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### COVID-19 PANDEMIC: A SYSTEMATIC REVIEW ON THE CORONAVIRUSES OF ANIMALS AND SARS-CoV-2

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#### ABSTRACT

Coronaviruses (CoVs), classified into four genera, viz., alpha-, beta-, gamma-, and Delta- CoV, represent an important group of diverse transboundary pathogens that can infect a variety of mammalian and avian species including humans, animals, poultry, and non-poultry birds. CoVs primarily infect lung and gut epithelial cells, besides monocytes and macrophages. CoVs have high mutation rates causing changes in host specificity, tissue tropism, and mode of virus excretion and transmissions. The recent CoV zoonoses are SARS, MERS, and COVID-19 that are caused by the transmission of beta-CoVs of bats to humans. Recently, reverse zoonoses of the COVID-19 virus have been detected in dogs, tigers, and minks. Beta-CoV strains also infect bovine (BCoV) and canine species (CRCoV); both these beta-CoVs might have originated from a common ancestor. Despite the high genetic similarity between BCoV, CRCoV, and HCoV-OC43, these differ in species specificity. Alpha-CoV strains infect canine (CCoV),

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feline (FIPV), swine (TGEV and PEDV), and humans (HCoV229E and NL63). Six coronavirus species are known to infect and cause disease in pigs, seven in human beings, and two in dogs. The high mutation rate in CoVs is attributed to error-prone 3'-5' exoribonuclease (NSP 14), and genetic recombination to template shift by the polymerase. The present compilation describes the important features of the CoVs and diseases caused in humans, animals, and birds that are essential in surveillance of diverse pool of CoVs circulating in nature, and monitoring interspecies transmission, zoonoses, and reverse zoonoses.

## 1 Introduction

Emerging infectious diseases, particularly those caused by viruses, such as severe acute respiratory syndrome (SARS, including COVID-19), Bird Flu (Avian influenza virus), Ebola, Zika, Crimean Congo hemorrhagic fever (CCHF), Nipah, HIV to name a few, are a major threat to life as a result of Epidemics and Pandemics involving a wide range of hosts. A diverse group of RNA viruses, including coronavirus (*coronaviridae*), rhinovirus (enterovirus; *picornaviridae*), pneumovirus (respiratory syncytial virus, *pneumoviridae*), parainfluenza virus (*paramyxoviridae*), and influenza virus (*orthomyxoviridae*), target the respiratory tract of man and animals and represent a large global burden of disease (Zhang et al., 2020). It infects the epithelial cells of the respiratory tract and rapidly triggers an innate immune response (Shang et al., 2020). CoVs are members of the *Coronaviridae* family of the Nidovirales order (Figure 1). These are enveloped viruses that bear a single-stranded positive-sense RNA genome. (Khailany et al., 2020).

There are four genera in the family *Coronaviridae* viz., Alphacoronavirus, Betacoronavirus, *Gammacoronavirus* and Deltacoronavirus (Figure 2). The genera  $\alpha$ - and BCoV infect mammals, while the genera  $\delta$ - and  $\gamma$ -CoV infect avian and certain mammals.

The length of the RNA genome ranges from 27,317 (HCoV-229E) to 31,357 nucleotides (murine hepatitis virus-A59); the largest among RNA viruses. The genome organization of CoVs is represented by 5'-leader-UTR-replicase/transcriptase(RdRp)-spike(S)-envelope(E)-membrane(M)-nucleocapsid(N)-3'UTR-poly(A) tail (Yin, 2020). Similarity in N and M genes indicate recent divergence of BCoV, TCoV, and HCoV-OC43 (Laha et al., 2020).

The basic organization of the *Coronaviridae* genome is shared with the family *Arteriviridae*. Till now, at least 12 coding regions (ORFs) have been predicted in the CoV genome (Zeng et al., 2004; Issa et al., 2020). The majority of T cell epitopes are located in the S and N proteins of the virus (Dearlove et al., 2020). The viral proteases generate up to 16 non-structural proteins (NSPs) from ORF1ab (Ou et al., 2020). The NSPs are involved in genome replication, sub-genomic mRNA synthesis, and processing of polyprotein, and are encoded within the 5'- two-thirds of the

genome, whereas the structural proteins are encoded within the 3'-one-third of the genome.

Coronaviruses have great potential for interspecies transmission. The replication cycle of CoVs occurs entirely in the cytoplasm and involves the generation of a series of sub-genomic RNAs. Viruses of the genera Alpha, Beta, and Gamma- CoVs cause host cell shutoff through their NSP 1, and accessory protein 5b (Fan et al., 2020; Premkumar et al., 2020; Chan et al., 2020; Poran et al., 2020; Tung, 2020; Subbarao & Mahanty, 2020; Thielen et al., 2020).

Beta-CoVs are highly variable and use several different attachment and entry receptors. They attach to the glycan layer on the cell surface (e.g., sialic acids or heparan sulfate), then interact with the entry receptor, viz., carcinoembryonic antigen-cell adhesion molecule (CEACAM1) for MHV, angiotensin-converting enzyme 2 (ACE2) for SARS-CoV-1 and 2, dipeptidyl peptidase 4 (DPP4) for MERS-CoV, Human leukocyte antigen class I (HLA-I) for HCoV-OC43 and HCoV-HKU1, neural cell adhesion molecule for PHEV (Chen et al., 2020). Maximum parsimony tree based on polymerase gene in ORF1b revealed four major antigenic groups, viz., *Group I* (HCoV229E, PEDV, TGEV, CCoV, and FIPV), *Group II* (MHV, Rat SADV, PHEV, BCoV, and HCoVOC43), *Group III* (Avian IBV and Turkey CoV), and *Group IV* that comprises of SARS virus (Ma et al., 2019b). (Figure 3)

## 2 Human CoVs and SARS-CoV-2 (beta- CoV; sarbecovirus subgenus)

There are seven species of virus included in human infectious coronavirus, including  $\alpha$ -CoV (HCoV-NL63 and HCoV-229E) and BCoV (SARS-CoV, SARS-CoV-2, HCoV-OC43, HCoV-HKU1, and MERS-CoV) (Ye et al., 2020). The ongoing COVID-19 pandemic caused by SARS-CoV-2, a beta- CoV, has affected 213 countries on all five Continents. The virus affects both respiratory and enteric systems that have a preponderance of viral receptors. The SARS-CoV-2, popularly known as the COVID-19 virus, affects human of all ages with respiratory sickness of different degree; however, it has been observed to be fatal in elderly people due to acute respiratory distress syndrome (ARDS) complicated by Cytokine Storm (Leghari et al., 2016; Hassan et al., 2019), as observed earlier in Feline Infectious Peritonitis (FIP), a fatal disease

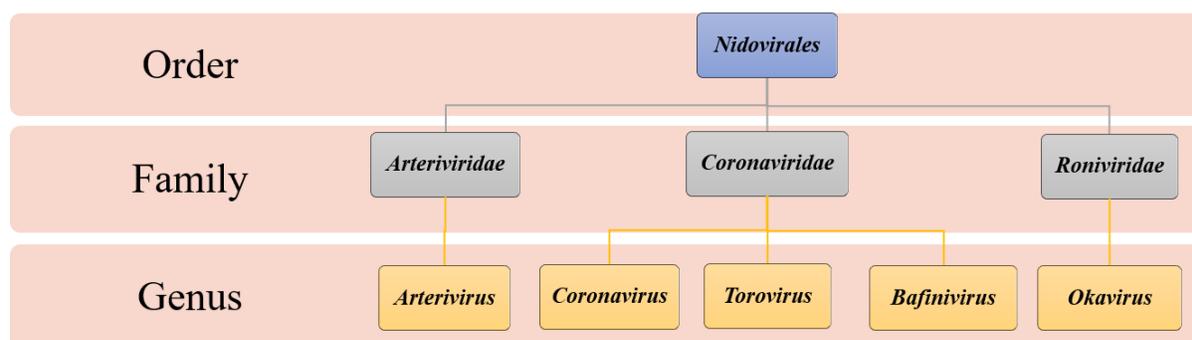


Figure 1 Nidovirales classification tree (Van Dorp et al., 2020)

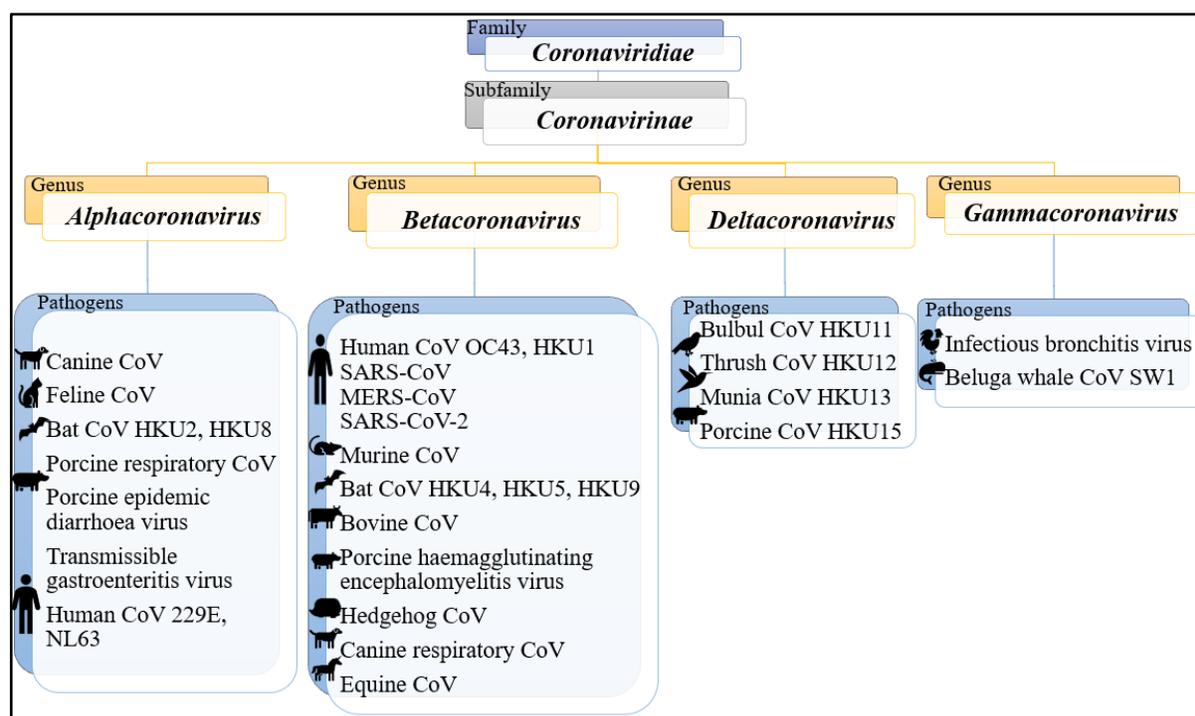


Figure 2 Classification of genera coronavirinae along with few pathogens of each genus

of cats caused by feline CoV (Khataby et al., 2016). Similarly, antibody dependent enhancement (ADE), as described earlier during the evaluation of an FIPV vaccine, has been suspected to occur in COVID-19 (Cavanagh, 2007; De et al., 2011; Valastro et al., 2016).

Genetically, SARS-CoV-2 is closely related (79% homology) to SARS-CoV of 2003, but distinct (50% homology) from MERS-CoV of 2012 (Xu et al., 2018). All these three respiratory human CoVs are of bat origin and zoonotic; transmission from bat to human is facilitated by intermediate animal hosts that are civet cat for SARS, dromedary camel for MERS, and pangolin for COVID-19 (Simon & Holmes, 2011). Reverse zoonoses have also been detected in tiger and mink.

In late March 2020, a sick Malayan tiger at the Bronx Zoo in New York City tested positive for the virus. Recently, Oreshkova et al. (2020) reported SARS-CoV-2 infection of minks in two farms in the Netherlands and showed that humans can become a source of infection for minks. Ferrets, poultry, and companion animals of humans were all screened for SARS-CoV-2 susceptibility by Shi et al (2020a). The researchers discovered that SARS-CoV-2 infects ferrets' upper respiratory tracts (Shi et al., 2020b).

The genome contains 13 open reading frames (ORFs) that produce 20 non-structural proteins (NSPs) and four structural proteins (SPs) viz., Spike (S), Membrane (M), Envelope (E), and Nucleocapsid (N)

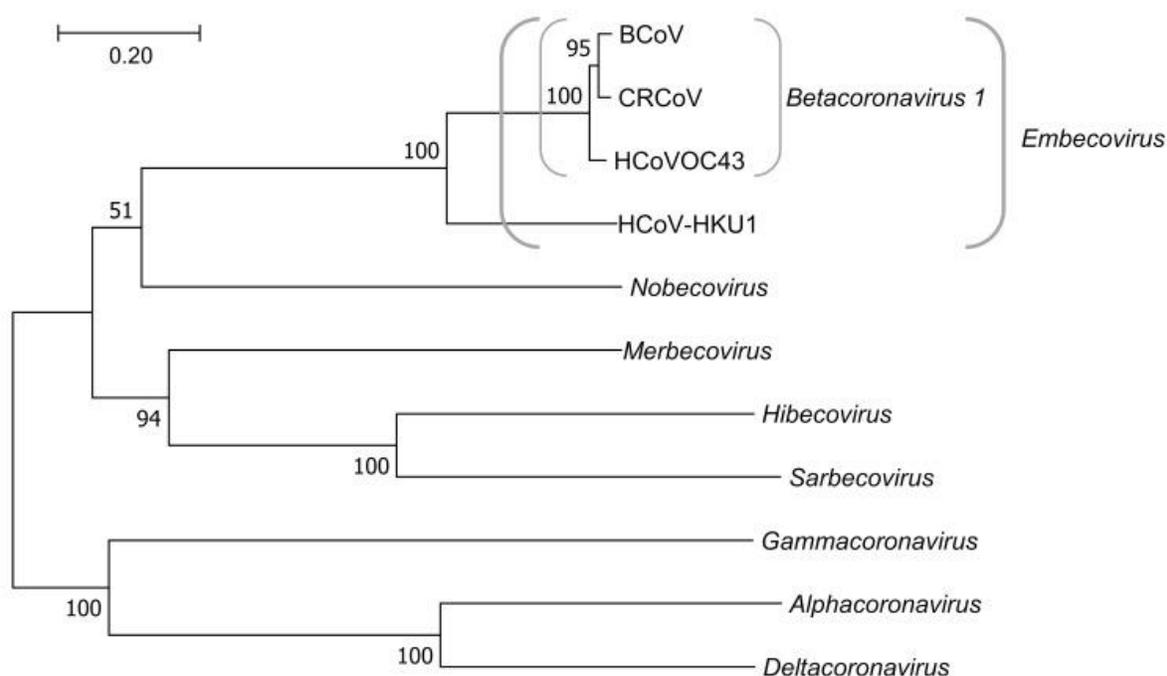


Figure 3 Maximum likelihood phylogenetic tree of Orthocoronavirinae (Szczepanski et al., 2019)

(Takano et al., 2011; Honeycutt et al., 2016; Amarasinghe et al., 2017; Li et al., 2017; Channappanavar & Perlman, 2017; Abbasi et al., 2020). The RNA genome attaches to the host cell ribosomes, resulting in the translation of 2 co-terminal and large polyproteins that are further processed by proteolytic enzymes 3CLpro and PLpro, and with the involvement of RdRp enzyme new virions are produced (Lin & Chen, 2017; Adabor, 2019; Safavi et al., 2020).

Since the beginning of the COVID-19 pandemic, two mutations across the virus genome have become consensus; P4715L in ORF1ab (nucleotide 14143, C to T) and D614G in S (nucleotide 23403, A to G) (Zheng et al., 2008). Using 18514 sequences, they found limited diversity across SARS-CoV-2 genomes. Out of 7559 polymorphic sites detected, only 11 mutations were found in >5% of sequences. Examining 114 sequences, Thielen et al. (2020) identified 153 unique, unambiguous single nucleotide variants across all sequences (54 synonymous variants, 91 non-synonymous variants, 8 noncoding variants) compared to the Wuhan-Hu-1 SARS-CoV-2 reference genome (accession: MN908947.3) with a range of 2–14 variants per genome. Nucleotide sequence alignment of 86 complete or near-complete genomes of SARS-CoV-2 revealed 93 mutations over the entire genome (Jordan, 2017). There were 42 missense mutations in all the major non-structural and structural proteins, other than the envelope protein. There were three mutations (D354, Y364, and F367) in the receptor-binding domain (RBD), and such mutations in the RBD might lead to conformational changes and changes in antigenicity

(Sumi et al., 2012; Patel et al., 2015). Recurrent mutations were observed at three positions in Orf1ab (11083, 13402, 16887) in the regions encoding NSPs 6, 11 and 13, and one in the S protein (21575) (Jackwood, 2012). Analysis of ~660 SARS-CoV-2 genome sequences revealed that, among the 11 genes of the virus, S glycoprotein, nucleocapsid, ORF1ab, and ORF8 had frequent mutations, whereas envelope, membrane, ORF6, ORF7a, and ORF7b were conserved in the amino acid sequence (Zheng et al., 2018). The study identified frequently mutated variants among COVID-19 patients. The ORFs 6, 7a, 10, E, and M were mostly conserved. The ORF3a encodes a minor structural protein of 274 aa residues in SARS-CoV (Masters, 2016). A total of 51 different non-synonymous mutations were detected in the 3a proteins among 2,782 SARS-CoV-2 strains. The 3a protein of SARS-CoV-1 and 2 has three transmembrane domains, and is essential for disease pathogenesis; six functional domains linked to virulence were identified in it (Hulswit et al., 2016; Jackwood, 2012).

### 3 Bovine Coronavirus (BCoV; beta- CoV; embecovirus subgenus)

Group 2 coronaviruses include BCoV, MHV, HCoV-OC43, PHEV, CRCoV, and equine coronavirus, and these are antigenically related. A beta- CoV in the subgenus Embecovirus, has an additional shorter spike protein HE (Fung et al., 2016). It causes severe neonatal calf diarrhea, calf enteritis, winter dysentery in adult cattle and also enzootic pneumonia complex in calves leading

to economic losses to the livestock industry (Siu et al., 2014). The BCoV, a member of subgenus Embecovirus, in addition to S protein, has an additional shorter spike protein HE (Kint et al., 2016). The virus has a broad host range with dual tropism for the respiratory and gastrointestinal tracts and a zoonotic potential (Kameka et al., 2014). BCoV's broad host range can be due to the HE protein, which allows the virus to bind to a variety of cell types (Jordan, 2016). Due to fecal contamination, calves born to BCoV carrier dams are more likely to develop diarrhea. Shedding of BCoV via the respiratory tract and enteric route in cattle has been recorded (Rohaim et al., 2020). Persistent infection of BCoV in cattle has been detected (Cavanagh, 2003; Franzo et al., 2019). Wild ruminants can transmit BCoV-like a virus to cattle and other animals. The BCoV exists in two genomic clades (clade 1 and 2) which can be differentiated antigenically (Yan et al., 2018). Members of the Beta-CoV infect not only cattle and wild ruminants, but also equines (equine coronavirus; ECoV), humans (HCoV OC43) and pigs (PHEV).

BCoV has >31kb positive-sense RNA genome, and five structural proteins, viz., M, E, HE, S, and N (Lewis et al., 2015; Emmeler et al., 2020). Recombination event in the HE gene of BCoV has been identified between the esterase and lectin domain of HE (Fehr & Perlman, 2015; Snijder et al., 2016). Virulent and avirulent strains differ in the S1 that is the hypervariable region. The virus enters the host cell by binding to the N-acetyl-9-O-acetylneuraminic acid receptor (Porter et al., 2014; Felten et al., 2017; Doki et al., 2018; Li et al., 2019; Kennedy, 2020).

There is an evolutionary relationship between PHEV, BCoV, and HCoV-OC43 (Vuong et al., 2020). It is speculated that inter-species transmission events have occurred before the emergence of PHEV, BCoV, and HCoV-OC43. The amino acid sequences of both the N and M proteins of the turkey enteric coronavirus (TCoV) were >99% similar to BCoV (Murphy et al., 2018). The extensive similarity of the N protein of TCoV with MHV (70%) and HCoV-OC43 (98%) has been observed. There was 86% similarity between the M proteins of TCoV and MHV. Such similarities suggest that BCoV, TCoV, and HCoV-OC43 must have diverged recently.

BCoV is a significant pathogen in the bovine respiratory disease complex (BRDC). Vaccine against BCoV is widely employed in cattle to protect against enteric and respiratory disease in young calves (Hsieh & Chueh, 2014).

BCoV has a wide range of interspecies transmission. Different BCoV-like CoVs have been detected in domesticated ruminants (water buffalo, cow, donkey, dromedary camel, llama, and alpaca), wild ruminants (deer, wild cattle, antelopes, giraffes, and wild goats), dogs, and humans as enteric and/or respiratory pathogens (Leghari et al., 2016; Kipar et al., 2006; Czajka, 2016). The

presence of antibodies to BCoV in virus neutralization and haemagglutination inhibition assays was linked to the detection of BCoV-like CoVs in water buffalo (Ntasis et al., 2013; Pedersen, 2014; Decaro et al., 2015; Felten & Hartmann, 2019).

#### 4 Infectious Bronchitis Virus (IBV; gamma- CoV)

Avian infectious bronchitis, caused by IBV, a gamma-CoV, was first described in 1930 (Sanchez et al., 2004; Ma et al., 2018;). The RNA genome of approximately 27 kb; the 3' end of the genome encodes four structural proteins, S, E, M, and N, and four non-structural accessory proteins, 3a, 3b, 5a, and 5b, and the 5' end of the genome encodes two polyproteins (1a and 1ab) that are necessary for RNA replication (Enjuanes et al., 2000). The spike protein comprises about 1145 amino acids, contains 29 putative asparagines (N)-linked glycosylation sites, and undergoes post-translational cleavage to form S1 and S2 subunits (Licitra et al., 2014; Naylor et al., 2002; Philips et al., 2017; Li et al., 2019; Timurkan et al., 2021). The recombination events arise from template switching mechanisms during RNA replication (Munir & Corte, 2015). Nucleotide sequencing of the S1 region discriminates between all IBV strains (Vijgen et al., 2016; Castells et al., 2019; Luk et al., 2019; Yachou et al., 2020). The S1 subunit contains virus-neutralizing epitopes, serotype-specific determinants, and has the highest variability leading to the emergence of new virus genotypes, serotypes, and variants (Terada et al., 2014; Tizard, 2020). Cytotoxic T lymphocyte epitopes in the N protein can protect chickens from IBV infection (Fulton et al., 2013; Wang et al., 2019a). Macrophage numbers are elevated in the respiratory tract of IBV infected chickens, and productive infection in macrophages has been confirmed (Szczepanski et al., 2019). Macrophages play an important role in the pathogenesis of some animal and human viruses; viz., Marek's disease virus in birds, FIPV, HIV, and SARS-CoV (Nemoto et al., 2017; Kanno et al., 2018; Kim et al., 2018; Tortorici et al., 2019; Keha et al., 2019; Shin et al., 2019; Qian et al., 2020).

Current IBV vaccines are either live-attenuated or killed, and are used extensively (Amer, 2018). Vaccination is only partially successful due to the continual emergence of antigenic variants of IBV (Szczepanski et al., 2019). The presence of multiple antigenic types requires multivalent (more than one antigenic type) vaccines. Vaccines against IBV are widely used, compared to vaccines for CoV diseases caused by bovine, canines, felines and porcine CoVs (Decaro et al., 2015; Burimuah et al., 2020).

A new classification of the S1 gene has been proposed, which comprises 32 lineages, six genotypes (GI to G VI), and many inter-lineage recombinants (Woo et al., 2014; Byukusenge et al., 2018). Some lineages are prevalent in several continents and countries, while others are geographically confined. In India, IBV strains have been isolated. Genetic recombination in the spike gene

leading to the emergence of a novel genotype/serotype (GVII-1) with a lower affinity to the respiratory tract in chickens comparing to one of its parental virus ck/CH/LGX/111119 has been reported (Zhou et al., 2017; Tortorici et al., 2019).

Many IBV variants have been found to have originated by recombination with other existing strains (Wang et al., 2018b). Surveillance for IBV serotypes and identification of variants is extremely important for the control of the disease. Because IBV exists as multiple serotypes with no cross-protection, it is very difficult to control.

### 5 Canine Coronavirus (alpha and beta- CoV)

The phylogenetic relationship between CCoV-I and FCoV-I, and CCoV-II and FCoV-II, indicate the possibility of interspecies transmission. Clinically, CCoV is often detected in the presence of other viruses such as canine adenovirus type 1 or canine parvovirus type 2 (Xia et al., 2018). The virus binds to the APN (aminopeptidase N) receptor and enters the host cell. CCoV type II is split into two subtypes: CCoV-IIa (classical strains) and CCoV-IIb (recombination of CCoV-IIa and TGEV) (Ma et al., 2019a). In Europe, highly virulent pantropic CCoV- IIa strains have been discovered in dogs (Zhang et al., 2017; Chen et al., 2019a; Li et al., 2019). Nucleotide sequence of ORF1b, M and S genes identified divergent CCoVs (Zhang et al., 2019; Guo et al., 2020). Analysis of various regions of the S and polymerase genes revealed that the CCoV- UWSMN-1 strain isolated from an outbreak of fatal gastroenteritis is widely divergent from other CCoV and FCoV strains; the strain could be a novel subtype of CCoV (Hu et al., 2015; Mou et al., 2016; Saif & Jung, 2020).

Like FIPV, TGEV, porcine respiratory CoV, and HCoV 229E, the S protein of CCoV lack a proteolytic cleavage site present in many other coronavirus S proteins (Magtoto et al., 2019). In contrast to the amino-terminus of the S protein, homology in the carboxy-terminus between the canine, feline and porcine S proteins ranged from 90.8% to 96.8%. Phylogenetic analysis showed that CCoVs are evolutionarily more related to the feline than to the porcine CoVs. Recombinant S protein of CCoV could be immunoprecipitated by Anti-FCoV antibodies. The phylogenetic relationship between CCoV-I and FCoV-I, and CCoV-II and FCoV-II, indicates the possibility of interspecies transmission.

### 6 Feline Infectious Peritonitis Virus (FIPV; alpha- CoV)

The FIPV belongs to the genus Alpha-CoV that includes CCoV and TGEV (Saif, 2014; Huan et al., 2020; Wang et al., 2019b; Chen et al., 2019b). The genome of FCoV consists of >29,000 nucleotides and 11 ORFs that encode structural, non-structural, and accessory genes (Lee, 2015; Wicht et al., 2014). The important NSPs are, ssRNA-binding protein (NSP9), RdRP (NSP12),

helicase and NTPase (NSP13), 3'→5' exoribonuclease (ExoN) and N7-methyltransferase (NSP14), uridylate-specific endonuclease (NSP 15), and 2'-O-methyltransferase (NSP 16) (Li et al., 2016; Gerdt & Zakhartchouk, 2017). The genome organization of SARS-CoV-2 is similar to FCoV.

The most important feature in FCoV infection is that some infected animals remain healthy whilst others develop FIP, which occurs when FCoV mutates within the host to a highly virulent biotype and the immune response fails to control the infection; mutations in the S gene contribute to the change in virulence by facilitating virus replication in macrophages (Channappanavar et al., 2014; Lin et al., 2016; Oreshkova et al., 2020; Xiao et al., 2020), and it leads to replication of the virus in large quantities in monocyte-macrophages (Decaro et al., 2020; Hirano & Murakami, 2020) that further leads to priming of the monocytes/macrophages by the virus and these primed mononuclear cells interact with endothelial cells and cause granulomatous phlebitis and peri-phlebitis, the morphological features of initial lesion of FIP (Holshue et al., 2020). There were genetic distances in the M and NSP 7b genes that demonstrated distinct virulent and avirulent strains, co-circulating in natural cat populations (Chen et al., 2020; Hu et al., 2021). Similar features have been recorded in severe COVID-19 human patients. The clinical feature of hypergammaglobulinemia-associated FIP is indicative of virus-induced immune dysregulation (Ciotti et al., 2020; Lu et al., 2020). A similar untoward immune reaction leading to pathology is not expected in the COVID-19 vaccines under trial. However, the immune complex reaction might occur after the application of COVID-19 vaccination in areas with high seroprevalence.

### 7 Porcine Coronaviruses (PCoVs)

Swine coronavirus is divided into respiratory (PRCoV) and enteropathogenic, such as transmissible gastroenteritis virus (TGEV), porcine epidemic diarrhea virus (PEDV), and porcine delta coronavirus (PDCoV). TGEV and PEDV are Alphacoronavirus. The number of accessory genes, between ORFs for structural genes, varies between them; TGEV has 3 accessory genes, PDCoV has 2, whereas PEDV has only one (Khailanya et al., 2020). The adaptive immune response is based on secretory antibodies (IgA, IgG, and IgM) and cytotoxic T cells.

#### 7.1 Porcine Respiratory Coronavirus (PRCoV; alpha- CoV)

PRCoV is an S gene deletion mutant of TGEV first identified in Belgium in 1984 (Ahmed et al., 2020; Iwasaki & Yang, 2020). There is a deletion between nt 672 and 681 at the 5' end of the S gene of TGEV (Ganji et al., 2020). European and American isolates of PRCoV differ and developed independently from TGEV. A novel deletion in ORF3a in three field strains of TGEV, similar to the deletion found in PRCoV, was detected showing a

relationship between the TGEV and PRCoV (Sahu et al., 2020). Recombination has been observed between TGEV and PRCoV (Yuki et al., 2020). Though related to TGEV, PRCoV is not enteropathogenic rather causes minor respiratory symptoms. There is serologic cross-reactivity between TGEV and PRCoV (Boniotti et al., 2016; Shi et al., 2020a; Wang et al., 2020).

### 7.2 Transmissible Gastroenteritis Virus (TGEV; alpha- CoV)

The pathogenic porcine-transmissible gastroenteritis virus is responsible for high morbidity and mortality in suckling piglets. Other members of Alphacoronavirus1 are FIPV and CCoV (Belsham et al., 2016; Mora et al., 2019). The virus enters its host cell by binding to the APN (aminopeptidase N) receptor. The RNA genome is >28.5Kb in size and contains seven ORFs (Yachou et al., 2020). The genome of TGEV is arranged in the order 5'-Replicase-S-3a-3b-E-M-N-7-3' with a leader sequence at the 5' end and a poly (A) tail at the 3' end. It encodes four structural proteins, S, E, M and N, and five NSPs, including replicases pp1a and pp1ab, 3a, 3b and 7 (Shi et al., 2018). Activation of nuclear factor-kappa B (NF- $\kappa$ B) and expression of pro-inflammatory cytokines by NSP2 of the virus is important in the pathogenesis (Hoffmann et al., 2018). The NSP papain-like (PL) protease suppresses IFN expression to overcome host innate immunity. Induction of IFN- $\alpha/\beta$  is a crucial antiviral mechanism of the innate immune system. CoVs encode two types of papain-like proteases, PL1 and PL2, contained in NSP5 and NSP3, respectively, that help in processing pp1a and pp1ab polyproteins. Long noncoding RNAs (LncRNAs), transcripts that are not translated, have been found to play important roles in inflammation response in TGE. Natural recombination between Purdue and the Miller strains of TGEV has been detected.

### 7.3 Porcine Epidemic Diarrhea Virus (PEDV; alpha- CoV)

PEDV similar to TGEV is an important swine enteropathogenic coronavirus. Both are transboundary agents and antigenically different, as TGEV antisera failed to neutralize PEDV, and vice versa. This enteric disease of swine was initially described as "epidemic viral diarrhea" in the 1970s in Europe. The incubation period of PEDV ranges from 1 to 8 days, and morbidity approaches 100 % in piglets. PEDV, an alpha-CoV as TGEV, infects gut epithelial cells and macrophages, inducing diarrhea and causing high mortality in piglets. LncRNAs play role in activating the immune system within the ileum. PEDV mutates constantly and recombination occurs frequently among PEDV strains and sometimes between PEDV and other coronaviruses. The ORFs in the 3'-proximal genome regions encode four structural proteins, viz., S, M, E and N. PEDV replicates efficiently in porcine enterocytes, and uses porcine aminopeptidase N (pAPN) on the surface of epithelial cells as the cellular receptor. Trypsin cleaves the S protein into S1 and S2 subunits to facilitate entry of PEDV

into Vero cells, and also release, which helps in efficient viral replication and spreading in vitro. Attenuated and inactivated vaccines have been used to control PED. The vaccine in common use consists of an inactivated whole virus formulated with an adjuvant. The same approach has also been used in developing COVID-19 vaccines (Jain et al., 2020).

### 7.4 Porcine Hemagglutinating Encephalomyelitis Virus (PHEV; beta- CoV, Embecovirus subgenus)

The virus is prevalent worldwide, The PHEV/2008 strain genome was 30,684 bp, with a minimum of 11 ORFs flanked by 5' and 3' untranslated regions, and 16 NSPs, and clustered within lineage A of the genus beta-CoV, relatively close to BCoV and HCoV-OC43 (Shi et al., 2018). The virus attaches to N-acetyl-9-O-acetylneuraminic acid receptors on erythrocytes. Two different genotypes referred to as genotype I (GI-1 to GI-2) and genotype II (GII-1 to GII-3), of the virus, are detected.

### Conclusion

Coronaviruses cause respiratory, and also enteric diseases in man, animals, and birds. Diverse coronaviruses infect domestic species, viz., cattle, dogs, cats, pigs, and poultry. The CoVs have great potential for interspecies transmission, and also mutation and recombination. FCoV and IBV mutate within the host to escape immune response to cause disease. Novel IBV lineages have been emerging continuously. PEDV mutates constantly and recombination occurs frequently among PEDV strains and sometimes with other coronaviruses. Bovine CoV extensively crosses the interspecies barrier, and BCoV-like CoVs have been identified as enteric and/or respiratory pathogens in domesticated and wild ruminants, dogs, and humans. Human CoV-OC43 likely evolved from BCoV and both are beta-CoVs of Embecovirus subgenus. There is an evolutionary relationship between BCoV, HCoV-OC43 and PHEV. Further, turkey enteric coronavirus is similar to BCoV in N and M genes. Given the broad antigenicity and wider prevalence of BCoVs, in the present COVID-19 pandemic, it would be epidemiologically and immunologically important to examine humans for antibodies to BCoV, and surveillance for the possibility of cross-protection by BCoV. The SARS-CoV-2 lacks HE antigen that is present on the surface of BCoV, and surveillance for antibodies to BCoV- HE antigen in humans is likely to explore new ground. IBV is the first CoV that was described in 1930. IBV variants have been isolated from immunized chicken flocks. A similar situation might arise once COVID-19 vaccination is introduced on large scale. And it will be a challenging task to monitor the efficiency of future COVID-19 vaccines. The S protein of CoVs is important in virus-host interaction and contributes to antigenic differences between strains. Mutations in the S gene contribute to the change in virulence and may facilitate virus replication in macrophages. Macrophages are

associated with the pathogenesis of FIP, PED, and SARS-CoV. The S gene of CCoV is closely related to FCoVs type II, TGEV, and PRCoV. CCoVs are evolutionarily closer to the FCoVs. PRCoV is an S gene deletion mutant of TGEV and offers cross-protection as a heterologous vaccine. Many species of the CoV infect one host species, opening the chances of genetic recombination. Seven CoVs (2 alpha- and 5 beta- CoV) infect humans, whereas six (4 alpha-, and 1 each of beta- and delta- CoV) infect pigs. Dogs are infected by both alpha- and beta-CoVs. There is a similarity in the pathogenesis of FIPV and COVID-19 in terms of cytokine storm and ADE. Animal CoV inactivated vaccines suffer from a relatively short duration of protective immunity. The situation could be similar in the case of inactivated whole virus COVID-19 vaccines. However, COVID-19 vaccines must elicit protective immunity without causing immunopathology, as described in the case of vaccine for FIPV. New generation vaccines for TGE, S1-DNA vaccine, induced excellent humoral and cellular immune response. Single-chain fragment variable (scFv) antibodies have been used for both prevention and treatment of TGEV infection in swine. A deep understanding of animal CoVs, their distribution in nature, host tropism and genetic variations, pathogenesis, and genomic and antigenic similarities with human CoVs are essential in planning control strategies for COVID-19.

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**Conflict of Interest:** Nil

### References

- Abassi Z, Knaney Y, Karram T, Heyman SN (2020) The Lung Macrophage in SARS-CoV-2 Infection: A Friend or a Foe?. *Frontiers in immunology* 11: 1312.
- Adabor ES (2019) Anticipating time-dependent antigenic variants of influenza A (H3N2) viruses. *Infection, Genetics and Evolution* 67: 67–72.
- Ahmed SF, Quadeer AA, McKay MR (2020) Preliminary Identification of Potential vaccine targets for the COVID-19 Coronavirus (SARS-CoV-2) based on SARS-CoV immunological studies. *Viruses* 12:254.
- Amarasinghe A, Abdul-Cader MS, Nazir S, De Silva Senapathi U, van der Meer F, Cork SC, Gomis S, Abdul-Careem MF (2017) Infectious bronchitis corona virus establishes productive infection in avian macrophages interfering with selected antimicrobial functions. *PLoS One* 12(8): e0181801.
- Amer HM (2018) Bovine-like coronaviruses in domestic and wild ruminants. *Animal Health Research Reviews* 19(2):113-124.
- Belsham GJ, Rasmussen TB, 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. *Transboundary and Emerging Diseases* 63:595–601.
- Boniotti MB, 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. *Emerging infectious diseases* 22(1):83–87.
- Burimuah V, Sylverken A, Owusu M, El-Duah P, Yeboah R, Lamptey J, et al. (2020) Molecular-based cross-species evaluation of bovine coronavirus infection in cattle, sheep and goats in Ghana. *BMC veterinary research* 16(1): 405.
- Byukusenge M, Nissly RH, Kasibhatla SM, Li L, Russell R, Springer H, et al. (2018) Complete Genome Sequences of Four Bovine Coronavirus Isolates from Pennsylvania. *Genome Announcements* 6(22): e00467-18.
- Castells M, Giannitti F, Caffarena RD, Casaux ML, Schild C, Castells D, Riet-Correa F, Victoria M, Parreño V, Colina R (2019) Bovine coronavirus in Uruguay: genetic diversity, risk factors and transboundary introductions from neighboring countries. *Archives of Virology* 164(11): 2715–2724.
- Cavanagh D (2003) Severe acute respiratory syndrome vaccine development: experiences of vaccination against avian infectious bronchitis coronavirus. *Avian Pathology* 32(6): 567–582.
- Cavanagh D (2007) Coronavirus avian infectious bronchitis virus. *Veterinary research* 38:281–297.
- Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, Yuen KY (2020) Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. *Emerging Microbes & Infections* 9(1): 221–236.
- Channappanavar R, Perlman S (2017) Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Seminars in immunopathology* 39(5): 529–539.
- Channappanavar R, Zhao J, Perlman S (2014) T cell-mediated immune response to respiratory coronaviruses. *Immunologic Research* 59(1-3):118–128.

- Chen J, Zhang C, Zhang Na, Liu G (2019a) Porcine endemic diarrhoea virus infection regulates long noncoding RNA expression. *Virology* 527: 89-97.
- Chen Y, Liu Q, Guo D (2020) Emerging coronaviruses: Genome structure, replication, and pathogenesis. *Journal of Medical Virology* 92(4): 418–423.
- Chen F, Knutson TP, Rossow S, Saif LJ, Marthaler DG (2019b) Decline of transmissible gastroenteritis virus and its complex evolutionary relationship with porcine respiratory coronavirus in the United States. *Scientific reports* 9(1):3953.
- Ciotti M, Angeletti S, Minieri M, Giovannetti M, Benvenuto D, Pascarella S, et al. (2020) COVID-19 outbreak: An overview. *Chemotherapy* 17(6):2094.
- Czaja AJ (2016) Diagnosis and Management of Autoimmune Hepatitis: Current Status and Future Directions. *Gut and liver* 10(2): 177–203.
- De Wit JJ, Nieuwenhuisen-van Wilgen J, Hoogkamer A, van de Sande H, Zuidam GJ, Fabri TH (2011) Induction of cystic oviducts and protection against early challenge with infectious bronchitis virus serotype D388 (genotype QX) by maternally derived antibodies and by early vaccination. *Avian Pathology* 40(5): 463–471.
- Dearlove B, Lewitus E, Bai H, Li Y, Reeves D B, Joyce M G, Scott P T, Amare M F, et al. (2020) A SARS-CoV-2 vaccine candidate would likely match all currently circulating variants. *Proceedings of the National Academy of Sciences of the United States of America* 117(38): 23652–23662.
- Decaro N, Mari V, Dowgier G, Elia G, Lanave G, Colaianni ML, Buonavoglia C (2015) Full-genome sequence of pantropic canine coronavirus. *Genome announcements* 3(3): e00401-15.
- Decaro N, Martella V, Saif LJ, Buonavoglia C (2020) COVID-19 from veterinary medicine and one health perspectives: What animal coronaviruses have taught us. *Research in Veterinary Science* 131: 21-23.
- Doki T, Yabe M, Takano T, Hohdatsu T (2018) Differential induction of type I interferon by type I and type II feline coronaviruses in vitro. *Research in veterinary science* 120: 57–62.
- Emmler L, Felten S, Matiasek K, Balzer HJ, Pantchev N, Leutenegger C, Hartmann K (2020) Feline coronavirus with and without spike gene mutations detected by real-time RT-PCRs in cats with feline infectious peritonitis. *Journal of Feline Medicine and Surgery* 22(8): 791–799.
- Enjuanes L, Brian D, Cavanagh D, Holmes K, Lai MMC, Laude H, Masters P, Rottier P, Siddell S, Spaan WJM, Taguchi F, Talbot P (2000) Coronaviridae In: van Regenmortel MHV, Fauquet CM, Bishop DHL, et al. (Eds.) *Virus Taxonomy, Seventh Report of the International Committee on Taxonomy of Viruses*. San Diego: Academic Press 827–834.
- Fan Wu, Aojie Wang, Mei Liu, Qimin Wang, Jun Chen, Shuai Xia, Yun Ling, et al. (2020) Neutralizing antibody responses to SARS-CoV-2 in a COVID-19 recovered patient cohort and their implications. *MedRxiv* 20047365. doi: <https://doi.org/10.1101/2020.03.30.20047365>.
- Fehr AR, Perlman S (2015) Coronaviruses: an overview of their replication and pathogenesis. *Methods in Molecular Biology (Clifton, N.J.)* 1282: 1–23.
- Felten S, Hartmann K (2019) Diagnosis of Feline Infectious Peritonitis: A Review of the Current Literature. *Viruses* 11(11): 1068.
- Felten S, Leutenegger CM, Balzer HJ, Pantchev N, Matiasek K, Wess G, Egberink H, Hartmann K (2017) Sensitivity and specificity of a real-time reverse transcriptase polymerase chain reaction detecting feline coronavirus mutations in effusion and serum/plasma of cats to diagnose feline infectious peritonitis. *BMC veterinary research* 13(1): 228.
- Franzo G, Legnardi M, Tucciarone CM, Drigo M, Martini M, Cecchinato M (2019) Evolution of infectious bronchitis virus in the field after homologous vaccination introduction. *Veterinary Research* 50(1): 92.
- Fulton RW, Ridpath JF, Burge LJ (2013) Bovine coronaviruses from the respiratory tract: antigenic and genetic diversity. *Vaccine* 31(6):886-92.
- Fung TS, Liao Y, Liu DX (2016) Regulation of stress responses and translational control by coronavirus. *Viruses* 8(7):184.
- Ganji A, Farahani I, Khansarinejad, B, Ghazavi A, Mosayebi G (2020) Increased expression of CD8 marker on T-cells in COVID-19 patients. *Blood Cells, Molecules and Diseases* 83:102437.
- Gerds V, Zakhartchouk A (2017) Vaccines for porcine epidemic diarrhoea virus and other swine coronaviruses. *Veterinary Microbiology* 206:45–51.
- Guo R, Fan B, Chang X, Zhou J, Zhao Y, Shi D, Yu Z, He K, Li B (2020) Characterization and evaluation of the pathogenicity of a natural recombinant transmissible gastroenteritis virus in China. *Virology* 545:24-32.
- Hassan MSH, Ojkic D, Coffin CS, Cork SC, van der Meer F, Abdul-Careem MF (2019) Delmarva (DMV/1639) Infectious Bronchitis Virus (IBV) Variants Isolated in Eastern Canada Show Evidence of Recombination. *Viruses* 11(11): 1054.

- Hirano T, Murakami M (2020) COVID-19: A new virus, but a familiar receptor and cytokine release syndrome. *Immunity* 52(5):731-733.
- Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. (2018) SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. *Cell* 181(2): 271-280.
- Holshue ML, DeBolt C, Lindquist S, Lofy KH, Wiesman J, Bruce H, Spitters C, Ericson K, Wilkerson S, Tural A, Diaz G, Cohn A, Fox L, Patel A, Gerber SI, Kim L, Tong S, Lu X, Lindstrom S, Pallansch MA, Weldon WC, Biggs HM, Uyeki TM, Pillai SK, Washington State 2019-nCoV Case Investigation Team (2020) First Case of 2019 Novel Coronavirus in the United States. *The New England Journal of Medicine* 382(10): 929–936.
- Honeycutt JB, Wahl A, Baker C, Spagnuolo RA, Foster J, Zakharova O, Wietgreffe S, et al. (2016) Macrophages sustain HIV replication in vivo independently of T cells. *The Journal of Clinical Investigation* 126(4): 1353–1366.
- Hsieh LE, Chueh LL (2014) Identification and genotyping of feline infectious peritonitis-associated single nucleotide polymorphisms in the feline interferon- $\gamma$  gene. *Veterinary Research* 45(1):57.
- Hu B, Guo H, Zhou P, Shi ZL (2021) Characteristics of SARS-CoV-2 and COVID-19. *Nature reviews. Microbiology* 19(3): 141–154.
- Hu X Jr, Li N Jr, Tian Z Jr, Yin X Jr, Qu L, Qu J (2015) Molecular characterization and phylogenetic analysis of transmissible gastroenteritis virus HX strain isolated from China. *BMC Veterinary Research* 11: 72.
- Huan C, Pan H, Fu S, Xu W, Gao Q, Wang X, Gao S, Chen C, Liu X (2020) Characterization and evolution of the coronavirus porcine epidemic diarrhoea virus HLJBY isolated in China. *Transboundary and Emerging Diseases* 67(1): 65–79.
- Hulswit RJ, de Haan CA, Bosch BJ (2016) Coronavirus Spike Protein and Tropism Changes. *Advances in Virus Research* 96: 29–57.
- Issa E, Merhi G, Panossian B, Salloum T, Tokajian S (2020) SARS-CoV-2 and ORF3a: Nonsynonymous Mutations, Functional Domains, and Viral Pathogenesis. *mSystems* 5(3): e00266-20.
- Iwasaki A, Yang Y (2020) The potential danger of suboptimal antibody response in COVID-19. *Nature* 20:339-341.
- Jackwood MW (2012) Review of infectious bronchitis virus around the world. *Avian Diseases* 56(4):634-41.
- Jain AS, Sushma P, Dharmashekar C, Beelagi MS, Prasad SK, Shivamallu C, Prasad A, Syed A, Marraiki N, Prasad KS (2020) In silico evaluation of flavonoids as effective antiviral agents on the spike glycoprotein of SARS-CoV-2. *Saudi Journal of Biological Sciences* 28(1): 1040-1051.
- Jordan B (2017) Vaccination against infectious bronchitis virus: A continuous challenge. *Veterinary microbiology* 206: 137–143.
- Kameka AM, Haddadi S, Sun Kim DS, Cork SC, Abdul-Careem MF (2014) Induction of innate immune response following infectious bronchitis corona virus infection in the respiratory tract of chickens. *Virology* 450-451: 114-21.
- Kanno T, Ishihara R, Hatama S, Uchida I (2018) A long-term animal experiment indicating persistent infection of bovine coronavirus in cattle. *The Journal of Veterinary Medical Science* 80(7):1134-1137.
- Keha A, Luo Xue, Shen Yan, Hua Yue, Cheng Tang (2019) Prevalence of a novel bovine coronavirus strain with a recombinant hemagglutinin/esterase gene in dairy calves in China. *Transboundary and Emerging Diseases* 66(5): 1971–1981.
- Kennedy MA (2020) Feline Infectious Peritonitis: Update on Pathogenesis, Diagnostics, and Treatment. *The Veterinary clinics of North America. Small Animal Practice* 50(5): 1001–1011.
- Khailanya R A, Safdarb M, Ozaslan M (2020) Genomic characterization of a novel SARS-CoV-2. *Gene Reports* 19:100682.
- Khataby K, Souiri A, Kasmi Y, Loutfi C, Ennaji MM (2016) Current situation, genetic relationship and control measures of infectious bronchitis virus variants circulating in African regions. *Journal of Basic & Applied Zoology* 76: 20–30.
- Kim JH, Jang JH, Yoon SW, Noh JY, Ahn MJ, Kim Y, Jeong DG, Kim HK (2018) Detection of bovine coronavirus in nasal swab of non-captive wild water deer, Korea. *Transboundary and Emerging Diseases* 65(3):627-631.
- Kint J, Langereis MA, Maier HJ, Britton P, van Kuppeveld FJ, Koumans J, Wiegertjes GF, Forlenza M (2016) Infectious Bronchitis Coronavirus Limits Interferon Production by Inducing a Host Shutoff That Requires Accessory Protein 5b. *Journal of Virology* 90(16): 7519–7528.
- Kipar A, Meli ML, Failing K, Euler T, Gomes-Keller MA, Schwartz D, Lutz H, Reinacher M (2006) Natural feline coronavirus infection: differences in cytokine patterns in association with the outcome of infection. *Veterinary Immunology and Immunopathology* 112(3-4):141–55.

- LahaS, Chakraborty J, Das S, Manna SK, Biswas S, Chatterjee R (2020) Characterizations of SARS-CoV-2 mutational profile, spike protein stability and viral transmission. *Infection, Genetics and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases* 85:104445.
- Lee C (2015) Porcine epidemic diarrhoea virus: An emerging and re-emerging epizootic swine virus. *Virology Journal* 12:193.
- Leghari RA, Fan B, Wang H, Bai J, Zhang L, Abro SH, Jiang P (2016) Full-length genome sequencing analysis of avian infectious bronchitis virus isolate associated with nephropathogenic infection. *Poultry science* 95(12): 2921–2929.
- Lewis CS, Porter E, Matthews D, Kipar A, Tasker S, Helps CR, Siddell SG (2015) Genotyping coronaviruses associated with feline infectious peritonitis. *The Journal of General Virology* 96 (6): 1358–1368.
- Li C, Liu Q, Kong F, Guo D, Zhai J, Su M, Sun D (2019) Circulation and genetic diversity of Feline coronavirus type I and II from clinically healthy and FIP-suspected cats in China. *Transboundary and Emerging Diseases* 66(2): 763–775.
- Li S, Bai L, Dong J, Sun R, Lan K (2017) Kaposi's Sarcoma-Associated Herpesvirus: *Epidemiology and Molecular Biology. Advances in Experimental Medicine and Biology* 1018: 91–127.
- Li W, van Kuppeveld FJM, He Q, Rottier PJM, Bosch BJ (2016) Cellular entry of the porcine epidemic diarrhea virus. *Virus Research* 226:117-127.
- Licitra BN, Duhamel GE, Whittaker GR (2014) Canine enteric coronaviruses: emerging viral pathogens with distinct recombinant spike proteins. *Viruses* 6(8): 3363–3376.
- Lin C M, Saif L J, Marthaler D, Wang Q (2016) Evolution, antigenicity and pathogenicity of global porcine epidemic diarrhea virus strains. *Virus Research* 226: 20–39.
- Lin SY, Chen HW (2017) Infectious Bronchitis Virus Variants: Molecular Analysis and Pathogenicity Investigation. *International Journal of Molecular Sciences* 18(10):2030.
- Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y, et al. (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Genomic characterization, and epidemiology of 2019 novel coronavirus: Implications for virus origins and receptor binding. Lancet* 395(10224): 565–574.
- Luk HKH, Li X, Fung J, Lau SKP, Woo PCY (2019) Molecular epidemiology, evolution and phylogeny of SARS coronavirus. *Infection, genetics and evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases* 71: 21–30.
- Ma T, Xu L, Ren M, Shen J, Han Z, Sun J, Zhao Y, Liu S (2019a) Novel genotype of infectious bronchitis virus isolated in China. *Veterinary Microbiology* 230:178-186.
- Ma X, Zhao X, Wang K, Tang X, Guo J, Mi M, Qi Y, Chang L, Huang Y, Tong D (2019b) Identification and analysis of long non-coding RNAs that are involved in inflammatory process in response to transmissible gastroenteritis virus infection. *BMC Genomics* 20:806.
- Ma Y, Wang C, Xue M, Fu F, Zhang X, Li L, Yin L, Xu W, Feng L, Liu P (2018) The Coronavirus Transmissible Gastroenteritis Virus Evades the Type I Interferon Response through IRE1 $\alpha$ -Mediated Manipulation of the MicroRNA miR-30a-5p/SOCS1/3 Axis. *Journal of Virology* 92(22): e00728-18.
- Magtoto R, Poonsuk K, Baum D, Zhang J, Chen Q, Ji J, Piñeyro P, Zimmerman J, Giménez-Lirola LG (2019) Evaluation of the Serologic Cross-Reactivity between Transmissible Gastroenteritis Coronavirus and Porcine Respiratory Coronavirus Using Commercial Blocking Enzyme-Linked Immunosorbent Assay Kits. *mSphere* 4(2):e00017-19.
- Masters PS (2016) The molecular biology of coronaviruses. *Advance Virus Research* 66:193–292.
- Mora-Díaz JC, Piñeyro PE, Houston E, Zimmerman J, Giménez-Lirola LG (2019) Porcine Hemagglutinating Encephalomyelitis Virus: A Review. *Frontiers in veterinary science* 6:53.
- Mou C, Zhu L, Xing X, Lin J, Yang Q (2016) Immune responses induced by recombinant *Bacillus subtilis* expressing the spike protein of transmissible gastroenteritis virus in pigs. *Antiviral Research* 131:74-84.
- Munir M, Cortey M (2015) Estimation of evolutionary dynamics and selection pressure in coronaviruses. *Methods in molecular biology (Clifton, N.J.)* 1282: 41–48.
- Murphy BG, Perron M, Murakami E, Bauer K, Park Y, Eckstrand C, Liepnieks M, Pedersen NC (2018) The nucleoside analog GS-441524 strongly inhibits feline infectious peritonitis (FIP) virus in tissue culture and experimental cat infection studies. *Veterinary Microbiology* 219: 226–233.
- Naylor MJ, Walia CS, McOrist S, Lehrbach PR, Deane EM, Harrison GA (2002) Molecular characterization confirms the presence of a divergent strain of canine coronavirus (UWSMN-1) in Australia. *Journal of Clinical Microbiology* 40(9):3518-22.

- Nemoto M, Kanno T, Bannai H, Tsujimura K, Yamanaka T, Kokado H (2017) Antibody response to equine coronavirus in horses inoculated with a bovine coronavirus vaccine. *The Journal of Veterinary Medical Science* 79(11):1889-1891.
- Ntafis V, Mari V, Decaro N, Papanastassopoulou M, Pardali D, Rallis TS, Kanellos T, Buonavoglia C, Xylouri E (2013) Canine coronavirus, Greece. Molecular analysis and genetic diversity characterization. *Infection, Genetics and Evolution* 16:129-36.
- Oreshkova N, Molenaar RJ, Vreman S, Harders F, Oude Munnink BB, Hakze-van der Honing RW, et al. (2020) SARS-CoV-2 infection in farmed minks, the Netherlands, April and May 2020. *Euro surveillance: bulletin Europeen sur les maladies transmissibles. European Communicable Disease Bulletin* 25(23):2001005.
- Ou X, Liu Y, Lei X, Li P, Mi D, Ren L, Guo L, Guo R, Chen T, Hu J, Xiang Z, Mu Z, Chen X, Chen J, Hu K, Jin Q, Wang J, Qian Z (2020) Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. *Nature Communications* 11(1):1620.
- Patel BH, Bhimani MP, Bhandari BB, Jhala MK (2015) Isolation and molecular characterization of nephropathic infectious bronchitis virus isolates of Gujarat state, India. *Virus Disease* 26:42-47.
- Pedersen NC (2014) An update on feline infectious peritonitis: Virology and immunopathogenesis. *Veterinary Journal* 201(2): 123-132.
- Phillips JM, Gallagher T, Weiss SR (2017) Neurovirulent Murine Coronavirus JHM.SD Uses Cellular Zinc Metalloproteases for Virus Entry and Cell-Cell Fusion. *Journal of Virology* 91(8): e01564-16.
- Poran A, Harjanto D, Malloy M, Arieta CM, Rothenberg DA, Lenkala D, van Buuren MM, Addona TA, Rooney MS, Srinivasan L, Gaynor RB (2020) Sequence-based prediction of SARS-CoV-2 vaccine targets using a mass spectrometry-based bioinformatics predictor identifies immunogenic T cell epitopes. *Genome Medicine* 12:70.
- Porter E, Tasker S, Day MJ, Harley R, Kipar A, Siddell SG, Helps CR (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. *Veterinary Research* 45(1):49.
- Premkumar L, Segovia-Chumbez B, Jadi R, Martinez DR, Raut R, Markmann A, et al. (2020) The receptor binding domain of the viral spike protein is an immunodominant and highly specific target of antibodies in SARS-CoV-2 patients. *Science Immunology* 5(48): eabc8413.
- Qian S, Gao Z, Cao R, Yang K, Cui Y, Li S, Meng X, He Q, Li Z (2020) Transmissible Gastroenteritis Virus Infection Up-Regulates FcRn Expression via Nucleocapsid Protein and Secretion of TGF- $\beta$  in Porcine Intestinal Epithelial Cells. *Frontiers in microbiology* 10: 3085.
- Rohaim MA, El Nagggar RF, Abdelsabour MA, Mohamed MHA, El-Sabagh IM, Munir M (2020) Evolutionary Analysis of Infectious Bronchitis Virus Reveals Marked Genetic Diversity and Recombination Events. *Genes* 11(6): 605.
- Safavi A, Kefayat A, Mahdevar E, Abiri A, Ghahremani F (2020) Exploring the out of sight antigens of SARS-CoV-2 to design a candidate multi-epitope vaccine by utilizing immunoinformatics approaches. *Vaccine* 38(48): 7612-7628.
- Sahu KK, Mishra AK, Lal A (2020) COVID-19: update on epidemiology, disease spread and management. *Monaldi Archives Chest Disease* 90(1).
- Saif LJ (2014) Animal coronavirus vaccines: lessons for SARS. *Developments in Biologicals* 119:129-40.
- Saif LJ, Jung K (2020) Comparative Pathogenesis of Bovine and Porcine Respiratory Coronaviruses in the Animal Host Species and SARS-CoV-2 in Humans. *Journal of Clinical Microbiology* 58(8): e01355-20.
- Sanchez-Morgado JM, Poynter S, Morris TH (2004) Molecular characterization of a virulent canine coronavirus BGF strain. *Virus Research* 104(1): 27-31.
- Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, Geng Q, Auerbach A, Li F (2020) Structural basis of receptor recognition by SARS-CoV-2. *Nature* 581(7807):221-224.
- Shi J, Wen Z, Zhong G, Yang H, Wang C, Huang B, Liu R, He X, Shuai L, Sun Z, et al. (2020) Susceptibility of ferrets, cats, dogs, and other domesticated animals to SARS-coronavirus 2. *Science* 368(6494):1016-1020.
- Shi J, Zhao K, Lu H, Zi Li, Lv X, Lan Y, Guan J, He W, Gao F (2018) Genomic characterization and pathogenicity of a porcine hemagglutinating encephalomyelitis virus strain isolated in China. *Virus Genes* 54(5): 672-683.
- Shi Y, Wang Y, Shao C, Huang J, Gan J, Huang X, Bucci E, Piacentini M, Ippolito G, Melino G (2020) COVID-19 infection: the perspectives on immune responses. *Cell Death & Differentiation* 27:1451-1454.

- Shin J, Tark D, Le VP, Choe S, Cha RM, Park GN, Cho IS, Nga BTT, Lan NT, An DJ (2019) Genetic characterization of bovine coronavirus in Vietnam. *Virus Genes* 55(3): 415–420.
- Simon-Loriere E, Holmes EC (2011) Why do RNA viruses recombine? *Nature reviews Microbiology* 9(8): 617–626.
- Siu KL, Chan CP, Kok KH, Woo PC, Jin DY (2014) Comparative analysis of the activation of unfolded protein response by spike proteins of severe acute respiratory syndrome coronavirus and human coronavirus HKU1. *Cell & Bioscience* 4(1):3.
- Snijder EJ, Decroly E, Ziebuhr J (2016) The Nonstructural Proteins Directing Coronavirus RNA Synthesis and Processing. *Advances in Virus Research* 96: 59–126.
- Subbarao K, Mahanty S (2020) Respiratory Virus Infections: Understanding COVID-19. *Immunity* 52:905-09.
- Sumi V, Singh SD, Dhama K, Gowthaman V, Barathidasan R, Sukumar K (2012) Isolation and molecular characterization of infectious bronchitis virus from recent outbreaks in broiler flocks reveals emergence of novel strain in India. *Tropical Animal Health and Production* 44(7):1791–1795.
- Szczepanski A, Owczarek K, Bzowska M, Gula K, Drobot I, Ochman M, Maksym B, Rajfur Z, Mitchell JA, Pyrc K (2019) Canine Respiratory Coronavirus, Bovine Coronavirus, and Human Coronavirus OC43: Receptors and Attachment Factors. *Viruses* 11(4):328.
- Takano T, Tomiyama Y, Katoh Y, Nakamura M, Satoh R, Hohdatsu T (2011) Mutation of neutralizing/antibody-dependent enhancing epitope on spike protein and 7b gene of feline infectious peritonitis virus: influences of viral replication in monocytes/macrophages and virulence in cats. *Virus Research* 156: 72–80.
- Terada Y, Matsui N, Noguchi K, Kuwata R, Shimoda H, Soma T, Mochizuki M, Maeda K (2014) Emergence of pathogenic coronaviruses in cats by homologous recombination between feline and canine coronaviruses. *PLoS One* 9(9):e106534.
- Thielen PM, Wohl S, Mehoke T, Ramakrishnan S, Kirsche M, Falade-Nwulia O, et al. (2020) Genomic Diversity of SARS-CoV-2 during Early Introduction into the United States National Capital Region. *MedRxiv* 20174136. <https://doi.org/10.1101/2020.08.13.20174136>.
- Timurkan MO, Aydin H, Dincer E, Coskun N (2021) Molecular characterization of canine coronaviruses: an enteric and pantropic approach. *Archives of Virology* 166(1): 35–42.
- Tizard IR (2020) Vaccination against coronaviruses in domestic animals. *Vaccine* 38(33): 5123–5130.
- Tortorici MA, Walls AC, Lang Y, Wang C, Li Z, Koerhuis D, Boons GJ, Bosch BJ, et al. (2019) Structural basis for human coronavirus attachment to sialic acid receptors. *Nature Structural & Molecular Biology* 26(6): 481–489.
- Tung P (2020) Genetic diversity and evolution of SARS-CoV-2. *Infection, Genetics and Evolution* 81:104260.
- Valastro V, Holmes EC, Britton P, Fusaro A, Jackwood MW, Cattoli G, Monne I (2016) S1 gene-based phylogeny of infectious bronchitis virus: an attempt to harmonize virus classification. *Infection, Genetics and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases* 39:349–364.
- Van Dorp L, Acman M, Richard D, Shaw LP, Ford CE, Ormond L, Owen CJ, Pang J, Tan CCS, Boshier FAT, Ortiz AT, Balloux F (2020) Emergence of genomic diversity and recurrent mutations in SARS-CoV-2. *Infection, Genetics and Evolution* 83:104351.
- Vijgen L, Keyaerts E, Lemey P, Maes P, Van Reeth K, Nauwynck H, Pensaert M, Van Ranst M (2016) Evolutionary History of the Closely Related Group 2 Coronaviruses: Porcine Hemagglutinating Encephalomyelitis Virus, Bovine Coronavirus, and Human Coronavirus OC43. *Journal of Virology* 80(14): 7270–7274.
- Vuong W, Khan MB, Fischer C, Arutyunova E, Lamer T, Shields J, Saffran HA, McKay RT, van Belkum MJ, Joyce MA, Young HS, Tyrrell DL, Vederas JC, Lemieux MJ (2020) Feline coronavirus drug inhibits the main protease of SARS-CoV-2 and blocks virus replication. *Nature Communications* 11(1): 4282.
- Wang C, Liu Z, Chen Z, Huang X, Xu M, He T, Zhang Z (2020) The establishment of reference sequence for SARS-CoV-2 and variation analysis. *Journal of Medical Virology* 92(6): 667–674.
- Wang D, Chen J, Yu C, Zhu X, Xu S, Fang L, Xiao S (2019a) Porcine Reproductive and Respiratory Syndrome Virus nsp11 antagonizes type I Interferon signalling by targeting IRF9. *Journal of Virology* 93(15): e00623-19.
- Wang L, Qiao X, Zhang S, Qin Y, Guo T, Hao Z, Sun L, Wang X, Wang Y, Jiang Y, Tang L, Xu Y, Li Y (2018b) Porcine transmissible gastroenteritis virus non-structural protein 2 contributes to inflammation via NF- $\kappa$ B activation. *Virulence* 9(1):1685-1698.
- Wang Q, Vlasova AN, Kenney SP, Saif LJ (2019b) Emerging and re-emerging coronaviruses in pigs. *Current Opinion in Virology* 34:39–49.

- Wicht O, Li W, Willems L, Meuleman TJ, Wubolts RW, van Kuppeveld FJ, Rottier PJ, Bosch BJ (2014) Proteolytic activation of the porcine epidemic diarrhoea coronavirus spike fusion protein by trypsin in cell culture. *Journal of Virology* 88(14):7952-7961.
- Woo PC, Lau SK, Wernery U, Wong EY, Tsang AK, Johnson B, Yip CC, Lau CC, Sivakumar S, Cai JP, Fan RY, Chan KH, Mareena R, Yuen KY (2014) Novel betacoronavirus in dromedaries of the Middle East, 2013. *Emerging Infectious Diseases* 20:560-572.
- Xia L, Yang Y, Wang J, Jing Y, Yang Q (2018) Impact of TGEV infection on the pig small intestine. *Virology journal* 15(1): 102.
- Xiao K, Zhai J, Feng Y, Zhou N, Zhang X, Zou JJ, Li N, Guo Y, Li X, Shen X, Zhang Z, et al. (2020) Isolation of SARS-CoV-2-related coronavirus from Malayan pangolins. *Nature* 583(7815):286-289.
- Xu L, Han Z, Jiang L, Sun J, Zhao Y, Liu S (2018) Genetic diversity of avian infectious bronchitis virus in China in recent years. *Infection, Genetics and Evolution: Journal of Molecular Epidemiology and Evolutionary Genetics in Infectious Diseases* 66:82-94.
- Yachou Y, El Idrissi A, Belapasov V, Ait Benali S (2020) Neuroinvasion, neurotropic, and neuroinflammatory events of SARS-CoV-2: understanding the neurological manifestations in COVID-19 patients. *Neurological sciences: official journal of the Italian Neurological Society and of the Italian Society of Clinical Neurophysiology* 41(10): 2657-2669.
- Yan S, Zhao J, Xie D, Huang X, Cheng J, Guo Y, Liu C, Ma Z, Yang H, Zhang G (2018) Attenuation, safety, and efficacy of a QX-like infectious bronchitis virus serotype vaccine. *Vaccine* 36(14):1880-1886.
- Ye ZW, Yuan S, Yuen KS, Fung SY, Chan CP, Jin DY (2020) Zoonotic origins of human coronaviruses. *International Journal of Biological Sciences* 16(10): 1686-1697.
- Yin C (2020) Genotyping coronavirus SARS-CoV-2: methods and implications. *Genomics* 112:3588-3596.
- Yuki K, Fujiogi M, Koutsogiannaki S (2020) COVID-19 pathophysiology: A review. *Clinical Immunology* 215:108427.
- Zeng R, Yang RF, Shi MD, Jiang MR, Xie YH, Ruan HQ, Jiang XS, Shi L, Zhou H, et al. (2004) Characterization of the 3a protein of SARS-associated coronavirus in infected Vero E6 cells and SARS patients. *Journal of Molecular Biology* 341(1):271-279.
- Zhang F, Chen Y, Yang L, Zhu J (2019) Construction and characterization of porcine single-chain fragment variable antibodies that neutralize transmissible gastroenteritis virus in vitro. *Archives of Virology* 164(4):983-994.
- Zhang L, Lin D, Sun X, Curth U, Drosten C, Sauerhering L, Becker S, Rox K, Hilgenfeld R (2020) Crystal structure of SARS-CoV-2 main protease provides a basis for design of improved  $\alpha$ -ketoamide inhibitors. *Science* 368(6489):409-412.
- Zhang X, Zhu Y, Zhu X, Shi H, Chen J, Shi D, Yuan J, Cao L, Liu J, Dong H, Jing Z, Zhang J, Wang X, Feng L (2017) Identification of a natural recombinant transmissible gastroenteritis virus between Purdue and Miller clusters in China. *Emerging microbes & infections* 6(8): e74.
- Zheng D, Chen G, Guo B, Cheng G, Tang H (2008) PLP2, a potent deubiquitinase from murine hepatitis virus, strongly inhibits cellular type I interferon production. *Cell Research* 18(11):1105-1113.
- Zheng J, Yamada Y, Fung TS, Huang M, Chia R, Liu DX (2018) Identification of N-linked glycosylation sites in the spike protein and their functional impact on the replication and infectivity of coronavirus infectious bronchitis virus in cell culture. *Virology* 513:65-74.
- Zhou Y, He C, Wang L, Ge B (2017) Post-translational regulation of antiviral innate signaling. *European Journal of Immunology* 47(9): 1414-1426.