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.

Virus Research 290 (2020) 198175

Contents lists available at ScienceDirect

Virus Research

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

Review

Zoonotic evolution and implications of microbiome in viral transmission and infection

Riya Rajeev [a], R. Prathiviraj [a], George Seghal Kiran [b], Joseph Selvin [a,*]

[a] Department of Microbiology, Pondicherry University, Puducherry 605014, India
[b] Department of Food Science and Technology, Pondicherry University, Puducherry 605014, India

ARTICLE INFO

Keywords:
Covid-19
Zoonotic evolution
Human microbiome
Viral infection
Zoonotic infection
Synthetic virus

ABSTRACT

The outbreak and spread of new strains of coronavirus (SARS-CoV-2) remain a global threat with increasing cases in affected countries. The evolutionary tree of SARS-CoV-2 revealed that Porcine Reproductive and Respiratory Syndrome virus 2, which belongs to the Beta arterivirus genus from the *Arteriviridae* family is possibly the most ancient ancestral origin of SARS-CoV-2 and other *Coronaviridae*. This review focuses on phylogenomic distribution and evolutionary lineage of zoonotic viral cross-species transmission of the *Coronaviridae* family and the implications of bat microbiome in zoonotic viral transmission and infection. The review also casts light on the role of the human microbiome in predicting and controlling viral infections. The significance of microbiome-mediated interventions in the treatment of viral infections is also discussed. Finally, the importance of synthetic viruses in the study of viral evolution and transmission is highlighted.

1. Introduction

In the end of December 2019, the world witnessed its new devastating pandemic outbreak in the form of an acute respiratory illness, caused by a novel coronavirus, SARS-CoV-2, first reported in Wuhan, Hubei Province, in central China (Chan et al., 2020; Chen et al., 2020). In the absence of specific antiviral drugs and vaccines, the conventional treatment strategies seem to be less effective in controlling the virus spread which makes it an international public health emergency with a huge number of individuals being infected each day all over the globe (Sun et al., 2020). Genome sequencing of human SARS-CoV-2 reveals 96.2 % match with bat SARS-related coronavirus, BatCoV RaTG13 which indicates that bats might be a natural host (Guo et al., 2020; Zhou et al., 2020). Pangolin-CoV which is 91.02 % identical to SARS-CoV-2 is reported to be its next closest relative (Zhang et al., 2020). Despite the knowledge of the process of emergence of the infectious agents, it is not yet possible to predict the outbreak in the earlier stages. But now, it has become necessary for the researcher to intrude even before the pathogen infects the humans, and to develop the precautionary measures (Morse et al., 2012).

Several studies have been conducted to reveal the evolutionary basis of coronavirus (Andersen et al., 2020; Ye et al., 2020), but the exact origin, diversity and transmission of SARS CoV-2 from animals to humans remain unclear. The host-microbiome-virus co-evolution, that has been taking place since millennia is very crucial since each element of this relationship exerts selective pressures on the others, thus affect the overall evolutionary process (Kuss et al., 2011; Zohdy et al., 2019). Viral zoonotic outbreaks can be predicted to some extent if there is a detailed understanding of the virus population associated with the key reservoir or intermediate host in the upcoming outbreak (Donaldson et al., 2010). Various studies have revealed that the human microbiome can be useful to predict the susceptibility of infectious diseases and therefore the microbiome modulation can aid in lowering the chances of infection (Unger and Bogaert, 2017).

This review focuses on phylogenomic distribution and evolutionary lineage of zoonotic viral cross-species transmission of the *Coronaviridae* family. Here, we also discuss the importance and involvement of the microbiome of the possible reservoir host in the study of the evolutionary aspects and epidemiology of a pathogen; and how the human microbiome can be useful in predicting and controlling infectious diseases. Finally, the importance of synthetic viruses in the study of viral evolution and transmission is discussed.

* Corresponding author.
E-mail addresses: rheanambiar9@gmail.com (R. Rajeev), raj.prathivi@gmail.com (R. Prathiviraj), seghalkiran@gmail.com (G.S. Kiran), josephselvinss@gmail.com, jselvin.mib@pondiuni.edu.in (J. Selvin).

https://doi.org/10.1016/j.virusres.2020.198175
Received 29 July 2020; Received in revised form 20 September 2020; Accepted 21 September 2020
Available online 29 September 2020

2. Zoonotic viral evolution and transmission

Based on various factors such as physiology, life history, ecology, etc., the tendency of various animals to transmit viruses to human beings vary (Mollentze and Streicker, 2020). Zoonotic viral infections emerge due to few factors such as phylogenetic similarity of the reservoir host to humans (Mollentze and Streicker, 2020; Olival et al., 2017), animal taxonomy and range overlap with human populations (Olival et al., 2017). The study of interspecific viral transmission plays key roles in comprehending the viral evolution, disease spread to humans, and the overall global change (Albery et al., 2020). Various shreds of evidence support that CoVs show higher genetic diversity, which makes them highly susceptible to adaptive mutation due to the spike protein which can easily exploit various cellular receptors and therefore helps in host jumps (Forni et al., 2020). The variations in the functional sites of the receptor-binding domain (RBD) present in the spike of SARS-CoV-2 and pangolin SARSr-CoVs is mainly attributed to natural selection apart from recombination (Tang et al., 2020). It is very important to trace the zoonotic origins of human CoVs, as it helps to comprehend the natural history, dynamics and restriction factors of species jumping along with any other possible intermediate, reservoir, or amplifying host so that any future spillovers could be avoided (Ye et al., 2020). So far several mutations and genomic variants have been reported in SARS-CoV-2 (Islam et al., 2020; Prathiviraj et al., 2020), and it is known to have very high infectivity and host specificity, which reflects the chances of increased disease transmission from animals to humans (Allocati et al., 2016; Harapan et al., 2020; Prathiviraj et al., 2020). Here, we provide a keen understanding of the origin and diversity of SARS-CoV-2 and how it has been transmitted from animals to human beings.

The phylogenomic large-scale supertree was constructed by retrieving the complete genome sequence of 53 coronavirus related isolates including the recent isolates of Wuhan-Hu-1 from different hosts from the NCBI (https://www.ncbi.nlm.nih.gov/) (Supplementary Table S1), using the MEGA X (Kumar et al., 2018) and Interactive Tree of Life (iTOL) v4 (Letunic and Bork, 2019). The phylogenomic tree is clustered into four major groups such as Alpha (α), Beta (β), Gamma (γ)

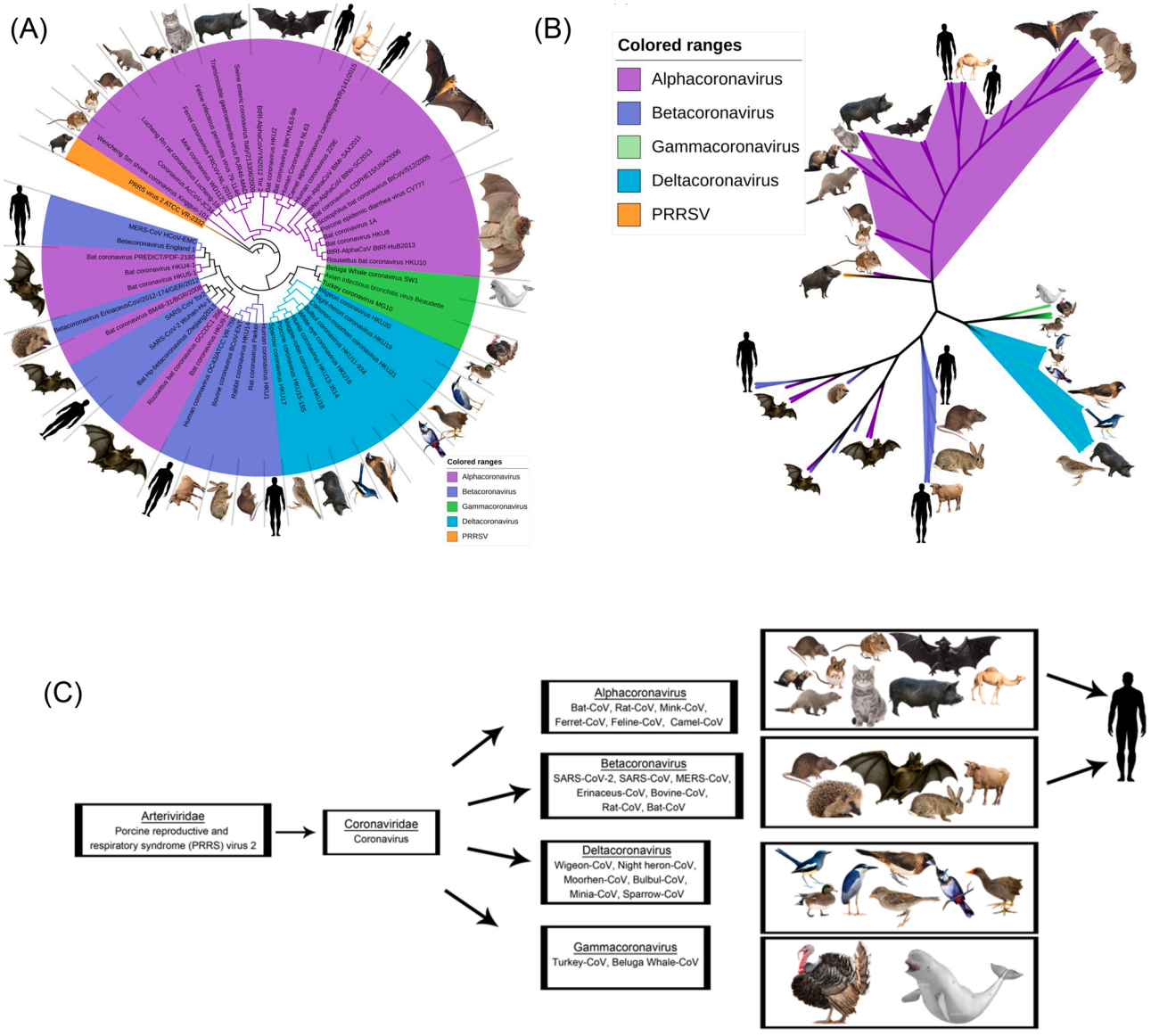

Fig. 1. A Phylogenomic distribution of zoonotic viral cross-species transmission of the Coronaviridae family. (A) Circular view of zoonotic viral transmission of SARS-CoV-2 from its origin, (B) Unrooted evolutionary tree, (C) graphical abstract view of transmission between animals to 2019-CoV. The phylogenomic tree was constructed using Neighbor joining method. Using the Maximum composite likelihood substitution model, the tree was generated with 1000 bootstrap replicates. Branch lengths are proportional based on the evolutionary distances. All selected Taxa, were classified and grouped into different color according to its genomic features of transmission.

and Delta (δ) coronavirus (Fig. 1a; Supplementary Figure S1). The evolutionary tree revealed that Porcine Reproductive and Respiratory Syndrome (PRRS) virus 2, which belongs to the Beta arterivirus genus from the *Arteriviridae* family is possibly the most ancient ancestral origin of SARS-CoV-2 and other *Coronaviridae* (Fig. 1a).

PRRS was initially known as the 'Mystery Swine Disease', in the United States in the late 1980s after which it spread throughout the swine-rearing areas of North America and Europe, and eventually throughout the world (Murtaugh et al., 2010; Wensvoort et al., 1991). The first PRRS report in China was in 1995; and in May 2006, South China faced another highly pathogenic PRRS virus (HP-PRRSV) outbreak which rapidly spread across the country, infecting above 20 million pigs, which re-emerged again in 2009, in central China (Li et al., 2007, 2011; Tian et al., 2007). PRRSV has been transmitted to humans due to the oral consumption of infected pig's meat (Raymond et al., 2017). This virus has undergone rapid evolution and also gained the ability to overcome the host immune responses. A vaccine like strain was also reported in South China, which could be mostly due to the extensive use of the attenuated modified live PRRS vaccine which is capable of reverting to a virulent strain (Murtaugh et al., 2010; Karniychuk et al., 2010; Li et al., 2011; Xie et al., 2014). The outbreak of PRRS as a novel swine disease has been attributed to the availability of a huge number of hosts which aided the viral recombination and evolution rapidly (Murtaugh et al., 2010).

It is also evident that Alpha coronavirus can be transmitted through bat, rat, mink, ferret, cat and camel to humans, while Beta coronavirus is transmitted from SARS, MERS, Erinaceus, bovine species, rat, and bat to humans (Fig. 1b). Alpha- and Beta-coronavirus can be transmitted via oral consumption of infected animals or direct transmission (Xu, 2020). Delta- and Gamma-coronavirus share their evolutionary lineage between birds (Wigeon, Night-heron, Moorhen, Bulbul, Munia, Sparrow and Turkey) and Beluga Whale as shown in Fig. 1 C and does not involve human as a host. Hence, there is no possibility of direct transmission of Delta- and Gamma-coronavirus to humans, and this correlates with the previous studies (Forni et al., 2020; Shereen et al., 2020). The wildlife has a huge diversity of viruses that undergoes evolution, hence, the best way to decrease the risk of future outbreaks is to minimize the exposure to animal pathogens to the maximum extent (Zhang and Holmes, 2020). Decreased consumption of raw meat and maintaining a safe distance from wildlife harboring possible pathogens could also aid in lowering the chances of zoonotic infections.

3. Implications of bat microbiome in zoonotic viral transmission and infection

There have been enough studies in the past two decades on the host-microbial interactions which has shed light on the concept of mammalian holobiont, as a consequence of the co-evolution of the eukaryotic host cells and its prokaryotic partners (Thaiss et al., 2016). The virome of few common bat species of North America (*Eptesicus fuscus, Perimyotis subflavus* and *Myotis lucifugus*) were analyzed and viral sequences having similarity to novel group 1 coronavirus, insect virus, plant virus and novel bacteriophages were identified, which indicates the possibility of bats being potential carriers of viruses which can infect various other organisms (Donaldson et al., 2010). As it is not feasible to study the microbiome of all the existing mammals, it becomes important to identify a particular clade, which could serve as a docile starting point for analyzing the evolution of microbiome among closely related species with various ecological habitats (Ingala et al., 2018). Since bats are a well-known natural reservoir of many deadly pathogenic microbes, mainly viruses, bats and their associated microbial population are being considered as vital components of zoonotic infection cycles (Mühldorfer, 2012; Veikkolainen et al., 2014; Banskar et al., 2016; Wolkers-Rooijackers et al., 2018; Henry et al., 2018; Selvin et al., 2019), and can serve as outstanding models for studying the microbiome evolution. Due to the excellent diversity, immunity, longevity and crucial roles displayed by them in the ecosystem, their microbiome can reveal the involvement and importance of microbes in host evolution and emergence of zoonotic pathogens, which could give us a better understanding of the epidemiology of such novel infections (Olival et al., 2017; Peixoto et al., 2018; Ingala et al., 2018). The majority of the SARS-CoV-2 genome is similar to SARSr-Ra-BatCoV-RaTG13 present in intermediate horseshoe bat in Yunnan, China, while the receptor-binding domain (RBD) is very similar to the pangolin-SARSr-CoV/MP789/Guangdong/2019 present in smuggled pangolins in Guangzhou, China. The pangolin SARSr-CoVs could be originated from the bats, as they are known to be the main reservoir of SARSr-CoVs. Hence, it could be inferred that the SARS-CoV-2 is most probably a recombinant virus which has its origin from bats (Lau et al., 2020).

Bats can harbor pathogenic microorganisms (Schountz et al., 2017; Banerjee et al., 2020), such as viruses which cause long-term persistent infections (Plowright et al., 2016), because such viruses could easily be adapted to the bat (Schountz et al., 2017), and hence are non-pathogenic to them; whereas such microbes are virulent in humans and other such hosts (Banskar et al., 2016; Halpin et al., 2011; Paweska et al., 2016; Schountz et al., 2017; Schuh et al., 2017; Gorbunova et al., 2020). This could be due to the high interferon-mediated immune response displayed by the bats, which supports the rapid cell-to-cell virus transmission rates within the host. Quickly-transmitting viruses, which have evolved with the bat immune system would display boosted virulence after its emergence into secondary hosts having different type of immune system (Brook et al., 2020).

The interspecies transmissions of such viruses from bats to other animals including human beings occur due to possible contact between the two, which causes the outbreak of serious zoonotic diseases (Allocati et al., 2016). The growing rate of bat-associated contagions is likewise supported by an increasing overlap between bat and human habitats (Chen et al., 2014). The swapping of bat microbiome with human beings and other animals can occur due to their flexible roosting behavior and their existence in close proximity (Sanderson et al., 2006; Ingala et al., 2018), consumption of fruits partially consumed by bats (Yob et al., 2001; Ingala et al., 2018) or coming in contact with bat guano (Field, 2016; Ingala et al., 2018). Hence, further studies on bat microbiome could provide better insights into zoonotic viral transmission and infection, and it could also aid in the prediction of any future outbreaks.

4. The role of human microbiome in viral transmission

The implications of the microbiome in infectious (Hanada et al., 2018) and non-infectious disease (Cryan et al., 2020) has been well documented. The theory of sterile lungs has been shifted to "lung microbiome", the resident microflora of the respiratory system (Dickson et al., 2016), however contagion specific fingerprint of lung microbiome remains to be fully established. The development and establishment of lung microbiome and lung-gut-axis play a critical role in respiratory diseases (Unger and Bogaert, 2017; Enaud et al., 2020). The usefulness of the nose/throat microbiome is being utilized in the prediction of vulnerability to influenza and also modulation of the microbiome can lower the chances of infection (Fanos et al., 2020). Tsang et al. (2019) observed that increased abundance of *Streptococcus* spp. reduced the vulnerability to influenza A(H3N2) and influenza B infection by 48 % and 25 % respectively, whereas a ten times greater abundance of *Prevotella salivae* reduced the vulnerability to influenza virus A(H3N2) by 63 % and increased the vulnerability to influenza B infection by 83 %.

SARS-CoV-2 gain access to the cell via the angiotensin-converting enzyme 2 (ACE-2) receptor (Yan et al., 2020; Zhou et al., 2020). The single-cell RNA sequencing (scRNA-seq) revealed that ACE-2 is present in various organs where they are located on specific cell types such as ileum and esophagus epithelial cells, type II alveolar cells (AT2) in lungs, proximal tubule cells in the kidney, myocardial cells and bladder urothelial cells, which indicates the vulnerability of these organs to COVID-19 infection. Individuals have reported certain clinical

symptoms such as acute cardiac injury and kidney failure along with common symptoms like dyspnea and diarrhea which could be attributed to the invasion of SARS-CoV-2 into the heart and kidney along with lung, upper respiratory tract and ileum (Zou et al., 2020). The microbiome present in the lung tissue of patients who were deceased due to COVID-19 was studied and results reveal that the most predominant bacterial members were of the genera *Acinetobacter, Burkholderia, Chryseobacterium, Sphingobium, Brevundimonas* and *Enterobacteriacea*; and the fungal members included *Aspergillus* spp., *Issatchenkia* spp., *Candida* spp., *Alternaria* spp., and *Cladosporium* spp., which are well known opportunistic invasive pathogens in immunocompromised patients. Hence, a combination of bacterial and fungal infections was observed (Fan et al., 2020).

ACE-2 receptors are also present in oral cells, mainly in tongue epithelial cells as per the recent report (Xu et al., 2020), which indicates that SARS-CoV-2 could interact with the oral microbiome, hence causing co-infection between the oral microbiome and SARS-CoV-2 in the lungs of the infected individuals (Bao et al., 2020). *Capnocytophaga, Veillonella* (Chen et al., 2020) and potential pathogens such as *Pseudomonas, Acinetobacter, Escherichia* and *Streptococcus* were present in the Bronchoalveolar lavage fluid (BALF) of COVID-19 patients (Ren et al., 2020).

The SARS-CoV-2 could hinder the nutrient absorption by binding to ACE-2 receptors which leads to gastroenteritis-related symptoms and disturbance of gut homeostasis (Gu et al., 2020). The individuals suffering from respiratory illness also undergo gut dysbiosis which indicates the presence of gut-lung crosstalk (Fanos et al., 2020). The gut-lung axis is bidirectional because the microbial metabolites and endotoxins produced in the gut reach the lungs via blood, also any infection or inflammation in the lungs affects the gut microbiome (Dumas et al., 2018; Dhar and Mohanty, 2020). The action of ACE-2, present on the surface of the lumen of the intestine is known to be influenced by the gut microbial community in COVID-19 (Yan et al., 2020). Hence, it indicates the impact of SARS-CoV-2 infection on the gut microbiome. Also, various studies have revealed the alteration in the gut microbiome during respiratory infections (Dhar and Mohanty, 2020; Groves et al., 2020).

Viral as well as the cytokine storm-driven variations enhance the gut permeability and lead to dysbiosis, which reduces the amounts of short-chain fatty acid (SCFAs) such as butyrate, and carries lipopolysaccharide (LPS) into the circulation (Anderson and Reiter, 2020). The 'colonization resistance' strategy used by the host microbiome prevents the colonization of pathogens whereby the beneficial microbes occupy the pathogen's niche or the mucosal entry points specific to the pathogens and also initiating the innate immune response (Thaiss et al., 2016). And few viruses can take over and manipulate the signaling interactions such as Lipopolysaccharide-Toll-like receptor 4 (LPS-TLR4) signaling between the microbiome and immune system, hence benefiting their own proliferation and spread (Domínguez-Díaz et al., 2019). Enteric viruses like Poliovirus, Norovirus and mouse mammary tumor virus have been found to utilize the microbial components like lipopolysaccharides to evade the host immune response (Kane et al., 2011; Robinson et al., 2014; Berger and Mainou, 2018); and the virion thermostability of reovirus was enhanced due to its interaction with bacterial cells (Berger et al., 2017; Berger and Mainou, 2018). A study revealed that allogeneic hematopoietic cell transplantation (HCT) recipients having higher loads of butyrate-synthesizing bacteria were at five times lower risk to develop viral lower respiratory tract infection (LRTI). Hence, a higher abundance of butyrate-synthesizing bacteria is associated with higher resistance against LRTI in allo−HCT recipients (Haak et al., 2018).

The gut microbiome composition of individuals infected with COVID-19 showed a significant reduction in bacterial diversity with an increase in the abundance of opportunistic pathogens like *Rothia, Streptococcus, Actinomyces* and *Veillonella*, and a reduction in beneficial microbial partners when compared with the healthy control group (Gu et al., 2020). A study revealed that individuals infected with COVID-19 had persistent shifts in the fecal microbiome when compared with the healthy control group which was associated with the fecal levels of SARS-CoV-2 and also the COVID-19 severity. In severe cases of COVID-19, opportunitistic pathogens like *Coprobacillus, Clostridium hathewayi* and *Clostridium ramosum* were observed. The disease severity was inversely proportional to the abundance of an anti-inflammatory bacterium, *Faecalibacterium prausnitzii* and also few other beneficial bacteria like *Eubacterium ventriosum, Faecalibacterium prausnitzii, Roseburia, Lachnospiraceae* (Zuo et al., 2020). Hence, the modulation of the gut microbiome might lower the disease severity. A study in China reported that few patients with COVID-19 also revealed gut microbial dysbiosis with a reduced abundance of *Lactobacillus* and *Bifidobacterium* (Mak et al., 2020; Xu et al., 2020). Changes in gut virome due to viral infections and their impact on liver health could provide better insights into the treatment of viral hepatic diseases (Scarpellini et al., 2020). Further investigation is required to provide a better understanding of the effect of the mutation in SARS-CoV-2 on shift in the microbiome due to zoonotic transmission.

Various factors influence the lung microbiome such as microbial composition, lifestyle, smoking, diet, use of chemotherapeutics, and the host immune response (Toraldo and Conte, 2019), and the COVID-19 severity is influenced by old age (Chen et al., 2020), cardiovascular disease (CVD), diabetes mellitus, hypertension, respiratory disorders, etc. Also, recently obesity has been linked to severe COVID-19. Obesity is also associated with dysbiosis and poor immune response against viral infections (Alberca et al., 2020). A high-fat and fructose-rich diet which is mainly associated with obesity (Namekawa et al., 2017), also reduces the ACE-2 levels significantly (Bundalo et al., 2016). The consumption of higher amounts of processed food increases sodium intake which leads to higher oxidative stress and reduced ACE-2 expression in kidneys (Bernardi et al., 2012), along with hypertension and CVD (Hendriksen et al., 2014). Lowered expression of ACE-2 is closely linked with higher COVID-19 severity (Alghatrif et al., 2020).

Nutritional interventions and the use of probiotics could prove beneficial in boosting the immunity of the host. Modulation and manipulation of microbiome via probiotics, prebiotics and high-fiber diet consumption may lower inflammation and dysbiosis by maintaining a healthy gut microbiome and also boosts the immune response (Toraldo and Conte, 2019). The beneficial activity of probiotics on pro-inflammatory and immune-regulatory cytokines leads to a reduction in the virus load, acute respiratory distress syndrome (ARDS) and also lowers the tissue damage caused by the cytokine storm which occurs in individuals with severe COVID-19 (Baud et al., 2020). Supplementation of combined prebiotics, probiotics, synbiotics and nutrition-enriched plant bioactives modify the bacterial composition and can protect against viral infections of the respiratory tract to some extent (Shinde et al., 2020). Due to various positive aspects of probiotics, such as anti-viral action, gut microbiome rebiosis, anti-inflammatory activity, easy availability, ease of administration, safety, and affordable nature, it could prove helpful in the treatment of COVID-19 (Angurana and Bansal, 2020). Hence, it is proposed that well documented probiotic strains should be considered and used for clinical trials to treat COVID-19 (Giannoni et al., 2020). In the coming days, the use of metabolomics could decipher the furtive dialects between the microbiome and its host (Fanos et al., 2020). Therefore, microbiome-mediated treatment strategies could be implemented to boost immunity, and also further studies in this field could support the present treatment strategies to some extent.

5. Conclusion

The extreme genetic diversity of the microbes enables them to evolve continuously to overcome host immune response and survive in new ecological niches, which leads to novel infectious outbreaks every time. Therefore, it is necessary to carefully analyze the phylogenomics of the microbe to identify the evolutionary and transmission patterns (Moratorio and Vignuzzi, 2018). To understand the evolutionary pattern in

the laboratory condition, experimental evolution is of great importance, where evolutionary dynamics of the newly emerging mutation is studied in controlled laboratory conditions. For this purpose, synthetic viruses synthesized from non-viral protein cages mimicking the evolutionary steps of primitive viruses could be used. Such artificial viruses can be safely used to identify the evolutionary pattern of each virus in a bottom-up fashion (Terasaka et al., 2018). Such an approach can help to understand the virulence patterns, predict its immediate future, host range and response to antiviral drugs, which can possibly help us to predict future outbreaks (Moratorio and Vignuzzi, 2018). Hence, further investigations using such synthetic viruses are highly recommended to provide a better understanding of evolutionary patterns of viruses.

Ethics approval and consent to participate

Not Applicable

Consent for publication

Not applicable

Availability of data and material

Not applicable

Funding

JS is thankful to Science and Engineering Research Board (SERB), New Delhi, India for the project on Human Microbiome. PR thankfully acknowledge the NPDF scheme (Sanction No. PDF/2019/002762/ Dated: 23/12/2019), SERB, New Delhi, India.

Authors' contributions

RR and PR performed the analysis and preparation of the draft manuscript; GSK and JS guided literature review, analysis and preparation of the manuscript.

Declaration of Competing Interest

The authors declare that they have no competing interests

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.virusres.2020.198175.

References

Alberca, R.W., Oliveira, L.D.M., Branco, A.C.C.C., Pereira, N.Z., Sato, M.N., 2020. Obesity as a risk factor for COVID-19: an overview. Crit. Rev. Food Sci. Nutr. https://doi.org/10.1080/10408398.2020.1775546.

Albery, G.F., Eskew, E.A., Ross, N., Olival, K.J., 2020. Predicting the global mammalian viral sharing network using phylogeography. Nat. Commun. 11, 2260. https://doi.org/10.1038/s41467-020-16153-4.

AlGhatrif, M., Cingolani, O., Lakatta, E.G., 2020. The dilemma of coronavirus disease 2019, aging, and cardiovascular disease: insights from cardiovascular aging science. JAMA Cardiol. 5 (7), 747–748. https://doi.org/10.1001/jamacardio.2020.1329.

Allocati, N., Petrucci, A.G., Giovanni, P., Di Masulli, M., Di, Ilio C., Laurenzi, V.De., 2016. Bat – man disease transmission : zoonotic pathogens from wildlife reservoirs to human populations. Cell Death Discov. 2, 16048. https://doi.org/10.1038/cddiscovery.2016.48.

Andersen, K.G., Rambaut, A., Lipkin, W.I., Holmes, E.C., Garry, R.F., 2020. The proximal origin of SARS-CoV-2. Nat. Med. 26 (4), 450–452. https://doi.org/10.1038/s41591-020-0820-9.

Anderson, G., Reiter, R.J., 2020. Melatonin: roles in influenza, Covid-19, and other viral infections. Rev. Med. Virol. 30 (3), e2109. https://doi.org/10.1002/rmv.2109.

Angurana, S.K., Bansal, A., 2020. Probiotics and COVID-19: think about the link. Br. J. Nutr. 1–26. https://doi.org/10.1017/S000711452000361X.

Banerjee, A., Baker, M.L., Kulcsar, K., Misra, V., Plowright, R., Mossman, K., 2020. Novel insights into immune systems of bats. Front. Immunol. 11, 26. https://doi.org/10.3389/fimmu.2020.00026.

Banskar, S., Bhute, S.S., Suryavanshi, M.V., Punekar, S., Shouche, Y.S., 2016. Microbiome analysis reveals the abundance of bacterial pathogens in Rousettus leschenaultii guano. Sci. Rep. 6 (1), 1–13. https://doi.org/10.1038/srep36948.

Bao, L., Zhang, C., Dong, J., Zhao, L., Li, Y., Sun, J., 2020. Oral microbiome and SARS-CoV-2: beware of lung Co-infection. Front. Microbiol. 11, 1840. https://doi.org/10.3389/fmicb.2020.01840.

Baud, D., Agri, V.D., Gibson, G.R., Reid, G., Giannoni, E., 2020. Using probiotics to flatten the curve of coronavirus disease COVID-2019 pandemic. Front. Public Health 8, 186. https://doi.org/10.3389/fpubh.2020.00186.

Berger, A.K., Mainou, B.A., 2018. Interactions between enteric Bacteria and eukaryotic viruses impact the outcome of infection. Viruses 10 (1), 19. https://doi.org/10.3390/v10010019.

Berger, A.K., Yi, H., Kearns, D.B., Mainou, B.A., 2017. Bacteria and bacterial envelope components enhance mammalian reovirus thermostability. PLoS Pathog. 13 (12), e1006768. https://doi.org/10.1371/journal.ppat.1006768.

Bernardi, S., Toffoli, B., Zennaro, C., Tikellis, C., Monticone, S., Losurdo, P., Johnston, C. I., Bellini, G., Thomas, M.C., Fallo, F., Veglio, F., Johnston, C.I., Fabris, B., 2012. High-salt diet increases glomerular ACE/ACE2 ratio leading to oxidative stress and kidney damage. Nephrol. Dial. Transplant. 27 (5), 1793–1800. https://doi.org/10.1093/ndt/gfr600.

Brook, C.E., Boots, M., Chandran, K., Dobson, A.P., Drosten, C., Graham, A.L., Van Leeuwen, A., Grenfell, B.T., Muller, M.A., Ng, M., Wang, L.F., 2020. Accelerated viral dynamics in bat cell lines, with implications for zoonotic emergence. Elife 9, e48401. https://doi.org/10.7554/eLife.48401.

Bundalo, M.M., Zivkovic, M.D., Romic, S.D., Tepavcevic, S.N., Koricanac, G.B., Djuric, T. M., Stankovic, A.D., 2016. Fructose-rich diet induces gender-specific changes in expression of the renin–angiotensin system in rat heart and upregulates the ACE/AT1R axis in the male rat aorta. J. Renin-angiotensin-aldosterone Syst. Jraas 17 (2). https://doi.org/10.1177/1470320316642915, 1470320316642915.

Chan, J.F., Yuan, S., Kok, K., To, K.K., Chu, H., Yang, J., Xing, F., Liu, J., Yip, C.C., Poon, R.W., Tsoi, H.W., Lo, S.K., Chan, K.H., Poon, V.K., Chan, W.M., Ip, J.D., Cai, J. P., Cheng, V.C., Chen, H., Hui, C.K., Yuen, K.Y., 2020. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission : a study of a family cluster. Lancet 395 (10223), 514–523. https://doi.org/10.1016/S0140-6736(20)30154-9.

Chen, L., Liu, B., Yang, J., Jin, Q., 2014. DBatVir : the database of bat-associated viruses. Database 2014. https://doi.org/10.1093/database/bau021.

Chen, L., Liu, W., Zhang, Q., Xu, K., Ye, G., Wu, W., Sun, Z., Liu, F., Wu, K., Zhong, B., Mei, Y., Zhang, W., Chen, Y., Li, Y., Shi, M., Lan, K., Liu, Y., 2020a. RNA based mNGS approach identifies a novel human coronavirus from two individual pneumonia cases in 2019 Wuhan outbreak. Emerg. Microbes Infect. 9 (1), 313–319. https://doi.org/10.1080/22221751.2020.1725399.

Chen, G., Wu, D., Guo, W., Cao, Y., Huang, D., Wang, H., Wang, T., Zhang, X., Chen, H., Yu, H., Zhang, X., Zhang, M., Wu, S., Song, J., Chen, T., Han, M., Li, S., Luo, X., Zhao, J., Ning, Q., 2020b. Clinical and immunological features of severe and moderate coronavirus disease 2019. J. Clin. Invest. 130 (5), 2620–2629. https://doi.org/10.1172/JCI137244.

Chen, N., Zhou, M., Dong, X., Qu, J., Gong, F., Han, Y., Qiu, Y., Wang, J., Liu, Y., Wei, Y., Xia, J., Yu, T., Zhang, X., Zhang, L., 2020c. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China : a descriptive study. Lancet 395 (10223), 507–513. https://doi.org/10.1016/S0140-6736(20)30211-7.

Cryan, J.F., O'Riordan, K.J., Sandhu, K., Peterson, V., Dinan, T.G., 2020. The gut microbiome in neurological disorders. Lancet Neurol. 19 (2), 179–194. https://doi.org/10.1016/S1474-4422(19)30356-4.

Dhar, D., Mohanty, A., 2020. Gut microbiota and Covid-19-possible link and implications. Virus Res. 285, 198018 https://doi.org/10.1016/j.virusres.2020.198018.

Dickson, R.P., Erb-Downward, J.R., Martinez, F.J., Huffnagle, G.B., 2016. The microbiome and the respiratory tract. Annu. Rev. Physiol. 78, 481–504. https://doi.org/10.1146/annurev-physiol-021115-105238.

Domínguez-Díaz, C., García-Orozco, A., Riera-Leal, A., Padilla-Arellano, J.R., Fafutis-Morris, M., 2019. Microbiota and its role on viral evasion: is it with us or against us? Front. Cell. Infect. Microbiol. 9, 256. https://doi.org/10.3389/fcimb.2019.00256.

Donaldson, E.F., Haskew, A.N., Gates, J.E., Huynh, J., Moore, C.J., Frieman, M.B., 2010. Metagenomic analysis of the viromes of three north american bat species : viral diversity among different bat species that share a common habitat. J. Virol. 84 (24), 13004–13018. https://doi.org/10.1128/JVI.01255-10.

Dumas, A., Bernard, L., Poquet, Y., Lugo-Villarino, G., Neyrolles, O., 2018. The role of the lung microbiota and the gut–lung axis in respiratory infectious diseases. Cell. Microbiol. 20 (12), e12966. https://doi.org/10.1111/cmi.12966.

Enaud, R., Prevel, R., Ciarlo, E., Beaufils, F., Wieërs, G., Guery, B., Delhaes, L., 2020. The gut-lung Axis in health and respiratory diseases : a place for inter-organ and inter-kingdom crosstalks. Frontiers in Cell and Infection Microbiology 10, 9. https://doi.org/10.3389/fcimb.2020.00009.

Fan, J., Li, X., Gao, Y., Zhou, J., Wang, S., Huang, B., Wu, J., Cao, Q., Chen, Y., Wang, Z., Luo, D., Zhou, T., Li, R., Shang, Y., Nie, X., 2020. The lung tissue microbiota features of 20 deceased patients with COVID-19. J. Infect. 81 (3), e64–e67. https://doi.org/10.1016/j.jinf.2020.06.047.

Fanos, V., Pintus, M.C., Pintus, R., Marcialis, A., 2020. Lung microbiota in the acute respiratory disease : from coronavirus to metabolomics. Journal of Pediatric and Neonatal Individualized Medicine 9 (1), e090139. https://doi.org/10.7363/090139.

Field, H.E., 2016. Hendra virus ecology and transmission. Curr. Opin. Virol. 16, 120–125. https://doi.org/10.1016/j.coviro.2016.02.004.
Forni, D., Cagliani, R., Clerici, M., Sironi, M., 2020. Molecular evolution of human coronavirus genomes. Trends Microbiol. 25 (1), 35–48. https://doi.org/10.1016/j.tim.2016.09.001.
Giannoni, E., Baud, D., Agri, V.D., Gibson, G.R., Reid, G., 2020. Probiotics and COVID-19. Lancet Gastroenterol. Hepatol. 5 (8), 720–721. https://doi.org/10.1016/S2468-1253(20)30195-3.
Gorbunova, V., Seluanov, A., Kennedy, B.K., 2020. The world goes bats: living longer and tolerating viruses. Cell Metab. 32 (1), 31–43. https://doi.org/10.1016/j.cmet.2020.06.013.
Groves, H.T., Higham, S.L., Moffatt, M.F., Cox, M.J., Tregoning, J.S., 2020. Respiratory viral infection alters the gut microbiota by inducing inappetence. Mbio 11 (1). https://doi.org/10.1128/mBio.03236-19.
Gu, S., Chen, Y., Wu, Z., Chen, Y., Gao, H., Lv, L., Guo, F., Zhang, X., Luo, R., Huang, C., Lu, H., Zheng, B., Zhang, J., Yan, R., Zhang, H., Jiang, H., Xu, Q., Guo, J., Gong, Y., Tang, L., Li, L., 2020. Alterations of the gut microbiota in patients with COVID-19 or H1N1 influenza. Clin. Infect. Dis. https://doi.org/10.1093/cid/ciaa709.
Guo, Y., Cao, Q., Hong, Z., Tan, Y., Chen, S., Jin, H., Tan, K.S., Wang, D.Y., Yan, Y., 2020. The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the staus. Military Medical Reserch 7 (1), 11. https://doi.org/10.1186/s40779-020-00240-0.
Haak, B.W., Littmann, E.R., Chaubard, J.L., Pickard, A.J., Fontana, E., Adhi, F., Gyaltshen, Y., Ling, L., Morjaria, S.M., Peled, J.U., van den Brink, M.R., Geyer, A.I., Cross, J.R., Pamer, E.G., Taur, Y., 2018. Impact of gut colonization with butyrate-producing microbiota on respiratory viral infection following allo-HCT. Blood 131 (26), 2978–2986. https://doi.org/10.1182/blood-2018-01-828996.
Halpin, K., Hyatt, A.D., Fogarty, R., Middleton, D., Bingham, J., Epstein, J.H., Rahman, S.A., Hughes, T., Smith, C., Field, H.E., Daszak, P., 2011. Pteropid bats are confirmed as the reservoir hosts of henipaviruses: a comprehensive experimental study of virus transmission. Am. J. Trop. Med. Hyg. 85 (5), 946–951. https://doi.org/10.4269/ajtmh.2011.10-0567.
Hanada, S., Pirzadeh, M., Carver, K.Y., Deng, J.C., 2018. Respiratory viral infection-induced microbiome alterations and secondary bacterial pneumonia. Front. Immunol. 9, 2640. https://doi.org/10.3389/fimmu.2018.02640.
Harapan, H., Itoh, N., Yufika, A., Winardi, W., Keam, S., Te, H., Megawati, D., Hayati, Z., Wagner, A.L., Mudatsir, M., 2020. Coronavirus disease 2019 (COVID-19): a literature review. J. Infect. Public Health 13 (5), 667–673. https://doi.org/10.1016/j.jiph.2020.03.019.
Hendriksen, M.A., Hoogenveen, R.T., Hoekstra, J., Geleijnse, J.M., Boshuizen, H.C., van Raaij, J.M., 2014. Potential effect of salt reduction in processed foods on health. Am. J. Clin. Nutr. 99 (3), 446–453. https://doi.org/10.3945/ajcn.113.062018.
Henry, R., Galbraith, P., Coutts, S., Prosser, T., Boyce, J., Mccarthy, T., 2018. What' s the risk? Identifying potential human pathogens within grey-headed flying foxes faeces. PLoS One 13 (1), e0191301. https://doi.org/10.1371/journal.pone.0191301.
Ingala, M.R., Simmons, N.B., Perkins, L., 2018. Bats are an untapped system for understanding microbiome evolution in mammals. MShpere 3 (5). https://doi.org/10.1128/mSphere.00397-18 e00397-18.
Islam, M.R., Hoque, M.N., Rahman, M.S., Alam, A.S.M.R.U., Akther, M., Puspo, J.A., Akter, S., Sultana, M., Crandall, K.A., Hossain, M.A., 2020. Genome-wide analysis of SARS-CoV-2 virus strains circulating worldwide implicates heterogeneity. Sci. Rep. 10 (114004) https://doi.org/10.1038/s41598-020-70812-6.
Kane, M., Case, L.K., Kopaskie, K., Kozlova, A., MacDearmid, C., Chervonsky, A.V., Golovkina, T.V., 2011. Successful transmission of a retrovirus depends on the commensal microbiota. Science 334 (6053), 245–249. https://doi.org/10.1126/science.1210718.
Karniychuk, U.U., Geldhof, M., Vanhee, M., Doorsselaere, J., Van Saveleva, T.A., Nauwynck, H.J., 2010. Pathogenesis and antigenic characterization of a new East European subtype 3 porcine reproductive and respiratory syndrome virus isolate. BMC Vet. Res. 6, 30. https://doi.org/10.1186/1746-6148-6-30.
Kumar, S., Stecher, G., Li, M., Knyaz, C., Tamura, K., 2018. MEGA X : molecular evolutionary genetics analysis across computing platforms. Mol. Biol. Evol. 35 (6), 1547–1549. https://doi.org/10.1093/molbev/msy096.
Kuss, S.K., Best, G.T., Etheredge, C.A., Pruijssers, A.J., Frierson, J.M., Hooper, L.V., Dermody, T.S., Pfeiffer, J.K., 2011. Intestinal microbiota promote enteric virus replication and systemic pathogenesis. Science 334 (6053), 249–252. https://doi.org/10.1126/science.1211057.
Lau, S.K.P., Luk, H.K.H., Wong, A.C.P., Li, K.S.M., Zhu, L., He, Z., Fung, J., Chan, T.T.Y., Fung, K.S.C., Woo, P.C.Y., 2020. Possible bat origin of severe acute respiratory syndrome coronavirus 2. Emerging Infect. Dis. 26 (7), 1542–1547. https://doi.org/10.3201/eid2607.200092.
Letunic, I., Bork, P., 2019. Interactive Tree of Life (iTOL) v4 : recent updates and new developments. Nucleic Acids Res. 47 (W1), W256–W259. https://doi.org/10.1093/nar/gkz239.
Li, Y., Wang, X., Bo, K., Wang, X., Tang, B., Yang, B., Jiang, W., Jiang, P., 2007. Emergence of a highly pathogenic porcine reproductive and respiratory syndrome virus in the Mid-Eastern region of China. Vet. J. 174 (3), 577–584. https://doi.org/10.1016/j.tvjl.2007.07.032.
Li, B., Fang, L., Guo, X., Gao, J., Song, T., Bi, J., He, K., Chen, H., Xiao, S., 2011. Epidemiology and evolutionary characteristics of the porcine reproductive and respiratory syndrome virus in China between 2006 and 2010. J. Clin. Microbiol. 49 (9), 3175–3183. https://doi.org/10.1128/JCM.00234-11.
Mak, J.W.Y., Chan, F.K.L., Ng, S.C., 2020. Probiotics and COVID-19 : one size does not fit all. Lancet Gastroenterol. Hepatol. S2468-1253 (20), 30122–30129. https://doi.org/10.1016/S2468-1253(20)30122-9.
Mollentze, N., Streicker, D.G., 2020. Viral zoonotic risk is homogenous among taxonomic orders of mammalian and avian reservoir hosts. Proc. Natl. Acad. Sci. 117 (17), 9423–9430. https://doi.org/10.1073/pnas.1919176117.
Moratorio, G., Vignuzzi, M., 2018. Monitoring and redirecting virus evolution. PLoS Pathog. 14 (6), e1006979. https://doi.org/10.1371/journal.ppat.1006979.
Morse, S.S., Mazet, J.A.K., Woolhouse, M., Parrish, C.R., Carroll, D., Karesh, W.B., Zambrana-Torrelio, C., Lipkin, W.I., Daszak, P., 2012. Prediction and prevention of the next pandemic zoonosis. Lancet 380 (9857), 1956–1965. https://doi.org/10.1016/S0140-6736(12)61684-5.
Mühldorfer, K., 2012. Bats and bacterial pathogens : a review. Zoonoses Public Health 60 (1), 93–103. https://doi.org/10.1111/j.1863-2378.2012.01536.x.
Murtaugh, M.P., Stadejek, T., Abrahante, J.E., Lam, T.T.Y., Leung, F.C., 2010. The ever-expanding diversity of porcine reproductive and respiratory syndrome virus. Virus Res. 154 (1–2), 18–30. https://doi.org/10.1016/j.virusres.2010.08.015.
Namekawa, J., Takagi, Y., Wakabayashi, K., Nakamura, Y., Watanabe, A., Nagakubo, D., Shirai, M., Asai, F., 2017. Effects of high-fat diet and fructose-rich diet on obesity, dyslipidemia and hyperglycemia in the WBN/Kob-Leprfa rat, a new model of type 2 diabetes mellitus. J. Vet. Med. Sci. 17–0136. https://doi.org/10.1292/jvms.17-0136.
Olival, K.J., Hosseini, P.R., Zambrana-torrelio, C., Ross, N., Bogich, T.L., Daszak, P., 2017. Host and viral traits predict zoonotic spillover from mammals. Nature 546 (7660), 646–650. https://doi.org/10.1038/nature22975.
Paweska, J.T., Storm, N., Grobbelaar, A.A., Markotter, W., Kemp, A., Jansen van Vuren, P., 2016. Experimental inoculation of Egyptian fruit bats (Rousettus aegyptiacus) with Ebola virus. Viruses 8 (2), 29. https://doi.org/10.3390/v8020029.
Peixoto, F.P., Braga, P.H.P., Mendes, P., 2018. A synthesis of ecological and evolutionary determinants of bat diversity across spatial scales. BMC Ecol. 18 (1), 18. https://doi.org/10.1186/s12898-018-0174-z.
Plowright, R.K., Peel, A.J., Streicker, D.G., Gilbert, A.T., McCallum, H., Wood, J., Baker, M.L., Restif, O., 2016. Transmission or within-host dynamics driving pulses of zoonotic viruses in reservoir–host populations. PLoS Negl. Trop. Dis. 10 (8), e0004796. https://doi.org/10.1371/journal.pntd.0004796.
Prathiviraj, R., Kiran, G.S., Selvin, J., 2020. Phylogenomic proximity and comparative proteomic analysis of SARS-CoV-2. Gene Rep. 20, 100777 https://doi.org/10.1016/j.genrep.2020.100777.
Raymond, P., Bellehumeur, C., Nagarajan, M., Longtin, D., Ferland, A., Müller, P., Bissonnette, R., Simard, C., 2017. Porcine reproductive and respiratory syndrome virus (PRRSV) in pig meat. Can. J. Vet. Res. 81 (3), 162–170.
Ren, L.L., Wang, Y.M., Wu, Z.Q., Xiang, Z.C., Guo, L., Xu, T., Jiang, Y.Z., Xiong, Y., Li, Y.J., Li, X.W., et al., 2020. Identification of a novel coronavirus causing severe pneumonia in human: a descriptive study. Chin. Med. J. 133 (9), 1015–1024. https://doi.org/10.1097/CM9.0000000000000722.
Robinson, C.M., Jesudhasan, P.R., Pfeiffer, J.K., 2014. Bacterial lipopolysaccharide binding enhances virion stability and promotes environmental fitness of an enteric virus. Cell Host Microbe 15 (1), 36–46. https://doi.org/10.1016/j.chom.2013.12.004.
Sanderson, K.J., Jaeger, D.A., Bonner, J.F., Jansen, L., 2006. Activity patterns of bats at house roosts near Adelaide. Aust. Mammal. 28 (2), 137–145. https://doi.org/10.1071/AM06023.
Scarpellini, E., Fagoonee, S., Rinninella, E., Rasetti, C., Aquila, I., Larussa, T., Ricci, P., Luzza, F., Abenavoli, L., 2020. Gut microbiota and liver interaction through immune system cross-talk: a comprehensive review at the time of the SARS-COV-2 pandemic. J. Clin. Med. 9 (8), 2488. https://doi.org/10.3390/jcm9082488.
Schountz, T., Baker, M.L., Butler, J., Munster, V., 2017. Immunological control of viral infections in bats and the emergence of viruses highly pathogenic to humans. Front. Immunol. 8, 1098. https://doi.org/10.3389/fimmu.2017.01098.
Schuh, A.J., Amman, B.R., Sealy, T.K., Spengler, J.R., Nichol, S.T., Towner, J.S., 2017. Egyptian rousette bats maintain long-term protective immunity against Marburg virus infection despite diminished antibody levels. Sci. Rep. 7 (1), 1–7. https://doi.org/10.1038/s41598-017-07824-2.
Selvin, J., Lanong, S., Syiem, D., Mandal, S.De, Kayang, H., Kumar, N.S., Kiran, G.S., 2019. Microbial Pathogenesis Culture-dependent and metagenomic analysis of lesser horseshoe bats' gut microbiome revealing unique bacterial diversity and signatures of potential human pathogens. Microb. Pathog. 137, 103675 https://doi.org/10.1016/j.micpath.2019.103675.
Shereen, M.A., Khan, S., Kazmi, A., Bashir, N., Siddique, R., 2020. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J. Adv. Res. https://doi.org/10.1016/j.jare.2020.03.005.
Shinde, T., Hansbro, P.M., Sohal, S.S., Dingle, P., Eri, R., Stanley, R., 2020. Microbiota modulating nutritional approaches to countering the effects of viral respiratory infections including SARS-CoV-2 through promoting metabolic and immune fitness with probiotics and plant bioactives. Microorganisms 8 (6), 921. https://doi.org/10.3390/microorganisms8060921.
Sun, J., He, W., Wang, L., Lai, A., Ji, X., Zhai, X., Li, G., Suchard, M.A., Tian, J., Zhou, J., Veit, M., Su, S., 2020. COVID-19 : epidemiology, evolution, and cross-disciplinary perspectives. Trends Mol. Med. 26 (5), 483–495. https://doi.org/10.1016/j.molmed.2020.02.008.
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. 7 (6), 1012–1023. https://doi.org/10.1093/nsr/nwaa036.
Terasaka, N., Azuma, Y., Hilvert, D., 2018. Laboratory evolution of virus-like nucleocapsids from nonviral protein cages. PNAS 115 (21), 5432–5437. https://doi.org/10.1073/pnas.1800527115.
Thaiss, C.A., Zmora, N., Levy, M., Elinav, E., 2016. The microbiome and innate immunity. Nature 535 (7610), 65–74. https://doi.org/10.1038/nature18847.
Tian, K., Yu, X., Zhao, T., Feng, Y., Cao, Z., Wang, C., et al., 2007. Emergence of fatal PRRSV variants: unparalleled outbreaks of atypical PRRS in China and molecular

dissection of the unique hallmark. PLoS One 2 (6), e526. https://doi.org/10.1371/journal.pone.0000526.
Toraldo, D.M., Conte, L., 2019. Influence of the lung microbiota Dysbiosis in chronic obstructive pulmonary disease exacerbations: the controversial use of corticosteroid and antibiotic treatments and the role of Eosinophils as a disease marker. J. Clin. Med. Res. 11 (10), 667–675. https://doi.org/10.14740/jocmr3875.
Tsang, T.K., Lee, K.H., Foxman, B., Balmaseda, A., Gresh, L., Sanchez, N., Ojeda, S., Lopez, R., Yang, Y., Kuan, G., Gordon, A., 2019. Association between the respiratory microbiome and susceptibility to influenza virus infection. Clin. Infect. Dis. 1–9. https://doi.org/10.1093/cid/ciz968.
Unger, S.A., Bogaert, D., 2017. The respiratory microbiome and respiratory infections. J. Infect. 74, S84–S88. https://doi.org/10.1016/S0163-4453(17)30196-2.
Veikkolainen, V., Vesterinen, E.J., Lilley, T.M., Pulliainen, A.T., 2014. Bats as reservoir hosts of human bacterial pathogen, Bartonella mayotimonensis. Emerging Infect. Dis. 20 (6), 960. https://doi.org/10.3201/eid2006.130956.
Wensvoort, G., Terpstra, C., Pol, J.M., Ter Laak, E.A., Bloemraad, M., De Kluyver, E.P., et al., 1991. Mystery swine disease in the Netherlands: the isolation of Lelystad virus. Vet. Q. 13 (3), 121–130. https://doi.org/10.1080/01652176.1991.9694296.
Wolkers-Rooijackers, J., Rebmann, K., Bosch, T., Hazeleger, W.C., 2018. Fecal bacterial communities in insectivorous bats from the Netherlands and their role as a possible vector for foodborne diseases. Acta Chiropt. 20 (2), 475–483. https://doi.org/10.3161/15081109ACC2018.20.2.017.
Xie, J., Cui, T., Cui, J., Chen, Y., Zhang, M., Zhou, P., Deng, S., Su, S., Zhang, G., 2014. Epidemiological and evolutionary characteristics of the PRRSV in Southern China from 2010 to 2013. Microb. Pathog. 75, 7–15. https://doi.org/10.1016/j.micpath.2014.08.001.
Xu, Y., 2020. Unveiling the origin and transmission of 2019-nCoV. Trends Microbiol. 28 (4), 239–240. https://doi.org/10.1016/j.tim.2020.02.001.
Xu, K., Cai, H., Shen, Y., Ni, Q., Chen, Y., Hu, S., Li, J., et al., 2020a. Management of corona virus disease-19 (COVID-19): the Zhejiang experience. Journal of Zhejiang University (medical science) 49 (2), 147–157. https://doi.org/10.3785/j.issn.1008-9292.2020.02.02.
Xu, H., Zhong, L., Deng, J., Peng, J., Dan, H., Zeng, X., Li, T., Chen, Q., 2020b. High expression of ACE2 receptor of 2019-nCoV on the epithelial cells of oral mucosa. Int. J. Oral Sci. 12 (8) https://doi.org/10.1038/s41368-020-0074-x.
Yan, R., Zhang, Y., Li, Y., Xia, L., Guo, Y., Zhou, Q., 2020. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. Science 367 (6485), 1444–1448. https://doi.org/10.1126/science.abb2762.
Ye, Z., Yuan, S., Yuen, K., Fung, S., Chan, C., Jin, D., 2020. Zoonotic origins of human coronaviruses. Intrnational Journal of Biological Sciences 16 (10), 1686–1697. https://doi.org/10.7150/ijbs.45472.
Yob, J.M., Field, H., Rashdi, A.M., Morrissy, C., van der Heide, B., Rota, P., et al., 2001. Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia. Emerging Infect. Dis. 7 (3), 439. https://doi.org/10.3201/eid0703.010312.
Zhang, Y.Z., Holmes, E.C., 2020. A genomic perspective on the origin and emergence of SARS-CoV-2. Cell 181 (2), 223–227. https://doi.org/10.1016/j.cell.2020.03.035.
Zhang, T., Wu, Q., Zhang, Z., 2020. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Curr. Biol. https://doi.org/10.1016/j.cub.2020.03.022.
Zhou, P., Yang, X., Wang, X., Hu, B., Zhang, L., Zhang, W., et al., 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 579 (7798), 270–273. https://doi.org/10.1038/s41586-020-2012-7.
Zohdy, S., Schwartz, T.S., Oaks, J.R., 2019. The coevolution effect as a driver of spillover. Trends Parasitol. 35 (6), 399–408. https://doi.org/10.1016/j.pt.2019.03.010.
Zou, X., Chen, K., Zou, J., Han, P., Hao, J., Han, Z., 2020. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Front. Med. 14 (2), 185–192. https://doi.org/10.1007/s11684-020-0754-0.
Zuo, T., Zhang, F., Lui, G.C., Yeoh, Y.K., Li, A.Y., Zhan, H., et al., 2020. Alterations in Gut Microbiota of patients with COVID-19 during time of hospitalization. Gastroenterology 149 (3), 944–955. https://doi.org/10.1053/j.gastro.2020.05.0484 e8.