

Diseases

Disease	Causative agent	Affected organisms	Disease characteristics	Transmission route/vector	Treatment	Geographic distribution
Transmissible gastroenteritis	Alphacoronavirus-1 (TGEV)	Domestic and wild pigs	Diarrhoea, high mortality in newborns	Faecal-oral	Only symptomatic	Worldwide
Swine respiratory disease	Alphacoronavirus-1 (PRCoV, respiratory variant of TGEV)	Domestic and wild pigs	Sneezing, coughing, nasal discharge	Aerosol	Only symptomatic	Worldwide
Porcine epidemic diarrhoea	PEDV	Swine	Diarrhoea, high mortality in weaning pigs	Faecal-oral	Only symptomatic	Europe, Asia, not North America
Feline enteritis	Alphacoronavirus-1 (FCoV)	Cats	Diarrhoea	Faecal-oral	Only symptomatic	Worldwide
Feline infectious peritonitis	Alphacoronavirus-1 (FIPV)	Cats	Peritonitis, granulomatous inflammation in multiple organs	Not transmissible (in-vivo FCoV variant)	Only symptomatic	Worldwide
Canine enteritis	Alphacoronavirus-1 (CCoV)	Dogs	Diarrhoea, some mortality in young pups	Faecal-oral	Only symptomatic	Worldwide
Canine pantropic coronavirosis	Alphacoronavirus-1 (pantropic CCoV)	Dogs	Lymphopenia, diarrhoea, fever, depression, mortality	Unknown, maybe faecal-oral	Only symptomatic	Europe
Human common cold	HCoV-229E	Humans	Common cold (sneezing, coughing, nasal discharge)	Aerosol	Only symptomatic	Worldwide
Human respiratory disease	HCoV-NL63	Humans	Fever, cough, coryza, sore throat, bronchiolitis, bronchitis, pneumonia and croup	Aerosol	Only symptomatic	Worldwide
Ferret epizootic catarrhal enteritis	FrCoV (FrECoV)	Ferrets	Diarrhoea	Faecal-oral	Only symptomatic	North America, Europe
Ferret systemic coronavirosis	FrCoV (FrSCoV)	Ferrets	FIP-like disease (dry form)	Unknown	Only symptomatic	North America, Europe
Mink epizootic catarrhal gastroenteritis	MiCoV	Mink	Diarrhoea, mortality	Faecal-oral	Only symptomatic	North America, Europe

Diagnosis

Method	Species	Sample material	Detection target	References
Monoclonal time-resolved fluoroimmunoassay	HCoV-229E	respiratory samples	Viral antigens	Hierholzer et al (1994)
nested PCR amplification of the spike protein gene	HCoV-229E	Respiratory samples	Viral RNA	Myint et al (1994)
L132 cell culture and indirect immunofluorescence assay with monoclonal antibodies	HCoV-229E	Respiratory samples	Viral antigens	Sizun et al (1998)
RT-PCR amplification of the nucleocapsid protein gene	HCoV-NL63	Respiratory samples	Viral RNA	Moes et al (2005)
RT-PCR amplification of the spike protein gene	HCoV-NL63	Respiratory samples	Viral RNA	Bastien et al (2005)
Direct immunofluorescence assay and HuH7 cell culture	HCoV-229E	Respiratory samples	Viral antigens	Freymuth et al (2006)
Microarray using standard amplification and hybridization techniques	HCoV-229E	Respiratory samples	Viral RNA	Lodes et al (2007)
RT-PCR amplification of the nucleocapsid protein gene	HCoV-229E	Respiratory samples	Viral RNA	Dominguez et al (2009)
Nested PCR amplification of the nucleocapsid protein gene	HCoV-229E, HCoV-NL63	Respiratory samples	Viral RNA	Gaunt et al (2010)
Multiplex real-time RT-PCR amplification of the nucleocapsid protein gene	HCoV-229E, HCoV-NL63	Respiratory samples	Viral RNA	Gaunt et al (2010)
Vero cell culture and direct immunofluorescence assay	PEDV	Faeces, intestine	Viral antigens	Kim and Chae (1999)
Monoclonal antibody-based immunohistochemistry	PEDV	Formalin-fixed paraffin-embedded gut sections	Viral antigens	Kim, et al (1999)
Duplex RT-PCR amplification of the spike protein gene	Alphacoronavirus-1 (TGEV), PEDV	Faeces	Viral RNA	Kim et al (2001)
ELISA	PEDV	Faeces	Viral antigens	Rodák et al (2005)
Multiplex RT-PCR amplification of the spike protein gene	Alphacoronavirus-1 (TGEV), PEDV	Faeces	Viral RNA	Song et al (2006)
Double antibody sandwich enzyme-linked immunosorbent assay	PEDV	Faeces	Viral antigens	Sozzi et al (2010)
ST cell culture and immunofluorescence assay	Alphacoronavirus-1 (TGEV)	Faeces, intestine; respiratory samples (PRCoV)	Viral antigens	McClurkin and Norman (1966)
Immunoelectron microsopy	Alphacoronavirus-1 (TGEV)	Faeces, intestinal content	particle morphology	Saif et al (1977)
Immunofluorescence assay	Alphacoronavirus-1 (TGEV)	Intestinal sections	Viral antigens	Solorzano et al (1978)
Sandwich ELISA	Alphacoronavirus-1 (TGEV)	Faeces, intestinal content	Viral antigens	Bernard et al (1986)

Method	Species	Sample material	Detection target	References
Immunogold silver staining	Alphacoronavirus-1 (TGEV)	Formalin-fixed paraffin-embedded gut sections	Viral antigens	Larochelle and Magar (1993)
Immunohistochemistry	Alphacoronavirus-1 (TGEV)	Formalin-fixed paraffin-embedded gut sections	Viral antigens	Shoup et al (1996)
Nested PCR amplification of the spike protein gene discriminating TGEV from PRCoV	Alphacoronavirus-1 (TGEV, PRCoV)	Faeces, intestinal content	faeces, intestinal content, respiratory samples	Kim et al (2000)
Real-time RT-PCR assay with LUX primer targeting the spike protein gene	Alphacoronavirus-1 (TGEV)	Faeces, intestinal content	Viral RNA	Chen et al (2004)
Internally-controlled real-time TaqMan RT-PCR assay targeting the spike protein gene	Alphacoronavirus-1 (TGEV)	Faeces, intestinal content	Viral RNA	Vemulapalli et al (2009)
A-72 cell culture and immunofluorescence assay	Alphacoronavirus-1 (CCoV)	Faeces, intestinal content	Viral antigens	Keenan et al (1976)
Electron microscopy	Alphacoronavirus-1 (CCoV)	Faeces, intestibal content	particle morphology	Appel et al (1979)
Sandwich ELISA	Alphacoronavirus-1 (CCoV)	Faeces, intestinal content	Viral antigens	Tuchiya et al (1991)
Nested PCR amplification of the membrane protein gene	Alphacoronavirus-1 (CCoV)	Faeces, intestinal content	Viral RNA	Pratelli et al (1999)
Real-time RT-PCR amplification of the membrane protein gene	Alphacoronavirus-1 (CCoV)	Faeces, intestinal content	Viral RNA	Decaro et al (2004)
Genotype-specific real-time RT-PCR amplifications of the membrane protein gene discriminating CCoV-I and CCoV-II	Alphacoronavirus-1 (CCoV)	Faeces, intestinal content	Viral RNA	Decaro et al (2005)
Indirect immunofluorescence assay	Alphacoronavirus-1 (FIPV)	Serum	anti-viral antibodies	Pedersen (1976)
Immunfluorescence assay	Alphacoronavirus-1 (FCoV, FIPV)	Intestine (FCoV), internal organs (FIPV)	Viral antigens	Hoshino and Scott (1980)
Electron microscopy	Alphacoronavirus-1 (FCoV, FIPV)	Faeces, intestine (FCoV), internal organs (FIPV)	particle morphology	Hoshino and Scott (1980)
Immunohistochemistry	Alphacoronavirus-1 (FIPV)	Internal organs	Viral antigens	Boyle et al (1984)
CrFK cell culture and immunofluorescence assay	FCoV. FIPV	Faeces, intestine (FCoV); internal organs (FIPV)	Viral antigens	McKeirnan et al (1987)
RT-PCR amplification of the spike protein gene	Alphacoronavirus-1 (FCoV, FIPV)	Faeces, intestine (FCoV); internal organs (FIPV)	Viral RNA	Li and Scott (1994)
RT-PCR amplification of the 3′-untranslated region	Alphacoronavirus-1 (FCoV, FIPV)	Faeces, intestine (FCoV); internal oragns (FIPV)	Viral RNA	Herrewegh et al (1995)

Method	Species	Sample material	Detection target	References
Real-time RT-PCR amplification of the 3′-untranslated region	Alphacoronavirus-1 (FCoV, FIPV)	Faeces, intestine (FCoV); internal organs (FIPV)	Viral RNA	Gut et al (1999)
RT-PCR amplification of the subgenomic mRNA of the membrane protein gene	Alphacoronavirus-1 (FIPV)	Blood	Viral mRNA	Simons et al (2005)

Vaccine Strains

Strain	Attenuation process	Additional information	References
Alphacoronavirus-1 TGEV vaccine-Diamond	Passage in ST cells	MLV; limited efficacy	Moxley et al. (1989)
Alphacoronavirus-1 TGEV vaccine-Ambico	Passage at low pH in presence of enzymes	Oral MLV; limited efficacy	Lai et al (1991)
Alphacoronavirus-1 TGEV Nouzilly	Passage in cell culturess	Resists to proteases and acidity; limited efficacy	Aynaud et al (1991)
Alphacoronavirus-1 CCoV vaccine Insavc-1	Passage in cell culture	MLV; limited efficacy; post-vaccination adverse reactions reported	Horsburgh et al (1992)
Alphacoronavirus-1 CCoV vaccine TN449	Inactivated vaccine	Limited efficacy	Fulker et al (1995)
Alphacoronavirus-1 CCoV feline enteric coronavirus vaccine	Inactivated vaccine	Heterologous vaccine prepared with FECV; limited efficacy	Gill et al (1998)
Alphacoronavirus-1 FIPV temperature-sensitive vaccine strain DF2	Passage in cell culture	Temperature-sensitive MLV; limited efficacy	Addie et al (2009)

Vector Constructs

Vector name	Backbone strain	Application	Insertion capacity (kb)	Additional information	References
vHCoV-inf-1 and vHCoV-inf-2	HCoV-229E	Expression	27.3	Recombinant vaccinia virus containing the full-length genome of HCoV-229E	Thiel et al (2001)
TGEV M33 and M39	Alphacoronavirus-1 TGEV PUR46-MAD	Expression	5	Helper dependent expression system	Izeta et al (1999)
pBAC-TGEV (FL)	Alphacoronavirus-1 TGEV PUR46-MAD	Reverse genetics	28.7	Infectious bacterial artificial chromosome	Almazán et al (2000)
icTGEV	Alphacoronavirus-1 TGEV Purdue	Reverse genetics	28.5	Full-length genome infectious clone constructed through ligation of six inserts	Yount et al (2000)

Vector name	Backbone strain	Application	Insertion capacity (kb)	Additional information	References
pBRDI1	Alphacoronavirus-1 FCoV-II 79-1146	Reverse genetics	9–10	Used for targeted RNA recombination to obtain chimeric FIPV	Haijema et al (2003)
vrecFCoV	Alphacoronavirus-1 FCoV-I Black	Reverse genetics	26.3	Recombinant vaccinia virus containing the full-length genome of FCoV	Tekes et al (2008)
icNL63	HCoV-NL63	Reverse genetics	27.7	Full-length genome infectious clone constructed through ligation of five inserts	Donaldson et al (2008)

References

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