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Research on the structural characteristics, mutation evolution and prevention and control strategies of SARS-CoV-2

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Abstract. OVID-19, or novel coronavirus pneumonia, is a global infectious disease caused by SARS-CoV-2, which has had a profound impact on public health, socioeconomics, and people's daily lives since its outbreak in 2019. This article reviews the structural composition, mutation evolution, transmission characteristics, and prevention and control measures of SARS-CoV-2. Studies have shown that the virus is mainly composed of spike protein, nucleocapsid protein, and viral RNA. The spike protein mediates viral invasion of host cells by binding to the human ACE2 receptor and is an important target for vaccine and antiviral drug development. The nucleocapsid protein plays a crucial role in viral RNA protection and replication. As the virus continues to spread, JN.1 and its derived variants have gradually become the main circulating strains globally, and their transmissibility and immune evasion capabilities have been enhanced through continuous mutation accumulation. To prevent and control the spread of infectious diseases, wear masks, wash hands regularly, improve ventilation, receive vaccinations, maintain social distancing, stay home when ill, etc., and thereby reduce the risk of disease transmission. Among them, a multi-layered, combined prevention and control strategy will be more protective.

Keywords: COVID-19; SARS-CoV-2; Spike protein; Variant evolution and immune evasion.

1. Introduction

COVID-19 is a virus that has affected people's lives around the world. It was first reported in 2019, and since then, millions of people have fallen ill around the world, causing various health crises. Schools and businesses were closed, people had to stay home during the lockdown, and hospitals were severely overstressed. In response to the spread of the virus, the government has implemented all kinds of countermeasures to help reduce the spread: wearing masks, social distancing, handwashing, testing and vaccination. Although the above measures reduced the spread of COVID-19, life and study were also disrupted for many people [1,2].

Scientists have studied COVID-19 to better understand how it spreads and what causes it in SARS-CoV-2. Research has shown that the parts of the virus include the spike protein, nucleocapsid protein and viral RNA. The spike protein is used to bind with the ACE2 receptor on human cells to enter the body of the virus. Spike proteins are involved in infection and thus are the targets of vaccines and treatments. Recently, a study has shown that the nucleocapsid protein binds to viral RNA to promote an increase in the number of these viruses.

With the spread of the virus, new variants have also emerged in different parts of the world, such as XDV.1, JN.1.67 and KP.2. Some variants spread more easily and showed stronger immune evasion, making the spread of the pandemic more severe. Research on COVID-19 variants has also shown that the virus is continuously changing over time. In addition, researchers have found that the virus can remain on different surfaces for an extended period; thus, regular disinfection of these surfaces and scrupulous hand hygiene have been required to curb the spread during the pandemic [3].

This paper will introduce the structure of COVID-19, various types of new-generation variants, how the virus spreads, and the public health measures taken during the pandemic.

2. Functional Characteristics of SARS-CoV-2 Structural Proteins and Their Therapeutic Prospects

2.1. Nucleocapsid Protein: A Highly Conserved Target inside the Virus

The highly conserved target of the nucleocapsid protein (N protein) in the virus is located inside the virus. It is highly conserved in all types of coronaviruses, and their sequences and structures have changed very little. It is suitable for developing an anti-viral drug at this time. The first job of the N protein is to link up with the virus's genetic material to create an RNP complex. The above mechanism will prevent damage to genomic RNA and regulate the replication and expression of the virus; at the same time, it can help form new viruses [4]. The N protein is needed to protect the fragile viral genomic RNA and help it replicate and assemble.

2.2. Regulation Mechanism of Phosphorylation for the N Protein

There is a Serine- and Arginine-rich region (SR region) in the middle of the N protein. After the virus infects the cell, this area will be heavily phosphorylated by kinases in the cell. When all eight specific phosphorylation sites in the SR region are modified, this area will undergo a change in spatial conformation and directly occupy the location on the N protein that was originally used for RNA binding, thus physically inhibiting the binding of RNA to the N protein. This is because at certain times during viral replication, it needs to be separated from RNA for a while so that RNA replication and transcription can be performed, and phosphorylation serves as this "reversible switch" function [4].

2.3. Spike Protein: The First Molecule of Virus Entry

The spike protein (S protein) binds to the receptors on the surface of host cells and is thus recognised. It is now one of the main subjects for vaccine development and therapeutic antibody screening. The two parts of the S protein are S1 and S2. The S1 subunit is at the N-terminus of the protein, and it has a receptor-binding domain (RBD) that binds to the ACE2 receptor. The S2 subunit is at the C-terminus of the protein and guides the fusion of the viral envelope with the host cell membrane [3]. The equilibrium dissociation constant (KD) of the S protein of SARS-CoV-2 for ACE2 is 14.7 nmol/L, and that of the S protein of the SARS virus is 325.8 nmol/L. The reason for the 22-fold higher transmissibility of the COVID-19 virus compared to the 2003 SARS virus [3] is that it is easier to transmit [unfounded].

2.4. Mutation of the S Protein and Immune Evasion

Antigenic variation of the COVID-19 virus causes it to continuously evade immune recognition by developing many mutations at the RBD binding site. Mutations in the RBD region and the S1/S2 cleavage site are also important functional sites of the S protein. This site can be recognised and cut by the furin protease in the host cell. Cleavage must occur first before the S protein is in its active state and can promote membrane fusion. If this site is deleted, the virus will also be less infectious. The multiple base cleavage sites are one of the reasons for the difference in structure between the SARS and COVID-19 viruses and are also closely linked to their high transmissibility [2].

2.5. Vaccine and Drug Development Strategies

As the mutant strains are continuously evolving, so too must the vaccine antigens be adjusted. The S protein is a target for vaccines, therapeutic antibodies and diagnostic reagents. At present, most of the first-generation COVID-19 vaccines are based on the S protein or its RBD as antigens to stimulate the immune system in people to produce anti-S protein antibodies that prevent infection [1, 2]. Vaccines and antibody drugs targeting the S protein have been developed, and as the N protein is highly conserved among coronaviruses, drugs targeting the N protein may have broad-spectrum anti-coronavirus effects and are less likely to develop drug resistance due to viral mutations. Research has shown that the compound PJ34 can also bind to the same binding site on the N-NTD of AMP and

inhibit the binding activity of the N protein to RNA, thereby suppressing viral replication. Another compound, 5-benzyloxygramine, can prevent the formation of the RNP complex and the assembly of virus particles by inducing abnormal aggregation of MERS-CoV N-NTD [4]. In particular, Arg259 and Lys338 are two amino acid residues that must be present for RNA binding at the N-CTD domain. Researchers have found that when both of these sites are mutated to alanine, the binding affinity of the N protein for RNA is also reduced to some extent. Therefore, small-molecule drugs that target this binding pocket may be used to design new types of antiviral drugs [4].

3. Biological Characteristics, Evolution, and Host Immune Response of SARS-CoV-2

3.1. Viral Structure and Cellular Entry Mechanism

SARS-CoV-2 is a beta-coronavirus that has a genome of about 30,000 nucleotides and four primary structural proteins: spike (S), envelope (E), membrane (M) and nucleocapsid (N) [5]. Homotrimers of S proteins on the viral envelope are responsible for the infectious ability of the virus. The S1 subunit has a receptor-binding domain (RBD) and the S2 subunit mediates membrane fusion [5].

Viral entry is initiated by the particular recognition of the host Angiotensin-converting enzyme 2 (ACE2) receptor by the RBD. The main site for this interaction is type II pneumocytes in the respiratory system. Attached, the S2 subunit enables fusion after proteolytic cleavage by host proteases, such as transmembrane serine protease 2 (TMPRSS2) [5]. ACE2-dependent mechanism of viral tropism and the main target for neutralizing antibodies.

3.2. Evolution Trajectory: Alpha to Omicron

Although SARS-CoV-2 has a proofreading mechanism (nsp14) and is thus subject to a relatively low mutation rate compared with influenza, extensive transmission has led to the emergence of fitter variants [6]. Transmission and immune evasion have both varied in recent years due to the pandemic.

The Alpha variant (B.1.1.7) was the first to show that some mutations in the S-protein can increase transmissibility. The Delta variant (B.1.617.2), which appeared in late 2020, had mutations (e.g., L452R, P681R) that increased the binding affinity and cleavage efficiency of ACE2, thus raising viral load. Delta achieved world-class transmission and had a value of 5-7 [6].

On the other hand, in November 2021, the Omicron variant (B.1.1.529) had undergone substantial changes. More than 30 mutations in the S protein (15 in the RBD) have been accumulated by Omicron sublineages (BA.2, BA.5, XBB, JN.1) through convergent evolution [6]. XBB.1.5 gained the F486P substitution, and JN.1 showed that a single mutation (L455S) could improve both ACE2 binding and immune evasion. Therefore, the basic reproduction number for Omicron sublineages is around 9-10 and has reached the level of measles. Pre-symptomatic viral shedding and upper respiratory tract tropism are also present; thus, symptom-based screening will not be effective [6].

3.3. Host Immune Response and Public Health Implications

Upon entry of a virus into the host, the innate immune system will recognize the viral RNA through pattern recognition receptors (TLR3, TLR7, TLR8, RIG-I, MDA5) and trigger type I and III interferon (IFN) responses [7]. However, SARS-CoV-2 is also immune-evasive. The viral genome has a low CpG density to avoid TLR9 binding, and viral proteins (nsp1, nsp6, ORF6) suppress IFN signalling. A late or faulty early interferon response will likely lead to unchecked viral multiplication and, consequently, a "cytokine storm" that causes acute respiratory distress syndrome (ARDS) [7].

The first target of the adaptive immune response is an antibody that binds to the RBD and confers partial protection against infection [8]. However, due to the rapid mutation speed of SARS-CoV-2 in the XBB and JN.1 lineages, there has been significant evasion of vaccine- and infection-induced antibodies [8]. However, T cell responses to conserved epitopes remain strong and are necessary to prevent serious illness [7]. Immunological differentiation has now shifted the focus of public health

from preventing infection to reducing the severity of disease; vaccination and therapeutic intervention are used instead of general-population restrictions [6].

4. Prevention and Public Health Control Strategies for COVID-19

4.1. Mask-wearing

Now, a large number of people wear masks to prevent the spread of COVID-19. The main ways the virus spreads are through droplets and very fine airborne particles released when an infected person coughs, sneezes, talks or breathes. Masks can help to block the spread of these particles of the virus among people [9].

The kinds of masks are for different purposes. N95 masks are generally good at filtering out airborne particles and can be worn close to the face. Surgical masks offer some protection and have a looser fit than N95 masks [11]. In the process of reducing the spread of COVID-19, people in public spaces have started wearing face masks. Naturally, the previous measure of maintaining distance is still quite effective; by keeping away from others, one reduces the risk of inhaling virus-carrying droplets. At the beginning of the pandemic, many countries took measures to prevent the spread of the virus by social distancing [12].

To reduce the risk of transmission through close contact, many people have been avoiding crowded places and large gatherings. Stay away from people in poorly ventilated Areas or those not wearing masks.

4.2. Vaccination

Vaccination can reduce the risk of serious illness due to COVID-19 to some extent. Most vaccines are directed against the spike (S) protein of SARS-CoV-2 to help the immune system produce antibodies and T cells [13]. Antibodies cannot allow the virus to enter human cells, and T cells kill the infected cells.

In the beginning of the pandemic, vaccinations have reduced hospitalisation and death rates to some extent, thus easing the strain on the healthcare system and lowering the demand for critical care. Some of these are only partially protected by vaccines, but even so, they will be much less likely to cause serious disease after being vaccinated. Boosters are needed to increase the declining protective immunity with time. At the same time, the first rounds of vaccination have also changed the public health policies for vaccination requirements, travel, etc.

Nowadays, many countries have continued to update their vaccines in response to new variants and recommend regular booster shots for high-risk groups; thus, the management of the pandemic is slowly moving away from an emergency response towards an organized system for disease prevention.

4.3. Home Protection

If a person is unwell with a fever, cough, sore throat or fatigue, they should stay home and avoid contacting others to prevent the spread of the disease. SARS-CoV-2 can spread before showing any symptoms, and therefore, infected people may have spread it without realising it [9]. At home during illness can help break the transmission chain and protect vulnerable groups, such as older adults and those with weakened immune systems.

Frequent Handwashing is another good prevention method. Although the novel coronavirus spreads mainly through the air, it can still remain on surfaces for some time. Soap and water can wash away the virus from hands [10]. Soap works because it is in the form of a lipid-based membrane on the surface of SARS-CoV-2. Soap will break down this layer and render the virus harmlessly. Hand sanitiser with a lower limit of 60 per cent alcohol content can also be used to fight viruses. Do not touch eyes, nose and mouth with the hand that is dirty.

A reasonable Air-Exchange Environment can help to reduce the spread of COVID-19. Tiny virus particles can stay in the air for a long time in closed, poorly ventilated rooms [13]. Open windows, use fans to circulate the air, and run air purifiers to bring in fresh air and reduce the spread of viruses in the air. The air can circulate more freely in the outdoors, so it is relatively safe. Research in the past two years has shown that areas of indoor crowding with poor ventilation have had a higher rate of spread.

4.4. Layered Protection Strategies

A Single Prevention Method Will Not Prevent the Spread of COVID-19. Vaccines reduce the risk of serious illness but are not infections. Masks help reduce exposure, but they are not ideal. Ventilation can reduce the concentration of viruses in the air, but not all virus particles will be removed. Since all the prevention measures have certain defects, many should be used in combination.

This is called the "Swiss cheese model", and each prevention measure is regarded as a slice of Swiss cheese with holes. A single layer is not enough to stop the spread of the virus; there may still be a leak in one. However, when many slices are placed together, the holes are covered by other layers, and it is thus much more difficult for the virus to spread.

During the COVID-19 pandemic, the Swiss cheese model has gained attention as a public health concept that suggests that combining various measures, such as vaccination, masks, ventilation, handwashing and physical distancing, can provide a more robust level of protection than using any single measure alone [14].

COVID-19 has severely disrupted public health and life in society all over the world. SARS-CoV-2 is transmitted by droplets and small particles in the air, so the mechanism of this virus spreads to reduce the risk of infection. Every day, to reduce the spread of the virus, wear a mask, increase ventilation, wash hands often, get vaccinated, stay away from others, and stay home if sick.

No single way of preventing COVID-19 is sufficient to eliminate the virus. Multiple Safety Measures are being employed at the same time for strengthened protection. During the pandemic, public health experts have advocated for people to use a combination of vaccines, masks, ventilation, good hygiene habits, etc., to reduce transmission and protect vulnerable groups.

Although vaccines and other treatments have been developed since the start of the pandemic, COVID-19 still requires the attention of the public and scientists. To learn how to prevent the spread of COVID-19 and deal with further outbreaks of infectious diseases in the future.

5. Conclusion

This paper will introduce the molecular features, mutations and evolution of the new coronavirus, as well as prevention strategies, and draw the following conclusions. At the level of viruses, it is carried by nucleocapsid proteins and spike proteins. At the same time, it compares the novel coronavirus with the SARS virus in 2003 and explains the origin of the increased infectivity of the novel coronavirus. JN.1 and its derived mutant strains have become the dominant circulating strains around the world and, through continuous mutation accumulation, have evaded immune recognition. The Distribution of mutant strains is unevenly distributed across the regions. Everyday preventive measures at the level of prevention include wearing masks, improving ventilation, practising good hand hygiene, getting vaccinated, keeping a distance from others, and staying home when sick in isolation. As a single indicator is not sufficient to prevent the spread of viruses altogether, all kinds of prevention and control systems are deployed in an overlapping manner. Before the introduction of vaccines, the only way to control the spread of respiratory infectious diseases was through non-pharmaceutical intervention measures, but strict measures also incurred a relatively high socio-economic cost. The findings of this paper provide reference for responding to the emergence of respiratory infectious diseases in the future: First, swift coordination of non-pharmaceutical intervention measures is needed, but measures that cause significant economic damage should be avoided; second, the development of

broad-spectrum vaccines targeting conserved features of the virus is of great importance; finally, a multi-level combined prevention strategy should be incorporated into public health education. This essay also has certain deficiencies. Due to the continuous development of the virus, the data on the spread of mutant strains are now outdated. The full structure of the nucleocapsid protein is not known at present, and thus related drugs have not been developed. Future research will continue to study the laws of virus mutation, investigate the entire length structure of the nucleocapsid protein, and develop broad-spectrum anti-coronavirus drugs. At the same time, an adaptable public health response system will also be built in the future to control the spread of viruses more effectively.

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