



# COVID-19 And Some Trends Information About Epidomology Pathogensis, Immunotherputies And Vaccines: A Review

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#### **KEY WORDS**

COVID-19 Pandemic SARS-CoV Vaccines **Abstract:** Coronaviruses are an enveloped group of viruses that contain non-segmented, uniform and positive genomes of RNA. Apart from the economically significant variety of vertebrates such as pigs and chickens but also the climate, six coronaviruses evidently invaded man's hosts and caused disease. In recent decades, attempts have been made to develop vaccines such as MERS and SARS for human coronavirus infection (CoV). However, antiviral medication or vaccine has yet to be approved for MERS and SARS. A big emphasis on attempts to improve CoV vaccines and drugs is the pick or S protein which is the primary inducer of neutralizing antikoids. We do our utmost to clarify such emerging COVID-19 trends in this study.

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#### INTRODUCTION

Coronavirus (CoV) is a single-stranded, positive-sense RNA virus that infects a large-scale host and develops diseases from intermittent bloodless to severe lethal illnesses. Originally called the new virus "2019-nCoV", the new virus was found to be an Extreme Acute Respiratory Syndrovirus (SARS-CoV) sister virus which was found by the International Commission for Virus Taxonomy (ICTV) Coronavirus Study Community. The new virus was also called the "SARS-CoV-2", virus<sup>[1]</sup>.

However, approx. 15% of pneumonia development and approximately 5% rise of acute respiratory difficulties (ABA), septic shock and/or other organ

failures have shown that mild to reasonable symptoms escalate in most COVID-19 patients sooner or later<sup>[2]</sup>.

Medical therapy for patients who suffer from impaired respiratory conditions is based on symptomatic administration and treatment of oxygen and artificial ventilation. During an active analysis of a variety of antivirals, none of which have been primarily approved for COVID-19 are nuclear analog remdesivir. Apart from the production of vaccines and methods to combat immunopathology for contamination, virus or blockage are now without delay a major priority<sup>[3]</sup>.

Bats are regarded historically as a natural coronavirus reservoir which can be transmitted to

humans and other animals after genetic mutation. Seven human coronaviruses were considered including SARS-CoV-2. Four of these have been found to circulate in a moderate symptom human setting (HCoV-HKU1, HCoV-OC43, HCoV-229E and HCoV-NL63)<sup>[4]</sup>. After Severe Acute Respiratory Syndrome (SARS) outbreak coronavirus became more widespread<sup>[5]</sup>. There is no human vaccine to avoid COVID-19 on the market and there is an immediate need to encourage a safe and fine vaccine to prevent this significantly infectious condition.

The focus of this analysis is on recent trends in genomic, morphological, clinical and molecular aspects of the protein COVID-19.

Genome of COVID-19: Comparison of genome sequences COVID-19, SARS-CoV and MERS-CoV verified that 2019-CoV is better identical with SARS-CoV than with the MERS CoV series<sup>[2]</sup>. The COVID-19 amino acid sequence differs from different coronaviruses in areas with 1av polyprotein and glycoprotein or s-protein surface only. The S-protein has two subunits with a subunit binding immediately to the host receptor to aid the infection of the virus. The RNA binding area of the S-protein is more compatible with COVID-19 in SARS EuropeanCoV. Although, the receptor is connected by some of the residues, they are universal. Non identical residues. Studies COVID-19 may be performed to suggest that the human COVID-19 receiver is angiotensin converter enzyme 2 (ACE2)<sup>[6]</sup> (Fig. 1).

While various studies of coronaviral vaccines focused on particular structural proteins, the majority of efforts came to an end soon after the SARS and MERS outbreak. Research on Coronavirus Vaccines needs to be resumed with the present COVID-19 pandemic as soon as possible. In an urgent response to the ongoing pandemic, the first clinical trials of the mRNA-based vaccine which focuses on the S protein SARS-CoV-2, started on 16 March 2020.

The most superficial and protrusive protein, coronaviral protein, plays a major role as mediator in virus entry. The full-scale S proteins (sub-compatible with the receptor domain binding domain S1) have been used frequently as vaccine antigen for developing the SARS vaccines because of their ability to neutralize host cell antibodies research confirmed that S protein-based vaccination did now not grant full safety and every so often elevate protection concerns<sup>[7,8]</sup>.

**Epidemiology of coronavirus:** China has already recounted the likelihood that there is a new outbreak of the virus in the future which has harassed the importance, in the waking of the stipulations arising from the SARS epidemic and the intense criticism of global establishments in terms of delayed provision of and sharin, of formulating a health system improvement and preparedness<sup>[9]</sup>.

The people with the disease had nothing to do with the economy at the beginning. Surprisingly, some high-performance patients with COVID-19 have no longer entered this market. Health staff in a variety of countries have an effect on the infected patient. This shows that COVID-19 is most vulnerable to human transmission<sup>[10]</sup>. Other than aerosols and large respiratory dropples, COVID-19 can also be seen in stools and urine of infected patients with diarrheal symptoms. As of 12 February 2020, the WHO recorded 45,171 cases and 1115 worldwide deaths related to the COVID-19. According to statistics, 99% of infections and 99,9% of COVID-19 deaths in China were reported. Activities are carried out by WHO to reflect developments of the COVID-1929 WHO scenarial reviews as of 12 February 2020. Working in Wuhan, China, drug trials are being carried out to enhance COVID-19 drugs[11].

The COVID-19 infection has become evident through publicity of a virus that is both susceptible to immune suppression and regularity. It is also apparent. Some

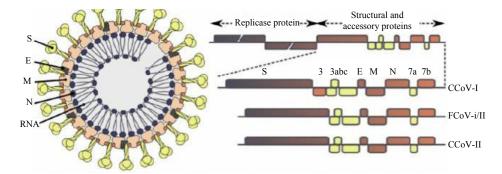


Fig. 1: Coronavirus structure

studies have shown that people aged 25-89 should be distributed. The majority of adults with Tongji Hospital between the ages of 35 and 55 and the cases of young people and children have been reported to be less large<sup>[12, 13]</sup>. The median age of the patients ranged from 15-89 years while most (5%) men reported Early Transmission Dynamics findings<sup>[14]</sup>. Having found that those with a dreadful immune system like the elderly with renal and hepatic disorders could be the population most vulnerable, COVID-19 has expanded the spectrum of transmissibility and pandemic risks relative to SARSCoV, since, COVID-19 (2.9) estimates that the reproductive effectiveness (R) is higher than the high quadratic species listed. The basic copy (R0) of COVID-19 was estimated at 2.6-4.71. Different research estimated to vary between 2-9<sup>[14]</sup> days from 4.8±2.6 and 5.2 days from 4.1-7<sup>[14]</sup> at one time. The typical incubation period of COVID-19 was once estimated to be 4.8±2.6. The trendy hints from Chinese health authorities noted an common incubation period of 7 days, ranging from two to 14 days<sup>[15]</sup>.

Mechanism action of human coronaviruses: Both coronaviruses contain genes which encode proteins for viruses, nucleocapsides and spikes in downstream areas of ORF1<sup>[16]</sup>. The spikes in glycoproteine on the external surface of coronavirus induce infection of the virus into host cells Hence the virus can infect more than a host. The receptor-associating area (RBD) between viruses is unwavering. SARS-CoV and MERS-CoV in other coronaviruses are exopeptidated by others as a key receptor in human cells<sup>[17]</sup>. Coronavirus entry is based on mobile proteases such as HAT, cathepsins and transmembrane protease serine 2)

TMPRSS2 that divide and aggregate spike-protein. Penetration shifts<sup>[18, 19]</sup>. The MERS-coronavirus uses four Dipeptidyl Peptidase (DPP4) and the two angiotensin modified enzymes (ACE2) as the main receptor for HCoV-NL63 and SARS-coronavirus<sup>[17, 20]</sup> are needed.

The SARS-CoV-2 spike protein has a three-dimensional structure in the region of the RBD to retain van der Waals'<sup>[10]</sup> powers. The 394 residue of glutamine in the RBD region of SARS-CoV-2 is located on the human ACE2 receptor via. essential lysine 31<sup>[21]</sup>. The full pathogenicity mechanism for SARS-CoV-2 from replication attachment (Fig. 2).

Pathogenicity of corona virus: In the WHO study, about 82% of COVID-19 patients who had COVID-19 had no signs and were recovered immediately. By Feb. 20, 18264 (24%) cases were recovered in China and in the extreme cases Guang-dong recovery and death rates were 26.4% and 13.4%, respectively. In moderate and extreme cases, median signs began to heal once for two and three to 6 weeks. In addition, there have been four coronaviruses (HCOVs, HCoV 229E, NL63, OC43, HKU1), non-extreme Acute Air Syndroma (SARS)-like coVs just one week before initiating and developing extreme symptoms, like hypoxia<sup>[22]</sup>, known as CoVs. They are mild and endemic all over the world. Three zoonotic CoVs have emerged during this two-year period and have caused a lot media and public hype, particularly pathogenic CoVs which have caused human disease deadly over the last two years. concern, such as the coronavirus SARS (SARS-CoV now called SARS-CoV-1) observed in November 2002, the coronavirus of the Middle East (MERS) (SERS-CoV)[23] and SARS-CoV-2, b. Coronavirus Diseases-2019 (COVID-19) is the disease

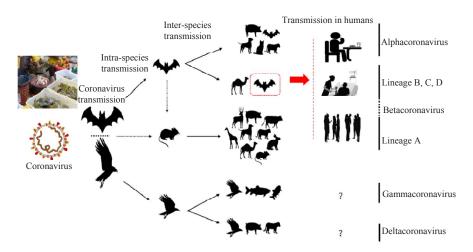


Fig. 2: The key reservoirs and mode of transmission of coronaviruses

caused by the use of SARS-CoV-2.19. For investigations outside mainland China, symptoms began once 22.2 days for recovery (95% self belief interval 18-83). Furthermore, the duration of beginning the symptoms varies from 20.2 days to 22.3 days<sup>[24, 25]</sup> (95% self-confidence range of 15.1-29.9). Even though the ages are a deterministic decisive factor in the severity of the symptoms, various aspects of the development of signs and symptoms including a record of underlying conditions or co-infection with various infections, like the flu virus or Klebsiella can speed up the development of the disease, resulting in negative disease pronostics<sup>[26]</sup>. The results of Singapore findings indicate, however, that infected patients without any background history are further strengthened by severe disease and want intensive treatment<sup>[27]</sup>.

**Laboratory diagnosis:** COVID-19 clinical diagnostics are focused primarily on epidemiological history, clinical evidence, and certain auxiliary exams, such as nucleic acid detection, CT scan, IgM/IgG point-of-care identification technology, enzyme-linked immunosorbent monitoring and the blood culture (ELISA).

**Nucleic acid detection technology:** The two most important scientific applications for SARS-CoV-2 nuclear acid are quantum chain reactions (RT-qPCR) and high performance real-time series. SARS-CoV-2 has become the definitive distinguishing solution to virus blood lifestyle and high efficiency genomic sequence<sup>[28]</sup>. However, due to his deployment of tools and overhead costs, technological know-how in medical prediction is restricted in high performance sequencing software. RT-qPCR is thus the best known, most popular and easy-to-use method for the identification of pathogenic viruses in respiratory and blood secretions<sup>[29]</sup>.

Following the outbreak of SARS-CoV-2 in China, several companies quickly adopted scientific diagnostic test kits for RT-qPCR. The Chinese CDC Center for Disease Control and Prevention (CCDC) recommend that SarS-CoV-2 be detected via. rt-qPCR in the gene regions ORF1ab and N, using various primers and samples. Chu *et al.* [30] identified 2 1-stage RT-qPCR tests to determine whether a virus genome can be detected separately in two extraordinary areas (ORF1b and N). If each goal is positive, the patient is determined to have a laboratory-confirmed infection. Both samples were recorded poorly controlled when samples were examined using this method in respiratory specimens from 2 infected SARS CoV-2 patients as beauty samples. Another observation showed the interesting RT-qPCR

fees for SRAS-CoV-2 (SYBR-based non-SYBR-based fluorescent signal)self-sacrificed saliva were typically. The saliva is promising non-invasive test for the identification, monitoring, and management of SARS-CoV-2 infection<sup>[30]</sup>. Additionally, excess resistance and specialty detection of SARS-CoV and MERS-CoV infection was confirmed by RT-qPCR<sup>[31]</sup>. However for SARS-CoV-2, 5 sufferers suffering from a weak RT-qPCR effect could eventually have confirmed that all affected persons are SARS-CoV-2 infected, as well as positive Chest-CT findings and repeated swab assessments (RT-qPCR). The protocol used to detector SARSA coV with RT-qPCR can only achieve sensitivities of 50-79% by using the form and variations of scientific samples obtained<sup>[32]</sup>.

CT scans and other diagnostic methods: In the case of COVID-19, it is special to RT-qPCR but because of the severe diagnosis penalties it cannot leave its false negative burden. Too many clinicians recommended CT scans as an important auxiliary diagnostic method should be more sensitive. Even if you have excessive scientific concern about SARS-CoV-2 with weak RT-qPCR screening, a mixture of repeated RT-QPCR controls and CT scans may be helpful. The high-resolution CT (HRCT) is required for chest patients, in particular in the early analysis and assessment of disease severity in the SARS-CoV-2<sup>[33]</sup>. CT snap shots of SARS-CoV-2 contaminated patients have been tested in various research studies<sup>[34, 35]</sup>. The common images of CT show bilateral pulmonary pulmonary glass and lung opacity consolidating, each with rounded morphology and lung distribution peripherals. Besides SARS CoV and MERS- BesidesCoV infections, lung engagement with The peripheral prevalence has been seen and the development of ground-glass opacity and consolidation close to that of SARS-CoV-2 infections has been confirmed by chest CT<sup>[36]</sup>. Due to the vulnerabilities present in nuclear detection and COVID-19 predictive CT scanning, certain immunological detection kits aimed at viral antigens or antibodies should be taken by scientific labs as soon as possible. Currently, IgM/IgG and ELISA POCT for SARS-CoV-2 have also been developed and pre-tested by several firms with rates of detection being shown to be higher than nucleic acid detection. The IgG ELISA (94.7%) in SARS-CoV N-based is significantly more sensitive than the SARS CoV in IgG ELISA (58.9%)[37].

**Immunopathology of COVID-19:** Currently, data are not available for the specific role of both humoral and mobile immunity or innate immunity of COVID-19 patients. Only

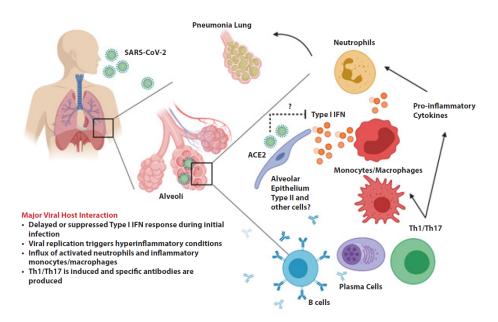


Fig. 3: Proposed host immune responses during SARS-CoV-2 infection

extraordinary advanced laboratories may perform experiments to analyze the immune reactions to class I and class-lirestricted viral epitopes, respectively, mediated with CD8+ and CD4+ T lymphocytes, to prove the presumption that mobile immunity to SARS-CoV (rather than humoural immunity) is suspected.

In a separate study by Wuhan, entire lymphatic cells were decreased statistically in 40 one patient with accelerated neutrophils compared with other ICU patients. More severity of the disease and death was associated with increased neutrophils and lowered lymphocytes. In addition, ICU patients had larger plasma levels of multiple native cytokines, IP-10, MCP-1, MIP-1A and TNFa.2, which counseled the likelihood of participation in disease development and severity in an extraordinarily inflammatory state. SARS-CoV and MERS-CoV infections which suggested that a comparable cytokine-stormed infection may be comparable [31,38], also indicated an early rise in proinflammatory serum cytokin. Lymphopenia is also seen in SARS-CoV-2 infected patients, suggesting that mobile immune reactions can also occur be suppressed [12,39]. In this context, it becomes possible that a form of race decides the direction of events after contamination with SARS-CoV-2. Or the motivation for a nation of immunosuppression which weakens and sometimes overwhelms its defense in the best-case scenario with the exception of any or mild scientific symptoms of the infection, the preliminary dose of the viral inoculum major in contamination can also

play an important role in all subsequent occurrences, whether the cellular immune reaction rapidly clears SARS-CoV-2<sup>[38]</sup> (Fig. 3).

Efficient inborn immune responses to viral infections are closely associated with interferon type 1 and downstream (IFN) reaction, contributing to the regulation of viral replication and activation of higher-end adaptive immune responses. Although, the ACE2 input receiver continues to share SARS-CoV and SARS-CoV2 the MERS-CoV uses the DPP-4 as a separate recipient<sup>[40]</sup>. Innate immune cells also use patterns to recognise the infection of the virus to create an antiviral reaction (PAMPs). For RNA viruses such as coronavirus, both endosomal RNA receptors, TLR3 and TLR7 and cytosomal RNA sensors are known to be utilized for identifying PAMPs, along with dsRNA, endosomal RNA, TLR3 and TLR7 and RIG-I/MDA5 as a virus genomatic RNA or intermediate viral replication, cytosolic RNA sensors are known. This focal point tour leads to the downstream signaling cascade activation, i.e. Aid of their nuclear translocation was supported by NF-SB and IRF3. The nuclei are the elements that provide transcription for expression of type IFN and various pro-inflammatory cytokins and the first line defense against viral infection at the entry site are provided in this preliminary response<sup>[8]</sup>.

Vaccines for SARS-CoV-2: Such an antiviral antimicrobial agent SAR S-CoV is currently unavailable, just like SARS-CoV and Meds-CoV<sup>[8, 2]</sup>. Help therapy, including

oxidation, fluid preservation and the use of wide-ranging antibiotics to treat secondary bacterial infections<sup>[2]</sup>, are the most effective treatment strategies. Research on coronavirus molecular mechanisms<sup>[41]</sup> and the SARS COV-2 genomic company<sup>[5]</sup> have established various therapeutic aims to restructure or enhance the current antiviral functions.

The animals test for coV-SRAS-CoV are LIV-attended viruses, Viral Vectors, Inactivated Viruses, Unit Sub-Vaccines, Recombinant DNA Vaccines and Proteins<sup>[42]</sup>. Animals studies include: numerous methods of vaccination. Increased SARS-CoV vaccine will succeed with previous vacuum techniques. SARS-CoV strain recombinant protein used in urban strain mice and hamsters (AY278741) has contributed to an antibody neutralization and defense of SARS-CoV<sup>[43, 44]</sup>. SARS-CoV strain a large number of animal models were used to decrease the diameter of SAR S-CoV (AY278741)[24, 45] significantly by viruses and by the inactivated or live-vectored stresses. The inactivated and live-vectored vaccines that reduced viral load in animal models were developed by different lines of SARS-CoV. The following traces are given in Tor2 (AY274119)[46, 48].

In comparison to SARS-CoV-2, however, few vaccines are in the pipeline. In this study, 1 trial<sup>[49]</sup>, mRNA is primarily aimed and co-ordinated with the assistance of the United States National Institute for Allergy and Infectious Diseases for SARS-CoV-2. INO-4800-The predominantly reliant vaccine for humans to be tested could easily be accessible<sup>[50]</sup>. Cheung *et al.*<sup>[51]</sup> focuses on the improvement of the virus inactivation vaccine, a hub in China for disease control and prevention. Primarily based on the pattern of vaccine mRNA (prepared by Stermirna Therapeutics)<sup>[52]</sup> is to be present in the future<sup>[53]</sup>. While a recombinant 2019-nCoV S sub-unit trimer dependent mainly vaccine has to be developed at Clover biopharmaceuticals<sup>[54]</sup>.

It is extremely important for the international promotion of lucrative organized therapies to fight against the COVID-19 pandemic in severe cases. The combined application of antiviral and anti-inflammatory drugs may be of extra benefit than the use of both. Centralized on in vitro evidence to prevent replication of SARS-CoV-2 and block SARS-CoV-2 mediated cytokine inhibition<sup>[55]</sup>.

## **REFERENCES**

01. Gorbalenya, A.E., S.C. Baker, R. Baric, R.J.D. Groot and C. Drosten *et al.*, 2020. Severe acute respiratory syndrome-related coronavirus: The species and its viruses-a statement of the Coronavirus Study Group. BioRxiv, Vol. 1, 10.1101/2020.02.07.937862

- Huang, C., Y. Wang, X. Li, L. Ren and J. Zhao et al., 2020. Clinical features of patients infected with 2019 novel Coronavirus in Wuhan, China. Lancet, 395: 497-506.
- 03. Xu, Z., L. Shi, Y. Wang, J. Zhang and L. Huang *et al.*, 2020a. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Resp. Med., 8: 420-422.
- 04. Cabeca, T.K., C. Granato and N. Bellei, 2013. Epidemiological and clinical features of human coronavirus infections among different subsets of patients. Influenza Respir. Viruses, 7: 1040-1047.
- 05. Lu, R., X. Zhao, J. Li, P. Niu and B. Yang *et al.*, 2020. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395: 565-574.
- 06. Dong, E., H. Du and L. Gardner, 2020. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect. Dis., 20: 533-534.
- 07. Roper, R.L. and K.E. Rehm, 2009. SARS vaccines: Where are we?. Expert Rev. Vaccines, 8: 887-898.
- De Wit, E., N. van Doremalen, D. Falzarano and V.J. Munster, 2016. SARS and MERS: Recent insights into emerging coronaviruses. Nat. Rev. Microbiol., 14: 523-534.
- 09. Dong, N., X. Yang, L. Ye, K. Chen, E.W.C. Chan, M. Yang and S. Chen, 2020. Genomic and protein structure modelling analysis depicts the origin and infectivity of 2019-nCoV, a new coronavirus which caused a pneumonia outbreak in Wuhan, China. BioRxiv., Vol. 1, 10.12688/f1000research.22357.1
- Xu X., Chen P., Wang J., Feng J., Zhou H., Li X., Zhong W. and Hao P., 2020b. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. Sci., China Life Sci., 63: 457-460.
- 11. Cyranoski D., 2020. This scientist hopes to test coronavirus drugs on animals in locked-down Wuhan. Nature 577: 607-607.
- 12. Medical Expert Group of Tongji Hospital, 2020. Quick guide to the diagnosis and treatment of pneumonia for novel coronavirus infections. Medical Expert Group of Tongji Hospital, Wuhan, China.
- 13. Wang, D., B. Hu, C. Hu, F. Zhu and X. Liu *et al.*, 2020. Clinical characteristics of 138 hospitalized patients with 2019 novel Coronavirus—infected pneumonia in Wuhan, China. JAMA., 323: 1061-1069.
- Li, Q., X. Guan, P. Wu, X. Wang and L. Zhou et al., 2020. Early transmission dynamics in Wuhan, China, of novel coronavirus-infected pneumonia. N. Engl. J. Med., 382: 1199-1207.

- National Health Commission of People's Republic of China, 2020. Preventguideline of 2019-nCoV. National Health Commission of People's Republic of China, China.
- Van Boheemen, S., M. De Graaf, C. Lauber, T.M. Bestebroer and V.S. Raj et al., 2012. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. MBio, Vol. 3, No. 6. 10.1128/mBio.00473-12
- Wang, N., X. Shi, L. Jiang, S. Zhang and D. Wang et al., 2013. Structure of MERS-CoV spike receptor-binding domain complexed with human receptor DPP4. Cell Res., 23: 986-993.
- 18. Glowacka, I., S. Bertram, M.A. Muller, P. Allen and E. Soilleux *et al.*, 2011. Evidence that TMPRSS2 activates the severe acute respiratory syndrome coronavirus spike protein for membrane fusion and reduces viral control by the humoral immune response. J. Virol., 85: 4122-4134.
- 19. Bertram, S., I. Glowacka, M.A. Muller, H. Lavender and K. Gnirss *et al.*, 2011. Cleavage and activation of the severe acute respiratory syndrome coronavirus spike protein by human airway trypsin-like protease. J. Virol., 85: 13363-13372.
- 20. Raj, V.S., H. Mou, S.L. Smits, D.H.W. Dekkers and M.A. Muller *et al.*, 2013. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. Nature, 495: 251-254.
- Wan Y., Shang J., Graham R., Baric R.S. and Li F., 2020. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J. Virol., 94: e00127-e00127.
- 22. WHO., 2020. SARS (severe acute respiratory syndrome). World Health Organization, Geneva, Switzerland.
- 23. Zaki, A.M., S. van Boheemen, T.M. Bestebroer, D.M.E. Albert, D.V.M. Osterhaus and R.A.M. Fouchier, 2012. Isolation of a novel coronavirus from a man with pneumonia in Saudi Arabia. N. Engl. J. Med., 367: 1814-1820.
- 24. Jung, S.M., A.R. Akhmetzhanov, K. Hayashi, N.M. Linton and Y. Yang et al., 2020. Real-time estimation of the risk of death from novel coronavirus (COVID-19) infection: Inference using exported cases. J. Clin. Med., Vol. 9, No. 2. 10.3390/jcm9020523
- Dorigatti, I., L. Okell, A. Cori, N. Imai and M. Baguelin et al., 2020. Report 4: Severity of 2019-novel coronavirus (nCoV). Imperial College London, London.

- 26. Ng, L.F. and J.A. Hiscox, 2020. Coronaviruses in animals and humans. BMJ., Vol. 1, 10.1136/bmj.m634
- 27. Phelan, A.L., R. Katz and L.O. Gostin, 2020. The novel coronavirus originating in Wuhan, China: Challenges for global health governance. Jama, 323: 709-710.
- Zhao, Y., Z. Zhao, Y. Wang, Y. Zhou, Y. Ma and W. Zuo, 2020. Single- cell RNA expression profiling of ACE2, the putative receptor of Wuhan 2019-nCov. Am. J. Respir. Crit. Care Med., Vol. 1, 10.1101/2020.01.26.919985
- 29. Corman, V.M., O. Landt, M. Kaiser, R. Molenkamp and A. Meijer *et al.*, 2020. Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Eurosurveillance, Vol. 25, No. 3.
- 30. Chu D.K.W., Y. Pan, S.M.S. Cheng, K.P.Y. Hui and P. Krishnan *et al.*, 2020. Molecular Diagnosis of a Novel Coronavirus (2019-nCoV) Causing an Outbreak of Pneumonia. Clin. Chem., 66: 549-555.
- 31. Mahallawi, W.H., O.F. Khabour, Q. Zhang, H.M. Makhdoum and B.A. Suliman, 2018. MERS-CoV infection in humans is associated with a proinflammatory Th1 and Th17 cytokine profile. Cytokine, 104: 8-13.
- 32. Yam, W.C., K.H. Chan, L.L.M. Poon, Y. Guan, K.Y. Yuen, W.H. Seto and J.S.M. Peiris, 2003. Evaluation of reverse transcription-PCR assays for rapid diagnosis of severe acute respiratory syndrome associated with a novel coronavirus. J. Clin. Microbiol., 41: 4521-4524.
- 33. Shi H., Han X. and Zheng C., 2020. Evolution of CT Manifestations in a Patient Recovered from 2019 Novel Coronavirus (2019-nCoV) Pneumonia in Wuhan, China. Radiology 295: 20-20.
- 34. Chung, M., A. Bernheim, X. Mei, N. Zhang and M. Huang *et al.*, 2020. CT imaging features of 2019 novel coronavirus (2019-nCoV). Radiology, 295: 202-207.
- 35. Ooi, G.C., P.L. Khong, N.L. Muller, W.C. Yiu and L.J. Zhou *et al.*, 2004. Severe acute respiratory syndrome: Temporal lung changes at thin-section CT in 30 patients. Radiology, 230: 836-844.
- 36. Ajlan, A.M., R.A. Ahyad, L.G. Jamjoom, A. Alharthy and T.A. Madani, 2014. Middle East Respiratory Syndrome Coronavirus (MERS-CoV) infection: Chest CT findings. Am. J. Roentgenol., 203: 782-787.
- 37. Woo, P.C., S.K. Lau, B.H. Wong, H.W. Tsoi and A.M. Fung *et al.*, 2005. Differential sensitivities of severe acute respiratory syndrome (SARS) coronavirus spike polypeptide Enzyme-Linked Immunosorbent Assay (ELISA) and SARS coronavirus nucleocapsid protein ELISA for serodiagnosis of SARS coronavirus pneumonia. J. Clin. Microbiol., 43: 3054-3058.

- 38. Wong, C.K., C.W.K. Lam, A.K.L. Wu, W.K. Ip and N.L.S. Lee *et al.*, 2004. Plasma inflammatory cytokines and chemokines in severe acute respiratory syndrome. Clin. Exp. Immunol., 136: 95-103.
- 39. Zhang, J.J., X. Dong, Y.Y. Cao, Y.D. Yuan and Y.B. Yang et al., 2020. Clinical characteristics of 140 patients infected with SARS CoV 2 in Wuhan, China. Allergy, 75: 1730-1741.
- 40. Zhou, P., X.L. Yang, X.G. Wang, B. Hu and L. Zhang *et al.*, 2020. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature, 579: 270-273.
- 41. Groneberg, D.A., R. Hilgenfeld and P. Zabel, 2005. Molecular mechanisms of severe acute respiratory syndrome (SARS). Respir. Res., 6: 1-16.
- 42. Graham, R.L., E.F. Donaldson and R.S. Baric, 2013. A decade after SARS: Strategies for controlling emerging coronaviruses. Nature Rev. Microbiol., 11: 836-848.
- 43. Bisht, H., A. Roberts, L. Vogel, K. Subbarao and B. Moss, 2005. Neutralizing antibody and protective immunity to SARS coronavirus infection of mice induced by a soluble recombinant polypeptide containing an N-terminal segment of the spike glycoprotein. Virology, 334: 160-165.
- 44. Kam, Y.W., F. Kien, A. Roberts, Y.C. Cheung and E.W. Lamirande et al., 2007. Antibodies against trimeric S glycoprotein protect hamsters against SARS-CoV challenge despite their capacity to mediate FcγRII-dependent entry into B cells in vitro. Vaccine, 25: 729-740.
- 45. Stadler, K., A. Roberts, S. Becker, L. Vogel and M. Eickmann *et al.*, 2005. SARS vaccine protective in mice. Emerging Infect. Dis., Vol. 11, No. 8. 10.3201/eid1108.041003
- 46. See, R.H., A.N. Zakhartchouk, M. Petric, D.J. Lawrence and C.P. Mok et al., 2006. Comparative evaluation of two severe acute respiratory syndrome (SARS) vaccine candidates in mice challenged with SARS coronavirus. J. General Virol., 87: 641-650.

- 47. Weingartl, H., M. Czub, S. Czub, J. Neufeld and P. Marszal et al., 2004. Immunization with modified vaccinia virus ankara-based recombinant vaccine against severe acute respiratory syndrome is associated with enhanced hepatitis in ferrets. J. Virol., 78: 12672-12676.
- 48. Qu, D., B. Zheng, X. Yao, Y. Guan and Z.H. Yuan *et al.*, 2005. Intranasal immunization with inactivated SARS-CoV (SARS-associated coronavirus) induced local and serum antibodies in mice. Vaccine, 23: 924-931
- 49. McKay, B.L.P., 2020. Drugmakers rush to develop vaccines against China virus the wall street journal. The Wall Street Journal, China.
- 50. Inovio IP., 2020. Inovio selected by CEPI to develop vaccine against new coronavirus inovio. Inovio IP., Pennsylvania.
- 51. Cheung, E., 2020. China coronavirus: 2020 Hong Kong researchers have already developed vaccine but need time to test it, expert reveals. SCMP Group, China.
- 52. Xinhua News Agency, 2020. China fast-tracks novel coronavirus vaccine development Xinhua. Xinhua News Agency, Beijing, China.
- 53. Geo-Vax, 2020. Geovax and bravovax (Wuhan, China) to collaborate on development of coronavirus vaccine. GeoVax Biotechnology Company, China.
- 54. Clover, B., 2020. Clover initiates development of recombinant subunit-trimer vaccine for Wuhan coronavirus (2019-ncov). YAOZH.COM, China.
- 55. Runfeng, L., H. Yunlong, H. Jicheng, P. Weiqi and M. Qinhai *et al.*, 2020. Lianhuaqingwen exerts anti-viral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2). Pharmacol. Res., Vol. 156, 10.1016/j.phrs.2020.104761