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Unraveling SARS-CoV-2: A comprehensive review of origin, structure and therapeutic targets

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Abstract

The emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in late 2019 triggered the global COVID-19 pandemic, presenting an unprecedented public health challenge. This review synthesizes critical aspects of SARS-CoV-2, beginning with its origin, which genomic analyses trace to bat coronaviruses like RaTG13, though the exact transmission pathway to humans remains debated. The virus possesses a large ~30,000-nucleotide RNA genome encoding structural, non-structural, and accessory proteins that facilitate replication and pathogenesis. Key structural proteins include the Spike (S) protein, which mediates host cell entry via the ACE2 receptor. The review details the virus's epidemiological characteristics and the emergence of Variants of Concern (VOCs) such as Delta and Omicron, driven by viral evolution and selective pressures. A significant portion is dedicated to the functions of viral proteins, highlighting their roles in viral replication, immune evasion, and contributing to severe disease. Furthermore, the article surveys diagnostic methodologies, emphasizing molecular techniques like RT-PCR as the gold standard, and explores emerging biosensor technologies. Finally, it outlines therapeutic strategies, cataloguing antiviral drugs that target essential viral components, including the main protease and RNA-dependent RNA polymerase. This comprehensive overview underscores the multifaceted understanding required to combat SARS-CoV-2 through diagnostics, therapeutics, and public health measures.

Keywords: SARS-CoV-2; COVID-19; Pandemic; Structure; Diagnosis; Treatment.

1. Introduction

In 2019, a novel coronavirus called severe acute respiratory syndrome coronavirus (SARS-CoV-2) developed in Wuhan, Hubei province, China [1]. Coronavirus illness 19 (COVID-19) is a new and extremely contagious viral infection caused by SARS-CoV-2. Genomic investigations have showed that SARS-CoV-2 is phylogenetically close to severe acute respiratory syndrome-like (SARS-like) bat viruses, implying that bats could be the major reservoir [2]. The pandemic induced by the novel Betacoronavirus (-CoVs or Beta-CoVs), the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which triggered the epidemic of coronavirus disease 2019 (COVID-19), has been a serious public health problem worldwide [3]. On February 11, 2020, the World Health Organisation (WHO) officially designated the current coronavirus outbreak Coronavirus Disease-2019 (COVID-19), while the International Committee on Taxonomy of Viruses (ICTV) named the virus SARS-CoV-2 [4]. The Betacoronavirus is the most investigated genera because it contains airborne viral species capable of infecting people, such as severe acute respiratory syndrome-related coronaviruses (SARS-CoV) and Middle East respiratory disease coronaviruses (MERS-CoV). SARS-CoV-2 is extremely deadly because it spreads by sneezing and contact [5]. To multiply, viruses must enter a host cell and employ the cellular machinery to aid in the replication of their genetic material and the translation of viral proteins [6]. Older age, male sex, and several co-morbidities have been identified as risk factors for COVID-19 severity; however, these risk variables do not entirely explain the variations between asymptomatic, mild, and severe patients [7]. Although molecular methods

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for measuring SARS-CoV-2, such as reverse transcription-quantitative polymerase chain reaction (RT-qPCR) with primers and probes designed in the core coding region, cannot distinguish between non-infectious residual virions and infectious (replicative) virus particles, are widely used in clinical settings [8]. The investigated antiviral techniques are primarily based on current medications designed to treat viral infections or other disorders [9]. As a primary focus, the coronavirus spike (S) protein is critical in coronavirus infection, pathogenicity, transmission, and evolution [10].

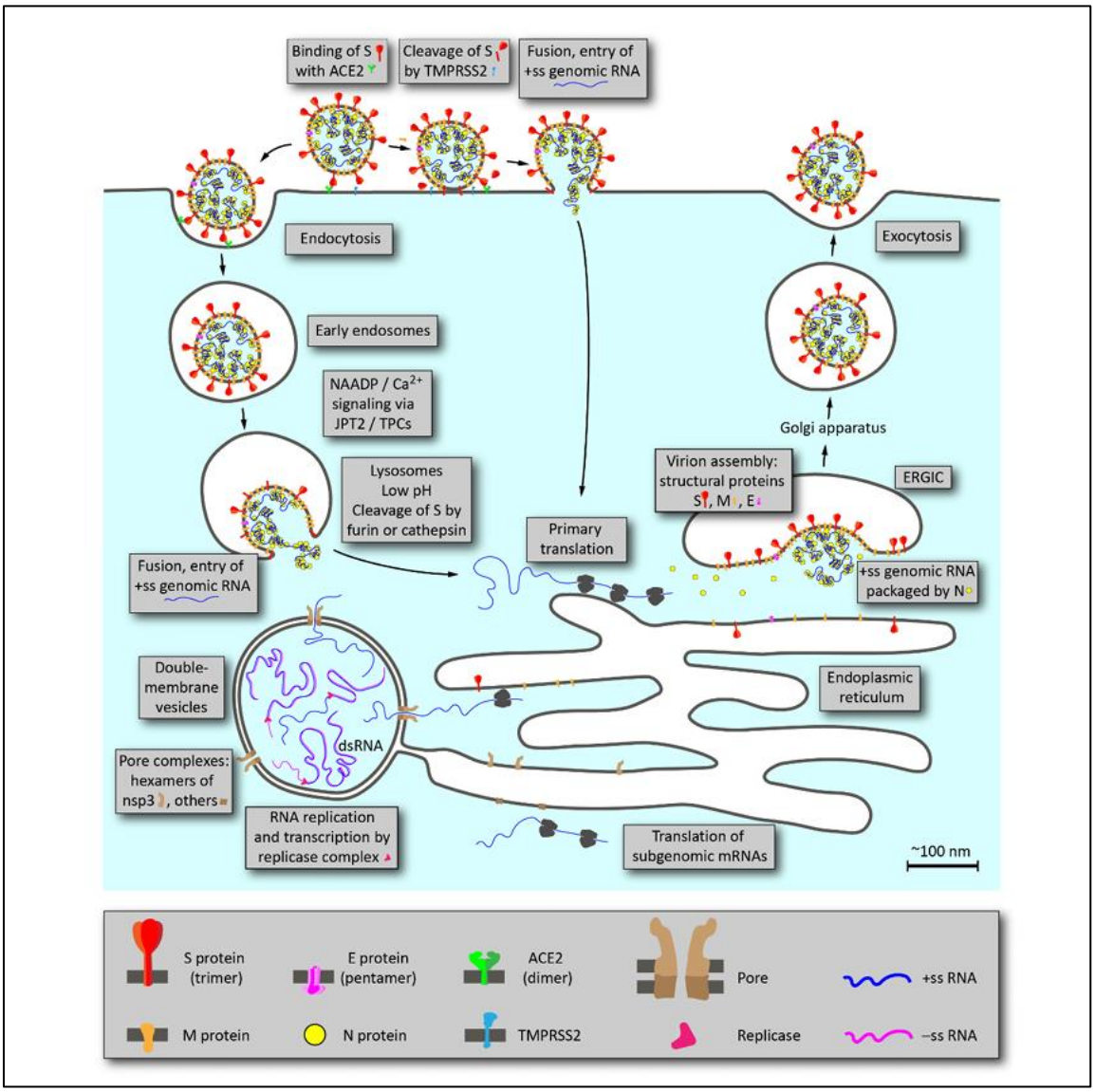

Figure 1 Schematic outline of SARS-CoV-2 life cycle [11].

2. Origin and Evolution

On December 31, 2019, the WHO China Country Office was notified of cases of pneumonia of unknown etiology discovered in Wuhan (Hubei Province, China), which was later identified as the epicenter of SARS-CoV-2 transmission [3]. Early in the Wuhan pneumonia pandemic, scientists obtained full genome sequences from five SARS-CoV-2-infected individuals [4]. Its genome consists of 14 open reading frames (ORFs), two-thirds of which encode 16 nonstructural proteins (nsp1-16) that comprise the replicase complex, and the remaining one-third encodes nine accessory proteins (ORF) and four structural proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N), with Spike mediating SARS-CoV entry into host cells [12]. Coronavirus can cause a variety of disorders in people, including common colds and the aforementioned deadly infections (SARS and MERS) [13]. SARS-CoV-2, like other coronaviruses, has a large RNA genome of around 30,000 nucleotides. Its replication is mediated by RNA-dependent RNA polymerase (RdRP) and an associated proofreading enzyme, exo ribonuclease (ExoN) [14].

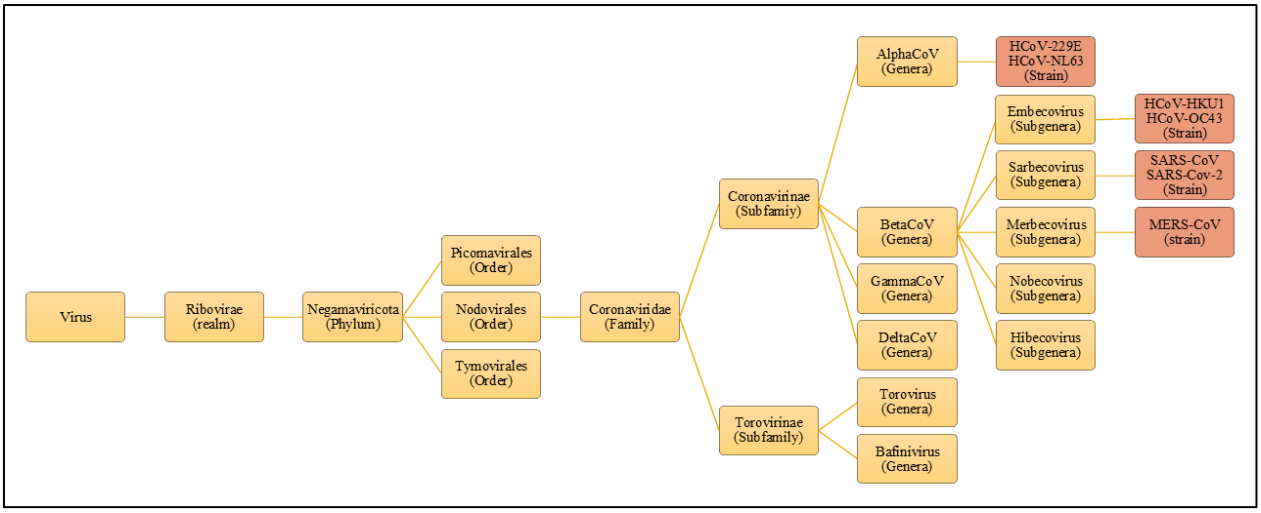

Figure 2 The taxonomic classification and positions for the known seven HcoVs [15].

The origin of SARS-CoV-2 is still contested, however the most closely related viruses originate from bats, such as the RaTG13 virus, which shares around 96% sequence homology and was isolated from the Rhinolophus affinis (i.e., intermediate horseshoe) bat [16]. Even though bats are presumably the primary source of SARS-CoV-2 transmission, it is unclear whether it is transferred directly from bats to people or via an intermediate host [17]. When studying the evolution of protein-coding sequences, it is critical to distinguish between nucleotide changes that change amino acids (and thus possibly impact the protein structure) and those that do not [18]. The SARS-CoV-2 genome was extensively sequenced, allowing for a thorough understanding of the evolutionary history of the virus's main lineages, particularly the variants of concern [19].

3. Epidemiological Characteristics:

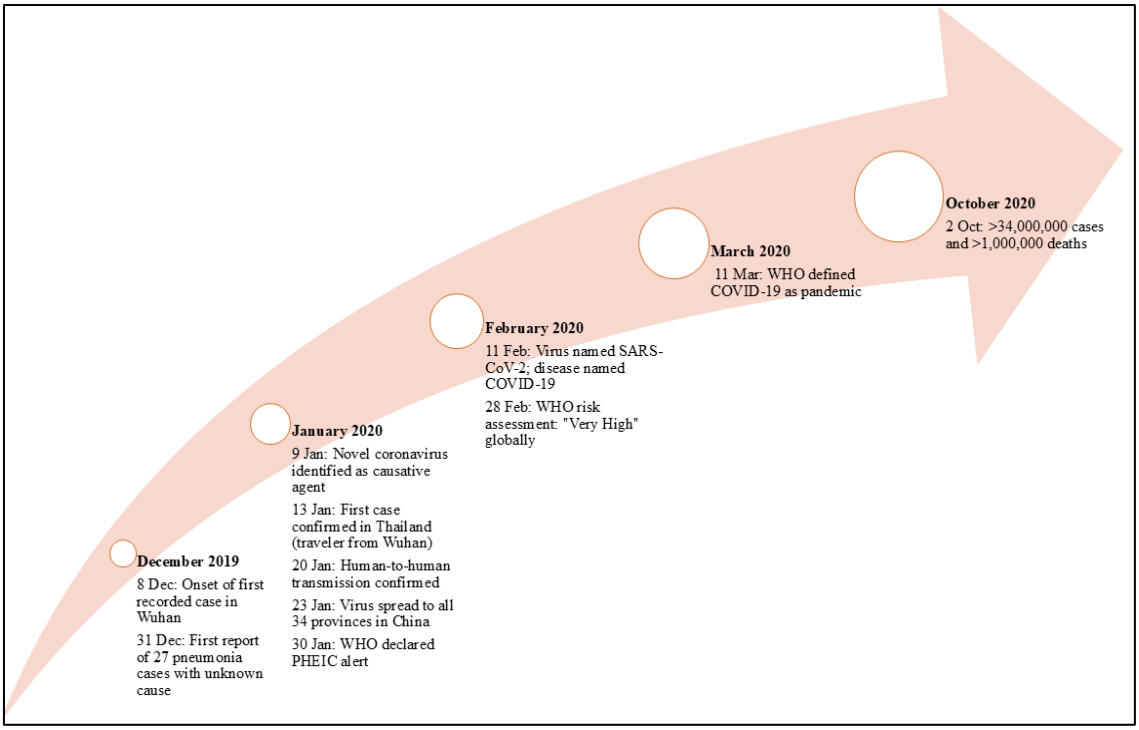

Figure 3 Timeline of the key events of the COVID-19 outbreak [23].

Since December 21, 2019, doctors in Wuhan, Hubei province, China, have seen an unusually high number of patients with atypical pneumonia [20]. According to the Johns Hopkins University dashboard, which was updated on November

4, 2020, the number of fatalities from COVID-19 has increased to 1,215,173, with a total of 47,491,193 impacted cases worldwide [21]. On December 14, 2020, England and Northern Ireland reported the first new strain of variant SARS-CoV-2. COVID-19 incidence varies over the world, and the WHO recorded about 84 million confirmed cases and 1.8 million documented deaths from 218 countries [22].

4. Variants

Viruses mutate or modify their genetic material during replication, resulting in variations [24]. Low replication fidelity enables RNA viruses to swiftly adapt to varied host conditions and selection forces, hence promoting viral replication [25]. WHO identifies five SARS-CoV-2 variants of concern (VOC): Alpha, Beta, Gamma, Delta, and Omicron, as well as two SARS CoV-2 variants of interest (VOI): Lambda and Mu (WHO SARS CoV-2 Variants) [26]. The evolution of the virus was influenced by social behaviors such as masking and social distancing, host immune status (naïve, vaccinated, and herd immunity), the development of passive countermeasures to treat vulnerable hosts, and the resulting selective pressures [27].

5. Structure

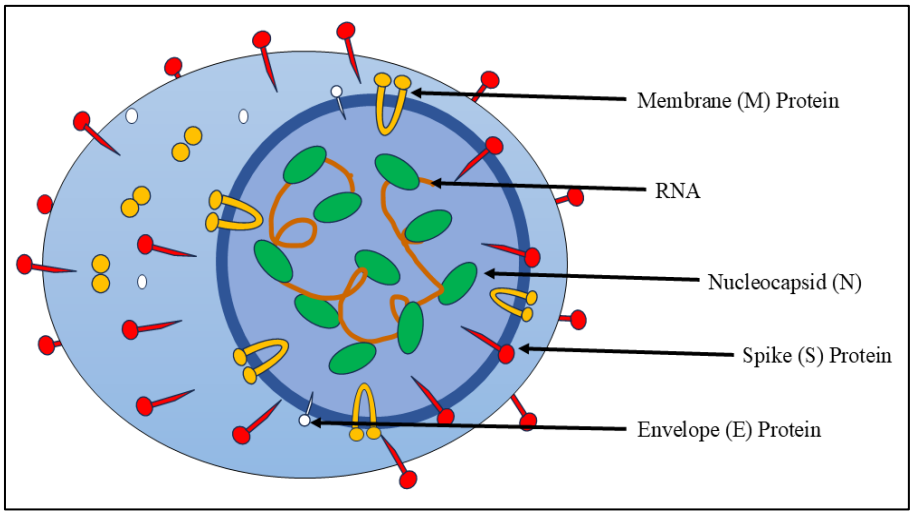

Figure 4 The principal structure of SARS-CoV-2 [3].

Understanding the structure and genome organisation of SARS-CoV-2 is critical for determining the mechanisms of viral replication, infectivity, and proteins that induce host immune responses, which could aid in the development of potential treatments and vaccines for COVID-19 prevention [28]. Coronaviruses belong to the Coronavirinae subfamily of the Coronaviridae family, which includes four genera: Alphacoronavirus, Betacoronavirus, Gammacoronavirus, and Deltacoronavirus [4]. SARS-CoV-2 follows the normal genomic organisation of β-coronaviruses. The genome is made up of 14 functional open reading frames (ORFs), two noncoding areas at either end, and several regions that encode nonstructural proteins (NSPs), accessory proteins, and structural proteins [29]. A comparative genomic investigation of 44 Sarbecoviruses revealed that SARS-CoV-2 ORF3a, ORF3c, ORF6, ORF7a, ORF7b, ORF8, and ORF9b encode accessory proteins designated using homology-based ORF nomenclature [30]. The coronavirus virion consists of structural proteins such as the nucleocapsid (N), membrane (M), envelope (E), and spike (S) [31]. Coronavirus infection begins with the specific binding of the coronavirus spike (S) protein to the cellular entry receptors, which have been identified for several coronaviruses and include human aminopeptidase N (APN; HCoV-229E), angiotensin-converting enzyme 2 (ACE2; HCoV-NL63, SARS-CoV and SARS-CoV-2), and dipeptidyl peptidase 4 (DPP4; MERS-CoV) [32]. Approximately two-thirds of the 5′ end of the SARS-CoV-2 genome encodes two overlapping polyproteins, pp1a and pp1ab12. Two viral proteases degrade these two polyproteins, resulting in 16 non-structural proteins (NSPs) required for viral replication and transcription [33].

Table 1 Functions of invasiveness and virulence of individual proteins of SARS-CoV-2.

Proteins	Functions	Reference
Nsp1	Suppresses the host protein synthesis (including IFN-I and RIG-I) through association with ribosomes. Inhibits IRF3 phosphorylation and IFN production; suppresses ISG induction due to Tyk2 and STAT2 depletion and inhibition of STAT1 phosphorylation. Changes the structure and function of the cytoskeleton.	[3]
Nsp2	Can participate in the binding of nucleic acids and the regulation of intracellular signaling pathways. Participates Nsp2 in the processes of viral replication. Proteins that interact with nsp2 are involved in several biological processes, such as endosomal transport and translation. Changes the synthesis and modification of lipids.	[29]
Nsp3	Papain-like protease (PLpro) and deubiquitinase. Participates in the proteolysis of 1a/1ab polyproteins. Cleaves IRF3. By removing ubiquitin in the structures of signaling pathways, they disrupt the development of antiviral cellular stress, including translocation of IRF3 into the cell nucleus and inhibition of RIG-I, STING, TRAF3, Nsp3 TBK1, IRF3. Nsp3 SARS-CoV-1 c promotes inactivation of conjugated ubiquitin-like molecules such as interferon, which is involved in different pathways of the innate antiviral immune response regulation. However, the deubiquitinase and IFN-blocking functions of nsp3 SARS-CoV-2 seem to be significantly lower than that of nsp3 SARS-CoV-1. Participates in the RTC formation.	[33,34]
Nsp4	AnER-localized transmembrane protein (as nsp3 and nsp6), is considered to be involved in the assembly of virus-induced cytoplasmic double-membrane vesicles. Participates in the RTC formation.	[35,36]
Nsp5	3-chymotrypsin-like “main” protease (3CLpro) is involved in the proteolysis of 1a/1ab polyproteins. Inhibits the translocation of IRF3 into the cell nucleus and promotes the degradation of IRF3. It regulates (by proteolysis) the Nsp5 development of pro-inflammatory stress in different directions: activating the formation of NLRP12 by inflammasomes and inhibiting kinase- TGF-beta activated kinase 1 (MAP3K7- mitogen-activated protein kinase 7) binding protein 1 (TAB1). Participates in the RTC formation.	[5,37]
Nsp6	Inhibits the phosphorylation of IRF3, STAT1, and STAT2 [110]. Potentially contributes to SARS-CoV-2 infection by Nsp6 impairing the ability of autophagosomes to deliver viral components to lysosomes for degradation. Probably, along with orf7a, can interact with sigma receptors, which are involved in lipid remodeling and the ER stress response. Participates in the RTC formation.	[14,38,39]
Nsp7	During viral RNA replication, the nsp12 cofactor forms a primase complex with nsp. Participates in the RTC formation.	[40,41]
Nsp8	The nsp12 cofactor in viral RNA replication. Participates in the formation of the RTC. Forms a primase complex with nsp7, which plays a decisive role in the regulation of the activity of RNA-dependent RNA polymerase (RdRP) nsp12. Suppresses the transport of membrane proteins in cells infected with SARS-CoV-2, disrupts IFN secretion.	[42,43]
Nsp9	RNA-binding protein, interacting with nsp12, is one of the key factors of RTC. Suppresses the transport of membrane proteins in cells infected with SARS-CoV-2, disrupts the secretion of IFN and some other cytokines. Interferes with the activation of IRF3 and the induction of IFN synthesis by inhibiting TBK1.	[29,44]
Nsp10	The cofactor of nsp14 and nsp16 forms functional complexes with them upon methylation of viral RNA. Nsp10 Acting on NKRF (NF-B-repressive factor), can regulate the levels of IL-8, NKRF and form a unique immune signature in COVID-19. Participates in the RTC formation.	[36,43,45]
Nsp11	Includes only 13 amino acid residues. The role of the nsp11 protein in cells infected with CoV has not yet been studied.	[34,41]
Nsp12	RNA-dependent RNA polymerase is a key enzyme mediating the synthesis of all viral RNA molecules. A key component of RTC.	[36,39,46]

Nsp13	Helicase, 5-triphosphatase. Inhibits the phosphorylation of TBK1, which leads to a decrease in IRF3 activation, inhibits Nsp13 the phosphorylation of STAT1 and STAT2. Participates in viral replication. Changes the structure and function of the cytoskeleton. Participates in the RTC formation.	[47,48]
Nsp14	3-5 exoribonuclease and N-7-methyltransferase. Inhibits nuclear translocation of IRF3. Participates in the RTC formation. As an exonuclease, it provides the ability to correct errors in the RNA synthesis complex, which allows SARS-CoV-2 to maintain its large genome.	[34,39,49]
Nsp15	NendoU, a uridylate-specific endoribonuclease. Inhibits nuclear translocation of IRF3. Participates in the RTC formation. Meanwhile, nsp15-deficient CoVs are viable and can replicate, but with some delay and errors. Another possible mechanism of nsp15 action is an evasion of viral double-stranded RNA recognition by host sensors in macrophages, including MDA5, PKR, and OAS/RNaseL.	[5,50,51]
Nsp16	2-O-methyltransferase, which blocks the recognition of viral RNA by PRR by forming the morpho-functional complexes with nsp10. Participates in the RTC formation.	[51,52,53]
Orf3a	Disrupts the IFN signaling pathways by inhibiting STAT1 phosphorylation. Can regulate the effects of IL-6 action by inhibiting STAT3 and STAT5. Promotes lysosomal degradation of the-chain of the IFN-I receptor (IFNAR1) and induces ER stress (shown in SARS-CoV-1). Forms transmembrane ionic potassium-specific Orf3a channels that facilitate the release of the virus from the cell. It is assumed that viral ion channels can also promote membrane fusion and regulate viral replication and/or the packaging of genomic RNA into viral particles. Activates NF-kB, NLRP3 inflammasomes, promoting cytokine storm. Blocks the fusion of autophagosomes with lysosomes, contributing to the survival of the virus.	[41,54,55]
Orf3b	Interferes with nuclear translocation of IRF3. Can cause a specific antibody response as N and orf8 proteins. Orf3b is not expressed in many strains of SARS-CoV-2, however, SARS-CoV-2 orf3b can suppress IFN-I induction more efficiently than its orthologue SARS-CoV-1.	[36,43]
Orf6	Inhibits IRF3 (via action on TBK1) phosphorylation. Binds to KPNA2 (karyopherin subunit alpha 2) and the Nup98-Rae1 complex, which inhibits nuclear translocation of IRF3 and STAT1. Causes changes in Orf6 signaling pathways that include the activation of apoptosis through caspase-3-mediated, ER stress, and JNK-dependent pathways (JNK-c-Jun N-terminal kinases). Inhibition of STAT1 causes compensatory hyperactivation of STAT3 in cells infected with SARS-CoV-2, which promotes overproduction and activation of plasminogen activator inhibitor-1 (PAI-1) and can lead to coagulopathy.	[19,30,49]
Orf7a	Inhibits the STAT2 phosphorylation. According to the results of in silico calculations, can interact with sigma receptors, as nsp6. Has structural homology to ICAM-1, binds to Mac-1 and the integrin receptor LFA-1 on leukocytes. The orf7a expression leads to apoptosis, blocking the cell cycle, activation of NF-kB, and mitogen-activated protein kinase (MAPK). Binds to CD14 (TLR4 cofactor), promoting the production of proinflammatory cytokines. Promotes the release of SARS-CoV-2 from the cell membrane by inhibiting the membrane protein BST-2.	[39,54]
Orf7b	Inhibits STAT1 and STAT2 phosphorylation.	[36,48]
Orf8	Interacts with a variety of host proteins and blocks the class 1 major histocompatibility complex (MHC-I) protein in the Orf8 ERlumen. Inhibits IFN signaling pathways and activation of ISG promoters. Orf8, being secreted into the extracellular space can activate the IL-17 signaling pathway by interacting with the host's IL17RA. Forms cation channels upon assembly in the lipid bilayer, like orf3a and E-protein.	[42,51]
Orf9b	Blocks the signaling pathways from TNF receptors by acting on TRAF3 and TRAF6 (TNF receptor-associated factor 3 and 6), disrupts IFN-I synthesis, and induces ATG5-mediated autophagy in host cells. Blocks TOM70, a key Orf9b adapter that transmits an antiviral signal from the mitochondrial RLR/MAVS pathway to TBK1/IRF3 to induce an IFN response. Interacts with RIG-I, MDA-5, MAVS, STING, and TBK1, prevents	[41,56]

	phosphorylation and nuclear translocation of IRF3, NF-B activation, and inhibits TRIF (TLR adapter).	
S	Plays a key role in the process of receptor recognition and cell membrane fusion. The structure of this protein allows it to interact with many receptors in host cells.	[1,38,44,57]
E	Promotes the assembly and release of the virus, has the properties of a viroporin membrane channel, which can contribute to damage to the epithelial barrier, the pathogenesis, and the severity of COVID-19. The function of E the ion channel is associated with the activation of inflammasomes and the development of hyperinflammation in the lungs. These effects of E-protein are capable of initiating a cytokine storm and the development of an experimental analog of ARDS.	[33,47,55]
M	The dominant structural protein can bind to other structural proteins such as S and E and determines the shape of the viral envelope. Participates in the packaging of the genome in the viral particle, structures the viral particle. M Inhibits STAT1 phosphorylation. M interacts with RIG-I, MAVS, and TBK1, thus preventing the formation of a multiprotein complex containing RIG-I, MAVS, TRAF3, and TBK1, and subsequently preventing phosphorylation, nuclear translocation, and activation of IRF3.	[15,50,53,55]
N	Binds viral RNA and protects the viral genome, participates in the assembly of the genomic RNA of the virus. Modifies the signaling pathway of the cytokine TGF-β, blocking the apoptosis of infected host cells, but can also induce apoptosis by activating the mitochondrial pathway. Promotes hyperinflammation by activating NLRP3 inflammasome. It interferes with RIG-I activation, interferes with the association between TBK1 and IRF3, and prevents nuclear translocation of IRF3. Inhibits the formation of G3BP1-dependent stress granules during the development of the cell's antiviral response and blocks the host mRNA.	[35,46,52,56]

Abbreviations of Table 1.

- CoV - Coronavirus
- Nsp- Non-Structural Protein
- Orf - Open Reading Frame (Accessory Protein)
- RTC - Replication-Transcription Complex
- S - Spike Protein
- E - Envelope Protein
- M - Membrane Protein
- N - Nucleocapsid Protein
- IFN / IFN-I - Interferon / Type I Interferon
- ISG - Interferon-Stimulated Gene
- IRF3- Interferon Regulatory Factor 3
- STAT1/2/3- Signal Transducer and Activator of Transcription
- NF-κB- Nuclear Factor Kappa B
- NLRP3- Inflammasome sensor
- RIG-I / MDA5- Viral RNA sensors
- MAVS- Mitochondrial Antiviral-Signaling Protein
- STING- Sensor for cytosolic DNA
- TBK1- Kinase that activates IRF3
- TRAF3/6- Signaling adaptor proteins
- ER- Endoplasmic Reticulum
- MHC-I- Major Histocompatibility Complex Class I
- ARDS - Acute Respiratory Distress Syndrome

6. Diagnosis

Early detection is critical for limiting the spread of COVID-19. COVID-19 can be clinically diagnosed using three major approaches: epidemiological history, clinical symptoms, and laboratory examinations such as nucleic acid detection, computed tomography (CT) imaging of the lung, and immunoassay-based tests such as enzyme-linked immunosorbent assay (ELISA) [56]. Molecular and serological diagnostic techniques are used to detect the target analyte against SARS-

CoV 2. Furthermore, the most commonly used molecular diagnostic techniques for SARS-CoV-2 diagnosis include PCR (Polymerase Chain Reaction), qRT-PCR (Quantitative Reverse Transcription Polymerase Chain Reaction), CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats), RT-LAMP (Reverse Transcription Loop-mediated Isothermal Amplification), and CT-imaging (Computed Tomography imaging) [57]. Saliva is an excellent choice for sampling since salivary glands, gingiva, oral mucosa, and the tongue may act as hosts for SARS-CoV-2 due to the expression of the hACE2 receptor [1]. Several molecular assays have been validated and are now available on the market to diagnose SARS-CoV-2 infection. Validated specimen types include nasopharyngeal swab, aspirate, oropharyngeal swab, bronchoalveolar lavage, and sputum [58]. Molecular detection of SARS-CoV-2 nucleic acid is the gold standard. There are numerous commercial viral nucleic acid detection assays available that target ORF1b (including RdRp), N, E, or S genes [23]. The CDC recommends two nucleocapsid protein targets (N1 and N2), but the WHO recommends the E gene for first-line screening, followed by the RdRp gene as a confirmatory test due to its better sensitivity and specificity [28]. The current method for diagnosing SARS-CoV-2 is to amplify the viral nucleic acid using reverse transcription polymerase chain reaction (RT-PCR), with ORF1ab and the N gene of SARS-CoV-2 [1].

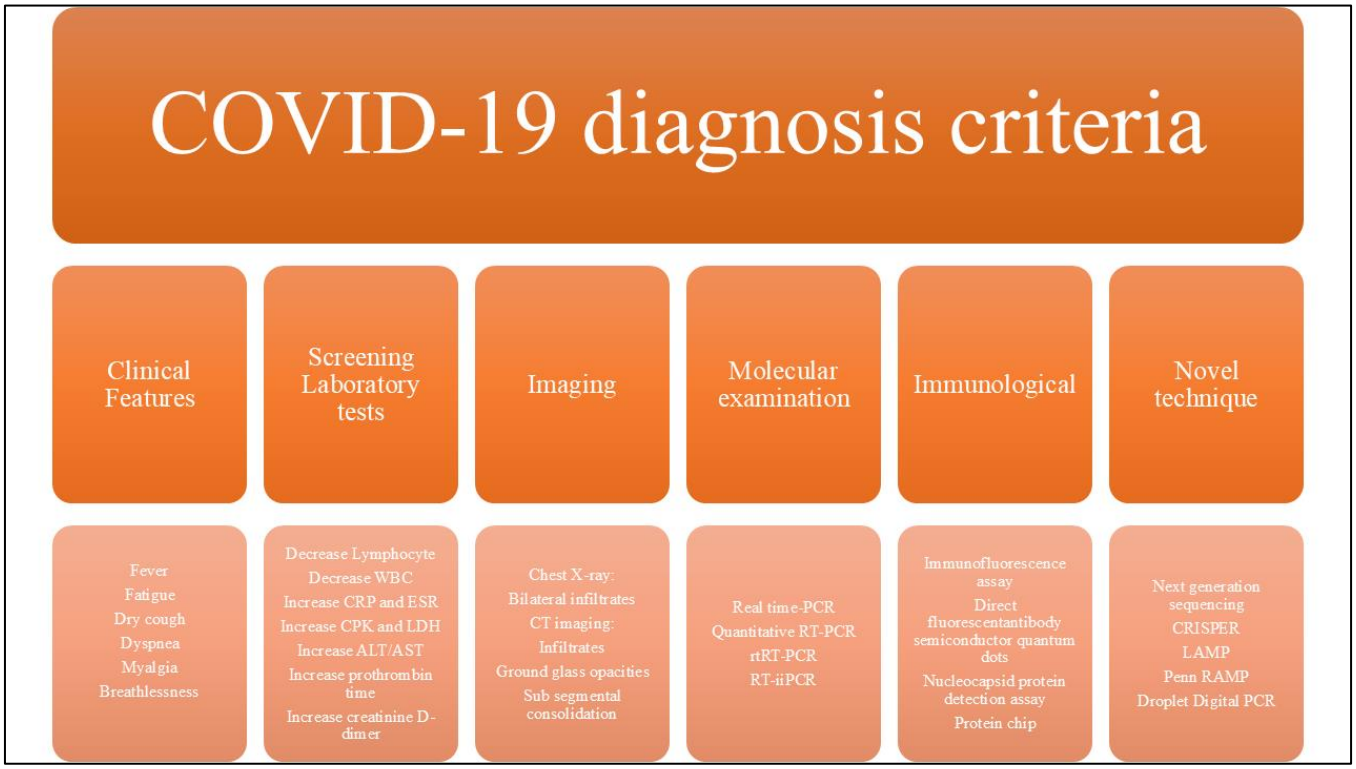

Figure 5 Diagnostic protocol has been recommended for COVID-19 [53].

The majority of lateral flow tests are designed to identify SARS-CoV-2 nucleocapsid protein as a surrogate for infectious virus in nasal or nasopharyngeal swabs [59].

Mass spectrometry (MS) is a promising analytical method for detecting viruses quickly and accurately from a variety of materials. Prior to the COVID-19 pandemic, outbreaks of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) in 2003 and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2012 encouraged efforts to create MS-based detection techniques for human coronaviruses [60]. Mass spectrometry (MS) techniques are used to diagnose SARS-CoV-2 in gargle or saliva samples [57].

A biosensor is an analytical tool made up of a biorecognition element that binds the analyte of interest and a transducer that generates the assay results [55]. It can also be classed based on the type of detection signal, such as optical or electrochemical sensor [61]. A photonic nanosensor targeting the SARS-CoV-2 RBD region using bioengineered nanobodies (Nb) has been developed, and bimodal waveguide (BiMW) interferometric technology is employed for rapid and direct detection of the SARS-CoV-2 virus's RBD [62]. Nanomaterials, specifically carbon-based, polymer-based, quantum-dot, and metal-based nanomaterials, are often used in biosensing applications to diagnose SARS-CoV 2 infection using various detection methods such as viral sequence, antibody, or antigen [63].

Various Biosensor techniques used in detection of SARS CoV-2: [64].

- Electrochemical Biosensors for SARS-CoV-2 RNA Detection
- Electrochemiluminescence-Based Biosensors
- Plasmonic-Based Biosensors
- Electrochemical Biosensors for Antibodies against SARS-CoV-2 Detection
- Ellipsometry- and SPR-Based Biosensors
- Photoluminescence-Based Biosensors
- Nanoplasmonic-Based Biosensors
- Field-Effect Transistor Based Biosensors
- Quartz Crystal Microbalance Based Biosensors
- Nanomaterial Based Sensor for the Diagnosis of COVID-19 in Exhaled Breath

7. Therapeutics

A healthy population with a strong immune system as a result of exercise, proper nutrition, and regular vitamin and mineral supplementation ensures safety against SARS CoV-2 [65]. Understanding the variations in structural and nonstructural proteins between SARS-CoVs and other coronaviruses may aid in the development of treatments for SARS-CoV-2 infection [4].

Table 2 Antiviral Drugs and their Viral targets [11,13,16,23,33,40,44,45,34,36,56,66,67].

Antiviral Drug	**Viral Target**
Bamlanivimab	Spike protein
Amubarvimab	Spike protein
Calpeptin	Spike protein
Sertraline	Spike protein
Arbidol	Spike protein
Simnotrelvir	Main protease
Leritrelvir	Main protease
Apixaban	Main protease
Nelfinavir	Main protease
Glycyrrhizin	Main protease
Lopinavir-ritonavir	Main protease
Nirmatrelvir	Main protease
Danoprevir	Main protease
Atazanavir	Main protease
Boceprevir	Main protease
Dipyridamole	Main protease
Carmofur	Main protease
Ebselen	Main protease
Darunavir	Main protease
Baicalein	Main protease & RNA-dependent RNA polymerase
Deuremidevir	RNA-dependent RNA polymerase
Remdesivir	RNA-dependent RNA polymerase

Favipiravir	RNA-dependent RNA polymerase
Avifavir	RNA-dependent RNA polymerase
Molnupiravir	RNA-dependent RNA polymerase
Ribavirin	RNA-dependent RNA polymerase

8. Conclusion

The review synthesizes current knowledge on SARS-CoV-2, covering its origins, genomic structure, and protein functions relevant to replication and immune evasion. The emergence of new variants presents challenges, while advancements in RT-PCR and biosensors improve diagnostics. Targeted antivirals and a strong immune response are vital in managing infections. This comprehensive understanding informs public health strategies, therapeutic developments, and vaccine creation, underscoring the need for ongoing research to combat viral evolution and prepare for future threats.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] Kumavath R, Barh D, Andrade BS, Imchen M, Aburjaile FF, Ch A, Rodrigues DLN, Tiwari S, Alzahrani KJ, Góes-Neto A, Weener ME, Ghosh P, Azevedo V. The Spike of SARS-CoV-2: Uniqueness and Applications. Front Immunol. 2021; 12:663912. doi: 10.3389/fimmu.2021.663912. PMID: 34305894; PMCID: PMC8297464.

[2] Sanyal S. How SARS-CoV-2 (COVID-19) spreads within infected hosts - what we know so far. Emerg Top Life Sci. 2020; 4(4):371-378. doi: 10.1042/ETLS20200165. PMID: 33269805; PMCID: PMC7733667.

[3] Gusev E, Sarapultsev A, Solomatina L, Chereshnev V. SARS-CoV-2-Specific Immune Response and the Pathogenesis of COVID-19. Int J Mol Sci. 2022; 23(3):1716. doi: 10.3390/ijms23031716. PMID: 35163638; PMCID: PMC8835786.

[4] Wang MY, Zhao R, Gao LJ, Gao XF, Wang DP, Cao JM. SARS-CoV-2: Structure, Biology, and Structure-Based Therapeutics Development. Front Cell Infect Microbiol. 2020; 10:587269. doi: 10.3389/fcimb.2020.587269. PMID: 33324574; PMCID: PMC7723891.

[5] Shamsi A, Mohammad T, Anwar S, Amani S, Khan MS, Husain FM, Rehman MT, Islam A, Hassan MI. Potential drug targets of SARS-CoV-2: From genomics to therapeutics. Int J Biol Macromol. 2021; 177:1-9. doi: 10.1016/j.ijbiomac.2021.02.071. Epub 2021 Feb 9. PMID: 33577820; PMCID: PMC7871800.

[6] Hoch NC. Host ADP-ribosylation and the SARS-CoV-2 macrodomain. Biochem Soc Trans. 2021; 49(4):1711-1721. doi: 10.1042/BST20201212. PMID: 34351418; PMCID: PMC8421052.

[7] Huang SW, Wang SF. SARS-CoV-2 Entry Related Viral and Host Genetic Variations: Implications on COVID-19 Severity, Immune Escape, and Infectivity. Int J Mol Sci. 2021; 22(6):3060. doi: 10.3390/ijms22063060. PMID: 33802729; PMCID: PMC8002537.

[8] Ge X, Zhou H, Shen F, Yang G, Zhang Y, Zhang X, Li H. SARS-CoV-2 subgenomic RNA: formation process and rapid molecular diagnostic methods. Clin Chem Lab Med. 2023; 62(6):1019-1028. doi: 10.1515/cclm-2023-0846. PMID: 38000044.

[9] Valle C, Martin B, Touret F, Shannon A, Canard B, Guillemot JC, Coutard B, Decroly E. Drugs against SARS-CoV-2: What do we know about their mode of action? Rev Med Virol. 2020; 30(6):1-10. doi: 10.1002/rmv.2143. Epub 2020 Aug 11. PMID: 32779326; PMCID: PMC7435512.

[10] Zhu C, He G, Yin Q, Zeng L, Ye X, Shi Y, Xu W. Molecular biology of the SARs-CoV-2 spike protein: A review of current knowledge. J Med Virol. 2021; 93(10):5729-5741. doi: 10.1002/jmv.27132. Epub 2021 Jun 14. Erratum in: J Med Virol. 2023 Jan;95(1):e28282. doi: 10.1002/jmv.28282. PMID: 34125455; PMCID: PMC8427004.

[11] Putlyaeva LV, Lukyanov KA. Studying SARS-CoV-2 with Fluorescence Microscopy. Int J Mol Sci. 2021; 22(12):6558. doi: 10.3390/ijms22126558. PMID: 34207305; PMCID: PMC8234815.

[12] Harrison AG, Lin T, Wang P. Mechanisms of SARS-CoV-2 Transmission and Pathogenesis. Trends Immunol. 2020; 41(12):1100-1115. doi: 10.1016/j.it.2020.10.004. Epub 2020 Oct 14. PMID: 33132005; PMCID: PMC7556779.

[13] Santos-López G, Cortés-Hernández P, Vallejo-Ruiz V, Reyes-Leyva J. SARS-CoV-2: basic concepts, origin and treatment advances. Gac Med Mex. 2021; 157(1):84-89. English. doi: 10.24875/GMM.M21000524. PMID: 34125824.

[14] Carabelli AM, Peacock TP, Thorne LG, Harvey WT, Hughes J; COVID-19 Genomics UK Consortium; Peacock SJ, Barclay WS, de Silva TI, Towers GJ, Robertson DL. SARS-CoV-2 variant biology: immune escape, transmission and fitness. Nat Rev Microbiol. 2023; 21(3):162-177. doi: 10.1038/s41579-022-00841-7. Epub 2023 Jan 18. PMID: 36653446; PMCID: PMC9847462.

[15] Kirtipal N, Bharadwaj S, Kang SG. From SARS to SARS-CoV-2, insights on structure, pathogenicity and immunity aspects of pandemic human coronaviruses. Infect Genet Evol. 2020; 85:104502. doi: 10.1016/j.meegid.2020.104502. Epub 2020 Aug 13. PMID: 32798769; PMCID: PMC7425554.

[16] Bakhiet M, Taurin S. SARS-CoV-2: Targeted managements and vaccine development. Cytokine Growth Factor Rev. 2021; 58:16-29. doi: 10.1016/j.cytogfr.2020.11.001. Epub 2020 Dec 1. PMID: 33293238; PMCID: PMC7706592.

[17] Tatsi EB, Filippatos F, Michos A. SARS-CoV-2 variants and effectiveness of vaccines: a review of current evidence. Epidemiol Infect. 2021; 149:e237. doi: 10.1017/S0950268821002430. PMID: 34732275; PMCID: PMC8632374.

[18] Singh D, Yi SV. On the origin and evolution of SARS-CoV-2. Exp Mol Med. 2021; 53(4):537-547. doi: 10.1038/s12276-021-00604-z. Epub 2021 Apr 16. PMID: 33864026; PMCID: PMC8050477.

[19] González-Vázquez LD, Arenas M. Molecular Evolution of SARS-CoV-2 during the COVID-19 Pandemic. Genes (Basel). 2023; 14(2):407. doi: 10.3390/genes14020407. PMID: 36833334; PMCID: PMC9956206.

[20] Alizon S, Sofonea MT. SARS-CoV-2 epidemiology, kinetics, and evolution: A narrative review. Virulence. 2025; 16(1):2480633. doi: 10.1080/21505594.2025.2480633. Epub 2025 Apr 8. PMID: 40197159; PMCID: PMC11988222.

[21] Khade SM, Yabaji SM, Srivastava J. An update on COVID-19: SARS-CoV-2 life cycle, immunopathology, and BCG vaccination. Prep Biochem Biotechnol. 2021; 51(7):650-658. doi: 10.1080/10826068.2020.1848869. Epub 2020 Nov 23. PMID: 33226885.

[22] Kannan S, Shaik Syed Ali P, Sheeza A. Evolving biothreat of variant SARS-CoV-2 - molecular properties, virulence and epidemiology. Eur Rev Med Pharmacol Sci. 2021; 25(12):4405-4412. doi: 10.26355/eurrev_202106_26151. PMID: 34227076.

[23] Hu B, Guo H, Zhou P, Shi ZL. Characteristics of SARS-CoV-2 and COVID-19. Nat Rev Microbiol. 2021r; 19(3):141-154. doi: 10.1038/s41579-020-00459-7. Epub 2020 Oct 6. Erratum in: Nat Rev Microbiol. 2022 May;20(5):315. doi: 10.1038/s41579-022-00711-2. PMID: 33024307; PMCID: PMC7537588.

[24] Jogalekar MP, Veerabathini A, Gangadaran P. SARS-CoV-2 variants: A double-edged sword? Exp Biol Med (Maywood). 2021; 246(15):1721-1726. doi: 10.1177/15353702211014146. Epub 2021 May 22. PMID: 34024159; PMCID: PMC8719041.

[25] Sarkar M, Madabhavi I. SARS-CoV-2 variants of concern: a review. Monaldi Arch Chest Dis. 2022; 93(3). doi: 10.4081/monaldi.2022.2337. PMID: 36305283.

[26] Liu H, Wei P, Kappler JW, Marrack P, Zhang G. SARS-CoV-2 Variants of Concern and Variants of Interest Receptor Binding Domain Mutations and Virus Infectivity. Front Immunol. 2022; 13:825256. doi: 10.3389/fimmu.2022.825256. PMID: 35154144; PMCID: PMC8828474.

[27] Case JB, Jain S, Suthar MS, Diamond MS. SARS-CoV-2: The Interplay Between Evolution and Host Immunity. Annu Rev Immunol. 2025; 43(1):29-55. doi: 10.1146/annurev-immunol-083122-043054. Epub 2024 Dec 20. PMID: 39705164.

[28] Salimi-Jeda A, Abbassi S, Mousavizadeh A, Esghaie M, Bokharaei-Salim F, Jeddi F, Shafaati M, Abdoli A. SARS-CoV-2: Current trends in emerging variants, pathogenesis, immune responses, potential therapeutic, and vaccine development strategies. Int Immunopharmacol. 2021; 101(Pt A):108232. doi: 10.1016/j.intimp.2021.108232. Epub 2021 Oct 16. PMID: 34673335; PMCID: PMC8519814.

[29] Bai C, Zhong Q, Gao GF. Overview of SARS-CoV-2 genome-encoded proteins. Sci China Life Sci. 2022; 65(2):280-294. doi: 10.1007/s11427-021-1964-4. Epub 2021 Aug 10. PMID: 34387838; PMCID: PMC8362648.

[30] Steiner S, Kratzel A, Barut GT, Lang RM, Aguiar Moreira E, Thomann L, Kelly JN, Thiel V. SARS-CoV-2 biology and host interactions. Nat Rev Microbiol. 2024; 22(4):206-225. doi: 10.1038/s41579-023-01003-z. Epub 2024 Jan 15. PMID: 38225365.

[31] Jackson CB, Farzan M, Chen B, Choe H. Mechanisms of SARS-CoV-2 entry into cells. Nat Rev Mol Cell Biol. 2022; 23(1):3-20. doi: 10.1038/s41580-021-00418-x. Epub 2021 Oct 5. PMID: 34611326; PMCID: PMC8491763.

[32] V'kovski P, Kratzel A, Steiner S, Stalder H, Thiel V. Coronavirus biology and replication: implications for SARS-CoV-2. Nat Rev Microbiol. 2021; 19(3):155-170. doi: 10.1038/s41579-020-00468-6. Epub 2020 Oct 28. PMID: 33116300; PMCID: PMC7592455.

[33] Yang H, Rao Z. Structural biology of SARS-CoV-2 and implications for therapeutic development. Nat Rev Microbiol. 2021; 19(11):685-700. doi: 10.1038/s41579-021-00630-8. Epub 2021 Sep 17. PMID: 34535791; PMCID: PMC8447893.

[34] Malone B, Urakova N, Snijder EJ, Campbell EA. Structures and functions of coronavirus replication-transcription complexes and their relevance for SARS-CoV-2 drug design. Nat Rev Mol Cell Biol. 2022; 23(1):21-39. doi: 10.1038/s41580-021-00432-z. Epub 2021 Nov 25. PMID: 34824452; PMCID: PMC8613731.

[35] Bai Z, Cao Y, Liu W, Li J. The SARS-CoV-2 Nucleocapsid Protein and Its Role in Viral Structure, Biological Functions, and a Potential Target for Drug or Vaccine Mitigation. Viruses. 2021; 13(6):1115. doi: 10.3390/v13061115. PMID: 34200602; PMCID: PMC8227405.

[36] van de Leemput J, Han Z. Understanding Individual SARS-CoV-2 Proteins for Targeted Drug Development against COVID-19. Mol Cell Biol. 2021; 41(9):e0018521. doi: 10.1128/MCB.00185-21. Epub 2021 Aug 24. PMID: 34124934; PMCID: PMC8384068.

[37] McCaig CD. SARS-CoV-2 Is an Electricity-Driven Virus. Rev Physiol Biochem Pharmacol. 2025; 187:361-410. doi: 10.1007/978-3-031-68827-0_18. PMID: 39838019.

[38] Kumar S, Saxena SK. Structural and molecular perspectives of SARS-CoV-2. Methods. 2021; 195:23-28. doi: 10.1016/j.ymeth.2021.03.007. Epub 2021 Mar 15. PMID: 33737214; PMCID: PMC7959701.

[39] Justo Arevalo S, Castillo-Chávez A, Uribe Calampa CS, Zapata Sifuentes D, Huallpa CJ, Landa Bianchi G, Garavito-Salini Casas R, Quiñones Aguilar M, Pineda Chavarría R. What do we know about the function of SARS-CoV-2 proteins? Front Immunol. 2023; 14:1249607. doi: 10.3389/fimmu.2023.1249607. PMID: 37790934; PMCID: PMC10544941.

[40] Citarella A, Scala A, Piperno A, Micale N. SARS-CoV-2 Mpro: A Potential Target for Peptidomimetics and Small-Molecule Inhibitors. Biomolecules. 2021; 11(4):607. doi: 10.3390/biom11040607. PMID: 33921886; PMCID: PMC8073203.

[41] Kaur M, Sharma A, Kumar S, Singh G, Barnwal RP. SARS-CoV-2: Insights into its structural intricacies and functional aspects for drug and vaccine development. Int J Biol Macromol. 2021; 179:45-60. doi: 10.1016/j.ijbiomac.2021.02.212. Epub 2021 Mar 1. PMID: 33662418; PMCID: PMC7919520.

[42] Arduini A, Laprise F, Liang C. SARS-CoV-2 ORF8: A Rapidly Evolving Immune and Viral Modulator in COVID-19. Viruses. 2023; 15(4):871. doi: 10.3390/v15040871. PMID: 37112851; PMCID: PMC10141009.

[43] Yan W, Zheng Y, Zeng X, He B, Cheng W. Structural biology of SARS-CoV-2: open the door for novel therapies. Signal Transduct Target Ther. 2022; 7(1):26. doi: 10.1038/s41392-022-00884-5. PMID: 35087058; PMCID: PMC8793099.

[44] Zhu Y. SARS-CoV-2: phylogenetic status, mutations and therapeutic research based on spike protein. Eur Rev Med Pharmacol Sci. 2021; 25(18):5843-5852. doi: 10.26355/eurrev_202109_26803. PMID: 34604976.

[45] Silva SJRD, Kohl A, Pena L, Pardee K. Recent insights into SARS-CoV-2 omicron variant. Rev Med Virol. 2023; 33(1):e2373. doi: 10.1002/rmv.2373. Epub 2022 Jun 4. PMID: 35662313; PMCID: PMC9347414.

[46] Ghimire D, Han Y, Lu M. Structural Plasticity and Immune Evasion of SARS-CoV-2 Spike Variants. Viruses. 2022; 14(6):1255. doi: 10.3390/v14061255. PMID: 35746726; PMCID: PMC9229035.

[47] Shajahan A, Pepi LE, Rouhani DS, Heiss C, Azadi P. Glycosylation of SARS-CoV-2: structural and functional insights. Anal Bioanal Chem. 2021; 413(29):7179-7193. doi: 10.1007/s00216-021-03499-x. Epub 2021 Jul 7. PMID: 34235568; PMCID: PMC8262766.

[48] Karges J, Cohen SM. Metal Complexes as Antiviral Agents for SARS-CoV-2. Chembiochem. 2021; 22(16):2600-2607. doi: 10.1002/cbic.202100186. Epub 2021 Jun 14. PMID: 34002456; PMCID: PMC8239769.

[49] Soares VC, Moreira IBG, Dias SSG. SARS-CoV-2 Infection and Antiviral Strategies: Advances and Limitations. Viruses. 2025; 17(8):1064. doi: 10.3390/v17081064. PMID: 40872778; PMCID: PMC12390440.

[50] Cao Y, Yang R, Lee I, Zhang W, Sun J, Wang W, Meng X. Characterization of the SARS-CoV-2 E Protein: Sequence, Structure, Viroporin, and Inhibitors. Protein Sci. 2021; 30(6):1114-1130. doi: 10.1002/pro.4075. Epub 2021 Apr 13. Erratum in: Protein Sci. 2021 Dec;30(12):2482. doi: 10.1002/pro.4216. PMID: 33813796; PMCID: PMC8138525.

[51] Wu, Cr., Yin, Wc., Jiang, Y. et al. Structure genomics of SARS-CoV-2 and its Omicron variant: drug design templates for COVID-19. Acta Pharmacol Sin. 2022; 43:3021–3033. doi: https://doi.org/10.1038/s41401-021-00851-w

[52] Bhat EA, Khan J, Sajjad N, Ali A, Aldakeel FM, Mateen A, Alqahtani MS, Syed R. SARS-CoV-2: Insight in genome structure, pathogenesis and viral receptor binding analysis - An updated review. Int Immunopharmacol. 2021; 95:107493. doi: 10.1016/j.intimp.2021.107493. Epub 2021 Feb 25. PMID: 33721758; PMCID: PMC7904465.

[53] Mohamadian M, Chiti H, Shoghli A, Biglari S, Parsamanesh N, Esmaeilzadeh A. COVID-19: Virology, biology and novel laboratory diagnosis. J Gene Med. 2021; 23(2):e3303. doi: 10.1002/jgm.3303. Epub 2021 Jan 6. PMID: 33305456; PMCID: PMC7883242.

[54] Zhang J, Hom K, Zhang C, Nasr M, Gerzanich V, Zhang Y, Tang Q, Xue F, Simard JM, Zhao RY. SARS-CoV-2 ORF3a Protein as a Therapeutic Target against COVID-19 and Long-Term Post-Infection Effects. Pathogens. 2024; 13(1):75. doi: 10.3390/pathogens13010075. PMID: 38251382; PMCID: PMC10819734.

[55] Ahirwar R, Gandhi S, Komal K, Dhaniya G, Tripathi PP, Shingatgeri VM, Kumar K, Sharma JG, Kumar S. Biochemical composition, transmission and diagnosis of SARS-CoV-2. Biosci Rep. 2021; 41(8):BSR20211238. doi: 10.1042/BSR20211238. PMID: 34291285; PMCID: PMC8350435.

[56] Beig Parikhani A, Bazaz M, Bamehr H, Fereshteh S, Amiri S, Salehi-Vaziri M, Arashkia A, Azadmanesh K. The Inclusive Review on SARS-CoV-2 Biology, Epidemiology, Diagnosis, and Potential Management Options. Curr Microbiol. 2021; 78(4):1099-1114. doi: 10.1007/s00284-021-02396-x. Epub 2021 Feb 27. PMID: 33638671; PMCID: PMC7913045.

[57] Ranjan P, Singhal A, Yadav S, Kumar N, Murali S, Sanghi SK, Khan R. Rapid diagnosis of SARS-CoV-2 using potential point-of-care electrochemical immunosensor: Toward the future prospects. Int Rev Immunol. 2021; 40(1-2):126-142. doi: 10.1080/08830185.2021.1872566. Epub 2021 Jan 15. PMID: 33448909.

[58] Ciotti M, Benedetti F, Zella D, Angeletti S, Ciccozzi M, Bernardini S. SARS-CoV-2 Infection and the COVID-19 Pandemic Emergency: The Importance of Diagnostic Methods. Chemotherapy. 2021; 66(1-2):17-23. doi: 10.1159/000515343. Epub 2021 Mar 19. PMID: 33744904; PMCID: PMC8089410.

[59] Puhach O, Meyer B, Eckerle I. SARS-CoV-2 viral load and shedding kinetics. Nat Rev Microbiol. 2023; 21(3):147-161. doi: 10.1038/s41579-022-00822-w. Epub 2022 Dec 2. PMID: 36460930; PMCID: PMC9716513.

[60] Bojórquez-Velázquez E, Llamas-García ML, Elizalde-Contreras JM, Zamora-Briseño JA, Ruiz-May E. Mass Spectrometry Approaches for SARS-CoV-2 Detection: Harnessing for Application in Food and Environmental Samples. Viruses. 2022; 14(5):872. doi: 10.3390/v14050872. PMID: 35632614; PMCID: PMC9144875.

[61] Wei H, Zhang C, Du X, Zhang Z. Research progress of biosensors for detection of SARS-CoV-2 variants based on ACE2. Talanta. 2023; 251:123813. doi: 10.1016/j.talanta.2022.123813. Epub 2022 Aug 6. PMID: 35952504; PMCID: PMC9356646.

[62] Taha BA, Al Mashhadany Y, Al-Jubouri Q, Rashid ARBA, Luo Y, Chen Z, Rustagi S, Chaudhary V, Arsad N. Next-generation nanophotonic-enabled biosensors for intelligent diagnosis of SARS-CoV-2 variants. Sci Total Environ. 2023; 880:163333. doi: 10.1016/j.scitotenv.2023.163333. Epub 2023 Apr 6. PMID: 37028663; PMCID: PMC10076079.

[63] Thapa S, Singh KR, Verma R, Singh J, Singh RP. State-of-the-Art Smart and Intelligent Nanobiosensors for SARS-CoV-2 Diagnosis. Biosensors (Basel). 2022; 12(8):637. doi: 10.3390/bios12080637. PMID: 36005033; PMCID: PMC9405813.

[64] Drobysh M, Ramanaviciene A, Viter R, Chen CF, Samukaite-Bubniene U, Ratautaite V, Ramanavicius A. Biosensors for the Determination of SARS-CoV-2 Virus and Diagnosis of COVID-19 Infection. Int J Mol Sci. 2022; 23(2):666. doi: 10.3390/ijms23020666. PMID: 35054850; PMCID: PMC8776074.

[65] Boretti A. Favipiravir use for SARS CoV-2 infection. Pharmacol Rep. 2020; 72(6):1542-1552. doi: 10.1007/s43440-020-00175-2. Epub 2020 Oct 27. PMID: 33108587; PMCID: PMC7590246.

[66] Lim SP. Targeting SARS-CoV-2 and host cell receptor interactions. Antiviral Res. 2023; 210:105514. doi: 10.1016/j.antiviral.2022.105514. Epub 2022 Dec 26. PMID: 36581047; PMCID: PMC9792186.

[67] Zarandi PK, Zinatizadeh MR, Zinatizadeh M, Yousefi MH, Rezaei N. SARS-CoV-2: From the pathogenesis to potential anti-viral treatments. Biomed Pharmacother. 2021; 137:111352. doi: 10.1016/j.biopha.2021.111352. Epub 2021 Feb 2. PMID: 33550050; PMCID: PMC7969672.