
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Veterinary Microbiology 244 (2020) 108693

Contents lists available at ScienceDirect

Veterinary Microbiology

journal homepage: www.elsevier.com/locate/vetmic

# Novel human coronavirus (SARS-CoV-2): A lesson from animal coronaviruses

Nicola Decaro[a,*], Alessio Lorusso[b]

[a] Department of Veterinary Medicine, University of Bari, Valenzano, Bari, Italy
[b] Istituto Zooprofilattico Sperimentale dell'Abruzzo e del Molise 'G. Caporale', Teramo, Italy

ARTICLE INFO

*Keywords:*
Novel human coronavirus
SARS-CoV-2
COVID-19
Animal coronaviruses
Genetic plasticity
Host switch
Tissue tropism

ABSTRACT

The recent pandemic caused by the novel human coronavirus, referrred to as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), not only is having a great impact on the health care systems and economies in all continents but it is also causing radical changes of common habits and life styles. The novel coronavirus (CoV) recognises, with high probability, a zoonotic origin but the role of animals in the SARS-CoV-2 epidemiology is still largely unknown. However, CoVs have been known in animals since several decades, so that veterinary coronavirologists have a great expertise on how to face CoV infections in animals, which could represent a model for SARS-CoV-2 infection in humans.

In the present paper, we provide an up-to-date review of the literature currently available on animal CoVs, focusing on the molecular mechanisms that are responsible for the emergence of novel CoV strains with different antigenic, biologic and/or pathogenetic features. A full comprehension of the mechanisms driving the evolution of animal CoVs will help better understand the emergence, spreading, and evolution of SARS-CoV-2.

## 1. Introduction

Eighteen years after the emergence of severe acute respiratory syndrome (SARS) in China and 8 years after the emergence of Middle East respiratory syndrome (MERS) in Saudi Arabia, a novel coronavirus (CoV) epidemic, recently classified as pandemic by the WHO, is threatening the human population worldwide (Zhou et al., 2020). The disease, now referred to as coronavirus disease 2019 (COVID-19), is caused by a novel human CoV, which was initially denominated 2019 novel coronavirus (2019-nCoV) and later renamed as SARS coronavirus 2 (SARS-CoV-2) the by Coronavirus Study Group of the International Committee on Taxonomy of Viruses (Gorbalenya et al., 2020). COVID-19 emerged in December 2019 in Wuhan City, Hubei Province, China, in humans exposed to wildlife at the Huanan seafood wholesale market, which is the largest seafood market in central China, and where different species of farm and wild animals are commonly sold (Lorusso et al., 2020). The epidemic has then expanded not only to neighbouring Asian countries, but also to other continents (https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200415-sitrep-86-covid-19.pdf?sfvrsn=c615ea20_2). .

A list of human CoVs is showed in Table 1. Historically, only two human CoVs (HCoVs) had been known before the SARS emergence, namely HCoV-229E, an alphacoronavirus originated in bats and transmitted to humans through alpacas, and HCoV-OC43, a betacoronavirus which had passed from rodents to humans through cattle (Corman et al., 2015, 2018). After 2002–2003 SARS epidemic, the renovated interest in HCoVs allowed the discovery of two additional viruses, the alphacoronavirus HCoV-NL63 and the betacoronavirus HCoV-HKU1, derived from bats and rodents, respectively (Tao et al., 2017). All these four viruses are usually responsible for mild respiratory symptoms in immunocompetent patients. SARS-CoV and MERS-CoV are two unrelated betacoronaviruses originated in bats and transmitted to humans by wild carnivores and dromedary camels, respectively. In contrast to other HCoVs, these two viruses displayed an increased virulence, causing severe pneumonia and even the death of affected people, with mortality rates of about 10 % and 30 %, respectively (Guarner, 2020).

The occurrence of three highly pathogenic CoVs with a zoonotic origin in less than two decades, highlights the role of animals in generating CoVs with increased virulence that can adapt to humans, causing epidemics (and eventually pandemics) with high impact on human health. Indeed, CoV infections of veterinary interest have been known since almost a century (Cavanagh, 2007; Pedersen, 2014; Decaro et al., 2020), so that animal CoVs are paradigmatic of how this large family of viruses evolves, generating strains with different biological properties. In addition, the efforts done in veterinary medicine

* Corresponding author at: Department of Veterinary Medicine, University of Bari, Strada per Casamassima Km 3, 70010, Valenzano, Bari, Italy.
*E-mail address:* nicola.decaro@uniba.it (N. Decaro).

https://doi.org/10.1016/j.vetmic.2020.108693
Received 10 March 2020; Received in revised form 10 April 2020; Accepted 10 April 2020

**Table 1**
Coronaviruses in humans.

| CoV genus | CoV subgenus | CoV species | CoV common name(s) | Possible ancestor | Associated disease | Reference |
|---|---|---|---|---|---|---|
| *Alphacoronavirus* | *Setracovirus* | *Human coronavirus NL63* | HCoV-NL63 | *NL63-related bat CoV strain BtKYNL63-9b* x *Hipposideros*-associated CoVs 229E like viruses | Mild respiratory disease | van der Hoek et al. (2004), Fouchier et al. (2004) |
| *Alphacoronavirus* | *Duvinacovirus* | *Human coronavirus 229E* | HCoV-229E | Alpaca(alpha)coronavirus ACoV | Mild respiratory disease | Hamre and Procknow (1966); Reed (1984) |
| *Betacoronavirus* | *Embecovirus* | *Betacoronavirus 1* | HCoV-OC43 | Bovine coronavirus (BCoV) | Mild respiratory disease | McIntosh et al. (1967) |
| *Betacoronavirus* | *Embecovirus* | *Human coronavirus HKU1* | HCoV-HKU1 | A coronavirus strain of *Rodentia*? | Mild respiratory disease | Woo et al. (2005) |
| *Betacoronavirus* | *Sarbecovirus* | *Severe acute respiratory syndrome-related coronavirus* | SARS-CoV, SARS-CoV-1 | Recombination between SARS-rCoVs of *Rhinolophus* bats. Intermediate host: palm masked civets and other wild carnivores | SARS, Severe respiratory distress, diarrhoea (1/3 patients); 10 % case fatality rate | Ksiazek et al. (2003) |
| *Betacoronavirus* | *Marbecovirus* | *Middle East respiratory syndrome-related coronavirus* | MERS-CoV | Probable common bat ancestor with *Neoromicia capensis* CoV. Intermediate host: dromedary camels | MERS, Severe respiratory distress, diarrhoea and vomiting (1/3 patients); 36 % case fatality rate | Zaki et al., 2012 |
| *Betacoronavirus* | *Sarbecovirus* | *Severe acute respiratory syndrome-related coronavirus* | SARS-CoV-2 | Unknown; 96.2 % of nucleotide identity with SARS-rCoV BatCoVRaTG13 | COVID-19, Severe respiratory distress and diarrhoea (10 % of patients), 3 – 4% case fatality rate | Zhou et al. (2020); Wu et al. (2020) |

to develop effective vaccines and antiviral therapies against well-known CoV infections of animals could be useful to set up prophylactic and therapeutical strategies against SARS-CoV-2.

The aim of this paper is to present a comprehensive review of the current literature on animal CoVs, their intermingled evolution, characterised by the continuous generation of strains with new pathobiological features and host range.

## 2. Coronaviruses: changing viruses in a changing world

Coronaviruses (subfamily *Orthocoronavirinae*, family *Coronaviridae*, order *Nidovirales*) are enveloped, single-strand, positive-sense RNA viruses. Currently, four different genera exist, i.e., *Alphacoronavirus*, *Betacoronavirus*, *Gammacoronavirus* and *Deltacoronavirus*, whose reservoirs are bats and rodents for alpha- and betacoronaviruses or birds for gamma- and deltacoronaviruses. From their natural reservoirs CoVs may jump to other animals, including humans, with the transmission to humans usually requiring an intermediate host (Lorusso et al., 2020). Each CoV genus is organised in subgenera that are presently 13, 5, 4 and 2 for alpha-, beta-, delta- and gammacoronaviruses, respectively (https://talk.ictvonline.org/taxonomy/).

Among RNA viruses, CoVs possess the largest genome, 27.6–31 kb in size. At the very 5'-end of the genome is a leader sequence, which plays critical roles in the gene expression of CoV during its discontinuous sub-genomic replication (Li et al., 2005). The 5′-most two-thirds of the genome comprises the replicase gene, which consists of two overlapping open reading frames, ORF 1a and 1b. Located downstream of ORF1b are 4 ORFs that code for a common set, to all CoVs, of structural proteins (spike (S), envelope (E), membrane (M) and nucleocapsid (N) proteins). The order of the structural protein genes is always conserved in all CoVs. The S protein mediates viral attachment to specific cell receptors and fusion between the envelope and plasma membrane and it is the main inducer of virus-neutralising antibodies. The small membrane (E) protein plays an important role in viral envelope assembly, but it is not essential for virus propagation. The membrane (M) protein, the most abundant structural component, is a type III glycoprotein consisting of a short amino-terminal ectodomain, a triple-spanning transmembrane domain, and a long carboxyl-terminal inner domain. The nucleocapsid (N) protein is a highly basic phosphoprotein that in addition to its function in the virion also modulates viral RNA synthesis. In addition to the common set of proteins, CoVs related to bovine coronavirus (BCoV), recently included in the subgenus *Embecovirus* (genus *Betacoronavirus*), possess an additional structural protein, the haemagglutinin-esterase (HE), closely related to the haemagglutinin-esterase fusion protein of influenza C virus. CoVs do also possess accessory genes coded by additional ORFs located downstream of ORF1b. Their number, nucleotide sequence and order can vary remarkably among different CoVs. The function of the accessory proteins is in most cases unknown and as a rule they are not essential for virus replication. They do play an important role, however, in virus host interactions as they are generally maintained during natural infection and their loss -either through spontaneous mutation or reversed genetics- results in reduced virulence (Brian and Baric, 2005; Decaro and Buonavoglia, 2008).

Replication of the CoV RNA involves the synthesis of a full-length negative-strand RNA that is present at low concentrations and serves as a template for the synthesis of full-length genomic RNA. The genes downstream of ORF1b are expressed through a 3'-coterminal nested set of subgenomic (sg) mRNAs. According to the generally accepted model for CoV transcription, sg minus-strand RNAs are produced via a discontinuous 3'-extension step, which is regulated by transcription regulating sequences (TRSs) that are present upstream of (most) ORFs and also at the 5'-end of the genome. The minus-strand RNAs in turn serve as templates for the synthesis of complementary sg mRNAs, of which only the 5' end is generally translated (Brian and Baric, 2005).

CoVs are characterised by an exceptional genetic plasticity and

evolve rapidly, changing their antigenic profile, tissue tropism or host range by means of two distinct mechanisms. The viral replicase (an RNA dependent-RNA polymerase) does not possess a good proof reading activity, therefore the incorporation of wrong nucleotides at each replication cycle and the consequent accumulation of mutations in the viral genome lead to a progressive differentiation of the viral progeny from the parental strain. This mechanism, which is well known for influenza viruses being responsible for the so called antigenic drift, may cause the progressive adaptation of the viral surface proteins to the cell receptors of new animal species, increasing the viral fitness. In addition, the particular replicating machinery of CoVs facilitates recombination events due to the presence of consensus sequences upstream each gene. Therefore, in the case of coinfection by more than one CoV strain, the RNA polymerase can jump from the RNA of a strain to that of the other one, synthetizing a hybrid RNA containing sequences from both viruses. Recombination can occur not only with genomic sequences of other CoVs (homologous recombination), but also with RNAs of different viruses and other organisms (heterologous recombination) (Luytjes et al., 1988; Banner and Lai, 1991; Lai, 1996; Zeng et al., 2008; Huang et al., 2016). Recombination is an alternative mechanism that let CoVs acquire novel biological properties in terms of virulence, host range and tissue tropism, so that CoV strains, which are non-pathogenic or low-pathogenic in the original host, may increase their pathogenicity in the same species or adapt to different species spreading in the new host with exceptional rapidity (Banner and Lai, 1991).

The occurrence of three human CoV epidemics in less than 20 years, along with the emergence of less pathogenic human CoVs, arises some questions on how these viruses that have their reservoirs in bats and rodents may overcome the species barriers jumping to humans. The animal-to-human transmission of viruses has been already occurred in the past, but it seems that its frequency has been increased in the last decades, involving in a short time span not only CoVs, but also a plethora of genetically and biologically different viruses with zoonotic potential, such as Ebola virus, influenza viruses, flaviviruses, Hendra and Nipah viruses (McMahon et al., 2018). Climate changes that are intensifying in this first quarter of the 21st century are favouring the spread of vector-borne diseases through increasing the proliferation of vectors and predisposing to their occupation of new ecological niches. The emergence in temperate climate areas such as Europe of vector-borne diseases caused by viruses considered exotic until few years ago (West Nile virus, Usutu virus, Chikungunya virus) accounts for a progressive geographic expansion of tropical diseases thanks to the ongoing phenomenon of tropicalisation (McMahon et al., 2018). Deforestation and urbanization are other major factors that facilitate the spill-over of zoonotic agents to humans by reducing the habitat of wildlife and increasing the chances of contacts between wild animals (like bats, rodents and birds) and human beings (Beena and Saikumar, 2019; Lorusso et al., 2020). This could be the case of Ebola virus, Hendra and Nipah viruses, hantavirus and coronavirus infections. In addition, the close contact between human beings and different animal species sold at the wet markets of East Asia represents the optimal situation for the host species jump and adaptation to humans of potentially zoonotic agents like CoVs. It is not a coincidence that two of the most severe zoonoses of the last two decades (highly pathogenic H5N1 avian influenza and SARS) have emerged in the same Chinese province of Guangdong where the contact between humans and animals is closer (Lorusso et al., 2020).

## 3. Animal coronaviruses

### 3.1. Coronaviruses in birds

Table 2 reports the most important avian CoV species recognised so far and their associated diseases. The number of avian species in which CoVs have been detected in the last years is humongous. Since the emergence of SARS-CoV in 2002, there has been increased interest in

**Table 2**
Main coronaviruses in domestic and domesticated avian species.

| Avian species | CoV genus | CoV subgenus | CoV species | CoV common name | Associated disease | Reference |
|---|---|---|---|---|---|---|
| Chicken (*Gallus gallus domesticus*) and other birds of different orders | *Gammacoronavirus* | *Igacovirus* | *Avian coronavirus* | Infectious bronchitis virus (IBV) | Respiratory disease, kidney injury and/ reproductive failures | Schalk and Hawn (1931); Beach and Schalm (1936); Beaudette and Hudson (1937) |
| Turkey (genus *Meleagris*) | *Gammacoronavirus* | *Igacovirus* | *Avian coronavirus* | Turkey coronavirus (TCoV) | Enteric disease | Panigrahy et al. (1973); Ritchie et al. (1973) |
| Quail (*Coturnix coturnix*) | *Gammacoronavirus* | *Igacovirus* | *Avian coronavirus* | Quail coronavirus (QCoV) | Enteric disease | Pascucci et al. (1983) |
| Guineafowl (fam. *Numididae*) | *Gammacoronavirus* | *Igacovirus* | *Avian coronavirus* | Guineafowl coronavirus (GfCoV) | Enteric disease | Ito et al. (1991) |
| Pheasant (*Phasianus colchicus*) | *Gammacoronavirus* | *Igacovirus* | *Avian coronavirus* | Pheasant coronavirus (PhCoV) | Respiratory and kidney disease | Spackman et al. (1983) |

CoVs in other species, including birds. Prior to that time, our knowledge of CoVs in avian species was limited largely to three birds of the order *Galliformes*, i.e., domestic fowl (*Gallus gallus*), turkeys (genus *Meleagris*) and pheasants (*Phasianidae*), with their infectious bronchitis virus (IBV), turkey coronavirus (TCoV), and pheasant coronavirus (PhCoV), respectively. These three viruses were considered for a long-time different species for several reasons such as the diverse pathotype (enterotropic or respirotropic), host range and genetic relatedness of the S protein (Cavanagh, 2007). This scenario radically changed after the discovery of several novel CoVs with high genetic diversity from different avian species and the novel rules for species designation of the Coronavirus Study Group (CSG https://talk.ictvonline.org/ictv-reports/ictv_9th_report/positive-sense-rna-viruses-2011/w/posrna_viruses/222/coronaviridae). All these viruses as well as analogous IBV-like CoVs detected in other birds including penguins, pigeons, peafowl, parrots, waterfowl, teal, quail, duck and whooper swan (Cavanagh et al., 2002; Circella et al., 2007; Domanska-Blicharz et al., 2014; Torres et al., 2013; Hughes et al., 2009; Liu et al., 2005; Wille et al., 2016; Jordan et al., 2015; Bande et al., 2016; Suryaman et al., 2019) have been assigned to the same viral species known as *Avian coronavirus* (ACoV) within the subgenus *Igacovirus* of genus *Gammacoronavirus*.

IBV and IBV-like strains are commonly detected in both gallinaceous and non-gallinaceous birds, also asymptomatically (Cavanagh, 2005). This might suggest that these species would act as wild reservoirs, spreading IBV strains over the world (de Wit et al., 2011). As for the huge economic impact of the disease it causes, IBV is one of the most studied CoVs over the last decades. IBV causes the infectious bronchitis (IB), a term adopted in 1931 for describing the main clinical characteristics of a transmissible respiratory disease of poultry detected for the first time in North Dakota (USA). IB has been now diagnosed worldwide and is one of the most important viral diseases of poultry characterised by respiratory signs, but it can also affect the kidneys and reproductive tract following viremia with a severity that differs depending on the involved viral strain (Cavanagh and Gelb, 2008). The disease also affects wild and ornamental birds (Liu et al., 2005; Chen et al., 2013).

IB control has been hampered by the intricate IBV evolution, which has been entailed, over the years, by the emergence of many different antigenic or genotypic types, commonly referred to as variants, with divergent molecular, biological, and antigenic properties. Being a CoV, IBV has, indeed, a considerable ability to change both by mutation and by homologous recombination events, which may cause, along with replicase stuttering or slippage, also insertions and deletions in the genome (Cavanagh and Gelb, 2008). If these mechanisms involve the hypervariable region S1, they frequently result in the emergence of new IBV variants. Although many new variants are not successful, a few may emerge, spread, causing devastating disease either worldwide or in limited geographic areas. Currently 32 lineages have been recognized, categorized into six genotypes (GI to GVI) (Valastro et al., 2016). Through their S protein, IBV and IBV-like viruses recognise as cellular host receptor the α2,3-linked sialic acid glycan, widely distributed in the respiratory tract and in several other host tissues, factor which may explain the tropism also for several organs of the infected host (Winter et al., 2006, 2008; Shahwan et al., 2013; Ambepitiya Wickramasinghe et al., 2011). Extensive use of vaccines has greatly contributed to the high variability of IBV strains thorough recombination between vaccine and field viruses and viral selection pressure resulting from vaccination and presence of partially immune birds (Gandon and Day, 2008; Gandon et al., 2001; Bande et al., 2017).

Important IBV-like strains are TCoV, responsible for enteritis in turkey (also known as bluecomb disease), guinea fowl coronavirus (GfCoV) and quail coronavirus (QCoV) responsible for fulminating enteric disease in guinea fowl and quail, respectively (Brown et al., 2016; Cavanagh, 2005; Liais et al., 2014).

TCoV, GfCoV and QCoV are evolutionarily distant from ACoV based on the S protein. While IBV is a primarily respiratory pathogen, TCoV causes gastrointestinal disease (Liais et al., 2014; Guy, 2008). Enterotropism has also been observed for some IBV serotypes; however, all IBV strains infect primarily the respiratory tract, resulting in mild to severe inflammation of the nasal and tracheal epithelia (Cavanagh, 2005, 2007). The S1 domain of the S protein is highly variable, with the amino acid sequences of IBV and TCoV from the USA sharing < 25 % sequence identity. Phylogenetic analysis of the S1 gene shows, indeed, grouping of IBV and IBV-like viruses on the one hand and TCoV-US, GfCoV and QCoV on the other hand (Ambepitiya Wickramasinghe et al., 2015a). Accordingly, the emergence of CoVs in turkeys in the USA was proposed to have resulted from recombination events involving IBVs and an as-yet-unidentified CoV donating a novel S gene. This switch contributed largely to determine the *in vivo* tissue tropism of TCoV and related viruses. Intriguingly, the S protein of these CoVs requires nonsialylated type 2 poly-LacNAc structures on N-glycan cores for binding. This is in marked contrast to the α2,3-linked sialic acid glycan binding of IBV and IBV-like viruses (Ambepitiya Wickramasinghe et al., 2015b).

The S1 subdomain of a TCoV isolate from France in 2008 (TCoV-FR) had only 42 % sequence identity to that of the TCoV-US strain (Maurel et al., 2011). This diversity was biologically evident by the prominent tropism for the epithelium of the bursa of Fabricius and only mild tropism for the small intestine of turkey. TCoV-FR S1 protein did not show, indeed, affinity for nonsialylated type 2 poly-LacNAc (Ambepitiya Wickramasinghe et al., 2015a). This genetic diversity between TCoVs is in accordance with several recombination events involving IBVs on different continents with several unknown CoVs. On the one hand, the S genes of GfCoV/Fr/2011 (isolated in France in 2011) and TCoV-US share significant genetic relationships, and thus these viruses must have acquired their S gene from a common ancestor. On the other hand, GfCoV/Fr/2011 and Fr TCoV have a very similar genetic background in other genes. Two recombination events may be responsible for the genesis of TCoV-US and Fr TCoV. A first event occurred between an IBV EU recipient strain and an unknown ACoV donor, resulting in a virus with a new S gene, whose evolution would have resulted in Fr TCoV and GfCoV/Fr/2011. A second recombination event involving a US IBV recipient and GfCoV/Fr/2011 would have generated US TCoV viruses, which share a stronger S gene similarity with GfCoV/Fr/2011 than with Fr TCoV (Brown et al., 2016).

Additional CoVs distinct from ACoVs and mainly circulating in ducks (duck coronavirus, DCoV), pigeons (pigeon coronavirus, PCoV), or geese (goose coronavirus, GCoV) have been identified (Cheng et al., 2013; Jonassen et al., 2005; Muradrasoli et al., 2010; Kim and Oem, 2014; Zhuang et al., 2015; Papineau et al., 2019). Although their genome seems to fulfill the official ICTV criteria required to distinguish a new species within the *Gammacoronavirus* genus, ICTV approval is still pending.

Historically, CoVs of birds were all included in the *Gammacoronavirus* genus and, in turn, all CoVs belonging to this genus were identified only in birds. However, this suggestion was rebutted by the evidence of a CoV belonging to the *Gammacoronavirus* genus in a beluga whale first discovered in 2008 (viral species *Beluga whale coronavirus SW1* species, subgenus *Cegacovirus*, genus *Gammacoronavirus*) (Mihindukulasuriya et al., 2008), and of three novel CoVs, BuCoV HKU1, ThCoV HKU12, and MuCoV HKU13 in birds of the order *Passeriformes*, namely bulbuls (*Pycnonotus jocosus*), thrushes (*Turdidae*) and munias (*Lonchura punctulate*), respectively, which did not cluster phylogenetically with extant CoVs identified in birds. These latter three viruses were distinct from known CoVs forming a unique cluster in the phylogenetic tree, which was the basis for generation of the *Deltacoronavirus* genus (Woo et al., 2009). Importantly, additional novel viruses belonging to this novel genus were detected in wild birds (Woo et al., 2012; Chu et al., 2011; Durães-Carvalho et al., 2015; Torres et al., 2016). These viruses cluster with previously unclassified CoVs detected in various Asian carnivores, i.e., the Asian leopard cat (*Prionailurus bengalensis*) and Chines ferret badger (*Nyctereutes procyonoides*) (Dong

et al., 2007). CoVs belonging to the *Betacoronavirus* genus, which are strictly related to mouse hepatitis virus (MHV), were also described in wild birds, including parrots, in Brazil (Durães-Carvalho et al., 2015). Interestingly, this was not the first detection of viruses belonging to the *Betacoronavirus* genus in birds. Often overlooked is the discovery over 38 years ago of a CoV from the Manx shearwater (*Puffinus puffinus*), a bird that visits the shores of Britain in summer (Nuttall and Harrap, 1982; Cavanagh et al., 2007). This virus was also related to MHV. However, at that time, considering the unusual finding and that the virus was isolated by passage of shearwater material in the brains of mice, it was speculated that the detected virus was an MHV strain already present in the mice before inoculation (Cavanagh, 2007).

### 3.2. Coronaviruses in bats

Bats are an ancient and heterogeneous group of ecologically important mammals, representing nearly a quarter of all mammalian diversity on earth. They belong to the order *Chiroptera* and further classified in two suborders *Yinpterochiroptera* and *Yangochiroptera*. The first includes the non-echolocating *Pteropodidae* family (megabats) and five echolocating *Rhinolophoidea* microbat superfamilies. *Yangochiroptera* contain thirteen echolocating microbat families (Tsagkogeorga et al., 2013). Bats are thought to host a large plethora of viruses. These include, amongst the others, lyssaviruses, filoviruses, henipaviruses, and reoviruses (Calisher et al., 2006).

Before SARS-CoV epidemic, bats were not known to host CoVs. Indeed, the first evidence of a bat CoV was published in 2005 (Poon et al., 2005). After the SARS epidemic, there was a boost in interest regarding searching for novel CoVs in various animals, including bats. To date, over 200 novel CoVs have been identified in bats and approximately 35 % of the bat virome sequenced to date is composed of CoVs (Chen et al., 2014). This data has been made available following the massive surveillance, coupled with the advent of next-generation sequencing (NGS) technology, which has been performed in wild animals (Woo et al., 2010; Banerjee et al., 2019). Just a small portion of these CoVs have been officially recognised by the ICTV; many others are still pending for official designation. CoV species detected in bats and officially recognised by the ICTV are listed in Table 3 and the following chapter reasonably discusses only officially recognized bat CoV species.

Bats can carry and transmit CoVs into local bat populations via migration even though little is known about the migratory patterns of these animals. Closely related CoVs can be detected in the same bat species living at locations separated by thousands of miles (Drexler et al., 2010) and different CoV species or genera can be found in different bat species living at the same roosting sites. However, some CoVs have been shown to be species-specific. Accordingly, regional patterns of bat CoV outbreaks at species level can be deduced from the population distribution of their respective bat hosts. Although bats seem to develop clinical diseases induced by several viruses and bacteria (Mühldorfer et al., 2011), generally CoVs do not cause apparently overt disease in these mammals, also experimentally. This phenomenon seems to be related with peculiar characteristics of their immune system (Ahn et al., 2019; Brook et al., 2020).

Based upon genomic data available so far, it is widely accepted that while birds represent the reservoir for CoVs belonging to genera *Gammacoronavirus* and *Deltacoronavirus*, bats are the natural reservoir for alpha- and betacoronaviruses. However, only betacoronaviruses of subgenera *Sarbecovirus*, *Merbecovirus*, *Nobecovirus* and *Hibecovirus* have been detected in bats so far. Given that several betacoronaviruses from the subgenus *Embecovirus* have been discovered in rodents, it was speculated that rodent CoVs may be the ancestors of currently circulating viruses belonging to this subgenus (Wong et al., 2019). CoVs have been detected at high frequency in bats in all continents, with alphacoronaviruses being more widespread than betacoronaviruses (Wong et al., 2019).

Subgenus *Colacovirus* (genus *Alphacoronavirus*) officially comprises the viral species *Bat coronavirus CDPHE15*, so far composed by two bat CoVs strains named CDPHE15/USA/2006 and *Myotis lucifugus* CoV (Myl-CoV), which share a 98.2 % nucleotide identity across the whole genome. Both strains have been detected in *Myotis lucifugus* bats (*Vespertilionidae*) also known as the northern American little brown bats. The former was detected in 2006 in Colorado (GenBank acc. no. KF430219), while the latter was reported in 2010 in Canada. This virus was identified in the intestines and lungs and associated with minimal pathology or inflammation (Subudhi et al., 2017). Subgenus *Decacovirus* (genus *Alphacoronavirus*) comprises the species *Rhinolophus ferrumequinum alphacoronavirus HuB-2013* composed so far by BtMs-AlphaCoV/GS2013 and BtRf-AlphaCoV/HuB2013 strains discovered in China in *Myotis* spp. and *Rhinolophus ferrumequinum* bats, respectively.

**Table 3**
Coronaviruses in bats[a].

| CoV genus | CoV subgenus | CoV species | Common ancestor with/ Possible descendant | Reference |
|---|---|---|---|---|
| *Alphacoronavirus* | *Colacovirus* | *Bat coronavirus CDPHE15* | Not determined | KF430219 |
| *Alphacoronavirus* | *Decacovirus* | *Rhinolophus ferrumequinum alphacoronavirus HuB-2013* | Not determined | Wu et al. (2016) |
| *Alphacoronavirus* | *Decacovirus* | *Bat coronavirus HKU10* | Not determined | Woo et al. (2007); Lau et al. (2012) |
| *Alphacoronavirus* | *Minunacovirus* | *Miniopterus bat coronavirus 1* | Not determined | Poon et al. (2005); Chu et al. (2008) |
| *Alphacoronavirus* | *Minunacovirus* | *Miniopterus bat coronavirus HK8* | Not determined | Poon et al. (2005); Chu et al. (2008) |
| *Alphacoronavirus* | *Myotacovirus* | *Myotis ricketti alphacoronavirus Sax-2011* | Not determined | Wu et al. (2016) |
| *Alphacoronavirus* | *Nyctacovirus* | *Nyctalus velutinus alphacoronavirus SC-2013* | Not determined | Wu et al. (2016) |
| *Alphacoronavirus* | *Pedacovirus* | *Scotophilus bat coronavirus 512* | Porcine epidemic diarrhoea virus | Tang et al. (2006) |
| *Alphacoronavirus* | *Rhinacovirus* | *Rhinolophus bat coronavirus HKU2* | Severe acute diarrhoea syndrome-coronavirus | Lau et al. (2005); Woo et al. (2006) |
| *Alphacoronavirus* | *Setracovirus* | *NL63-related bat coronavirus strain BtKYNL63−9b* | Human coronavirus NL63 | Tao et al. (2017) |
| *Betacoronavirus* | *Hibecovirus* | *Bat Hp-betacoronavirus Zhejiang2013* | Not determined | Wu et al. (2016) |
| *Betacoronavirus* | *Merbecovirus* | *Middle East respiratory syndrome-related coronavirus* | MERS-CoV | Lelli et al. (2013); De Benedictis et al. (2014); Corman et al. (2014a, b) |
| *Betacoronavirus* | *Merbecovirus* | *Pipistrellus bat coronavirus HKU5* | Not determined | Woo et al. (2006) |
| *Betacoronavirus* | *Merbecovirus* | *Tylonycteris bat coronavirus HKU4* | Not determined | Woo et al. (2006) |
| *Betacoronavirus* | *Nobecovirus* | *Rousettus bat coronavirus GCCDC1* | Not determined | Huang et al. (2016) |
| *Betacoronavirus* | *Nobecovirus* | *Rousettus bat coronavirus HKU9* | Not determined | Woo et al. (2007) |
| *Betacoronavirus* | *Sarbecovirus* | *Severe acute respiratory syndrome-related coronavirus* | SARS-CoV-1; SARS-CoV-2 | Li et al. (2005); Lau et al. (2005) |

[a] Only viral species officially recognised by the International Committee on Taxonomy of Viruses are reported.

These two viruses share very high sequence identities (higher than 98 %), which dramatically decrease in the S genes (only 85% nucleotide identity) (Wu et al., 2016). The viral species *Bat coronavirus* HKU10 (subgenus *Decacovirus*, genus *Alphacoronavirus*) was discovered in 2005 in China from *Rousettus* spp. and *Hipposideros* spp. bats. Additional strains from *Hipposideros* spp. bats were then discovered in 2006 and 2010 (Lau et al., 2012). A viral strain related to HKU10 was also identified in *Hipposideros pomona* in 2018 (GenBank acc. no. MN611523). Viral species *Miniopterus bat coronavirus 1 and Miniopterus bat coronavirus HK8* belong to subgenus *Minunacovirus* of genus *Alphacoronavirus* and were discovered in 2005 immediately after SARS epidemic. CoVs belonging to *Miniopterus bat coronavirus 1* are commonly detected in *Miniopterus* spp. (*Vespertilionidae*) including *Miniopterus magnater* (*Miniopterus* bat coronavirus 1A) and *Miniopterus pusillus* (*Miniopterus* bat coronavirus 1B) from China, whereas *Miniopterus bat coronavirus* HKU8 has been detected in *M. magnater*, *M. pusillus* and *Miniopterus schreibersii* (Poon et al., 2005; Chu et al., 2006, 2008). Co-infections of 1B and HKU8 were detected in seven *M. pusillus* specimens collected in 2004 and 2006 (Chu et al., 2008) but also in *Miniopterus* spp. bats in Kenya (Tong et al., 2009). *Myotis ricketti alphacoronavirus Sax-2011* (subgenus *Myotacovirus*, genus *Alphacoronavirus*) and *Nyctalus velutinus alphacoronavirus SC-2013* (subgenus *Nyctacovirus,* genus *Alphacoronavirus*) have been discovered in the last decade from samples collected in China from *Myotis ricketti* and *Nyctalus velutinus* bats (*Vespertilionidae*), respectively. *Scotophilus bat coronavirus 512 (*subgenus *Pedacovirus,* genus *Alphacoronavirus)* has been first discovered in 2005 from samples of *Scotophilus kuhlii*(*Vespertilionidae*). Antibodies specific to the N protein of *Scotophilus bat coronavirus 512* have been also detected in serum collected from three bat species, namely *Scotophilus kuhlii*, *Miniopterus fuliginosus*, and *Rhinolophus monoceros* (Chen et al., 2018). BtCoV/512/2005, the representative strain of this viral species, likely has a common evolutionary precursor with porcine epidemic diarrhoea virus (PEDV) (Banerjee et al., 2019) and this latter, indeed, is thought to be originated from a cross-species jump of a BtCoV/512/2005-like virus into pigs. A similar scenario is thought to have occurred with bat-CoV HKU2. This virus, identified for the first time from *Rhinolophus sinicus* (Lau et al., 2005; Woo et al., 2006) shares an 86 % sequence identity with severe acute diarrhoea syndrome-coronavirus (SADS-CoV) of pigs (Zhou et al., 2018). These two viruses are now included in the same viral species *Rhinolophus bat coronavirus* HKU2 (subgenus *Rhinacovirus,* genus *Alphacoronavirus*). Viral strains BtKYNL63-9a, BtKYNL63-9b, BtKYNL63-15 and BtKYNL63-9a, identified in 2010 in *Triaenops afer* bats from Kenya, form the viral species *NL63-related bat coronavirus strain BtKYNL63-9b* that is part of the subgenus *Setracovirus* (genus *Alphacoronavirus*) along with *Human coronavirus NL63* (Tao et al., 2017).

In this regard, a bat origin has been strongly suggested for two of the less-pathogenic HCoVs causing mild respiratory symptoms in immunocompetent people, namely HCoV-229E and HCoV-NL63, both belonging to the *Alphacoronavirus* genus. Whereas HCoV-229E (subgenus *Duvinacovirus*) recognises as direct ancestor an alphacoronavirus from alpacas, which in turn derives from 229E-related CoVs identified in hipposiderid bats (Corman et al., 2015), HCoV-NL63 is likely a recombinant virus originating from the distantly related 229E-related CoVs associated with hipposiderid bats and CoVs associated with *Triaenops afer* bats (Tao et al., 2017) (Table 1). The S protein of HCoV-NL63 is more closely related to that of 229E-related CoVs, whereas the rest of the genome with CoVs included in the *NL63-related bat coronavirus strain BtKYNL63-9b* species (Tao et al., 2017). Different from the bovine coronavirus (BCoV)-like viruses that cause enteric disease, in 2007 a novel alpaca CoV was associated to respiratory disease in California, USA. Full-length genome analysis showed that this respiratory alpaca CoV was closely related to the alphacoronavirus HCoV-229E (subgenus *Duvinacovirus*) (Crossley et al., 2012). More recently, close relatives of HCoV-229E were detected in African hipposiderid bats. Interestingly, both bat and alpaca viruses displayed an intact accessory gene ORF8 located at the genomic 3' end, while HCoV-229E retained only a conserved TRS preceding remnants of this ORF, suggesting its loss after acquisition of a 229E-related CoV by humans. Therefore, HCoV-229 is likely a descendant of the alpaca alphacoronavirus (Corman et al., 2015).

Strains forming the viral species *Bat Hp-betacoronavirus Zhejiang2013* (subgenus *Hibecovirus*, genus *Betacoronavirus*) were discovered in *Hipposideros pratti* bats from China in 2013 (Wu et al., 2016). Strain Ro-BatCoV GCCDC1 356 was identified from stools of *Rousettus leschenaultii*, a species of fruit bats (*Pteropodidae*) of southern Asia, which were collected in Yunnan province, China, in 2014 (Huang et al., 2016). Ro-BatCoV GCCDC1 356 shows a small intact ORF of 276 nucleotides embedded between the N and NS7a genes. This ORF has no homology to any known coronavirus, and the encoded protein exhibited 54.9 % amino acid identity with the p10 protein encoded by the first ORF of segment S1 of bat fusogenic orthoreoviruses (genus *Orthoreovirus*, species *Nelson Bay orthoreovirus*, also known as pteropine orthoreovirus). These viruses are double-stranded segmented RNA viruses, belonging to the family *Reoviridae*, and are able to cause severe pneumonia in humans (Chua et al., 2007; Lorusso et al., 2015). Ro-BatCoV GCCDC1 356 is included in the viral species *Rousettus bat coronavirus GCCDC1* within the subgenus *Nobecovirus*, genus *Betacoronavirus*.

*Rousettus bat coronavirus HKU9*, belonging to subgenus *Nobecovirus*, was also identified in *Rousettus leschenaultii* and in other bat species (Mendenhall et al., 2017). This virus was first detected in 2007 in Guangdong province in China (Woo et al., 2007). Subsequent studies suggested that the virus was widely distributed and is circulating in different bat species (Ge et al., 2012). CoVs from the BtHKU9-like cluster were also detected in *Hipposidereos commersoni* and *Rousettus aegyptiacus* bats in Kenya (Tong et al., 2009). Being a fruit bat, *Rousettus leschenaultii* has a wider flying range than most of the insectivorous bats in China, thus it may carry viruses over long distances. A comparison of the reported HKU9-CoV sequences showed a high genetic diversity within this viral species (Luo et al., 2018a, b; Lau et al., 2010; Ge et al., 2012).

When MERS-CoV was first isolated in the Middle East in 2012 and its genome sequenced, it was found that it was most closely related to Ty-BatCoV HKU4 discovered in *Tylonycteris pachypus* and Pi-BatCoV HKU5 discovered in *Pipistrellus abramus*, which were the only known members of subgenus *Merbecovirus* at that time. These two viruses are now the prototype strains of *Tylonycteris bat coronavirus HKU4* and *Pipistrellus bat coronavirus HKU5* viral species, respectively, within subgenus *Merbecovirus*, genus *Betacoronavirus*. Although MERS related CoVs (*MERS-rCoVs*) were lately discovered, MERS-CoV was much closer in the S1 region to HKU4-CoV than to MERS-rCoV or HKU5-CoV. Indeed, dipeptidyl peptidase 4 (DPP4), the receptor for MERS-CoV, is also the receptor for HKU4, but neither for HKU5 nor for early discovered MERS-rCoVs. However, HKU4 prefers bat DPP4 over human DPP4, whereas MERS-CoV shows the opposite trend (Yang et al., 2014). So far, HKU4-CoVs are only carried by *Tylonycteris* spp. bats (*T. pachypus* and *T. robustula*) and are relatively conserved; HKU5-CoVs are found in different *Pipistrellus* spp. bats, including *P. abramus*, *P. pipistrellus* and *P. minus* (Fan et al., 2019).

Due to the current SARS-CoV-2 pandemic, attention should be given to the viral species *Severe acute respiratory syndrome-related coronavirus* (*SARS-rCoV,*subgenus *Sarbecovirus,* genus *Betacoronavirus*) and *Middle East respiratory syndrome-related coronavirus* (*MERS-rCoV,* subgenus *Merbecovirus,* genus *Betacoronavirus*), which enclose SARS-CoV and MERS-CoV, the first two highly pathogenic CoVs that were discovered in humans. In 2002, at the beginning of the SARS epidemic, almost all early human index patients had animal exposure in a market place, in Guangdong province, before developing disease. After SARS-CoV was identified, its RNA and/or specific antibodies were found in masked palm civets (*Paguma larvata*) and animal handlers in a market place. However, later investigations of farmed and wild- caught civets

revealed that SARS-CoV strains found in market civets were transmitted to them by other wild animals (Tu et al., 2004; Kan et al., 2005). Subsequently, novel CoVs related to human SARS-CoV (SARS-rCoVs) were discovered in horseshoe bats (genus *Rhinolophus*) in China and Hong Kong (Li et al., 2005; Lau et al., 2005). These SARS-rCoVs showed genome sequence identity of 88–90 % among themselves and 87–92 % identity to human or civet SARS-CoV isolates. SARS-rCoVs were detected in *Rhinolophus* spp. bats of other regions of China (Tang et al., 2006; Woo et al., 2006; Yuan et al., 2010; Ge et al., 2013). SARS-rCoVs with higher genetic diversity with respect to Chinese strains were also detected in rhinolophid bats from Slovenia, Bulgaria and Italy in Europe (Drexler et al., 2010; Rihtaric et al., 2010; Balboni et al., 2011). CoVs related to SARS-rCoV were also detected in *Hipposideros* spp. and *Chaerophon* spp. bats from Ghana, Kenya and Nigeria (Hu et al., 2015). These evidences suggested that bats may be the natural hosts for SARS-CoV and that wild carnivores were only intermediate hosts. Although these SARS-rCoVs showed high sequence identity to SARS-CoV, they were demonstrated to be unable to bind to the human cell angiotensin converting enzyme II (ACE2) receptor, the receptor of SARS-CoV, as a consequence of deletions in their S protein (Ren et al., 2008). Besides, the theory of bat origin of SARS-CoV lacked a powerful support due to the failure of direct isolation of this virus from bats. Thus, considering that no direct progenitor of SARS-CoV was found in bats and that RNA recombination is the fuel for CoV evolution, it has been proposed that SARS-CoV emerged through recombination of bat SARS-rCoVs. This hypothesis was made after the evidence of a single bat cave in Yunnan, China, with very high CoVs diversity and considering that, within the identified CoVs, all genetic elements needed to form SARS-CoV have been identified in that single cave (Ge et al., 2013). Recombination analysis also strongly supported the hypothesis that the civet SARS-CoV strain SZ3 originated following a recombination event of two existing bat strains, WIV16 and Rf4092 (Hu et al., 2017). Moreover, WIV1, the closest relative to SARS-CoV that has been found in bats so far (more than 95 % nucleotide identity, higher than that of any other bat SARS-rCoVs (76–92 %)), likely arose through recombination of two other prevalent bat SARS-rCoV strains. The most frequent recombination breakpoints were within the S gene and upstream of ORF8, which encodes an accessory protein. These genes were also involved in the crucial adaptation pathways of SARS-CoV from bats to wild carnivores, from wild carnivores to humans, and from human to human (Cui et al., 2019). WIV1 has been shown to have the capacity to bind to the human, civet and bat cell ACE2 receptor (Ge et al., 2013). The isolation in cell-culture of a highly related SARS-CoV strain, coupled with the evidence of a functional S protein capable of using the same ACE2 receptor, provided robust and conclusive evidence for the bat origin of SARS-CoV. An additional SARS-rCoV strain has been shown, by reverse genetics studies, to have the capacity to bind to the human ACE2 receptor (Menachery et al., 2015).

Quite the opposite, a direct bat CoV highly related to MERS-CoV of humans was never detected. Indeed, the genome sequences of MERS-CoV in human and dromedaries possess only around 65–80 % nucleotide identities to those of the other members of subgenus *Merbecovirus* from different bats. Human MERS-CoVs were instead almost identical to MERS-CoVs identified in dromedary camels (*Camelus dromedaries*). Lately, genomic sequence analyses indicated that CoVs now belonging to the *MERS-rCoV* species were found in several bat species from two bat families, *Vespertilionidae* and *Nycteridae* (Lelli et al., 2013; De Benedictis et al., 2014; Corman et al., 2014a, b; Anthony et al., 2017; Moreno et al., 2017; Wong et al., 2019). However, none of these MERS-rCoVs is a direct progenitor of MERS-CoV, as their S proteins differ substantially from that of the human virus. The closest relative to MERS-CoV of humans and dromedary camels is MERS-rCoV strain *Neoromicia*/5038 isolated from *Neoromicia capensis* bats in South Africa (Geldenhuys et al., 2018, Table 1). A short sequence (around 200 nucleotides) of viral RNA identical to that of MERS-CoV was also detected in a *Taphozous perforates* bat in Saudi Arabia (Memish et al., 2013). Overall, although it is widely accepted that MERS-CoV ancestor is in bats, further studies are warranted in order to discover the precise mechanisms of its emergence in dromedary camels and humans. It was suggested that MERS-CoV ancestors had been circulating in bats for very long time. MERS-CoV has evolved to adapt to use human receptor and the DPP4-recognising bat coronaviruses like HKU4 may follow up, thereby posing a serious risk to human health. Recent MERS-rCoVs were shown to have the capacity to bind to the DPP4 as entry cell receptor as they acquired the S1 through recombination with HKU4-like viruses (Luo et al., 2018a, b).

As for the recent and threatening COVID-19 outbreak in humans, we certainly know that SARS-CoV-2 belongs to the species *SARS-rCoV* together with SARS-CoV from humans and SARS-rCoVs from wild carnivores and horseshoe bats (genus *Rhinolophus*) (Gorbalenya et al., 2020; Zhou et al., 2020; Wu et al., 2020). Epidemiological investigations revealed that many initial patients were exposed to wildlife at the Huanan seafood wholesale market (South China Seafood Market), which is the largest seafood market in central China (Lorusso et al., 2020).

SARS-CoV-2 has been assigned to an existing species of hundreds of known viruses largely isolated from bats. These viruses have names derived from SARS-CoV, but only the viral isolates originating from the 2002–2003 outbreak have been confirmed to cause SARS in humans (Gorbalenya et al., 2020). Importantly, it has also been confirmed that SARS-CoV-2 uses the ACE2 receptor through the receptor binding domain (RBD) of the S protein (Hoffmann et al., 2020; Zhou et al., 2020). Likely, also SARS-CoV-2 has a bat origin. According to genome sequences available so far, the most closely related virus (96.2 % of nucleotide sequence identity) to SARS-CoV-2 is strain BatCoVRaTG13 identified from a bat, *Rhinolophus affinis*, from Yunnan province, China, followed by SARS-rCoVs identified from pangolins (Tang et al., 2020). The receptor-binding spike protein of SARS-CoV-2 is highly divergent from other CoVs with less than 75 % nucleotide sequence identity to all previously described SARS-rCoVs, except for a 93.1 % nucleotide identity to BatCoVRaTG13 (Zhou et al., 2020). Although SARS-CoV-2 uses the ACE2 receptor, five out six critical amino acid residues in RBD were different between SARS-CoV-2 and SARS-CoV; the same residues were instead identical to those of pangolin SARS-rCoVs and, in turn, only one of these residues was identical to those of BatCoVRaTG13 (Tang et al., 2020), although this latter shows the highest nucleotide sequence identity with SARS-CoV-2 along the whole genome. Thus, it was tempting to speculate that SARS-CoV-2 RBD region might have originated from recent recombination event in pangolins or that SARS-CoV-2 and SARS-rCoVs of pangolins represent the result of coincidental evolution (Lam et al., 2020; Tang et al., 2020). Overall, it remains to be solved whether also SARS-CoV-2 needed an intermediate (and amplification) host before being able to infect humans as it was the case for SARS-CoV and other HCoVs. Since a mammal reservoir has not yet been identified, a prudent use of specific antigens is strongly recommended for serological diagnosis of SARS-CoV-2 in animals as cross-reactions with viruses of the *Alphacoronavirus* genus, widespread in animals, might occur (Sun and Meng, 2004).

### 3.3. Coronaviruses in rodents

Analogously to bats, but with a lesser extent, also rodents have been recently demonstrated to play a significant role in the evolution of CoV, in particular of those belonging to subgenus *Embecovirus* of genus *Betacoronavirus*. *Rodentia* (rodents) is the largest order of mammals with more than 2000 species worldwide, representing a major source of zoonotic infectious diseases (Han et al., 2015). For decades, only one species of coronavirus, *Murine coronavirus* (subgenus *Embecovirus*, genus *Betacoronavirus*), has been associated with rodents. The prototype virus, which was named mouse hepatitis virus (MHV), was first isolated in mice in 1949 (Cheever et al., 1949). A MHV variant was lately identified in rats in 1970 (Parker et al., 1970). Rat coronavirus (RCoV) causes epidemics of respiratory disease in laboratory rat colonies. The two

**Table 4**
Coronaviruses in domestic swine and associated diseases.

| CoV genus | CoV subgenus | CoV species | CoV common name(s) | Possible ancestor | Associated disease | Reference |
|---|---|---|---|---|---|---|
| *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Transmissible gastroenteritis virus (TGEV) | Canine coronavirus | Gastroenteritis | Doyle and Hutchings, 1946 Doyle and Hutchings (1946) |
| *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Porcine respiratory coronavirus (PRCoV) | TGEV | Respiratory disease | Pensaert et al. (1986) |
| *Alphacoronavirus* | *Pedacovirus* | *Porcine epidemic diarrhoea virus* | Porcine epidemic diarrhoea virus (PEDV) | Common bat ancestor with *Scotophilus* bat coronavirus 512/2005 | Gastroenteritis | Wood (1977) |
| *Alphacoronavirus* | *Rhinacovirus* | *Rhinolophus bat coronavirus HKU2* | Severe acute diarrhoea syndrome-coronavirus (SADS-CoV), swine enteric alphacoronavirus (SeACoV) | Common bat ancestor with *Rhinolophus bat coronavirus HKU2* | Gastroenteritis | Gong et al. (2017) |
| *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Porcine haemagglutinating encephalomyelitis virus (PHEV) | Bovine coronavirus | Neurological and/or enteric disease | Greig et al. (1962) |
| *Deltacoronavirus* | *Buldecovirus* | *Coronavirus HKU15* | Porcine deltacoronavirus (PDCoV) | Avian deltacoronaviruses (Sparrow CoV HKU15 × bulbul CoV HKU11) | Gastroenteritis | Wang et al., (2014) |

prototype strains of RCoV are sialodacryoadenitis virus (SDAV) and Parker's RCoV (RCoV-P) (Bhatt et al., 1972; Parker et al., 1970). Both strains infect the respiratory tract, and SDAV can also infect the eye, salivary and lacrimal glands. Young rats are especially susceptible to RCoV with the infection occurring in the lower respiratory tract and developing into interstitial pneumonia (Parker et al., 1970).

Together with feline infectious peritonitis virus (FIPV) and IBV, MHV has been one of the most strictly animal CoV studied ever. MHV is a natural pathogen of mice, normally infecting the liver, gastrointestinal tract, and central nervous system, causing a wide range of disease, including hepatitis, gastroenteritis, and acute and chronic encephalomyelitis. Importantly, it served as model for CoV replication and pathogenesis, with emphasis for neuro-invasion and neurovirulence (Weiss and Navas-Martin, 2005). As for the additional structural protein HE, some strains (such as JHM) of MHV contain the HE protein, while others (such as A59) do not (Shieh et al., 1989; Yokomori et al., 1989).

The role of rodents in the evolution of CoVs belonging to embecoviruses has been recently highlighted by means of the discovery of a novel betacoronavirus in Norway rats (*Rattus norvegicus*) in China. This virus forms a separate species named *China Rattus coronavirus HKU24* (ChRCoV HKU24) within the *Embecovirus* subgenus. Although designated as a novel species, this virus possessed genome characteristics that resemble to those of both *Betacoronavirus-1* and *Murine coronavirus*, suggesting that ChRCoV HKU24 represents the murine origin of *Betacoronavirus-1*, with interspecies transmission from rodents to other mammals having occurred centuries ago (Lau et al., 2015).

Genus *Betacoronavirus* consists of five subgenera, with bat CoVs being including in all but one of subgenus *Embecovirus*, where rodent, human and bovine CoVs are included (https://talk.ictvonline.org/taxonomy/). This supports the hypothesis that rodent CoVs were the ancestors of embecoviruses of other animals, while bats are the natural reservoirs for all other betacoronaviruses. Importantly, rodent CoVs are not restricted to genus *Betacoronavirus*. A deep virological screening was performed in 1465 rodents sampled in Zhejiang province, China, during 2011–2013, with nearly 2% of rodents testing positive for CoV (Wang et al., 2015). In particular, CoVs were detected in 10 striped field mice (*Apodemus agrarius*), 4 Norway rats, 14 lesser ricefield rats (*Rattus losea*), 1 Asian house rat (*Rattus tanezumi*) and 1 Chinese white-bellied rat (*Niviventer confucianus*). Amplicons of the replicase gene sequences were recovered from 21 (70 %) of the CoV RNA positive rodent samples described above and whole genome or nearly whole genome sequences (> 98 %) were recovered from 1 and 4 CoV positive samples, respectively. By means of whole genome sequence analysis, authors were able to identify a divergent alphacoronavirus, which was lately officially designated as species *Lucheng Rn rat coronavirus* (LRNV) within the subgenus *Luchacovirus*, and two novel betacoronaviruses termed Longquan Aa mouse coronavirus (LAMV) and Longquan Rl rat coronavirus (LRLV) and assigned to the two established species *Betacoronavirus-1* and *Murine coronavirus*, respectively (Wang et al., 2015). Moreover, LRNV seems to be a recombinant virus as its N protein gene is more closely related to those of the genus *Betacoronavirus*. Overall, the discovery of rodent-associated CoVs belonging to subgenera that are distinct from those including bat CoVs warrants further investigations upon the role played by rodents in the evolution and emergence of these viruses.

SARS-CoV replication has been studied in mice, Syrian golden and Chinese hamsters. The most severe symptoms of SARS were observed in aged animals. Indeed, aged mouse model of SARS-CoV has been generated (Gretebeck and Subbarao, 2015). Transgenic mice expressing human ACE2 were also developed to closely mimic SARS-CoV infection in humans. Some animal models have been tested and analysed on the genomic and proteomic level to study the pathogenesis of SARS-CoV. Therefore, we have reason to believe that such models would work also for SARS-CoV-2. Quite the opposite, studies have demonstrated that mice, guinea pigs and hamsters are not susceptible to experimental MERS-CoV infection, mainly because their homologous DPP4 molecules

do not function as receptors for MERS-CoV entry (Cockrell et al., 2014). The first mouse model of MERS infection reported in 2014 involved transducing animals with recombinant adenovirus 5 encoding human DPP4 (hDPP4) molecules intranasally, and this resulted in replication of MERS-CoV in the lungs. This mouse model also showed clinical symptoms of interstitial pneumonia, including inflammatory cell infiltration, and thickened alveolar and mild oedema (Song et al., 2019).

### 3.4. Coronaviruses in swine

Currently, six CoVs are circulating in swine (Table 4). These include four alphacoronaviruses, transmissible gastroenteritis virus of swine (TGEV) and its derivative porcine respiratory coronavirus (PRCoV) (subgenus *Tegacovirus*), porcine epidemic diarrhoea virus (PEDV) (subgenus *Pedacovirus*) and SADS-CoV (subgenus *Rhinacovirus*), one betacoronavirus, porcine haemagglutinating encephalomyelitis virus (PHEV) (subgenus *Embecovirus*), and one deltacoronavirus, porcine deltacoronavirus (PDCoV) (subgenus *Buldecovirus*). TGEV, PEDV, SADS-CoV and PDCoV are responsible for acute gastroenteritis in swine, with fatal infections in piglets born to seronegative sows, PRCoV causes a mild respiratory disease and PHEV is the causative agent of neurological and/or digestive disease in pigs (Mora-Díaz et al., 2019; Wang et al., 2019).

TGEV was first described in UK in 1950s, representing the oldest known swine CoV. TGEV and PRCoV are closely related to canine coronavirus (CCoV) and feline coronavirus (FCoV) forming with these carnivore CoVs a unique species, referred to as *Alphacoronavirus-1*. Based on the analysis of the accessory protein gene ORF3, it has been postulated that TGEV has originated from CCoV type II (CCoV-II), since while CCoV type I (CCoV-I) exhibits an intact gene, both CCoV-II and TGEV, which are strictly related in the S gene, have only remnants of ORF3 (Lorusso et al., 2008). PRCoV, in turn, has derived from TGEV through the deletion of ≈600 nucleotides at the 5' end of the S gene (corresponding to ≈200 amino acids at the N-terminus of the spike protein) and consequent change of the major tissue tropism from the enteric to the respiratory epithelium. This large deletion caused the loss of sialic acid binding activity that allows the attachment to mucins and mucin-type glycoproteins, so that TGEV but not PRCoV is able overcome the intestinal mucus barrier, having access to the gut mucosa (Schwegmann-Wessels and Herrler, 2006). PRCoV shares some epitopes for neutralising antibodies with TGEV, so that its extensive circulation in swine herds has resulted in a drastic reduction of TGE outbreaks worldwide.

PEDV was introduced in the pig population in the 1970s, likely as a consequence of a spillover event from bats. The virus was first described in Europe and had been primarily maintained as an endemic pathogen in European and Asian swine populations until its introduction into North America in 2013. PEDV is more strictly related to a *Scotophilus bat coronavirus 512* than to other known alphacoronaviruses, including TGEV and human alphacoronaviruses HCoV-229E and HCoV-NL63. Therefore, PEDV and BtCoV/512/2005 likely have a common evolutionary precursor and a CoV cross-species transmission may have occurred between bats and pigs (Banerjee et al., 2019). Accordingly, PEDV contains signature motifs at the 5′-untranslated region that are shared by bat CoVs, thus providing further support of the evolutionary origin of PEDV from bats and potential cross-species transmission (Huang et al., 2013). Currently, different PEDV genotypes are described based on the S gene: i) G1a PEDV, including classical European and Asian strains with moderate virulence; ii) G2 PEDV, also called "original US PEDV", comprising highly virulent strains that originated in Asia and are now widespread in the USA; iii) G1b PEDV, which is represented by the so-called S-INDEL strains, i.e., strains presenting insertions and deletions in the S gene that are associated with mild clinical outbreaks. These strains are natural recombinant PEDVs with a G2-like genomic backbone carrying an S1 region of G1a strains; iv) S1 N-terminal domain-deletion (NTD-del) strains that are G2-like strains containing a 194 to 216-aa deletion within the N-terminal domain of the S1 subunit, also associated to mild clinical forms (Hou and Wang, 2019). Recombinant strains between PEDV and TGEV have been also reported in Europe (Akimkin et al., 2016; Belsham et al., 2016; Boniotti et al., 2016).

SADV-CoV, now referred to as swine enteric alphacoronavirus (SeACoV), is another virulent swine enteric alphacoronavirus that originated from bats, sharing an 86 % sequence identity with a bat alphacoronavirus HKU2-CoV. Since viruses displaying a 96–98 % sequence identity to SADS-CoV were detected in *Rhinolophus* spp. bats, SADS-CoV and HKU2-CoV likely descend from a common ancestor (Zhou et al., 2018). Accordingly, both viruses now belong to the unique species *Rhinolophus bat coronavirus HKU2*.

In contrast, PHEV, which was first described in 1957 in nursery pigs with encephalomyelitis in Ontario, Canada, has not derived from bat CoVs, but its evolutionary history is tightly intermingled with other two closely related betacoronavirus, HCoV-OC43 and the oldest known BCoV, with which PHEV may have common ancestors (Vijgen et al., 2006) and is included in the same viral species, *Betacoronavirus-1* (Corman et al., 2018). Most probably, HCoV-OC43 and PHEV descend from a rodent betacoronavirus through preliminary adaptation to BCoV, from which they may have emerged in the context of a pandemic recorded historically at the end of the 19th century (Corman et al., 2018).

PDCoV was recently detected in 2012 in Hong Kong during CoV molecular surveillance in avian and mammalian species. This swine deltacoronavirus seems to recognise another different ancestor, likely emerging from a host-switching event between avian and mammal CoVs. The most closely related PDCoV relative has been identified in quail deltacoronavrus UAE-HKU30 and the virus has been proposed to be a recombinant between other two avian deltacoronaviruses, sparrow CoV HKU15 and bulbul CoV HKU11. All these deltacoronavirus are now members of the same species *Coronavirus HKU15* (Lau et al., 2018).

Pigs were found to be susceptible to experimental infection with the betacoronavirus MERS-CoV (Vergara-Alert et al., 2017), while SARS-CoV RNA was detected in pigs and wild boars (Chen et al., 2005; Wang et al., 2005). In contrast, a recent experimental infection demonstrated that pigs are not susceptible to SARS-CoV-2 (Shi et al., 2020).

Few studies have been carried out to assess the circulation of CoVs in farmed or free-ranging wild boars (*Sus scrofa*). Antibodies against TGEV/PRCoV were detected in some animals in Slovenia (Vengust et al., 2006) and Croatia (Roic et al., 2012) and PEDV RNA was demonstrated in South Korea (Lee et al., 2016). A wild boar sold at a live animal market of Guangzhou, China, was positive for SARS-CoV RNA (Wang et al., 2005).

### 3.5. Coronaviruses in ruminants

The main CoVs infecting ruminants are reported in Table 5. The oldest known ruminant CoV is BCoV, which is also the prototype of the species *Betacoronavirus-1* (subgenus *Embecovirus*, genus *Betacoronavirus*). This virus is able to cause a variety of clinical forms, including enteric disease with high mortality rates in neonate calves, winter disease (a severe enteric form) in lactating cows (Decaro et al., 2008b), and a respiratory disease, also known as shipping fever, in cattle of all ages, with a higher prevalence in 2–3 month-old calves (Decaro et al., 2008a). It was postulated that the presence of genetic signatures differentiates enteric and respiratory BCoVs (Hasoksuz et al., 1999), but it was ultimately evident that the same virus strain could be responsible for simultaneous appearance of enteric and respiratory disease in the same animals (Chouljenko et al., 2001).

It has been postulated that BCoV originated from a rodent CoV (Corman et al., 2018). Very recently, a novel CoV, representing a new viral species, referred to as *China Rattus coronavirus HKU24* (ChRCoV-HKU24), was detected in Norway rats in China. This virus was phylogenetically distinct from MHV and HCoV-HKU1 and displayed genome

**Table 5**
Coronaviruses in domestic and domesticated ruminants and associated diseases.

| Ruminant species | CoV genus | CoV subgenus | CoV species | CoV common name | Possible ancestor | Associated disease | Reference |
|---|---|---|---|---|---|---|---|
| Cattle (*Bos taurus*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Bovine coronavirus (BCoV) | *China Rattus coronavirus HKU24* | Calf diarrhoea, winter dysentery, and/or respiratory disease | Kaye et al., (1975) |
| Sheep (*Ovis aries*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | BCoV-like coronavirus | BCoV | Gastroenteritis? | Tzipori et al. (1978) |
| Goat (*Capra hircus*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | BCoV-like coronavirus | BCoV | Gastroenteritis? | Muñoz et al. (1996) |
| Water buffalo (*Bubalus bubalis*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Bubaline coronavirus (BuCoV) | BCoV | Gastroenteritis | Decaro et al. (2008c) |
| Llama (*Lama lama*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | BCoV-like coronavirus | BCoV | Gastroenteritis | Cebra et al. (2003) |
| Alpaca (*Vicugna pacos*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Alpaca (beta)coronavirus (ACoV) | BCoV | Gastroenteritis and/or respiratory disease | Cebra et al. (2003) |
| Dromedary camel (*Camelus dromedarius*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Dromedary camel coronavirus UAE-HKU-23 (DcCoV UAE-HKU23) | BCoV? | Gastroenteritis | Woo et al., 2013 |
| Dromedary camel (*Camelus dromedarius*) | *Betacoronavirus* | *Merbecovirus* | *Middle East respiratory syndrome-related coronavirus* | Dromedary camel MERS-CoV | Common bat ancestor with *Neoromicia capensis* coronavirus | Mild respiratory disease | Haagmans et al. (2014) |
| Alpaca (*Vicugna pacos*) | *Alphacoronavirus* | *Duvinacovirus* | *Human coronavirus 229E* | Alpaca (alpha)coronavirus (ACoV) | African hypposiderid bat coronavirus | Mild respiratory disease | Crossley et al. (2012) |
| Dromedary camel (*Camelus dromedaries*) | *Alphacoronavirus* | *Duvinacovirus* | *Human coronavirus 229E* | Dromedary camel alphacoronavirus | African hypposiderid bat coronavirus | unknown | Sabir et al. (2016) |

features that were intermediate between BCoV and MHV. Therefore, ChRCoV HKU24 may represent the murine origin of BCoV and rodents are likely an important reservoir for ancestors of subgenus *Embecovirus* (Lau et al., 2015).

BCoV is paradigmatic of how CoVs are able to cross the interspecies barriers, establishing its derivatives as separate viral lineages affecting the respiratory and/or enteric tract of humans (HCoV-OC43), swine (PHEV), horses (equine coronavirus, ECoV), and dogs (canine respiratory coronavirus, CRCoV). A number of BCoV-related viruses, all currently included in the unique species *Betacoronavirus-1*, have been detected in the enteric and/or respiratory tract of domestic and wild ruminants. These BCoV-like CoVs include viruses of domestic and domesticated ruminants that were reported in sheep and goats (Reinhardt et al., 1995; Yang et al., 2008), water buffalo (*Bubalus bubalis*) (Decaro et al., 2008c), llamas (*Lama lama*) and alpacas (*Vicugna pacos*) (Cebra et al., 2003; Jin et al., 2007). In the wild, BCoV-like CoVs were demonstrated in six species of the *Cervidae* family, which are caribou/reindeer (*Rangifer tarandus caribou*), elk/wapiti (*Cervus elephus*), samber deer (*Cervus unicolor*), white-tailed deer (*Odocoileus virginianus*), sika deer (*Cervus nippon yesoensis*) and water deer (*Hydropotes inermis*) (Amer, 2018). Similar viruses were also found to circulate in the giraffe (*Giraffa camelopardalis*) (Hasoksuz et al., 2007), several species of antelopes (Alekseev et al., 2008; Chung et al., 2011), wisent (*Bison bonasus*), Himalayan tahr (*Hemitragus jemlahicus*) (Chung et al., 2011), and dromedary camels (*Camelus dromedarius*) (Woo et al., 2014). The last strain, detected in the United Arab Emirates and consequently named dromedary camel coronavirus UAE-HKU-23 (DcCoV UAE-HKU23), was slightly divergent from other BCoV-like viruses (Woo et al., 2014).

Dromedary camels are susceptible to MERS-CoV infection, developing asymptomatic infections or mild upper respiratory disease, so that they are considered the natural host of MERS-CoV, with adult animals in many countries in the Middle East as well as in North and East Africa showing > 90 % seroprevalence to the virus (Hemida et al., 2017b). Although human-to-human transmission has occurred outside Middle East due to travel-associated patients with MERS and has caused large clusters of human cases within healthcare facilities in Saudi Arabia, Jordan and United Arab Emirates, it remains inefficient and sustained community transmission has not being documented so far, thus suggesting multiple virus introduction into the human population by infected dromedaries (Hemida et al., 2017b). More recently, a phylogenetic study of 173 MERS-CoV full-genome sequences revealed recombination signatures that defined five major phylogenetically stable lineages, all of which contained human and camel MERS-CoV sequences (Sabir et al., 2016). In the same study, an alphacoronavirus strictly related to HCoV-229E was found in the respiratory tract of dromedary camels of Saudi Arabia (Sabir et al., 2016). Although some studies ruled out the susceptibility of other domestic ruminants to MERS-CoV (Reusken et al., 2013; Adney et al., 2016), a recent study detected specific antibodies and RNA in sera and nasal secretions, respectively, of domestic ruminants raised in Africa, including sheep, goats and cattle (Kandeil et al., 2019). Llamas were found to be susceptible to experimental infections with MERS-CoV (Vergara-Alert et al., 2017).

### 3.6. Coronaviruses in equines

The only CoV that has been so far known in horses is ECoV, which is a BCoV-descendant betacoronavirus (subgenus *Embecovirus*). ECoV was first isolated from the faeces of a diarrhoeic foal in 1999 (ECoV-NC99) in North Carolina, USA (Guy et al., 2000), and was initially believed to only affect foals. Since 2010, the virus has been recognised in Japan, Europe and the USA as a new, clinically important, enteric virus of adult horses (Pusterla et al., 2018).

Despite MERS-CoV was successfully adapted to the *in-vitro* growth in equine cell lines (Meyer et al., 2015), serological and molecular

**Table 6**
Coronaviruses in domestic and domesticated carnivores and associated diseases.

| Carnivore species | CoV genus | CoV subgenus | CoV species | CoV common name | Possible ancestor | Associated disease | Reference |
|---|---|---|---|---|---|---|---|
| Dog (*Canis lupus familiaris*) | *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Canine coronavirus I (CCoV-I) | Unknown | Mild enteritis | Pratelli et al. (2004) |
| Dog (*Canis lupus familiaris* | *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Canine coronavirus II (CCoV-II) | Canine coronavirus I | Mild enteritis, systemic disease (pantropic strains) | Binn et al. (1974) |
| Cat (*Felis catus*) | *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Feline coronavirus I (FCoV-I) | Unknown | Mild enteritis, asymptomatic infection (FECV), feline infectious peritonitis (FIPV) | Jakob, 1914Jacob (1914), Pedersen et al. (1984) |
| Cat (*Felis catus*) | *Alphacoronavirus* | *Tegacovirus* | *Alphacoronavirus-1* | Feline coronavirus II (FCoV-II) | Feline coronavirus I × Canine coronavirus II | Mild enteritis, asymptomatic infection (FECV), feline infectious peritonitis (FIPV) | Jacob (1914), Pedersen et al. (1984) |
| American mink (*Neovison vison*), European mink (*Mustela lutreola*) | *Alphacoronavirus* | *Minacovirus* | *Mink coronavirus 1* | Mink coronavirus (MCV) | Unknown | Epizootic catarrhal gastroenteritis | Larsen and Gorham (1975) |
| Ferret (*Mustela putorius furo*) | *Alphacoronavirus* | *Minacovirus* | *Ferret coronavirus* | Ferret coronavirus (FRCoV) | Unknown | Epizootic catarrhal enteritis (FRECV), systemic disease (FRSCV) | Williams et al. (2000) |
| Dog (*Canis lupus familiaris*) | *Betacoronavirus* | *Embecovirus* | *Betacoronavirus-1* | Canine respiratory coronavirus (CRCoV) | Bovine coronavirus | Canine infectious respiratory disease | Erles et al. (2003) |

investigations have demonstrated that horses are not naturally infected by MERS-CoV (Meyer et al., 2015; Hemida et al., 2017a), nor they are susceptible to experimental infection (Adney et al., 2016; Vergara-Alert et al., 2017). However, surprisingly, MERS-CoV RNA was detected in respiratory specimens of three donkeys of 42 from Egypt (Kandeil et al., 2019), a finding that requires further confirmation.

A molecular survey aimed to assess CoV circulation in horses in Saudi Arabia and Oman has detected two DcCoV UAE-HKU23 strains in enteric samples of horses (Hemida et al., 2017a).

Scarce data are available about CoV circulation in donkeys. These equids are susceptible to ECoV infection since positive RT-PCR results were obtained from a donkey in Ireland (Nemoto et al., 2019). In addition, three donkeys (7.1 %) of 42 from Egypt tested positive for MERS-CoV RNA in their nasal secretions (Kandeil et al., 2019).

### 3.7. Coronaviruses in carnivores

CoVs of carnivores are listed in Table 6. Three CoVs are known in dogs, i.e., two alphacoronaviruses of the subgenus *Tegacovirus*, namely CCoV-I and CCoV-II, and one betacoronavirus of the subgenus *Embecovirus*, namely CRCoV.

CCoVs (species *Alphacoronav-irus-1*) are commonly responsible for mild, self-limiting enteritis in pups (Decaro and Buonavoglia, 2008). Although they are neglected viruses and vaccination is not recommended due to the absence of an effective challenge model, two independent studies have demonstrated their significant involvement in the onset of acute canine enteritis (Duijvestijn et al., 2016; Dowgier et al., 2017). The evolutionary history of CCoVs is tightly intermingled with that of TGEV and FCoVs. CCoV-I possesses a divergent spike protein and the intact form of an additional gene, ORF3, whose remnants are present in CCoV-II and, at a lesser extent, in TGEV. Therefore, CCoV-II has likely emerged as a consequence of recombination between the original CCoV-I and an unknown CoV in the S gene and of progressive loss of ORF3 (Lorusso et al., 2008). A further recombination occurred in the very 5' end of the S gene between CCoV-II and TGEV, giving rise to back recombinant CCoV-II strains, also known as TGEV-like CCoVs, having a spike protein N-terminus of TGEV in a CCoV-II backbone (Decaro et al., 2009, 2010). Consequently, the CCoV taxonomy was revised, with classical and TGEV-like strains being referred to as CCoV-IIa and CCoV-IIb, respectively. While CCoVs are usually involved in mild forms of diarrhoea, there are some hypervirulent strains that are associated to severe, haemorrhagic, sometimes fatal gastroenteritis. In addition, CCoV-IIa strains, designated pantropic CCoV, that are able to spread systemically and cause severe disease and the death of infected dogs have been reported in Italy (Buonavoglia et al., 2006; Alfano et al., 2020), other European countries (Decaro et al., 2013) and South America (Pinto et al., 2014). Genomic sequences from pantropic CCoVs were analysed, but no obvious genetic signatures that may have caused the switch in pathogenicity were found (Decaro and Buonavoglia, 2011; Decaro et al., 2013).

Different from CCoV-I and CCoV-II, the betacoronavirus CRCoV is associated with mild respiratory signs and has been proposed as an etiological agent of canine infectious respiratory disease (CIRD) together with other viral and bacterial agents (Decaro and Buonavoglia, 2008). The virus was first detected firstly in UK in 2003 (Erles et al., 2003) and subsequently in other European and extra-European countries (Decaro et al., 2007, 2016; Mitchell et al., 2017; Maboni et al., 2019; Piewbang et al., 2019; More et al., 2020). Being a BCoV derivative, CRCoV possesses the same genomic organisation, with some differences in accessory ORFs located between the S and E protein genes. In particular, while some CRCoVs possess a unique 8.8 kDa protein gene directly downstream of the S protein gene, other canine BCoV-like CoVs display the canonical set of BCoV accessory genes but with truncated forms of the 4.8 kDa protein gene (Lorusso et al., 2009).

In cats, two *Alphacornavirus-1* genotypes are known, namely FCoV type I (FCoV-I) and FCoV type II (FCoV-II), the latter being generated as

a consequence of recombination events between CCoV-II and FCoV-I that generated viruses with a CCoV-II genomic region, encompassing ORF1b, ORF2 (S gene), ORF3abc, ORF4 (E gene), and partial ORF5 (M gene), in the context of an FCoV-I backbone (Pedersen, 2014). Both genotypes are involved in the development of feline infectious peritonitis (FIP), a perivascular pyogranulomatosis of cats that may occur in two clinical forms, effusive and non-effusive FIP, which are characterised by prevalence of effusions in the body cavities and of pyogranulomatous lesion in organs, respectively. FIP occurs as a consequence of a change in tissue tropism of an enteric FCoV strain (feline enteric coronavirus, FECV), infecting enterocytes of the intestinal villi, that acquires the ability to infect monocytes/macrophages switching to the more virulent FIPV, which is responsible for systemic infections and dysregulation of the proinflammatory cytokines (Addie et al., 2009). The changes responsible for the pathogenetic shift have been investigated for many decades, being suggested to be variably represented by point mutations located in the S gene (Rottier et al., 2005), deletion/insertion in the group-specific genes 3c (Vennema et al., 1998; Chang et al., 2010), 7b (Vennema et al., 1998) or 7a (Kennedy et al., 2001a). However, none of these differences appeared to consistently correlate with disease phenotype. More recent studies have identified specific genetic signatures in the S gene of FCoV-I that are implicated in monocyte/macrophage tropism. Two amino acid substitutions, M1058 L and/or S1060A, corresponding to nucleotide mutations A23531 T/C and T23537 G, respectively, in the viral genome, together distinguished FCoVs found in the tissues of FIP cats from those found in the faeces of healthy cats without FIP in > 95 % of cases (Chang et al., 2012). However, subsequent studies concluded that these mutations are likely to be markers of systemic FCoV infection rather than FIP per se (Porter et al., 2014; Barker et al., 2017).

Two alphacoronaviruses, both belonging to subgenus *Minacovirus*, are currently known in mustelids, namely *Mink coronavirus 1* (MCoV-1) and *Ferret coronavirus* (FRCoV). MCoV-1 has been recently identified as the etiological agent of mink epizootic catarrhal gastroenteritis (ECG), an infectious disease of farmed American (*Neovison vison*) and European (*Mustela lutreola*) mink first described in 1975 (Larsen and Gorham, 1975) and later affecting several million mink in different countries (Vlasova et al., 2011). The disease is observed at greater frequency in mink of ≥4 months and is characterised by seasonality, high morbidity (approaching 100%) and low mortality (< 5%). Recent full-genome analysis demonstrated that MCoV-1 is phylogenetically distant from CCoVs and FCoVs, being closely related to FRCoV (Vlasova et al., 2011). Presently, the two viruses are considered separate species within subgenus *Minacovirus* (https://talk.ictvonline.org/taxonomy/).

FRCoV has been recognised as the causative agent of epizootic catarrhal enteritis (ECE), first described in 1993 in domestic ferrets (*Mustela putorius furo*) in the eastern part of the USA (Williams et al., 2000) and subsequently reported in domestic and laboratory ferrets throughout the world (Murray et al., 2010). Analogous to FCoV, FRCoV exists in two different pathotypes: i) ferret enteric coronavirus (FRECV) is associated to ECE, a highly contagious diarrhoeal disease also known as green slime disease, which affects mainly young ferrets with morbidity and mortality rates similar to those of ECG; ii) ferret systemic coronavirus (FRSCV) is responsible for a systemic diseases of ferrets, which is characterised by pyogranulomatous perivasculitis and peritonitis resembling to those of FIP (Murray et al., 2010). Similar to FIP, Wise et al. (2010) have shown that FRECV and FRSCV differ significantly in spike protein and that deletions in FRCoV 3c may also correlate with the severe pathotype of FRSCV. Recombination in the S, 3c and E genes between different FRCoV has been also reported (Lamers et al., 2016).

Different CoVs were found to circulate in wild carnivores. CCoVs were detected in wolves (*Canis lupus*), red foxes (*Vulpes vulpes*), Eurasian otters (*Lutra lutra*), common genets (*Genetta genetta*) (Alfano et al., 2019; Rosa et al., 2020). CCoV-like viruses were also found in African wild carnivores, including spotted hyenas (*Crocuta crocuta*) and silver-backed jackals (*Canis mesomelas*) (Goller et al., 2013). FCoVs have a wide circulation in non-domestic felids (Kennedy et al., 2002, 2003), with FIP cases being reported in servals (*Felis serval*) (Juan-Salles et al., 1997), cheetah (*Acinonyx jubatus*) (Kennedy et al., 2001b), mountain lion (*Puma concolor*) (Stephenson et al., 2013), and European wildcat (*Felis silvestris*) (Watt et al., 1993).

Divergent *Alphacoronavirus-1* viruses were detected in Chinese ferret badger (*Nyctereutes procyonoides*) and raccoon dog (*Melogale moschata*) (Dong et al., 2007). The same study reported the identification in Asian leopard cat (*Prionailurus bengalensis*) and Chinese ferret badger of an unclassified CoV, which was closely related to gammacoronaviruses in most parts of the genome, whereas the S gene displayed the highest sequence identity to alphacoronaviruses (Dong et al., 2007). With the discovery of deltacoronaviruses, these viruses were later included in this novel genus along with avian and porcine strains (Woo et al., 2009; Wang et al., 2014).

Some domestic and wild carnivores are also susceptible to SARS-CoV infection. While the potential natural reservoirs are horseshoe bats, SARS-like CoV strains were found to be widespread in masked palm civets (*Paguma larvata*) and raccoon dogs, which were suspected to be intermediate hosts (Guan et al., 2003). Full-genomic comparative analysis has shown that SARS-like CoVs isolated from palm civets are under strong selective pressure and are genetically most closely related to SARS-CoV strains infecting humans early in the outbreaks (Song et al., 2005). Sequence analysis of the SARS-CoV-like virus in masked palm civets indicated that they were highly homologous to human SARS-CoV with nucleotide identity over 99.6 %, indicating the virus has not been circulating in the population of masked palm civets for a very long time (Shi and Hu, 2008). A Chinese ferret-badger (*Melogale moschata*) was found to have neutralising antibodies against SARS-CoV (Guan et al., 2003), whereas SARS-CoV RNA was detected in naturally infected cats and red foxes (*Vulpes vulpes*), but not in domestic dogs (Wang et al., 2005). There was, however, a single dog testing positive for SARS-CoV (https://apps.who.int/iris/bitstream/handle/10665/70863/WHO_CDS_CSR_GAR_2003.11_eng.pdf). Among carnivores, SARS-CoV-2 is able to infect cats, ferrets and, at a lesser extent, dogs (Shi et al., 2020).

### 3.8. Coronaviruses in other species

In 2008, a highly divergent CoV, tentatively named SW1, was discovered a deceased beluga wale *(Delphinapterus leucas*) with pneumonia and hepatic necrosis (Mihindukulasuriya et al., 2008). The virus was only distantly related to IBV, so that it now represents the prototype of the single mammalian CoV species belonging to the genus *Gammacoronavirus*, namely *Beluga wale coronavirus SW1* (BWCoV-SW1) (subgenus *Cegacovirus*). Few years later, related gammacoronaviruses were retrieved from faecal samples of three Indo-Pacific bottlenose dolphins (*Tursiops aduncus*), which were named bottlenose dolphin CoV (BdCoV) HKU22. Comparative genome analysis showed that BdCoV-HKU22 and BWCoV-SW1 have similar genome characteristics and structures, displaying a 98 % nucleotide sequence identity each to other (Woo et al., 2014).

A novel betacoronavirus distantly related to MERS-CoV was detected in the faeces of European hedgehogs (*Erinaceus europaeus*), an insectivorous mammal belonging to a related order of *Chiroptera*, from Germany. The virus was tentatively referred to as *Erinaceus* CoV (EriCoV) (Corman et al., 2014b) and CoVs found in hedgehogs in France, England and Italy had an identity from 92% to 98 % with the EriCoV (Monchatre-Leroy et al., 2017; Saldanha et al., 2019; Delogu et al., 2020). These hedgehog CoVs are are now included in a unique species, *Hedgehog coronavirus 1* (subgenus *Merbecovirus*). The virus was not associated to any form of disease, so that Western European hedgehog is a reservoir host of EriCoV in the absence of apparent disease, suggesting that hedgehogs in addition to bats may contribute to the evolution of *Merbecovirus* (Saldanha et al., 2019). A slightly

divergent *Merbecovirus* was later found in Amur hedgehogs (*Erinaceus amurensis*) in China and was poposed as a prototype of a separate species, namely *Erinaceus amurensis* hedgehog coronavirus HKU31 (Ea-HedCoV HKU31) (Lau et al., 2019). A novel coronavirus, named Wénchéng shrew coronavirus (WESV) was detected in shrews (*Suncus murinus*) in China (Wang et al., 2017). WESV is highly divergent from other alphacoronaviruses, exhibiting less than 71.1 % amino acid similarity to any known members of the genus *Alphacoronavirus* in the coronavirus-wide conserved domains of the replicase polyprotein pp1ab and less than 61.3 % amino acid similarity to the other three coronavirus genera. However, taking into account the current ICTV criteria, WESV is sufficiently divergent to be considered a distinct member of the genus *Alphacoronavirus*, but not a new genus of the subfamily *Orthocornavirinae* (Wang et al., 2017).

## 4. Synoptic summary

CoVs have been known in veterinary medicine since many decades; some of these viruses, such as IBV, swine enteric CoVs, BCoV and mustelid CoVs, can cause diseases that have a great impact on the farm industry. Other CoVs, namely FIPV, FRSCV and MHV, cause severe disease in companion (cats, ferrets) or laboratory (mice) animals. Animal CoVs are paradigmatic on how CoVs evolve through accumulation of point mutations and homologous (and heterologous) recombination, generating different genotypes and pathotypes. These virus variants may have different antigenic properties, escaping the host immunity induced by vaccines, as is the case of IBV. Alternatively, they may have a different tissue tropism in the same host that can increase or decrease the virus pathogenicity, as observed for the virus pairs FECV/FIPV or FRECV/FRSCV and TGEV/PRCoV, respectively. In other circumstances, the CoV evolution may result in the switch of the host range from one animal species to another one or from animals to humans. The former event is well documented in veterinary medicine, with a plethora of viruses being originated from IBV and BCoV that adapted to different animal species. However, the most interesting scenario is the jumping and further adaptation of an animal CoV to humans. There is increasing evidence that all HCoVs currently known recognise an animal origin, with bat or rodent CoVs being the most probable ancestors. In most instances, it was suggested that other mammals served as intermediate hosts prior to final adaptation to humans, i.e., alpacas and cattle for the low-pathogenic HCoV-229E and HCoV-OC43, respectively, and wild carnivores and dromedary camels for the high-pathogenic SARS-CoV and MERS-CoV, respectively. Other two HCoVs, namely HCoV-NL63 and HCoV-HKU1, were likely derived from bats and rodents, respectively, but whether this transmission required an intermediate mammalian host is presently unknown. The origin of SARS-CoV-2 should be zoonotic, since highly related sequences were detected in bats, but a definitive intermediate host has been not identified so far. What should we expect from the current pandemic? When HCoV-OC43 crossed the species barrier to infect humans from domestic livestock around 1890, an epidemic of respiratory infection was recorded. Even though, several years later, influenza was suspected to be the cause of it, in that pandemic involvement of central nervous system was more pronounced than in other influenza outbreaks. This evidence is further supported by molecular studies claiming that the most recent common ancestor of BCoV and HCoV-OC43 emerged around 1890 (Vijgen et al., 2005) and by the fact that HCoV-OC43 can be neuroinvasive (Arbour et al., 2000). Likely, HCoV-OC43 crossed species to infect dogs becoming established in this species as CRCoV (Lorusso et al., 2009). A similar scenario could be observed with SARS-CoV-2 with dogs and, at a greater extent, cats. Apparently, cats represent, within the domestic animals which have been experimentally infected, the host, together with ferrets, which is able to sustain more efficiently SARS-CoV-2 replication (Shi et al., 2020). Furthermore, based on structural studies and biochemical experiments, SARS-CoV-2 seems to have an RBD that binds with high affinity to ACE2 also from ferrets and cats (Andersen et al., 2020). Reasonably, a full comprehension of the animal CoV molecular evolution, host range and pathobiology is beneficial to better understand the mechanism driving the emergence and adaptation to humans of zoonotic CoVs.

## 5. Conclusions

The present review has highlighted that in the last 18 years, also thanks to the availability of novel sequencing technologies, we have witnessed a large number of novel CoVs being discovered in a large number of animals. Truth to be told, it was difficult for us to summarise, in this single review, all CoVs detected in animals and the tight interaction existing between them and human CoVs. Among animals, it is evident that bats are the group of mammals that harbor the largest number of CoVs and that many other animal CoVs recognise their ancestors in bat CoVs.

In an excellent review (Cui et al., 2019) written by the group coordinated by Dr. Zheng-Li Shi of the Wuhan Institute of Virology, Hubei, (China), city infamously known for being the epicenter and origin of the COVID-19 outbreak, authors stated that "*...given the prevalence and great genetic diversity of bat SARS-rCoVs, their close coexistence and the frequent recombination of CoVs, it is expected that novel variants will emerge in the future*". This forecasting statement was not surprising to coronavirologists and it was not, importantly, surprising to those scientists that daily deal with the plethora of viruses existing at the human/animal health interface. Although scientists were well aware of this hazard, no substantial actions were taken forward the limitations of strict and repeated contacts between humans and wildlife. Indeed, whereas biological mechanisms underlying viral evolution are not under human control, social and cultural habits can be modified accordingly through a deep and pounding informative campaigns. If to the human habits we sum the impact of modern agricultural practices and urbanization and the decrease of vital space for wildlife, it is quite easy to understand that, if countermeasures are not taken, we will face novel serious health emergencies of animal origin in the following years with tremendous social and economic impact on our lives. As clearly demonstrated by the SARS-CoV-2 emergence, CoVs are the main characters of this intricate puzzle characterised by the interactions of viral biological mechanisms and human habits.

Our review was reasonably prepared also to highlight (once more!) how CoVs originate, evolve, jump, mutate and infect their host. Could have the current COVID-19 outbreak been avoided? Answering this question is not relevant now, but actions to avoid the next viral spillover from animals to humans is certainly a priority. This task needs to be coupled with massive genomic surveillance in wild animals not limited to CoVs. Massive sequencing of SARS-CoV-2 strains detected in humans and CoVs of wildlife will help further assess the origin of this novel human pandemic and plan future measures able to reduce the risk of emergence of new CoV spillover events. However, additional tasks should be provisionally addressed in order to reduce the risk of future CoV pandemic like the current one. These include: i) prevention of animal-to-human infections through a ban of the wet markets and a more friendly management of the environment; ii) studies on CoV-host interactions to be performed both *in vitro* (cell cultures, ex-vivo explants of the respiratory tract) and *in vivo* (animals susceptible to SARS-CoV-2 infection); iii) development of new anticoronaviral drugs and evaluation of their efficacy in cell cultures and animal models.

## Acknowlegment

Funding were provided by the Italian Ministry of Health, IZS AM 08/19 RC , Ricerca Corrente 2019 "NGS e diagnostica molecolare in Sanità Animale: Fast D2", recipient Alessio Lorusso.

## Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.vetmic.2020.108693.

## References


Addie, D.D., Belák, S., Boucraut-Baralon, C., Egberink, H., Frymus, T., Gruffydd-Jones, T., Hartmann, K., Hosie, M.J., Lloret, A., Lutz, H., Marsilio, F., Pennisi, M.G., Radford, A.D., Thiry, E., Truyen, U., Horzinek, M.C., 2009. Feline infectious peritonitis. ABCD guidelines on prevention and management. J. Feline Med. Surg. 11, 594–604.

Adney, D.R., Brown, V.R., Porter, S.M., Bielefeldt-Ohmann, H., Hartwig, A.E., Bowen, R.A., 2016. Inoculation of goats, sheep, and horses with MERS-CoV does not result in productive viral shedding. Viruses 8, E230.

Ahn, M., Anderson, D.E., Zhang, Q., Tan, C.W., Lim, B.L., Luko, K., Wen, M., Chia, W.N., Mani, S., Wang, L.C., Ng, J.H.J., Sobota, R.M., Dutertre, C.A., Ginhoux, F., Shi, Z.L., Irving, A.T., Wang, L.F., 2019. Dampened NLRP3-mediated inflammation in bats and implications for a special viral reservoir host. Nat. Microbiol. 4, 789–799.

Akimkin, V., Beer, M., Blome, S., Hanke, D., Hoper, D., Jenckel, M., Pohlmann, A., 2016. New chimeric porcine coronavirus in swine feces, Germany, 2012. Emerg. Infect. Dis. 22, 1314–1315.

Alekseev, K.P., Vlasova, A.N., Jung, K., Hasoksuz, M., Zhang, X., Halpin, R., Wang, S., Ghedin, E., Spiro, D., Saif, L.J., 2008. Bovine-like coronaviruses isolated from four species of captive wild ruminants are homologous to bovine coronaviruses, based on complete genomic sequences. J. Virol. 82, 12422–12431.

Alfano, F., Dowgier, G., Valentino, M.P., Galiero, G., Tinelli, A., Nicola, D., Fusco, G., 2019. Dentification of pantropic canine coronavirus in a wolf (*Canis lupus italicus*) in Italy. J. Wildl. Dis. 55, 504–508.

Alfano, F., Fusco, G., Mari, V., Occhiogrosso, L., Miletti, G., Brunetti, R., Galiero, G., Desario, C., Cirilli, M., Decaro, N., 2020. Circulation of pantropic canine coronavirus in autochthonous and imported dogs, Italy. Transbound. Emerg. Dis. https://doi.org/10.1111/tbed.13542.

Ambepitiya Wickramasinghe, I.N., de Vries, R.P., Gröne, A., de Haan, C.A., Verheije, M.H., 2011. Binding of avian coronavirus spike proteins to host factors reflects virus tropism and pathogenicity. J. Virol. 85, 8903–8912.

Ambepitiya Wickramasinghe, I.N., de Vries, R.P., Weerts, E.A., van Beurden, S.J., Peng, W., McBride, R., Ducatez, M., Guy, J., Brown, P., Eterradossi, N., Gröne, A., Paulson, J.C., Verheije, M.H., 2015a. Novel receptor specificity of avian gammacoronaviruses that cause enteritis. J. Virol. 89, 8783–8792.

Ambepitiya Wickramasinghe, I.N., de Vries, R.P., Eggert, A.M., Wandee, N., de Haan, C.A., Gröne, A., Verheije, M.H., 2015b. Host tissue and glycan binding specificities of avian viral attachment proteins using novel avian tissue microarrays. PLoS One 10, e0128893.

Amer, H.M., 2018. Bovine-like coronaviruses in domestic and wild ruminants. Anim. Health Res. Rev. 19, 113–124.

Andersen, K.G., Rambaut, A., Lipkin, W.I., Holmes, E.C., Garry, R.F., 2020. The proximal origin of SARS-CoV-2. Nat. Med. https://doi.org/10.1038/s41591-020-0820-9.

Anthony, S.J., Gilardi, K., Menachery, V.D., Goldstein, T., Ssebide, B., Mbabazi, R., Navarrete-Macias, I., Liang, E., Wells, H., Hicks, A., Petrosov, A., Byarugaba, D.K., Debbink, K., Dinnon, K.H., Scobey, T., Randell, S.H., Yount, B.L., Cranfield, M., Johnson, C.K., Baric, R.S., Lipkin, W.I., Mazet, J.A., 2017. Further evidence for bats as the evolutionary source of Middle East respiratory syndrome coronavirus. mBio 8, e00373–17.

Arbour, N., Day, R., Newcombe, J., Talbot, P.J., 2000. Neuroinvasion by human respiratory coronaviruses. J. Virol. 74, 8913–8921.

Balboni, A., Palladini, A., Bogliani, G., Battilani, M., 2011. Detection of a virus related to betacoronaviruses in Italian greater horseshoe bats. Epidemiol. Infect. 139, 216–219.

Bande, F., Arshad, S.S., Omar, A.R., 2016. Isolation and metagenomic identification of avian leukosis virus associated with mortality in broiler chicken. Adv. Virol. 2016, 9058403.

Bande, F., Arshad, S.S., Omar, A.R., Hair-Bejo, M., Mahmuda, A., Nair, V., 2017. Global distributions and strain diversity of avian infectious bronchitis virus: a review. Anim. Health Res. Rev. 18, 70–83.

Banner, L.R., Lai, M.M., 1991. Random nature of coronavirus RNA recombination in the absence of selection pressure. Virology 185, 441–445.

Banerjee, A., Kulcsar, K., Misra, V., Frieman, M., Mossman, K., 2019. Bats and coronaviruses. Viruses 11, E41.

Barker, E.N., Stranieri, A., Helps, C.R., Porter, E.L., Davidson, A.D., Day, M.J., Knowles, T., Kipar, A., Tasker, S., 2017. Limitations of using feline coronavirus spike protein gene mutations to diagnose feline infectious peritonitis. Vet. Res. 48, 60.

Beach, J.R., Schalm, O.W., 1936. A filterable virus, distinct from that of laryngotracheitis, the cause of a respiratory disease of chicks. Poultry Sci. 15, 199–206.

Beaudette, F.R., Hudson, C.B., 1937. Cultivation of the virus of infectious bronchitis. J. Am. Vet. Med. Assoc. 90, 51–60.

Beena, V., Saikumar, G., 2019. Emerging horizon for bat borne viral zoonoses. Virus Dis. 30 (321), 328.

Belsham, G.J., Rasmussen, T.B., Normann, P., Vaclavek, P., Strandbygaard, B., Botner, A., 2016. Characterization of a novel chimeric swine enteric coronavirus from diseased pigs in Central Eastern Europe in 2016. Transbound. Emerg. Dis. 63, 595–601.

Bhatt, P.N., Percy, D.H., Jonas, A.M., 1972. Characterization of the virus of sialodacryoadenitis of rats: a member of the coronavirus group. J. Infect. Dis. 126, 123–130.

Binn, L.N., Lazar, E.C., Keenan, K.P., Huxsoll, D.L., Marchwicki, R.H., Strano, A.J., 1974. Recovery and characterization of a coronavirus from military dogs with diarrhea. Proc. Annu Meet. U. S. Anim. Health Assoc. 78, 359–366.

Boniotti, M.B., Papetti, A., Lavazza, A., Alborali, G., Sozzi, E., Chiapponi, C., Faccini, S., Bonilauri, P., Cordioli, P., Marthaler, D., 2016. Porcine epidemic diarrhea virus and discovery of a recombinant swine enteric coronavirus, Italy. Emerg. Infect. Dis. 22, 83–87.

Brian, D.A., Baric, R.S., 2005. Coronavirus genome structure and replication. Curr. Top. Microbiol. Immunol. 287, 1–30.

Brook, C.E., Boots, M., Chandran, K., Dobson, A.P., Drosten, C., Graham, A.L., Grenfell, B.T., Müller, M.A., Ng, M., Wang, L.F., van Leeuwen, A., 2020. Accelerated viral dynamics in bat cell lines, with implications for zoonotic emergence. Elife 9, e48401.

Brown, P.A., Touzain, F., Briand, F.X., Gouilh, A.M., Courtillon, C., Allee, C., Lemaitre, E., De Boisseson, C., Blanchard, Y., Eterradossi, N., 2016. First complete genome sequence of European turkey coronavirus suggests complex recombination history related with US turkey and guinea fowl coronaviruses. J. Gen. Virol. 97, 110–120.

Buonavoglia, C., Decaro, N., Martella, V., Elia, G., Campolo, M., Desario, C., Castagnaro, M., Tempesta, M., 2006. Canine coronavirus highly pathogenic for dogs. Emerg. Infect. Dis. 12, 492–494.

Calisher, C.H., Childs, J.E., Field, H.E., Holmes, K.V., Schountz, T., 2006. Bats: important reservoir hosts of emerging viruses. Clin. Microbiol. Rev. 19, 531–545.

Cavanagh, D., 2005. Coronaviruses in poultry and other birds. Avian Pathol. 34, 439–448.

Cavanagh, D., 2007. Coronavirus avian infectious bronchitis virus. Vet. Res. 38, 281–297.

Cavanagh, D., Gelb, J., 2008. Infectious bronchitis. In: Saif, Y.M., Fadly, A.M., Glisson, J.R., McDougald, L.R., Nolan, L.K., Swayne, D.E. (Eds.), Diseases of Poultry, 12th edition. Blackwell Publishing, Ames, Iowa, Ames, IA, pp. 117–135.

Cavanagh, D., Mawditt, K., Welchmand Dde, B., Britton, P., Gough, R.E., 2002. Coronaviruses from pheasants (*Phasianus colchicus*) are genetically closely related to coronaviruses of domestic fowl (Infectious Bronchitis Virus) and turkeys. Avian Pathol. 31, 81–93.

Cebra, C.K., Mattson, D.E., Baker, R.J., Sonn, R.J., Dearing, P.L., 2003. Potential pathogens in feces from unweaned llamas and alpacas with diarrhea. J. Am. Vet. Med. Assoc. 223, 1806–1808.

Chang, H.W., de Groot, R.J., Egberink, H.F., Rottier, P.J., 2010. Feline infectious peritonitis: insights into feline coronavirus pathobiogenesis and epidemiology based on genetic analysis of the viral 3c gene. J. Gen. Virol. 91, 415–420.

Chang, H.W., Egberink, H.F., Halpin, R., Spiro, D.J., Rottier, P.J., 2012. Spike protein fusion peptide and feline coronavirus virulence. Emerg. Infect. Dis. 8, 1089–1095.

Cheever, F.S., Daniels, J.B., Pappenheimer, A.M., Bailey, O.T., 1949. A murine virus JHM causing disseminated encephalomyelitis with extensive destruction of myelin. Isolation and biological properties of the virus. J. Exp. Med. 90, 181–194.

Chen, W., Yan, M., Yang, L., Ding, B., He, B., Wang, Y., Liu, X., Liu, C., Zhu, H., You, B., Huang, S., Zhang, J., Mu, F., Xiang, Z., Feng, X., Wen, J., Fang, J., Yu, J., Yang, H., Wang, J., 2005. SARS-associated coronavirus transmitted from human to pig. Emerg. Infect. Dis. 11, 446–448.

Chen, G.Q., Zhuang, Q.Y., Wang, K.C., Liu, S., Shao, J.Z., Jiang, W.M., Hou, G.Y., Li, J.P., Yu, J.M., Li, Y.P., Chen, J.M., 2013. Identification and survey of a novel avian coronavirus in ducks. PLoS One e72918.

Chen, L., Liu, B., Yang, J., Jin, Q., 2014. DBatVir: The Database of Bat-associated Viruses. pp. bau021.

Chen, Y.N., Su, B.G., Chen, H.C., Chou, C.H., Cheng, H.C., 2018. Detection of specific antibodies to the nucleocapsid protein fragments of severe acute respiratory syndrome-coronavirus and Scotophilus bat coronavirus-512 in three insectivorous bat species. Taiwan Vet. J. 44, 179–188.

Chouljenko, V.N., Lin, X.Q., Storz, J., Kousoulas, K.G., Gorbalenya, A.E., 2001. Comparison of genomic and predicted amino acid sequences of respiratory and enteric bovine coronaviruses isolated from the same animal with fatal shipping pneumonia. J. Gen. Virol. 82, 2927–2933.

Chu, D.K., Poon, L.L., Chan, K.H., Chen, H., Guan, Y., Yuen, K.Y., Peiris, J.S., 2006. Coronaviruses in bent-winged bats (*Miniopterus* spp.). J. Gen. Virol. 87, 2461–2466.

Chu, D.K., Peiris, J.S., Chen, H., Guan, Y., Poon, L.L., 2008. Genomic characterizations of bat coronaviruses (1A, 1B and HKU8) and evidence for co-infections in Miniopterus bats. J. Gen. Virol. 89, 1282–1287.

Chu, D.K., Leung, C.Y., Gilbert, M., Joyner, P.H., Ng, E.M., Tse, T.M., Guan, Y., Peiris, J.S., Poon, L.L., 2011. Avian coronavirus in wild aquatic birds. J. Virol. 85, 12815–12820.

Chua, K.B., Crameri, G., Hyatt, A., Yu, M., Tompang, M.R., Rosli, J., McEachern, J., Crameri, S., Kumarasamy, V., Eaton, B.T., Wang, L.F., 2007. A previously unknown reovirus of bat origin is associated with an acute respiratory disease in humans. Proc. Natl. Acad. Sci. U. S. A. 104 (27), 11424–11429.

Chung, J.Y., Kim, H.R., Bae, Y.C., Lee, O.S., Oem, J.K., 2011. Detection and characterization of bovine-like coronaviruses from four species of zoo ruminants. Vet. Microbiol. 148, 396–401.

Circella, E., Camarda, A., Martella, V., Bruni, G., Lavazza, A., Buonavoglia, C., 2007. Coronavirus associated with an enteric syndrome on a quail farm. Avian Pathol. 36, 251–258.

Cockrell, A.S., Peck, K.M., Yount, B.L., Agnihothram, S.S., Scobey, T., Curnes, N.R., Baric, R.S., Heise, M.T., 2014. Mouse dipeptidyl peptidase 4 is not a functional receptor for Middle East respiratory syndrome coronavirus infection. J. Virol. 88, 5195–5199.

Corman, V.M., Ithete, N.L., Richards, L.R., Schoeman, M.C., Preiser, W., Drosten, C., Drexler, J.F., 2014a. Rooting the phylogenetic tree of Middle East respiratory syndrome coronavirus by characterization of a conspecific virus from an African bat. J. Virol. 88, 11297–11303.

Corman, V.M., Kallies, R., Philipps, H., Göpner, G., Müller, M.A., Eckerle, I., Brünink, S., Drosten, C., Drexler, J.F., 2014b. Characterization of a novel betacoronavirus related to middle East respiratory syndrome coronavirus in European hedgehogs. J. Virol. 88, 717–724.

Corman, V.M., Baldwin, H.J., Tateno, A.F., Zerbinati, R.M., Annan, A., Owusu, M., Nkrumah, E.E., Maganga, G.D., Oppong, S., Adu-Sarkodie, Y., Vallo, P., da Silva Filho, L.V., Leroy, E.M., Thiel, V., van der Hoek, L., Poon, L.L., Tschapka, M., Drosten,

C., Drexler, J.F., 2015. Evidence for an ancestral association of human coronavirus 229E with bats. J. Virol. 89, 11858–11870.
Corman, V.M., Muth, D., Niemeyer, D., Drosten, C., 2018. Hosts and sources of endemic human coronaviruses. Adv. Virus Res. 100, 163–188.
Crossley, B.M., Mock, R.E., Callison, S.A., Hietala, S.K., 2012. Identification and characterization of a novel alpaca respiratory coronavirus most closely related to the human coronavirus 229E. Viruses 4, 3689–3700.
Cui, J., Li, F., Shi, Z.L., 2019. Origin and evolution of pathogenic coronaviruses. Nat. Rev. Microbiol 17, 181–192.
de Wit, J.J., Cook, J.K.A., van der Heijden, H.M.J.F., 2011. Infectious bronchitis virus variants: a review of the history, current situation and control measures. Avian Pathol 40, 223–235.
De Benedictis, P., Marciano, S., Scaravelli, D., Priori, P., Zecchin, B., Capua, I., Monne, I., Cattoli, G., 2014. Alpha and lineage C betaCoV infections in Italian bats. Virus Genes 48, 366–371.
Decaro, N., Buonavoglia, C., 2011. Canine coronavirus: not only an enteric pathogen. Vet. Clin. North Am. Small Anim. Pract. 41, 1121–1132.
Decaro, N., Desario, C., Elia, G., Mari, V., Lucente, M.S., Cordioli, P., Colaianni, M.L., Martella, V., Buonavoglia, C., 2007. Serological and molecular evidence that canine respiratory coronavirus is circulating in Italy. Vet. Microbiol. 121, 225–230.
Decaro, N., Campolo, M., Desario, C., Cirone, F., D'abramo, M., Lorusso, E., Greco, G., Mari, V., Colaianni, M.L., Elia, G., Martella, V., Buonavoglia, C., 2008a. Respiratory disease associated with bovine coronavirus infection in cattle herds in Southern Italy. J. Vet. Diagn. Invest. 20, 28–32.
Decaro, N., Mari, V., Desario, C., Campolo, M., Elia, G., Martella, V., Greco, G., Cirone, F., Colaianni, M.L., Cordioli, P., Buonavoglia, C., 2008b. Severe outbreak of bovine coronavirus infection in dairy cattle during the warmer season. Vet. Microbiol. 126, 30–39.
Decaro, N., Martella, V., Elia, G., Campolo, M., Mari, V., Desario, C., Lucente, M.S., Lorusso, A., Greco, G., Corrente, M., Tempesta, M., Buonavoglia, C., 2008c. Biological and genetic analysis of a bovine-like coronavirus isolated from water buffalo (*Bubalus bubalis*) calves. Virology 370, 213–222.
Decaro, N., Mari, V., Campolo, M., Lorusso, A., Camero, M., Elia, G., Martella, V., Cordioli, P., Enjuanes, L., Buonavoglia, C., 2009. Recombinant canine coronaviruses related to transmissible gastroenteritis virus of swine are circulating in dogs. J. Virol. 83, 1532–1537.
Decaro, N., Buonavoglia, C., 2008. An update on canine coronaviruses: viral evolution and pathobiology. Vet. Microbiol. 132, 221–234.
Decaro, N., Mari, V., Elia, G., Addie, D.D., Camero, M., Lucente, M.S., Martella, V., Buonavoglia, C., 2010. Recombinant canine coronaviruses in dogs, Europe. Emerg. Infect. Dis. 16, 41–47.
Decaro, N., Cordonnier, N., Demeter, Z., Egberink, H., Elia, G., Grellet, A., Le Poder, S., Mari, V., Martella, V., Ntafis, V., von Reitzenstein, M., Rottier, P.J., Rusvai, M., Shields, S., Xylouri, E., Xu, Z., Buonavoglia, C., 2013. European surveillance for pantropic canine coronavirus. J. Clin. Microbiol. 51, 83–88.
Decaro, N., Mari, V., Larocca, V., Losurdo, M., Lanave, G., Lucente, M.S., Corrente, M., Catella, C., Bo, S., Elia, G., Torre, G., Grandolfo, E., Martella, V., Buonavoglia, C., 2016. Molecular surveillance of traditional and emerging pathogens associated with canine infectious respiratory disease. Vet. Microbiol. 192, 21–25.
Delogu, M., Cotti, C., Lelli, D., Sozzi, E., Trogu, T., Lavazza, A., Garuti, G., Castrucci, M.R., Vaccari, G., De Marco, M.A., Moreno, A., 2020. Eco-Virological Preliminary Study of Potentially Emerging Pathogens in Hedgehogs (Erinaceus europaeus) Recovered at a Wildlife Treatment and Rehabilitation Center in Northern Italy. Animals (Basel).
Doyle, L.P., Hutchings, L.M., 1946. A transmissible gastroenteritis in pigs. J. Am. Vet. Med. A. 108, 257–259.
Decaro, N., Martella, V., Saif, L.J., Buonavoglia, C., 2020. COVID-19 from veterinary medicine and one health perspectives: what animal coronaviruses have taught us. Res. Vet. Sci. 131, 21–23.
Domanska-Blicharz, K., Jacukowicz, A., Lisowska, A., Wyrostek, K., Minta, Z., 2014. Detection and molecular characterization of infectious bronchitis-like viruses in wild bird populations. Avian Pathol. 43, 406–413.
Dong, B.Q., Liu, W., Fan, X.H., Vijaykrishna, D., Tang, X.C., Gao, F., Li, L.F., Li, G.J., Zhang, J.X., Peiris, J.S.M., Smith, G.J.D., Chen, H., Guan, Y., 2007. Detection of a novel and highly divergent coronavirus from Asian leopard cats and Chinese ferret badgers in southern China. J. Virol. 81, 6920–6926.
Dowgier, G., Lorusso, E., Decaro, N., Desario, C., Mari, V., Lucente, M.S., Lanave, G., Buonavoglia, C., Elia, G., 2017. A molecular survey for selected viral enteropathogens revealed a limited role of Canine circovirus in the development of canine acute gastroenteritis. Vet. Microbiol. 204, 54–58.
Drexler, J.F., Gloza-Rausch, F., Glende, J., Corman, V.M., Muth, D., Goettsche, M., Seebens, A., Niedrig, M., Pfefferle, S., Yordanov, S., Zhelyazkov, L., Hermanns, U., Vallo, P., Lukashev, A., Muller, M.A., Deng, H., Herrler, G., Drosten, C., 2010. Genomic characterization of severe acute respiratory syndrome-related coronavirus in European bats and classification of coronaviruses based on partial RNA-dependent RNA polymerase gene sequences. J. Virol. 84, 11336–11349.
Duijvestijn, M., Mughini-Gras, L., Schuurman, N., Schijf, W., Wagenaar, J.A., Egberink, H., 2016. Enteropathogen infections in canine puppies: (Co-)occurrence, clinical relevance and risk factors. Vet. Microbiol. 195, 115–122.
Durães-Carvalho, R., Caserta, L.C., Barnabé, A.C.S., Martini, M.C., Ferreira, H.L., Felippe, P.A.N., Santos, M.B., Arns, C.W., 2015. Coronaviruses detected in Brazilian wild birds reveal close evolutionary relationships with beta- and deltacoronaviruses isolated from mammals. J. Mol. Evol. 81, 21–23.
Erles, K., Toomey, C., Brooks, H.W., Brownlie, J., 2003. Detection of a group 2 coronavirus in dogs with canine infectious respiratory disease. Virology 310, 216–223.
Fan, Y., Zhao, K., Shi, Z.L., Zhou, P., 2019. Bat coronaviruses in China. Viruses 2 (3), E210 11.
Fouchier, R.A., Hartwig, N.G., Bestebroer, T.M., Niemeyer, B., de Jong, J.C., Simon, J.H., Osterhaus, A.D., 2004. A previously undescribed coronavirus associated with respiratory disease in humans. Proc. Natl. Acad. Sci. U. S. A. 101, 6212–6216.
Gandon, S., Day, T., 2008. Evidences of parasite evolution after vaccination. Vaccine 26 (Suppl. 3), C4–7.
Gandon, S., Mackinnon, M.J., Nee, S., Read, A.F., 2001. Imperfect vaccines and the evolution of pathogen virulence. Nature 414, 751–756.
Greig, A.S., Mitchell, D., Corner, A.H., Bannister, G.L., Meads, E.B., Julian, R.J., 1962. A hemagglutinating virus producing encephalomyelitis in baby pigs. Can. J. Comp. Med. Vet. Sci. 26, 49–56.
Ge, X., Li, Y., Yang, X., Zhang, H., Zhou, P., Zhang, Y., Shi, Z., 2012. Metagenomic analysis of viruses from bat fecal samples reveals many novel viruses in insectivorous bats in China. J. Virol. 86, 4620–4630.
Ge, X.Y., Li, J.L., Yang, X.L., Chmura, A.A., Zhu, G., Epstein, J.H., 2013. Isolation and characterization of a bat SARS-like coronavirus that uses the ACE2 receptor. Nature 503, 535–538.
Geldenhuys, M., Mortlock, M., Weyer, J., Bezuidt, O., Seamark, E.C.J., Kearney, T., Gleasner, C., Erkkila, T.H., Cui, H., Markotter, W., 2018. A metagenomic viral discovery approach identifies potential zoonotic and novel mammalian viruses in *Neoromicia* bats within South Africa. PLoS One 13, e0194527.
Gong, L., Li, J., Zhou, Q., Xu, Z., Chen, L., Zhang, Y., Xue, C., Wen, Z., Cao, Y., 2017. A new bat-HKU2-like coronavirus in swine, China. Emerg. Infect. Dis. 23.
Goller, K.V., Fickel, J., Hofer, H., Beier, S., East, M.L., 2013. Coronavirus genotype diversity and prevalence of infection in wild carnivores in the Serengeti National Park, Tanzania. Arch. Virol. 158, 729–734.
Gorbalenya, A.E., Baker, S.C., Baric, R.S., de Groot, R.J., Drosten, C., Gulyaeva, A.A., Haagmans, B.L., Lauber, C., Leontovich, A.M., Neuman, B.W., Penzar, D., Perlman, S., Poon, L.L.M., Samborskiy, D., Sidorov, I.A., Sola, I., Ziebuhr, J., 2020. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Coronaviridae study group of the international committee on taxonomy of viruses. Nat. Microbiol. 5, 536–544.
Gretebeck, L.M., Subbarao, K., 2015. Animal models for SARS and MERS coronaviruses. Curr. Opin. Virol. 13, 123–129.
Guan, Y., Zheng, B.J., He, Y.Q., Liu, X.L., Zhuang, Z.X., Cheung, C.L., Luo, S.W., Li, P.H., Zhang, L.J., Guan, Y.J., Butt, K.M., Wong, K.L., Chan, K.W., Lim, W., Shortridge, K.F., Yuen, K.Y., Peiris, J.S., Poon, L.L., 2003. Isolation and characterization of viruses related to the SARS coronavirus from animals in southern China. Science 302, 276–278.
Guarner, J., 2020. Three emerging coronaviruses in two decades. Am. J. Clin. Pathol. 153, 420–421.
Guy, J.S., 2008. Turkey coronavirus enteritis. In: Saif, Y.M., Fadly, A.M., Glisson, J.R., MacDougald, L.R., Nolan, L.K., Swayne, D.E. (Eds.), Diseases of Poultry, 12th ed. Blackwell Publishing, Oxford, United Kingdom, pp. 330–338.
Guy, J.S., Breslin, J.J., Breuhaus, B., Vivrette, S., Smith, L.G., 2000. Characterization of a coronavirus isolated from a diarrheic foal. J. Clin. Microbiol. 38, 4523–4526.
Hamre, D., Procknow, J.J., 1966. A new virus isolated from the human respiratory tract. Proc. Soc. Exp. Biol. Med. 121, 190–193.
Haagmans, B.L., Al Dhahiry, S.H., Reusken, C.B., Raj, V.S., Galiano, M., Myers, R., Godeke, G.J., Jonges, M., Farag, E., Diab, A., Ghobashy, H., Alhajri, F., Al-Thani, M., Al-Marri, S.A., Al Romaihi, H.E., Al Khal, A., Bermingham, A., Osterhaus, A.D., AlHajri, M.M., Koopmans, M.P., 2014. Middle East respiratory syndrome coronavirus in dromedary camels: an outbreak investigation. Lancet Infect Dis. 14, 140–145.
Han, B.A., Schmidt, J.P., Bowden, S.E., Drake, J.M., 2015. Rodent reservoirs of future zoonotic diseases. Proc. Natl. Acad. Sci. U. S. A. 112, 7039–7044.
Hasoksuz, M., Lathrop, S.L., Gadfield, K.L., Saif, L.J., 1999. Isolation of bovine respiratory coronaviruses from feedlot cattle and comparison of their biological and antigenic properties with bovine enteric coronaviruses. Am. J. Vet. Res. 60, 1227–1233.
Hasoksuz, M., Alekseev, K., Vlasova, A., Zhang, X., Spiro, D., Halpin, R., Wang, S., Ghedin, E., Saif, L.J., 2007. Biologic, antigenic, and full-length genomic characterization of a bovine-like coronavirus isolated from a giraffe. J. Virol. 81, 4981–4990.
Hemida, M.G., Chu, D.K.W., Perera, R.A.P.M., Ko, R.L.W., So, R.T.Y., Ng, B.C.Y., Chan, S.M.S., Chu, S., Alnaeem, A.A., Alhammadi, M.A., Webby, R.J., Poon, L.L.M., Balasuriya, U.B.R., Peiris, M., 2017a. Coronavirus infections in horses in Saudi Arabia and Oman. Transbound. Emerg. Dis. 64, 2093–2103.
Hemida, M.G., Elmoslemany, A., Al-Hizab, F., Alnaeem, A., Almathen, F., Faye, B., Chu, D.K., Perera, R.A., Peiris, M., 2017b. Dromedary camels and the transmission of Middle East respiratory syndrome coronavirus (MERS-CoV). Transbound. Emerg. Dis. 2017 (64), 344–353.
Hoffmann, M., Kleine-Weber, H., Schroeder, S., Krüger, N., Herrler, T., Erichsen, S., Schiergens, T.S., Herrler, G., Wu, N.H., Nitsche, A., Müller, M.A., Drosten, C., Pöhlmann, S., 2020. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell pii: S0092-8674(20)30229-4.
Hou, Y., Wang, Q., 2019. Emerging highly virulent porcine epidemic diarrhea virus: molecular mechanisms of attenuation and rational design of live attenuated vaccines. Int. J. Mol. Sci. 20, E5478.
Hu, B., Ge, X., Wang, L.F., Shi, Z., 2015. Bat origin of human coronaviruses. Virol. J. 12, 221.
Hu, B., Zeng, L.P., Yang, X.L., Ge, X.Y., Zhang, W., Li, B., Xie, J.Z., Shen, X.R., Zhang, Y.Z., Wang, N., Luo, D.S., Zheng, X.S., Wang, M.N., Daszak, P., Wang, L.F., Cui, J., Shi, Z.L., 2017. Discovery of a rich gene pool of bat SARS-related coronaviruses provides new insights into the origin of SARS coronavirus. PLoS Pathog. 13, e1006698.
Huang, Y.W., Dickerman, A.W., Piñeyro, P., Li, L., Fang, L., Kiehne, R., Opriessnig, T., Meng, X.J., 2013. Origin, evolution, and genotyping of emergent porcine epidemic diarrhea virus strains in the United States. mBio 4, e00737–13.
Huang, C., Liu, W.J., Xu, W., Jin, T., Zhao, Y., Song, J., Shi, Y., Ji, W., Jia, H., Zhou, Y., et al., 2016. A bat-derived putative cross-family recombinant coronavirus with a

reovirus gene. PLoS Pathog. 12, e1005883.
Hughes, L.A., Savage, C., Naylor, C., Bennett, M., Chantrey, J., Jones, R., 2009. Genetically diverse coronaviruses in wild bird populations of northern England. Emerg Infect. Dis. 15, 1091–1094.
Ito, N.M.K., Miyaji, C.I., Capellaro, C.E., 1991. Studies on broiler's IBV and IB-like virus from guinea fowl. In: Kaleta, E.F., Heffels-Redmann, U. (Eds.), I I International Symposium on Infectious Bronchitis. Justus Leibig University, Giessen, pp. 302–307.
Jakob, H., 1914. Therapeutische, kasuistische und statistische Mitteilungen aus der Klinik für kleine Haustiere an der Reichstierarzneischule in Utrecht (Holland). Jahrgang /13, Zsehr. Tiermed. 18, 193.
Jin, L., Cebra, C.K., Baker, R.J., Mattson, D.E., Cohen, S.A., Alvarado, D.E., Rohrmann, F., 2007. Analysis of the genome sequence of an alpaca coronavirus. Virology 365, 198–203.
Jonassen, C.M., Kofstad, T., Larsen, I.L., Lovland, A., Handeland, K., Follestad, A., Lillehaug, A., 2005. Molecular identification and characterization of novel coronaviruses infecting graylag geese Anser anser feral pigeons Columbia livia and mallards Anas platyrhynchos. J. Gen. Virol. 86, 1597–1607.
Jordan, B.J., Hilt, D.A., Poulson, R., Stallknecht, D.E., Jackwood, M.W., 2015. Identification of avian coronavirus in wild aquatic birds of the central and eastern USA. J. Wildl. Dis. 51, 218–221.
Juan-Salles, C., Domingo, M., Herraez, P., Fernandez, A., Fernandez, J., 1997. An outbreak of feline infectious peritonitis in captive servals (*Felis serval*): clinical, pathological, and immunohistochemical findings. In: Baer, C.K. (Ed.), Proceedings of the American Association of Zoo Veterinarians, pp. 224–226 Houston, Texas.
Kaye, H.S., Yarbrough, W.B., Reed, C.J., 1975. Calf diarrhea coronavirus. The Lancet. 306, 509.
Kan, B., Wang, M., Jing, H., Xu, H., Jiang, X., Yan, M., Liang, W., Zheng, H., Wan, K., Liu, Q., Cui, B., Xu, Y., Zhang, E., Wang, H., Ye, J., Li, G., Li, M., Cui, Z., Qi, X., Chen, K., Du, L., Gao, K., Zhao, Y.T., Zou, X.Z., Feng, Y.J., Gao, Y.F., Hai, R., Yu, D., Guan, Y., Xu, J., 2005. Molecular evolution analysis and geographic investigation of severe acute respiratory syndrome coronavirus-like virus in palm civets at an animal market and on farms. J. Virol. 79, 11892–11900.
Kandeil, A., Gomaa, M., Shehata, M., El-Taweel, A., Kayed, A.E., Abiadh, A., Jrijer, J., Moatasim, Y., Kutkat, O., Bagato, O., Mahmoud, S., Mostafa, A., El-Shesheny, R., Perera, R.A., Ko, R.L., Hassan, N., Elsokary, B., Allal, L., Saad, A., Sobhy, H., McKenzie, P.P., Webby, R.J., Peiris, M., Ali, M.A., Kayali, G., 2019. Middle East respiratory syndrome coronavirus infection in non-camelid domestic mammals. Emerg. Microbes Infect. 8, 103–108.
Kennedy, M., Boedeker, N., Gibbs, P., Kania, S., 2001a. Deletions in the 7a ORF of feline coronavirus associated with an epidemic of feline infectious peritonitis. Vet. Microbiol. 81, 227–234.
Kennedy, M., Citino, S., Dolorico, T., McNabb, A.H., Moffat, A.S., Kania, S., 2001b. Detection of feline coronavirus infection in captive cheetahs (*Acinonyx jubatus*) by polymerase chain reaction. J. Zoo Wildl. Med. 32, 25–30.
Kennedy, M., Citino, S., McNabb, A.H., Moffatt, A.S., Gertz, K., Kania, S., 2002. Detection of feline coronavirus in captive Felidae in the USA. J. Vet. Diagn. Invest. 14, 520–522.
Kennedy, M., Kania, S., Stylianides, E., Bertschinger, H., Keet, D., van Vuuren, M., 2003. Detection of feline coronavirus infection in southern African nondomestic felids. J. Wildl. Dis. 39, 529–535.
Kim, H.R., Oem, J.K., 2014. Surveillance of avian coronaviruses in wild bird populations of Korea. J. Wildl. Dis. 50, 964–968.
Ksiazek, T.G., Erdman, D., Goldsmith, C.S., Zaki, S.R., Peret, T., Emery, S., Tong, S., Urbani, C., Comer, J.A., Lim, W., Rollin, P.E., Dowell, S.F., Ling, A.E., Humphrey, C.D., Shieh, W.J., Guarner, J., Paddock, C.D., Rota, P., Fields, B., DeRisi, J., Yang, J.Y., Cox, N., Hughes, J.M., LeDuc, J.W., Bellini, W.J., Anderson, L.J., et al., 2003. A novel coronavirus associated with severe acute respiratory syndrome. N. Engl. J. Med. 348, 1953–1966.
Lai, M.M.C., 1996. Recombination in large RNA viruses. coronaviruses.
Lam, T.T., Shum, M.H., Zhu, H.C., Tong, Y.G., Ni, X.B., Liao, Y.S., Wei, W., Cheung, W.Y., Li, W.J., Li, L.F., Leung, G.M., Holmes, E.C., Hu, Y.L., Guan, Y., 2020. Identifying SARS-CoV-2 related coronaviruses in Malayan pangolins. Nature. https://doi.org/10.1038/s41586-020-2169-0.
Lamers, M.M., Smits, S.L., Hundie, G.B., Provacia, L.B., Koopmans, M., Osterhaus, A.D.M.E., Haagmans, B.L., Raj, V.S., 2016. Naturally occurring recombination in ferret coronaviruses revealed by complete genome characterization. J. Gen. Virol. 97, 2180–2186.
Larsen, A.E., Gorham, J.R., 1975. A new mink enteritis: an initial report. Vet. Med. Small Anim. Clin. 70, 291–292.
Lau, S.K., Woo, P.C., Li, K.S., Huang, Y., Tsoi, H.W., Wong, B.H., Wong, S.S., Leung, S.Y., Chan, K.H., Yuen, K.Y., 2005. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats. Proc. Natl. Acad. Sci. U. S. A. 102, 14040–14045.
Lau, S.K., Poon, R.W., Wong, B.H., Wang, M., Huang, Y., Xu, H., Guo, R., Li, K.S., Gao, K., Chan, K.H., Zheng, B.J., Woo, P.C., Yuen, K.Y., 2010. Coexistence of different genotypes in the same bat and serological characterization of Rousettus bat coronavirus HKU9 belonging to a novel Betacoronavirus subgroup. J. Virol. 84, 11385–11394.
Lau, S.K., Li, K.S., Tsang, A.K., Shek, C.T., Wang, M., Choi, G.K., Guo, R., Wong, B.H., Poon, R.W., Lam, C.S., Wang, S.Y., Fan, R.Y., Chan, K.H., Zheng, B.J., Woo, P.C., Yuen, K.Y., 2012. Recent transmission of a novel alphacoronavirus, bat coronavirus HKU10, from Leschenault's rousettes to pomona leaf-nosed bats: first evidence of interspecies transmission of coronavirus between bats of different suborders. J. Virol. 86, 11906–11918.
Lau, S.K., Woo, P.C., Li, K.S., Tsang, A.K., Fan, R.Y., Luk, H.K., Cai, J.P., Chan, K.H., Zheng, B.J., Wang, M., Yuen, K.Y., 2015. Discovery of a novel coronavirus, China Rattus coronavirus HKU24, from Norway rats supports the murine origin of Betacoronavirus 1 and has implications for the ancestor of Betacoronavirus lineage A. J. Virol. 89, 3076–3092.
Lau, S.K.P., Wong, E.Y.M., Tsang, C.C., Ahmed, S.S., Au-Yeung, R.K.H., Yuen, K.Y., Wernery, U., Woo, P.C.Y., 2018. Discovery and sequence analysis of four deltacoronaviruses from birds in the Middle East reveal interspecies jumping with recombination as a potential mechanism for avian-to-avian and avian-to-mammalian transmission. J. Virol. 92, e00265–18.
Lau, S.K.P., Luk, H.K.H., Wong, A.C.P., Fan, R.Y.Y., Lam, C.S.F., Li, K.S.M., Ahmed, S.S., Chow, F.W.N., Cai, J.P., Zhu, X., Chan, J.F.W., Lau, T.C.K., Cao, K., Li, M., Woo, P.C.Y., Yuen, K.Y., 2019. Identification of a novel betacoronavirus (*Merbecovirus*) in Amur hedgehogs from China. Viruses 11, E980.
Lee, D.U., Kwon, T., Je, S.H., Yoo, S.J., Seo, S.W., Sunwoo, S.Y., Lyoo, Y.S., 2016. Wild boars harbouring porcine epidemic diarrhea virus (PEDV) may play an important role as a PEDV reservoir. Vet. Microbiol. 192, 90–94.
Lelli, D., Papetti, A., Sabelli, C., Rosti, E., Moreno, A., Boniotti, M.B., 2013. Detection of coronaviruses in bats of various species in Italy. Viruses 5, 2679–2689.
Li, T., Zhang, Y., Fu, L., Yu, C., Li, X., Li, Y., Zhang, X., Rong, Z., Wang, Y., Ning, H., Liang, R., Chen, W., Babiuk, L.A., Chang, Z., 2005. Gene Ther. 12, 751–761.
Liais, E., Croville, G., Mariette, J., Delverdier, M., Lucas, M.N., Klopp, C., Lluch, J., Donnadieu, C., Guy, J.S., Corrand, L., Ducatez, M.F., Guerin, J.L., 2014. Novel avian coronavirus and fulminating disease in guinea fowl, France. Emerg. Infect. Dis. 20, 105–108.
Liu, S., Chen, J., Chen, J., Kong, X., Shao, Y., Han, Z., Feng, L., Cai, X., Gu, S., Liu, M., 2005. Isolation of avian infectious bronchitis coronavirus from domestic peafowl *Pavo cristatus* and teal Anas. J. Gen. Virol. 86, 719–725.
Lorusso, A., Decaro, N., Schellen, P., Rottier, P.J., Buonavoglia, C., Haijema, B.J., de Groot, R.J., 2008. Gain, preservation, and loss of a group 1a coronavirus accessory glycoprotein. J. Virol. 82, 10312–10317.
Lorusso, A., Desario, C., Mari, V., Campolo, M., Lorusso, E., Elia, G., Martella, V., Buonavoglia, C., Decaro, N., 2009. Molecular characterization of a canine respiratory coronavirus strain detected in Italy. Virus Res. 141, 96–100.
Lorusso, A., Teodori, L., Leone, A., Marcacci, M., Mangone, I., Orsini, M., Capobianco-Dondona, A., Camma', C., Monaco, F., Savini, G., 2015. A new member of the Pteropine Orthoreovirus species isolated from fruit bats imported to Italy. Infect. Genet. Evol. 30, 55–58.
Lorusso, A., Calistri, P., Petrini, A., Savini, G., Decaro, N., 2020. Novel coronavirus (SARS-CoV-2) epidemic: a veterinary perspective. Vet. Ital. https://doi.org/10.12834/VetIt.2173.11599.1.
Luo, Y., Li, B., Jiang, R.D., Hu, B.J., Luo, D.S., Zhu, G.J., Hu, B.J., Liu, H.Z., Zhang, Y.Z., Yang, X.L., et al., 2018a. Longitudinal surveillance of Betacoronaviruses in fruit bats in Yunnan province, China during 2009–2016. Virol. Sin. 33, 87–95.
Luo, C.M., Wang, N., Yang, X.L., Liu, H.Z., Zhang, W., Li, B., Hu, B., Peng, C., Geng, Q.B., Zhu, G.J., Li, F., Shi, Z.L., 2018b. Discovery of novel bat coronaviruses in South China that use the same receptor as Middle East respiratory syndrome coronavirus. J. Virol. 92, e00116–18.
Luytjes, W., Bredenbeek, P.J., Noten, A.F., Horzinek, M.C., Spaan, W.J., 1988. Sequence of mouse hepatitis virus A59 mRNA 2: indications for RNA recombination between coronaviruses and influenza C virus. Virology 166, 415–422.
Maboni, G., Seguel, M., Lorton, A., Berghaus, R., Sanchez, S., 2019. Canine infectious respiratory disease: new insights into the etiology and epidemiology of associated pathogens. PLoS One 14, e0215817.
Maurel, S., Toquin, D., Briand, F.X., Queguiner, M., Allee, C., Bertin, J., Ravillion, L., Retaux, C., Turblin, V., Morvan, H., Eterradossi, N., 2011. First full-length sequences of the S gene of European isolates reveal further diversity among turkey coronaviruses. Avian Pathol. 40, 179–189.
McIntosh, K., Dees, J.H., Becker, W.B., Kapikian, A.Z., Chanock, R.M., 1967. Recovery in tracheal organ cultures of novel viruses from patients with respiratory disease. Proc. Natl. Acad. Sci. U. S. A. 57, 933–940.
McMahon, B.J., Morand, S., Gray, J.S., 2018. Ecosystem change and zoonoses in the Anthropocene. Zoonoses Public Health 65, 755–765.
Memish, Z.A., Mishra, N., Olival, K.J., Fagbo, S.F., Kapoor, J.V., Epstein, H., Alhakeem, R., Durosinloun, A., Al Asmari, M., Islam, A., Kapoor, A., Briese, T., Daszak, P., Al Rabeeah, A.A., Lipkin, W.I., 2013. Middle East respiratory syndrome coronavirus in bats, Saudi Arabia. Emerg. Infect. Dis. 19, 1819–1823.
Menachery, V.D., Yount Jr., B.L., Debbink, K., Agnihothram, S., Gralinski, L.E., Plante, J.A., Graham, R.L., Scobey, T., Ge, X.Y., Donaldson, E.F., Randell, S.H., Lanzavecchia, A., Marasco, W.A., Shi, Z.L., Baric, R.S., 2015. A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. Nat. Med. 21, 1508–1513.
Mendenhall, I.H., Borthwick, S., Neves, E.S., Low, D., Linster, M., Liang, B., Skiles, M., Jayakumar, J., Han, H., Gunalan, V., Lee, B.P.Y., Okahara, K., Wang, L.F., Maurer-Stroh, S., Su, Y.C.F., Smith, G.J.D., 2017. Identification of a lineage d betacoronavirus in cave nectar bats (Eonycteris spelaea) in Singapore and an overview of lineage d reservoir ecology in SE Asian bats. Transbound. Emerg. Dis. 64, 1790–1800.
Meyer, B., García-Bocanegra, I., Wernery, U., Wernery, R., Sieberg, A., Müller, M.A., Drexler, J.F., Drosten, C., Eckerle, I., 2015. Serologic assessment of possibility for MERS-CoV infection in equids. Emerg. Infect. Dis. 21, 181–182.
Mihindukulasuriya, K.A., Wu, G., St Leger, J., Nordhausen, R.W., Wang, D., 2008. Identification of a novel coronavirus from a beluga whale by using a panviral microarray. J. Virol. 82, 5084–5088.
Mitchell, J.A., Cardwell, J.M., Leach, H., Walker, C.A., Le Poder, S., Decaro, N., Rusvai, M., Egberink, H., Rottier, P., Fernandez, M., Fragkiadaki, E., Shields, S., Brownlie, J., 2017. European surveillance of emerging pathogens associated with canine infectious respiratory disease. Vet. Microbiol. 212, 31–38.
Monchatre-Leroy, E., Boué, F., Boucher, J.M., Renault, C., Moutou, F., Ar Gouilh, M., Umhang, G., 2017. Identification of alpha and beta coronavirus in wildlife species in France: bats, rodents, rabbits, and hedgehogs. Viruses 9, E364.
Mora-Díaz, J.C., Piñeyro, P.E., Houston, E., Zimmerman, J., Giménez-Lirola, L.G., 2019. Porcine hemagglutinating encephalomyelitis virus: a review. Front. Vet. Sci. 6, 53.

More, G.D., Dunowska, M., Acke, E., Cave, N.J., 2020. A serological survey of canine respiratory coronavirus in New Zealand. N. Z. Vet. J. 68, 54–59.
Moreno, A., Lelli, D., De Sabato, L., Zaccaria, G., Boni, A., Sozzi, E., Prosperi, A., Lavazza, A., Cella, E., Castrucci, M.R., Ciccozzi, Mm, Vaccari, G., 2017. Detection and full genome characterization of two beta CoV viruses related to Middle East respiratory syndrome from bats in Italy. Virol. J. 14, 239.
Mühldorfer, K., Speck, S., Kurth, A., Lesnik, R., Freuling, C., Müller, T., Kramer-Schadt, S., Wibbelt, G., 2011. Diseases and causes of death in European bats: dynamics in disease susceptibility and infection rates. PLoS One 6, e29773.
Muñoz, M., Alvarez, M., Lanza, I., Cármenes, P., 1996. Role of enteric pathogens in the aetiology of neonatal diarrhoea in lambs and goat kids in Spain. Epidemiol. Infect. 117, 203–211.
Muradrasoli, S., Balint, A., Wahlgren, J., Waldenstrom, J., Belak, S., Blomberg, J., et al., 2010. Prevalence and phylogeny of coronaviruses in wild birds from the Bering Strait area (Beringia). PLoS One 5, e13640.
Murray, J., Kiupel, M., Maes, R.K., 2010. Ferret coronavirus-associated diseases. Vet. Clin. North Am. Exot. Anim. Pract. 13, 543–560.
Nemoto, M., Schofield, W., Cullinane, A., 2019. The first detection of equine coronavirus in adult horses and foals in Ireland. Viruses 11, E946.
Nuttall, P.A., Harrap, K.A., 1982. Isolation of a coronavirus during studies on puffinosis, a disease of the Manx shearwater (*Puffinus puffinus*). Arch. Virol. 73, 1–13.
Panigrahy, B., Naqi, S.A., Hall, C.F., 1973. Isolation and characterization of viruses associated with transmissible enteritis (bluecomb) of Turkeys. Avian Dis. 17, 430–438.
Papineau, A., Berhane, Y., Wylie, T.N., Wylie, K.M., Sharpe, S., Lung, O., 2019. Genome organization of Canada goose coronavirus, A novel species identified in a mass die-off of Canada geese. Sci. Rep. 9, 5954.
Parker, J.C., Cross, S.S., Rowe, W.P., 1970. Rat coronavirus (RCV): a prevalent, naturally occurring pneumotropic virus of rats. Arch. Gesamte Virusforsch. 31, 293–302.
Pascucci, S., Misciattelli, M.E., Giovanetti, L., Pacchioni, G., 1983. Isolamento di un coron-avirus simile da quaglie giapponesi (*Coturnixcoturnix japonica*) con sindrome respiratoria:Prima descrizione della malattia ed isolamentodel virus. Clin. Vet. 106, 33–34.
Pedersen, N.C., 2014. An update on feline infectious peritonitis: virology and immunopathogenesis. Vet. J. 201, 123–132.
Piewbang, C., Rungsipipat, A., Poovorawan, Y., Techangamsuwan, S., 2019. Cross-sectional investigation and risk factor analysis of community-acquired and hospital-associated canine viral infectious respiratory disease complex. Heliyon 5, e02726.
Pinto, L.D., Barros, I.N., Budaszewski, R.F., Weber, M.N., Mata, H., Antunes, J.R., Boabaid, F.M., Wouters, A.T., Driemeier, D., Brandão, P.E., Canal, C.W., 2014. Characterization of pantropic canine coronavirus from Brazil. Vet. J. 202, 659–662.
Pedersen, N.C., Black, J.W., Boyle, J.F., Evermann, J.F., McKeirnan, A.J., Ott, R.L., 1983. Pathogenic differences between various feline coronavirus isolates. Adv. Exp. Med. Biol. 173, 365–380.
Pensaert, M., Callebaut, P., Vergote, J., 1986. Isolation of a porcine respiratory, non-enteric coronavirus related to transmissible gastroenteritis. Vet. Quart. 8, 257–261.
Poon, L.L., Chu, D.K., Chan, K.H., Wong, O.K., Ellis, T.M., Leung, Y.H., Lau, S.K., Woo, P.C., Suen, K.Y., Yuen, K.Y., Guan, Y., Peiris, J.S., 2005. Identification of a novel coronavirus in bats. J. Virol. 79, 2001–2009.
Porter, E., Tasker, S., Day, M.J., Harley, R., Kipar, A., Siddell, S.G., Helps, C.R., 2014. Amino acid changes in the spike protein of feline coronavirus correlate with systemic spread of virus from the intestine and not with feline infectious peritonitis. Vet. Res. 45, 49.
Pusterla, N., Vin, R., Leutenegger, C.M., Mittel, L.D., Divers, T.J., 2018. Enteric coronavirus infection in adult horses. Vet. J. 231, 13–18.
Pratelli, A., Decaro, N., Tinelli, A., Martella, V., Elia, G., Tempesta, M., Cirone, F., Buonavoglia, C., 2004. Two genotypes of canine coronavirus simultaneously detected in the fecal samples of dogs with diarrhea. J. Clin. Microbiol. 7, 381–388.
Reed, S.E., 1984. The behaviour of recent isolates of human respiratory coronavirus in vitro and in volunteers: evidence of heterogeneity among 229E-related strains. J. Med. Virol. 13, 179–192.
Reinhardt, G., Zamora, J., Tadich, N., Polette, M., Aguilar, M., Riedemann, S., Palisson, J., 1995. Diagnosis of coronavirus in sheep in Valdivia province, Xth Region, Chile. Arch. Med. Vet. 27, 129–132.
Ren, W., Qu, X., Li, W., Han, Z., Yu, M., Zhou, P., Zhang, S.Y., Wang, L.F., Deng, H., Shi, Z., 2008. Difference in receptor usage between severe acute respiratory syndrome (SARS) coronavirus and SARS-like coronavirus of bat origin. J. Virol. 82, 1899–1907.
Reusken, C.B., Ababneh, M., Raj, V.S., Meyer, B., Eljarah, A., Abutarbush, S., Godeke, G.J., Bestebroer, T.M., Zutt, I., Muller, M.A., Bosch, B.J., Rottier, P.J., Osterhaus, A.D., Drosten, C., Haagmans, B.L., Koopmans, M.P., 2013. Middle East Respiratory Syndrome coronavirus (MERS-CoV) serology in major livestock species in an affected region in Jordan, June to September 2013. Euro Surveill. 18, 20662.
Rihtaric, D., Hostnik, P., Steyer, A., Grom, J., Toplak, I., 2010. Identification of SARS-like coronaviruses in horseshoe bats (*Rhinolophus hipposideros*) in Slovenia. Arch. Virol. 155, 507–514.
Ritchie, A.E., Deshmukh, D.R., Larsen, C.T., Pomeroy, B.S., 1973. Electron microscopy of coronavirus-like particles characteristic of turkey bluecomb disease. Avian Dis. 17, 546–558.
Roic, B., Jemersic, L., Terzic, S., Keros, T., Balatinec, J., Florijancic, T., 2012. Prevalence of antibodies to selected viral pathogens in wild boars (*Sus scrofa*) in Croatia in 2005–06 and 2009–10. J. Wildl. Dis. 48, 131–137.
Rosa, G.M., Santos, N., Grøndahl-Rosado, R., Fonseca, F.P., Tavares, L., Neto, I., Cartaxeiro, C., Duarte, A., 2020. Unveiling patterns of viral pathogen infection in free-ranging carnivores of northern Portugal using a complementary methodological approach. Comp. Immunol. Microbiol. Infect. Dis. 69, 101432.
Rottier, P.J., Nakamura, K., Schellen, P., Volders, H., Haijema, B.J., 2005. Acquisition of macrophage tropism during the pathogenesis of feline infectious peritonitis is determined by mutations in the feline coronavirus spike protein. J. Virol. 79, 14122–14130.
Sabir, J.S., Lam, T.T., Ahmed, M.M., Li, L., Shen, Y., Abo-Aba, S.E., Qureshi, M.I., Abu-Zeid, M., Zhang, Y., Khiyami, M.A., Alharbi, N.S., Hajrah, N.H., Sabir, M.J., Mutwakil, M.H., Kabli, S.A., Alsulaimany, F.A., Obaid, A.Y., Zhou, B., Smith, D.K., Holmes, E.C., Zhu, H., Guan, Y., 2016. Co-circulation of three camel coronavirus species and recombination of MERS-CoVs in Saudi Arabia. Science 351, 81–84.
Saldanha, I.F., Lawson, B., Goharriz, H., Rodriguez-Ramos Fernandez, J., John, S.K., Fooks, A.R., Cunningham, A.A., Johnson, N., Horton, D.L., 2019. Extension of the known distribution of a novel clade C betacoronavirus in a wildlife host. Epidemiol. Infect. 147, e169.
Schalk, A.F., Hawn, M.C., 1931. An apparently new respiratory disease of baby chicks. J. Am. Vet. Med. Assoc. 78 (1931), 413–416.
Schwegmann-Wessels, C., Herrler, G., 2006. Transmissible gastroenteritis virus infection: a vanishing specter. Dtsch. Tierarztl. Wochenschr. 113, 157–159.
Shahwan, K., Hesse, M., Mork, A.K., Herrler, G., Winter, C., 2013. Sialic acid binding properties of soluble coronavirus spike (S1) proteins: differences between infectious bronchitis virus and transmissible gastroenteritis virus. Viruses 5, 1924–1933.
Shi, Z., Hu, Z., 2008. A review of studies on animal reservoirs of the SARS coronavirus. Virus Res. 133, 74–87.
Shi, J., Wen, Z., Zhong, G., Yang, H., Wang, C., Liu, R., He, X., Shuai, L., Sun, Z., Zhao, Y., Liang, L., Cui, P., Wang, J., Zhang, X., Guan, Y., Chen, H., Bu, Z., 2020. Susceptibility of Ferrets, Cats, Dogs, and Different Domestic Animals to SARS-coronavirus-2. https://doi.org/10.1101/2020.03.30.015347. doi: bioRxiv preprint.
Shieh, C.K., Lee, H.J., Yokomori, K., La Monica, N., Makino, S., Lai, M.M., 1989. Identification of a new transcriptional initiation site and the corresponding functional gene 2b in the murine coronavirus RNA genome. J. Virol. 63, 3729–3736.
Song, H.D., Tu, C.C., Zhang, G.W., Wang, S.Y., Zheng, K., Lei, L.C., Chen, Q.X., Gao, Y.W., Zhou, H.Q., Xiang, H., Zheng, H.J., Chern, S.W., Cheng, F., Pan, C.M., Xuan, H., Chen, S.J., Luo, H.M., Zhou, D.H., Liu, Y.F., He, J.F., Qin, P.Z., Li, L.H., Ren, Y.Q., Liang, W.J., Yu, Y.D., Anderson, L., Wang, M., Xu, R.H., Wu, X.W., Zheng, H.Y., Chen, J.D., Liang, G., Gao, Y., Liao, M., Fang, L., Jiang, L.Y., Li, H., Chen, F., Di, B., He, L.J., Lin, J.Y., Tong, S., Kong, X., Du, L., Hao, P., Tang, H., Bernini, A., Yu, X.J., Spiga, O., Guo, Z.M., Pan, H.Y., He, W.Z., Manuguerra, J.C., Fontanet, A., Danchin, A., Niccolai, N., Li, Y.X., Wu, C.I., Zhao, G.P., 2005. Cross-host evolution of severe acute respiratory syndrome coronavirus in palm civet and human. Proc. Natl. Acad. Sci. 102, 2430–2435 U.S.A.
Song, Z., Xu, Y., Bao, L., Zhang, L., Yu, P., Qu, Y., Zhu, H., Zhao, W., Han, Y., Qin, C., 2019. From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses 11, E59.
Spackman, D., Cameron, I.R.D., 1983. Isolation of infectiousbronchitis virus from pheasants. Vet. Rec. 113, 354–355.
Stephenson, N., Swift, P., Moeller, R.B., Worth, S.J., Foley, J., 2013. Feline infectious peritonitis in a mountain lion (*Puma concolor*), California, USA. J. Wildl. Dis. 49, 408–412.
Subudhi, S., Rapin, N., Bollinger, T.K., Hill, J.E., Donaldson, M.E., Davy, C.M., Warnecke, L., Turner, J.M., Kyle, C.J., Willis, C.K.R., Misra, V., 2017. A persistently infecting coronavirus in hibernating *Myotis lucifugus*, the North American little brown bat. J. Gen. Virol. 98, 2297–2309.
Sun, Z.F., Meng, X.J., 2004. Antigenic cross-reactivity between the nucleocapsid protein of severe acute respiratory syndrome (SARS) coronavirus and polyclonal antisera of antigenic group I animal coronaviruses: implication for SARS diagnosis. J. Clin. Microbiol. 42, 2351–2352.
Suryaman, G.K., Soejoedono, R.D., Setiyono, A., Poetri, O.N., Handharyani, E., 2019. Isolation and characterization of avian coronavirus from healthy Eclectus parrots (*Eclectus roratus*) from Indonesia. Vet. World 12, 1797–1805.
Tang, X.C., Zhang, J.X., Zhang, S.Y., Wang, P., Fan, X.H., Li, L.F., Li, G., Dong, B.Q., Liu, W., Cheung, C.L., Xu, K.M., Song, W.J., Vijaykrishna, D., Poon, L.L., Peiris, J.S., Smith, G.J., Chen, H., Guan, Y., 2006. Prevalence and genetic diversity of coronaviruses in bats from China. J. Virol. 80, 7481–7490.
Tang, X., Wu, C., Li, X., Song, Y., Yao, X., Wu, X., Duan, Y., Zhang, H., Wang, Y., Qian, Z., Cui, J., Lu, J., 2020. On the origin and continuing evolution of SARS-CoV-2. Sci. Rev. https://doi.org/10.1093/nsr/nwaa036. nwaa036.
Tao, Y., Shi, M., Chommanard, C., Queen, K., Zhang, J., Markotter, W., Kuzmin, I.V., Holmes, E.C., Tong, S., 2017. Surveillance of bat coronaviruses in Kenya identifies relatives of human coronaviruses NL63 and 229E and their recombination history. J. Virol. 91, e01953–16.
Tong, S., Conrardy, C., Ruone, S., Kuzmin, I.V., Guo, X., Tao, Y., Niezgoda, M., Haynes, L., Agwanda, B., Breiman, R.F., Anderson, L.J., Rupprecht, C.E., 2009. Detection of novel SARS-like and other coronaviruses in bats from Kenya. Emerg. Infect. Dis. 15, 482–485.
Torres, C.A., Villarreal, L.Y.B., Ayres, G.G.R., Richtzenhain, L., Brandão, P.E., 2013. An avian coronavirus in quail with respiratory and reproductive signs. Avian Dis. 57, 295–299.
Torres, C.A., Hora, A., Tonietti, P.O., Taniwaki, S.A., Cecchinato, M., Villarreal, L.Y., Brandão, P.E., 2016. Gammacoronavirus and deltacoronavirus in Quail. Avian Dis. 60, 656–661.
Tsagkogeorga, G., Parker, J., Stupka, E., Cotton, J.A., Rossiter, S.J., 2013. Phylogenomic analyses elucidate the evolutionary relationships of bats. Curr. Biol. 23, 2262–2267.
Tzipori, S., Smith, M., Makin, T., McCaughan, C., 1978. Enteric coronavirus-like coronavirus particles in sheep. Aust. Vet. 54, 320–321.
Tu, C., Crameri, G., Kong, X., Chen, J., Sun, Y., Yu, M., Xiang, H., Xia, X., Liu, S., Ren, T., Yu, Y., Eaton, B.T., Xuan, H., Wang, L.F., 2004. Antibodies to SARS coronavirus in civets. Emerg. Infect. Dis. 10, 2244–2248.
Valastro, V., Holmes, E.C., Britton, P., Fusaro, A., Jackwood, M.W., Cattoli, G., Monne, I., 2016. S1 gene-based phylogeny of infectious bronchitis virus: an attempt to

harmonize virus classification. Infect. Genet. Evol. 39, 349–364.
van der Hoek, L., Pyrc, K., Jebbink, M.F., Vermeulen-Oost, W., Berkhout, R.J., Wolthers, K.C., Wertheim-van Dillen, P.M., Kaandorp, J., Spaargaren, J., Berkhout, B., 2004. Identification of a new human coronavirus. Nat. Med. 10, 368–373.
Vengust, G., Valencak, Z., Bidovec, A., 2006. A serological survey of selected pathogens in wild boar in Slovenia. J. Vet. Med. B Infect. Dis. Vet. Public Health 53, 24–27.
Vennema, H., Poland, A., Foley, J., Pedersen, N.C., 1998. Feline infectious peritonitis viruses arise by mutation from endemic feline enteric coronaviruses. Virology 243, 150–157.
Vergara-Alert, J., van den Brand, J.M., Widagdo, W., Muñoz 5th, M., Raj, S., Schipper, D., Solanes, D., Cordón, I., Bensaid, A., Haagmans, B.L., Segalés, J., 2017. Livestock susceptibility to infection with Middle East respiratory syndrome coronavirus. Emerg. Infect. Dis 23, 232–240.
Vijgen, L., Keyaerts, E., Moes, E., Thoelen, I., Wollants, E., Lemey, P., Vandamme, A.-M.-M., Van Ranst, A., 2005. Complete genomic sequence of human coronavirus OC43: molecular clock analysis suggests a relatively recent zoonotic coronavirus transmission event. J. Virol. 79, 1595–1604.
Vijgen, L., Keyaerts, E., Lemey, P., Maes, P., Van Reeth, K., Nauwynck, H., Pensaert, M., Van Ranst, M., 2006. Evolutionary history of the closely related group 2 coronaviruses: porcine hemagglutinating encephalomyelitis virus, bovine coronavirus, and human coronavirus OC43. J. Virol. 80, 7270–7274.
Vlasova, A.N., Halpin, R., Wang, S., Ghedin, E., Spiro, D.J., Saif, L.J., 2011. Molecular characterization of a new species in the genus *Alphacoronavirus* associated with mink epizootic catarrhal gastroenteritis. J. Gen. Virol. 92, 1369–1379.
Wang, M., Jing, H.Q., Xu, H.F., Jiang, X.G., Kan, B., Liu, Q.Y., Wan, K.L., Cui, B.Y., Zheng, H., Cui, Z.G., Yan, M.Y., Liang, W.L., Wang, H.X., Qi, X.B., Li, Z.J., Li, M.C., Chen, K., Zhang, E.M., Zhang, S.Y., Hai, R., Yu, D.Z., Xu, J.G., 2005. Surveillance on severe acute respiratory syndrome associated coronavirus in animals at a live animal market of Guangzhou in 2004. Zhonghua Liu Xing Bing Xue Za Zhi 26, 84–87.
Wang, L., Byrum, B., Zhang, Y., 2014. Detection and genetic characterization of deltacoronavirus in pigs, Ohio, USA, 2014. Emerg. Infect. Dis. 20, 1227–1230.
Wang, W., Lin, X.D., Guo, W.P., Zhou, R.H., Wang, M.R., Wang, C.Q., Ge, S., Mei, S.H., Li, M.H., Shi, M., Holmes, E.C., Zhang, Y.Z., 2015. Discovery, diversity and evolution of novel coronaviruses sampled from rodents in China. Virology 474, 19–27.
Wang, W., Lin, X.D., Liao, Y., Guan, X.Q., Guo, W.P., Xing, J.G., Holmes, E.C., Zhang, Y.Z., 2017. Discovery of a highly divergent coronavirus in the Asian house shrew from China illuminates the origin of the alphacoronaviruses. J. Virol. 91, e00764–17.
Wang, Q., Vlasova, A.N., Kenney, S.P., Saif, L.J., 2019. Emerging and re-emerging coronaviruses in pigs. Curr. Opin. Virol. 34, 39–49.
Watt, N.J., MacIntyre, N.J., McOrist, S., 1993. An extended outbreak of infectious peritonitis in a closed colony of European wildcats (*Felis silvestris*). J. Comp. Pathol. 108, 73–79.
Weiss, S.R., Navas-Martin, S., 2005. Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus. Microbiol. Mol. Biol. Rev. 69, 635–664.
Wille, M., Muradrasoli, S., Nilsson, A., Järhult, J.D., 2016. High prevalence and putative lineage maintenance of avian coronaviruses in Scandinavian waterfowl. PLoS One 11, e01510198.
Williams, B.H., Kiupel, M., West, K.H., Raymond, J.T., Grant, C.K., Glickman, L.T., 2000. Coronavirus-associated epizootic catarrhal enteritis in ferrets. J. Am. Vet. Med. Assoc. 217, 526–530.
Winter, C., Schwegmann-Wessels, C., Cavanagh, D., Neumann, U., Herrler, G., 2006. Sialic acid is a receptor determinant for infection of cells by avian infectious bronchitis virus. J. Gen. Virol. 87, 1209–1216.
Winter, C., Herrler, G., Neumann, U., 2008. Infection of the tracheal epithelium by infectious bronchitis virus is sialic acid dependent. Microbes Infect. 10, 367–373.
Wise, A.G., Kiupel, M., Garner, M.M., Clark, A.K., Maes, R.K., 2010. Comparative sequence analysis of the distal one-third of the genomes of a systemic and an enteric ferret coronavirus. Virus Res. 149, 42–50.
Wood, E.N., 1977. An apparently new syndrome of porcine epidemic diarrhoea. Vet Rec. 100, 243–244.
Wong, A.C.P., Li, X., Lau, S.K.P., Woo, P.C.Y., 2019. Global epidemiology of bat coronaviruses. Viruses 11 (2), E174.
Woo, P.C., Lau, S.K., Chu, C.M., Chan, K.H., Tsoi, H.W., Huang, Y., Wong, B.H., Poon, R.W., Cai, J.J., Luk, W.K., Poon, L.L., Wong, S.S., Guan, Y., Peiris, J.S., Yuen, K.Y., 2005. Characterization and complete genome sequence of a novel coronavirus, coronavirus HKU1, from patients with pneumonia. J. Virol. 79, 884–895.
Woo, P.C., Lau, S.K., Li, K.S., Poon, R.W., Wong, B.H., Tsoi, H.W., Yip, B.C., Huang, Y., Chan, K.H., Yuen, K.Y., 2006. Molecular diversity of coronaviruses in bats. Virology 351, 180–187.
Woo, P.C., Wang, M., Lau, S.K., Xu, H., Poon, R.W., Guo, R., Wong, B.H., Gao, K., Tsoi, H.W., Huang, Y., Li, K.S., Lam, C.S., Chan, K.H., Zheng, B.J., Yuen, K.Y., 2007. Comparative analysis of twelve genomes of three novel group 2c and group 2d coronaviruses reveals unique group and subgroup features. J. Virol. 81, 1574–1585.
Woo, P.C., Lau, S.K., Lam, C.S., Lai, K.K., Huang, Y., Lee, P., Luk, G.S., Dyrting, K.C., Chan, K.H., Yuen, K.Y., 2009. Comparative analysis of complete genome sequences of three avian coronaviruses reveals a novel group 3c coronavirus. J. Virol. 83, 908–917.
Woo, P.C., Huang, Y., Lau, S.K., Yuen, K.Y., 2010. Coronavirus genomics and bioinformatics analysis. Viruses. 2, 1804–1820.
Woo, P.C., Lau, S.K., Lam, C.S., Lau, C.C., Tsang, A.K., Lau, J.H., Bai, R., Teng, J.L., Tsang, C.C., Wang, M., Zheng, B.J., Chan, K.H., Yuen, K.Y., 2012. Discovery of seven novel Mammalian and avian coronaviruses in the genus deltacoronavirus supports bat coronaviruses as the gene source of alphacoronavirus and betacoronavirus and avian coronaviruses as the gene source of gammacoronavirus and deltacoronavirus. J. Virol. 86, 3995–4008.
Woo, P.C., Lau, S.K., Wernery, U., Wong, E.Y., Tsang, A.K., Johnson, B., Yip, C.C., Lau, C.C., Sivakumar, S., Cai, J.P., Fan, R.Y., Chan, K.H., Mareena, R., Yuen, K.Y., 2013. Novel betacoronavirus in dromedaries of the Middle East, 2013. Emerg. Infect. Dis. 20, 560–572.
Woo, P.C., Lau, S.K., Lam, C.S., Tsang, A.K., Hui, S.W., Fan, R.Y., Martelli, P., Yuen, K.Y., 2014. Discovery of a novel bottlenose dolphin coronavirus reveals a distinct species of marine mammal coronavirus in Gammacoronavirus. J. Virol. 88, 1318–1331.
Wu, Z., Yang, L., Ren, X., He, G., Zhang, J., Yang, J., Qian, Z., Dong, J., Sun, L., Zhu, Y., Du, J., Yang, F., Zhang, S., Jin, Q., 2016. Deciphering the bat virome catalog to better understand the ecological diversity of bat viruses and the bat origin of emerging infectious diseases. ISME J. 10, 609–620.
Wu, F., Zhao, S., Yu, B., Chen, Y.M., Wang, W., Song, Z.G., Hu, Y., Tao, Z.W., Tian, J.H., Pei, Y.Y., Yuan, M.L., Zhang, Y.L., Dai, F.H., Liu, Y., Wang, Q.M., Zheng, J.J., Xu, L., Holmes, E.C., Zhang, Y.Z., 2020. A new coronavirus associated with human respiratory disease in China. Nature 579, 265–269.
Yang, D.K., Hwang, I.J., Kim, B.H., Kweon, C.H., Lee, K.W., Kang, M.I., Lee, C.S., Cho, K.O., 2008. Serosurveillance of viral diseases in Korean native goats (*Capra hircus*). J. Vet. Med. Sci. 70, 977–979.
Yang, Y., Du, L., Liu, C., Wang, L., Ma, C., Tang, J., et al., 2014. Receptor usage and cell entry of bat coronavirus HKU4 provide insight into bat-to-human transmission of MERS coronavirus. Proc. Natl. Acad. Sci. U. S. A. 111, 12516–12521.
Yokomori, K., La Monica, N., Makino, S., Shieh, C.K., Lai, M.M., 1989. Biosynthesis, structure, and biological activities of envelope protein gp65 of murine coronavirus. Virology 173, 683–691.
Yuan, J., Hon, C.C., Li, Y., Wang, D., Xu, G., Zhang, H., et al., 2010. Intraspecies diversity of SARS-like coronaviruses in Rhinolophus sinicus and its implications for the origin of SARS coronaviruses in humans. J. Gen. Virol. 91, 1058–1062.
Zeng, Q., Langereis, M.A., van Vliet, A.L.W., Huizinga, E.G., de Groot, R.J., 2008. Structure of coronavirus hemagglutinin-esterase offers insight in corona and influenza virus evolution. Proc. Natl. Acad. Sci 105, 9065–9069.
Zaki, A.M., van Boheemen, S., Bestebroer, T.M., Osterhaus, A.D., Fouchier, R.A., 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N. Engl. J. Med. 367, 1814–1820.
Zhou, P., Fan, H., Lan, T., Yang, X.L., Shi, W.F., Zhang, W., Zhu, Y., Zhang, Y.W., Xie, Q.M., Mani, S., Zheng, X.S., Li, B., Li, J.M., Guo, H., Pei, G.Q., An, X.P., Chen, J.W., Zhou, L., Mai, K.J., Wu, Z.X., Li, D., Anderson, D.E., Zhang, L.B., Li, S.Y., Mi, Z.Q., He, T.T., Cong, F., Guo, P.J., Huang, R., Luo, Y., Liu, X.L., Chen, J., Huang, Y., Sun, Q., Zhang, X.L., Wang, Y.Y., Xing, S.Z., Chen, Y.S., Sun, Y., Li, J., Daszak, P., Wang, L.F., Shi, Z.L., Tong, Y.G., Ma, J.Y., 2018. Fatal swine acute diarrhoea syndrome caused by an HKU2 related coronavirus of bat origin. Nature 556, 255–258.
Zhou, P., Yang, X.L., Wang, X.G., Hu, B., Zhang, L., Zhang, W., Si, H.R., Zhu, Y., Li, B., Huang, C.L., Chen, H.D., Chen, J., Luo, Y., Guo, H., Jiang, R.D., Liu, M.Q., Chen, Y., Shen, X.R., Wang, X., Zheng, X.S., Zhao, K., Chen, Q.J., Deng, F., Liu, L.L., Yan, B., Zhan, F.X., Wang, Y.Y., Xiao, G.F., Shi, Z.L., 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579, 270–273.
Zhuang, Q.Y., Wang, K.C., Liu, S., Hou, G.Y., Jiang, W.M., Wang, S.C., Li, J.P., Yu, J.M., Chen, J.M., 2015. Genomic analysis and surveillance of the coronavirus dominant in ducks in China. PLoS One 10, e0129256.