Bulletin of Environment, Pharmacology and Life Sciences
Bull. Env. Pharmacol. Life Sci., Vol 9[12] November 2020 :182-188

Online ISSN 2277-1808
Journal's URL:http://www.bepls.com
CODEN: BEPLAD
Global Impact Factor 0.876
Universal Impact Factor 0.9804
NAAS Rating 4.95

REVIEW ARTICLE **OPEN ACCESS**

An overview of SARS-CoV-2 molecular diagnostics and therapeutics

S. Thangminlal Vaiphei & Robert Thangjam
Department of Biotechnology, Mizoram University, Aizawl
Email: mzut261@mzu.edu.in

ABSTRACT
During the on-going COVID-19 pandemic situation, various shortcomings in dealing with the crisis and difficulties in containing the coronavirus outbreak have been exacerbated by the absence of reliable rapid and efficient diagnostic tools. Moreover, the unavailability of approved therapeutic drugs against SARS-CoV-2 has become a major global concern. The prevailing diagnoses mostly rely on the detection of viral RNA as well as antibodies in response to viral infection of individuals. The combination of these assays has been recommended for affirmative diagnosis in several cases. However, it will take a while until therapeutic drugs and vaccines against COVID-19 will be available in the open market. Preventing the spread of SARS-CoV-2 by inculcating awareness and strict adherence to WHO guidelines are prerequisites at the moment until an efficacious solution emerges to tackle COVID-19. Various aspects of the prevailing diagnostics and potential interventive measures for COVID-19 are discussed in this article.
Keywords: *SARS-CoV-2, COVID-19, Therapeutics, Diagnosis, Coronavirus, Vaccines*

Received 17.09.2020 Revised 10.10.2020 Accepted 09.11.2020

INTRODUCTION

Coronaviruses (CoVs) are single-stranded RNA viruses that belong to the family Coronavirdiae. Recently, CoVs have emerged as human pathogens causing epidemics in large scale such as SARS-CoV or the severe acute respiratory syndrome CoV and MERS-CoV or the Middle East respiratory syndrome CoV [1,2]. The CoVs are classified into four different genera namely alpha-coronavirus (αCoV), beta-coronavirus (βCoV), delta-coronavirus (δCoV), and gamma-coronavirus (γCoV) [3]. Most CoVs have 8-10 open reading frames (ORFs), which are translated into several structural and non-structural proteins. The 2019 novel coronavirus has been named as SARS-CoV-2 by the International Committee of Taxonomy of Viruses (ICTV) and this virus can cause the disease named coronavirus disease 2019 or COVID-19 according to WHO/COVID-19/laboratory/2020.5 [4,5]. The SARS-CoV-2 belongs to the RNA beta-coronavirus and like the SARS and MERS, encodes structural proteins (e.g. spike glycoprotein) and non-structural proteins (e.g. 3-chymotrypsin-like protease, papain-like protease, helicase, and RNA-dependent RNA polymerase). The structural protein, spike glycoprotein is essential for the entrance of virus into the cell by means of virus–receptor interactions, and the four non-structural proteins are important enzymes in the viral life cycle [6]. With the declaration of pandemic status by World Health Organization (WHO) due to the recent outbreak, https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020, there has been an increasing demand and requirement for reliable fast and accurate diagnostics for preventing the wide spread of the SARS-CoV-2 infection. In response to this growing demand, multiple rapid testing diagnostic kits have emerged from different manufactures for commercial purposes. However, WHO has come up with strict guidelines that recommend the use of point-of–care immunodiagnostic COVID-19 tests only for research settings [7]. The high probability of false results may lead to misinterpretation of data and dissemination of wrong information. This work represents a comprehensive review related to the prevailing molecular diagnostic and therapeutic measures for COVID-19, and also highlights the relevant instructions according to WHO.

DIAGNOSIS BASED ON VIRAL RNA DETECTION

Since the COVID-19 outbreak, there has been a sudden surge in demand for efficient and reliable diagnostic methods for detection of SARS-CoV-2 infection. The first line of detection for COVID-19 cases relies on the presence of viral RNA (ribonucleic acid) using PCR (polymerase chain reaction) method. WHO has recommended the PCR testing in asymptomatic or mildly symptomatic contacts in the assessment of individuals who have had contacts with COVID-19 patients [5] (https://www.who.int /publications-detail/laboratory-testing-for-2019-novel-coronavirus-in-suspected-human-cases-2020 0117). According to the laboratory testings interim guideline by WHO dated March 19, 2020 (WHO/COVID-19/laboratory/2020.5) [5] rapid testing of suspected cases for clinical management and outbreak control should be carried out with nucleic acid amplification tests (NAAT), such as RT-PCR (Reverse transcriptase PCR) under the guidance of a laboratory expert. The real time RT-PCR assay has been found to be effective in detecting viral nucleic acids in patients suffering from acute respiratory viral infections [8,9]. Subsequently, following the outbreak in Wuhan, the genomic sequence of SARS-CoV-2 was published and made available for public with the GenBank accession number MN908947 [10]. The genomic sequence of the SARS-CoV-2 has been instrumental in development of PCR primers for COVID-19 targets such as ORF1a and ORF1b, RNA-dependent RNA polymerase (RdRp), nucleocapsid (N), and envelope (E) genes [11-13]. A comprehensive list of approved diagnostic PCR-assays manufactured by different companies are given in **Table 1** [14]. According to this table, the minimum time requirement for completion of a test varies from one hour to several hours. One of the major drawbacks of some of these assays is the time–consuming process. The RT-PCR-based screening method has been found to be beneficial in areas where there is a widespread of the COVID-19, however, it must be noted that the occurrence of false negatives in infected patients could be attributed by various factors such as poor quality of the specimens collected, the specimen was collected too early in the infection or too late, the sample was not handled appropriately, and other technical reasons [15,16].

Besides, the used of internal and external controls while performing NAAT tests is highly recommended [5]. In view of the current scenario, WHO has designated laboratories worldwide that can provide confirmatory testing for COVID-19 as shown in **Table 2** [17]. Laboratories with limited experience on COVID-19 virus testing or countries not having testing facilities could send their first five positives and first ten negative COVID-19 specimens to these WHO reference laboratories (https://www.who.int /emergencies/diseases/novel-coronavirus-2019/technical-guidance/laboratory-guidance).

Table 1: PCR-based diagnostic assays available from different companies [14]

Company	Product	Type	Time (Hour)
BioMerieux-BioFire Defense	BIOFIRE COVID-19 test	PCR	<1
Cepheid	Xpert Xpress SARS-CoV-2 test	PCR- PoC	<1
DiaSorin Molecular	Simplexa COVID-19 Direct	PCR	1
Mesa Biotech	Accula SARS-CoV-2 test	PCR- PoC	<1
Credo Diagnostics Biomedical	VitaPCR SARS-CoV2 Assay	PCR- PoC	<1
Qiagen (Thermo Fisher)	QIAstat-Dx Respiratory SARS-CoV-2 Panel	PCR	1
Co-Diagnostics	Logix Smart Coronavirus COVID-19 Test	PCR	1-2
GenMark Diagnostics	ePlex SARS-CoV-2-Test	PCR	2
Primerdesign	COVID-19 genesig Real-Time PCR assay	PCR	2
Anatolia Geneworks	Bosphore 2019-nCoV Detection Kit	PCR	2
CancerRop	Q-sens 2019-nCoV Detection Kit	PCR	2
SolGent	DiaPlexQ 2019-nCoV Detection Kit	PCR	2
BGI	Real-Time Fluorescent RT-PCR kit	PCR	3
Hologic	Panther Fusion SARS-CoV-2 Assay	PCR	3
Cer Test Biotech, BD	VIASURE SARS-CoV-2 real Time PCR	PCR	3
Luminex Molecular Diagnostics	NxTAG CoV extended Panel Assay	PCR	4
Thermo Fisher	TaqPath COVID-19 Combo Kit	PCR	4
Seegene	Allplex 2019-nCoV Assay	PCR	4
Abbot	RealTime SARS-CoV-2	PCR	4-6
PerkinElmer	New Coronavirus RT-PCR Kit	PCR	4-6
Quidel	Lyra SARS-CoV-2 Assay	PCR	4-6
3D Medicines	SARS-CoV-2+Influenza A&B RT-PCR Kit	PCR	4-6
AB ANALITICA	REALQUALITY RQ-2019-nCoV	PCR	4-6
AusDiagnostics	SARS-CoV-2, Influenza RSV Panel	PCR	4-6
Kogene Biotech	2019 Real-time PCR Kit	PCR	4-6
OsangHealthcare	GeneFinder COVID-19 RealAmp Kit	PCR	4-6
Beijing Applied Biological Technologies (XABT)	Multiple Real-time PCR Kit	PCR	4-6
Genomica/PharmMar Group	qCOVID-19, CLART COVID-19	PCR	5
Bioneer	AccuPower COVID-19 Real-Time RT-PCR Kit	PCR	8

Table 2: WHO reference laboratories providing confirmatory tests for COVID-19 (as of April 19, 2020).

Sl. No.	Laboratory	Location
1	Armed Forces Research Institute of Medical Science	Bangkok, Thailand
2	Centre for Respiratory Diseases and Meningitis, National Institute for Communicable Diseases	Johannesburg, South Africa
3	Central Public Health Laboratory	Muscat, Oman
4	China CDC	Beijing, China
5	Erasmus MC, Department Viroscience	Rotterdam, The Netherlands
6	German coronavirus diagnostic working group,Institute of Virology, Charité and Robert Koch Institute	Berlin, Germany
7	ICMR - National Institute of Virology	Pune, India
8	Instituto de Diagnóstico y Referencia, Epidemiológicos (InDRE)	Mexico City, Mexico
9	Institute of Tropical Medicine, Nagasaki University	Nagasaki, Japan
10	Institut Pasteur Dakar	Dakar, Senegal
11	Institut Pasteur Paris	Paris, France
12	National Institute of Infectious Diseases (INMI), L. Spallanzani	Rome, Italy
13	National Public Health Laboratory	Singapore, Singapore
14	National Institute of Health, Department of Medical Sciences, Ministry of Public Health	Nonthaburi, Thailand
15	Pasteur Institute of Cambodia	Phnom Penh, Cambodia
16	Public Health England	London, United Kingdom
17	Reference Lab for Infectious Diseases Abu Dhabi, Sheikh Khalifa Medical Center	Abu Dhabi, United Arab Emirates
18	Respiratory Viruses Diagnostic Laboratory, US-CDC	Atlanta, USA
19	Respiratory Virology Laboratory, Fio Cruz	Rio des Janeiro, Brazil
20	SAR Hong Kong School of Public Health University of Hong Kong	Hong Kong, China
21	The State Research Center of Virology and Biotechnology VECTOR	Koltsovo, Russian Federation
21	University Hospital of Geneva	Geneva, Switzerland
22	Victorial Infectious Diseases Reference Laboratory	Melbourne, Australia

DIAGNOSIS BASED ON SEROLOGICAL ANTIBODY TESTING

The occurrence of false negatives in NAAT assay is a major setback, however, serological tests can be helpful in such cases. If the suspected case has an epidemiological history that indicates strong correlations with COVID-19 infection, paired serum samples (in the acute and convalescent phase) could support diagnosis depending upon the availability of validated serology tests [5]. Serological testing based on antibody IgE and IgM against SARS-related virus (SARSr-CoV) Rp3 N antigen could be useful for detection of its SARS-CoV-2 counterparts due to their highly identical sequence [18-20]. A combined SARS-CoV-2 IgM-IgG antibody test for rapid screening of COVID-19 patients directly from blood samples was demonstrated using a lateral flow immunoassay [21]. The presence of IgM antibodies in the blood will indicate recent exposure to SARS-CoV2, whereas, the detection of IgG antibodies suggests that exposure to the coronavirus took place much earlier.

Antibody-based detection may also be useful in identification of asymptomatic carriers to prevent the widespread of COVID-19 virus [16, 22]. Besides, antibody-based serological testing will be more effective in recovery phase or asymptomatic carriers and not during the early stage of infection since the immune system takes several days to make antibody in response to COVID-19 infection [22]. Also, serological testing can help in identification of individuals, who might have developed immunity due to their earlier exposure to COVID-19 virus, as potential source for convalescent blood plasma (https://www.fda.gov/news-events/press-announcements/coronavirus-covid-19-update-serological-tests).

DIAGNOSTICS PIPELINE

As part of the global response to the ongoing pandemic, COVID-19 Diagnostics Resource Centre has been set up by the Foundation for Innovative New Diagnostics (FIND) in partnership with WHO to accelerate the development of diagnostics (https://www.finddx.org/covid-19/). The primary objective of this center

is to provide latest information to the healthcare providers and policymakers about SARS-CoV-2 diagnostics and testing for outbreak control and management. According to the SARS-CoV-2 diagnostic pipeline, most recent tracking results for commercialized immunoassays corresponds to a total number of approximately 241, whereas about 46 assays are still in development stage. For molecular assays like PCR, results indicate around 244 commercialized diagnostics with at least 43 in development stage.

WHO'S GUIDELINE ON RAPID IMMUNODIAGNOSTIC TESTS

Due to the increasing demand on COVID-19 diagnostic tests, multiple manufacturers have developed and commercialized rapid and simple test kits for testing outside the laboratory settings. According the recent scientific brief of WHO, dated April 8, 2020, (WHO/2019-nCoV/Sci_Brief/POC_ immunodiagnostics/2020.1), certain guidelines were laid down with regards to the use of point-of-care immunodiagnostics [7]. A rapid diagnostic kit can detect viral proteins (antigens) with antibodies fixed on a paper strip within half an hour. However, the test will be applicable only for acute or early infection since antigens are expressed only when the virus is actively replicating [7]. Besides, there are many factors governing whether the test will work or not, that includes concentration of viral particles, the quality of the collected samples, time from onset of illness, how sample is processed and other technical reasons. Based on past experience, the speculated success rate for this type of antigen based rapid detection test for COVID-19 is less than 50 %, which means that half or more of the infected patients might be missed by this test [7]. Moreover, the occurrence of false positives in non-infected individuals is another possibility if the antibodies used exhibit cross-reactivity with antigens from other human coronaviruses. Therefore, one must be cautious while confirming and interpreting such rapid diagnostic test results without the proper support of validated studies. Another rapid diagnostic kit detects the presence of antibodies in the blood of infected patients [21, 23]. However, antibodies are produced after several days following viral infection. And hence, diagnosis of COVID-19 infection based on antibody response will only be possible in the recovery phase. Besides, the chances of false positives may be also high if the antibodies recognize antigens from other pathogens including human coronaviruses [19,24,25]. WHO encourages the innovative efforts of researchers and manufacturers into furthering more research for improvement related to the epidemiology and disease surveillance of these diagnostics, however, use of such rapid immunodiagnostics in health care must strictly adhere to its guidelines.

POTENTIAL THERAPEUTICS FOR COVID-19

SARS-CoV-2 has spread rapidly since its identification causing a pandemic across the globe; however, there is still no therapeutics for treatment of COVID-19. Researchers and drug companies around the world are in the process of developing preventive and therapeutic drugs including monoclonal antibodies, vaccines, small-molecule drugs, peptides, oligonucleotides and interferon-based therapies for SARS-CoV-2 [26]. A list of therapeutic approaches based on antibody, antiviral as well as vaccines from various companies has been highlighted in **Table 3** [14, 27, 28]. In many countries, broad-spectrum antiviral drugs have been considered for treatment of COVID infected patients. The use of monoclonal antibodies against viruses has become popular in recent years, and some have already reached the clinical pipeline [29-31]. In the case of SARS-CoV and SARS CoV-2 infection, the interaction between the receptor binding domain of spike (S) protein and target receptor domain on the host cell surface angiotensis converting enzyme 2 (ACE2) is crucial for viral life cycle [32-35], while in the case of MERS-CoV, the host cell surface receptor is dipeptidyl peptidase-4 or DPP4 [36]. Therefore, disrupting this viral-host cell interaction with the help of monoclonal antibodies such as anti-ACE2 would prevent viral attachment and entry. The spike protein is the main antigenic component on the viral membrane and is indispensible for virus entry [37]. A list of monoclonal antibodies against S protein in SARS-CoV and MERS-CoV has been reviewed recently (please refer [38] for review).

Derivatives of adenine and guanine are also potential antiviral agents in human coronaviruses due to their inhibitory role in RNA-dependent RNA polymerase activity thereby, shutting down the viral RNA synthesis [26, 39]. These nucleoside analogues have been reported to be effective against a broad range of viruses including Ebola, influenza, yellow fever, chikungunya, norovirus and enterovirus [26, 39]. Therefore, approved nucleoside analogues such as favipiravir & ribavirin; and experimental nucleoside analogues including remdesivir & galidesivir may show promising therapeutic potentials against the SARS-CoV-2 coronavirus [26]. In a recent report, favipiravir (T-705), a guanine analogue and remdesivir, an analogue of adenine, both were shown to be effective agent against SARS-CoV-2 *in vitro* [40]. Clinical trials have started for protease inhibitors such as lopinavir and ritonavir for treatment of SARS-CoV-2 infection [26]. These drugs have been approved for treatment of HIV, which prevents replication of the viral gene. Another promising small-molecule agent against SARS coronavirus is the anti-malarial drug, chloroquine [41,42]. A recent study suggests that chloroquine is a promising therapeutic agent for

treatment against SARS-CoV-2 infected patients [43]. A comprehensive list of antiviral agents used against human coronaviruses for therapeutic options has been reported earlier [26]. Vaccines also offer promising prophylactic as well as therapeutic roles in controlling outbreak of infectious diseases including COVID-19. Based on earlier study of MERS-CoV vaccines, DNA vaccines have been developed based on the SARS-CoV-2 spike (S) sequence [44,45], which is expected to elicit a stronger immune response for effective control of the coronavirus infection. Pre-clinical trails have shown promising results for recombinant sub-unit vaccine developed from the S protein and of DNA vaccine targeted against SARS-CoV-2 [13]. These types of DNA vaccines are supposed to deliver the viral antigen, which activate the immune cells for production of therapeutic antibodies. Alternative vaccine strategies also include the use of fusion protein-based vaccines and mRNA-based vaccines. The mRNA-based vaccines overcome the need to integrate into the host genome and depend on the host machinery to translate the viral RNA into antigen [46,47]. However, one of the major bottlenecks in vaccine development is the high mutation rate of RNA viruses causing genetic variation to a large extent [48].

Table 3: Potential COVID-19 therapeutics and vaccines from different companies in phases of development [14, 26, 27]

Sl. No.	Company (Country)	Products	Stage
1	CytoDyn	Leronlimab (PRO 140)	Phase 2 for HIV and fast tracked for COVID-19
2	Eli Lilly	Antibody treatment	Preclinical
3	Regeneron Pharmaceuticals	Antibody treatment	Preclinical
4	Takeda	Treatment with Plasma antibodies from recovered patients	Preclinical
5	Vir Biotechnology/WuXi	Monoclonal antibodies	Preclinical
6	APEIRON Biologics	APN01 (rhACE2)	Phase 2
7	Innovation Pharmaceuticals	Brilacidin	Initial evaluation
8	Biocryst Pharma	Galidesivir	Advanced animal testing
9	Gilead Sciences	Remdesivir	Phase 3
10	Ascletis Pharma	Danoprevir & Ritonavir	Phase 1
11	Roche	Actemra	Phase 3
12	Humanigen	Lenzilumab	Phase 3
13	Ascletis	Ganovo+Ritonavir	Phase 4
14	OncoImmune	CD24Fc	Phase 3
15	Roche	Avastin	Phase 2/3
16	NeuroRx	Aviptadil	Phase 2
17	Novartis	Gilenya	Phase 2
18	Synairgen	SNG001	Phase 2
19	Roivant	Gimsilumab	Phase 1
20	EUSA Pharma	Sylvant	Observational
21	Moderna Therapeutics	mRNA Vaccine (mRNA-1273)	Phase 1
22	CanSino Biologics	Vaccine (Ad5-nCoV)	Phase 1
23	Arcturus Therapeutics	RNA vaccine with nanoparticle	Preclinical
24	BioNTech	mRNA Vaccine	Preclinical
25	CureVac	mRNA Vaccine	Preclinical
26	GlaxoSmithKline	Vaccine with adjuvants	Preclinical
27	Inovio Pharmaceuticals	DNA Vaccine	Preclinical
28	Johnson & Johnson	Vaccine &Treatment	Preclinical
29	Pfizer	Vaccine &Treatment	Preclinical
30	Sanofi	Vaccine &Treatment	Preclinical
31	Generex	Peptide Vaccine (Ii-Key)	Clinical programme development in China

CONCLUSION

The COVID-19 outbreak has resulted in uncertainty on an unprecedented scale across the globe. The sharing of knowledge and information such as the SARS-CoV-2 genome sequence has been extremely beneficial in development of diagnostics and therapeutic vaccine strategies for COVID-19. In response to the growing demand, multiple diagnostic assays have become available recently; however, prior validations and precautions must be taken while implementing rapid detection testing kits to ensure accurate interpretation of test results. Most importantly, adherence to WHO protocols and interim guidelines should be mandatory for handling of specimens and laboratory testings. Treatment drugs and

vaccines for prevention of COVID-19 may take some more time to be publicly available. However, outbreak control and management by spreading awareness and strictly following WHO guidelines are prerequisites until an efficacious solution emerges to tackle SARS-CoV-2. More research in the area of diagnostics, prevention and therapeutics must be accelerated in order to overcome the challenges due to COVID-19 outbreak.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Cheng VC, Lau SK, Woo PC, *et al.* (2007). Severe acute respiratory syndrome coronavirus as an agent of emerging and reemerging infection. *Clin Microbiol Rev*., vol. 20, no. 4, pp. 660–694.
2. Chan JF, Lau SK, To KK, *et al.* (2015). Middle East respiratory syndrome coronavirus: another zoonotic betacoronavirus causing SARS-like disease. *Clin Microbiol Rev*., vol, 28, no.2, pp. 465–522.
3. Chan JF, To KK, Tse H, *et al.* (2013). Interspecies transmission and emergence of novel viruses: lessons from bats and birds. *Trends Microbiol.*, vol. 21, no.10, pp. 544–555.
4. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. (2020). The species severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol*., vol. 5, no.4, pp. 536-544.
5. WHO. (2020). Laboratory testing for coronavirus disease (COVID-19) in suspected human cases. Interim Guidance, WHO/COVID-19/laboratory/2020.5
6. Zumla, A, Chan JF, Azhar El, *et al.* (2016). Coronaviruses—drug discovery and therapeutic options. *Nat Rev Drug Discov*., vol. 15, pp. 327–347.
7. WHO. Advice on the use of point-of-care immunodiagnostic tests for COVID-19. (2020). Scientific Brief.https://www.who.int/docs/default-source/coronaviruse/sb-2020-1-poc-immunodiagnostics-2020-04-08.pdf?sfvrsn=5b6820_2
8. Zhu N, Zhang D, Wang W, *et al.* (2020). A Novel Coronavirus from patients with pneumonia in China, 2019. *N Engl J Med*., vol. 382, pp. 727-733.
9. Wang C, Horby PW, Hayden FG, *et al.* (2020). A novel coronavirus outbreak of global health concern. *Lancet*, vol. 395, pp.: 470-473.
10. Wu F, Zhao S, Yu B, *et al.*. A new coronavirus associated with human respiratory disease in China. Nature, 2020, 579(7798): 265–269. doi: 10.1038/s41586-020-2008-3
11. Corman VM, Landt O, Kaiser M, *et al.* (2020). Detection of 2019 novel coronavirus (2019-nCoV) by real-time RT-PCR. Euro Surveill., vol. 25, no.3, pp.23-30.
12. Lu R, Zhao X, Li J, *et al.* (2020). Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet, vol. 395, no.10224, pp. 565-567.
13. Ahn DG, Shin HJ, Kim MH, *et al*. (2020). Current Status of Epidemiology, Diagnosis, Therapeutics, and Vaccines for Novel Coronavirus Disease 2019 (COVID-19*). J Microbiol Biotechnol.*, vol. 30, no.3, pp.313–324.
14. Routley N. (2020). Every Vaccine and Treatment in Development for COVID-19 — So Far. https://www.visualcapitalist.com/every-vaccine-treatment-covid-19-so-far/
15. Chan JF, Yuan SF, Kok KH, *et al*. (2020). A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet*, vol. 395, no.10223, pp. 514-523.
16. Zou LR, Ruan F, Huang M, *et al*. (2020). SARS-CoV-2 viral load in upper respiratory specimens of infected patients. *N Engl J Med.*, vol. 382, no.12, pp. 1177-1179.
17. WHO. (2020). Laboratories providing confirmatory testing for COVID-19. https://www.who.int/docs/default-source/coronaviruse/who-reference-laboratories-providing-confirmatory-testing-for-covid-19.pdf?sfvrsn=a03a01e6_8.
18. Zhou P, Yang XL, Wang XG, *et al*. (2020). A Pneumonia Outbreak Associated With a New Coronavirus of Probable Bat Origin. Nature, vol. 579, no.7798, pp.270-273.
19. Wang N, Li SY, Yang XL, *et al*. (2018). Serological evidence of bat SARS-related coronavirus infection in humans, China. *Virol Sin.*, vol. 33, pp. 104–107.
20. Zhang W, Du RH, Li B, *et al*. (2020). Molecular and serological investigation of 2019-nCoV infected patients: implication of multiple shedding routes. Emerg Microbes Infect, vol. 9, no.1, pp.386-389.
21. Li Z, Yi Y, Luo X, *et al*. (2020). Development and Clinical Application of A Rapid IgM-IgG Combined Antibody Test for SARS-CoV-2 Infection Diagnosis. *J Med Virol.,* doi:10.1002/jmv.25727
22. Rothe C, Schunk M, Sothmann P, *et al*. (2020). Transmission of 2019-nCoV Infection from an Asymptomatic Contact in Germany. *N Engl J Med.,* vol. 382 no. 10, pp. 970-971.
23. Pan Y, Li X, Yang G, *et al.* (2020). Serological immunochromatographic approach in diagnosis with SARS-CoV-2 infected COVID-19 patients. *J Infect*, vol. S0163-4453, no.20, pp. 30175-4.
24. Okba NMA, Muller MA, *et al*. (2020). Severe Acute Respiratory Syndrome Coronavirus 2-Specific Antibody Responses in Coronavirus Disease 2019 Patients. *Emerg Infect Dis*., vol. 26, no.7, pp. 1478-1488.
25. Che XY, Qiu LW, Liao ZY, *et al*. (2005). Antigenic cross-reactivity between severe acute respiratory syndrome-associated coronavirus and human coronaviruses 229E and OC43. J Infect Dis., vol. 191, no.12, pp. 2033–7.

26. Li G, De Clercq. (2020). Therapeutic options for the 2019 novel coronavirus (2019-nCoV). *E Nat Rev Drug Discov.,* vol. 19, no.3, pp.149-150.
27. Cahill J. (2020). Potential COVID-19 therapeutics currently in development. https://www.europeanpharmaceuticalreview.com/article/115842/potential-covid-19 therapeutics currently-in-development/
28. Garde D. (2020). An updated guide to the coronavirus drugs and vaccines in development. https://www.statnews.com/2020/03/19/an-updated-guide-to-the-coronavirus-drugs-and-vaccines-in-development/
29. Davey RT Jr, Dodd L, Proschan MA, Neaton J, *et a.l* (2016). A randomized, controlled trial of ZMapp for Ebola Virus infection. *N Engl J Med*., vol. 375, no.15, pp.1448-56.
30. Gupta P, Kamath AV, Park S, *et al*. (2016). Preclinical pharmacokinetics of MHAA4549A, a human monoclonal antibody to influenza A virus, and the prediction of its efficacious clinical dose for the treatment of patients hospitalized with influenza A. *MAbs*, vol.8, no.5, pp.991-7.
31. Caskey M, Klein F, Lorenzi JCC, *et al*. (2015). Viraemia suppressed in HIV-1-infected humans by broadly neutralizing antibody 3BNC117. Nature, vol. 522, no.7557, pp. 487-91.
32. Li W, Moore MJ, Vasilieva N, *et al*. (2003). Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature, vol. 426, no.6965, pp. 450-4.
33. Li F, Li W, Farzan M, *et al*. (2005). Structure of SARS coronavirus spike receptor- binding domain complexed with receptor. Science, vol. 309, no. 5742, pp. 1864-8.
34. Song Z, Xu Y, Bao L, *et al*. (2019). From SARS to MERS, thrusting coronaviruses into the spotlight. Viruses, vol. 11, no.1, pp. 59.
35. Wan Y, Shang J, Graham R, *et al*. (2020). Receptor recognition by novel coronavirus from Wuhan: An analysis based on decade-long structural studies of SARS. *J Virol.,* 94:e00127-20.
36. Raj VS, Mou H, Smits SL, *et al*. (2013). Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. *Nature*, vol. 495, no.7440, pp. 251-4.
37. Du L, Yang Y, Zhou Y, *et al*. (2017). MERS-CoV spike protein: a key target for antivirals. *Expert Opin Ther Targets*, vol. 21, no.2, pp. 131-43.
38. Shanmugaraj B, Siriwattananon K, Wangkanont K, *et al*. (2020). Perspectives on monoclonal antibody therapy as potential therapeutic intervention for Coronavirus disease-19 (COVID-19). *Asian Pac J Allergy Immunol.*, vol. 38, no.1, pp. 10-18.
39. De Clercq, E. (2019). New nucleoside analogues for the treatment of hemorrhagic fever virus infections. *Chem. Asian J.*, vol. 14, no.22, pp. 3962–3968.
40. Wang M, Cao R, Zhang L, *et al*. (2020). Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res*., vol. 30, pp.269-271.
41. Keyaerts E, Vijgen L, Maes P, *et al*. (2004). In vitro inhibition of severe acute respiratory syndrome coronavirus by chloroquine. *Biochem Biophys Res Commun*., vol. 323, pp.264-268.
42. Vincent MJ, Bergeron E, Benjannet S, *et al*. (2005). Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. *Virol J*., vol. 2, pp. 69.
43. Gao J, Tian Z, Yang X. (2020). Breakthrough: Chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci. Trends*, vol. 14, no.1, pp. 72-73.
44. Chi H, Zheng X, Wang X, *et al*. (2017). DNA vaccine encoding Middle East respiratory syndrome coronavirus S1 protein induces protective immune responses in mice. *Vaccine,* vol. 35, no.16, pp. 2069–2075.
45. Cohen, J. (2020). Scientists are moving at record speed to create new coronavirus vaccines—But they may come too late. 2020, doi: 0.1126/science.abb0612
46. Pardi N, Hogan MJ, Porter FW, *et al*. (2018). mRNA vaccines - a new era in vaccinology. *Nat Rev Drug Discov.*, vol.17, pp. 261-279.
47. Zhang C, Maruggi G, Shan H, *et al*. (2019). Advances in mRNA vaccines for infectious diseases. Front Immunol., vol. 10, pp. 594.
48. Duffy S. (2019). Why are RNA virus mutation rates so damn high? *PLoS Biol.,* 16(8): e3000003.

CITATION OF THIS ARTICLE

Vaiphei ST & Thangjam R. An overview of SARS-CoV-2 molecular diagnostics and therapeutics. Bull. Env. Pharmacol. Life Sci., Vol 9[12] November 2020 :182-188