Scientific Research Publishing

Journal of Biosciences and Medicines, 2022, 10, 153-164
https://www.scirp.org/journal/jbm
ISSN Online: 2327-509X
ISSN Print: 2327-5081

Telomere and SARS-CoV-2: A Correlation between Them

Alex He

Chengdu Shishi No. 4 High School, Chengdu, China
Email: Fukaforte@gmail.com

How to cite this paper: He, A. (2022) Telomere and SARS-CoV-2: A Correlation between Them. *Journal of Biosciences and Medicines*, **10**, 153-164.
https://doi.org/10.4236/jbm.2022.1011012

Received: September 26, 2022
Accepted: November 18, 2022
Published: November 21, 2022

Abstract Alex He

This article briefly reviews the history of coronavirus detection and states the structural characteristics and pathogenesis of the SARS-CoV-2 strain. Following the conclusion that cellular senescence is thought to contribute to SARS-CoV-2 susceptibility, this article continues to review the structure and function of telomeres. Finally, it briefly states the link between COVID-19 and telomeres caused by the SARS-CoV-2 strain.

Keywords

Senescence, SARS-CoV-2, Telomeres, Structure, Relationship, Structure, Function, Telomeres

1. Introduction

Covid-19 outbreaks caused by the SARS-CoV-2 strain have been ongoing globally for two years since 2020, and the disease has different clinical manifestations for other age groups. Patients with a global pandemic caused by the SARS-CoV-2 virus have been reported to have many different conditions and complications. Also, its strong contagiousness poses a threat to the elderly. It is thought to have the potential to cause inflammation and lead to accelerated ageing. Telomeres, on the other hand, are thought to be closely related to cellular ageing, so the SARS-CoV-2 virus may have a way of affecting telomeres. Therefore, this article will describe the history, structure, and pathogenesis of the SARS-CoV-2 strain; the possible associations and effects between it and telomeres will be briefly discussed.

2. COVID-19

2.1. History of Coronavirus and Introduction to SARS-CoV-2

Infectious coronaviruses were first discovered in the 1960s when there was little

epidemiological, genomic or causative information about these viruses, only that they contained membranes surrounded by "spike"-shaped proteins RNA [1]. The crowned appearance of these surface "spike" proteins gave the virus family its name, corona, Latin for the crown [2]. The earliest coronaviruses identified in humans, human HCoV-229E and HCoV-OC43, caused milder symptoms of infection and caused common upper respiratory tract disease [3]. Subsequently, two more coronavirus strains were discovered, namely HCoV-HKU1 and HCoV-NL63 [4]. Three other strains of coronaviruses (SARS-CoV, MERS-CoV, and SARS-CoV-2) were later found that, unlike the four common strains, have the potential to cause severe illness and even death [5].

The SARS-CoV strain, which first emerged in November 2002 in Guangdong Province, China, causes severe acute respiratory syndrome (SARS) with symptoms of fever, chills, chills, cough, and headache [6]. In addition, the patient's past medical history and age, Etc., will impact the patient outcome. The incubation period for SARS-CoV strains is 2 - 10 days [7]. The virus was found to target respiratory epithelial cells and cause damage to the lungs [8].

The outbreak caused by SARS-CoV lasted approximately 114 days and caused about 8098 infections, including 774 deaths; a total of 29 countries were affected [9]. This strain is derived from civet cats and is a zoonotic transfer to humans [10]. SARS cases have been dormant since the last case was reported in 2004. Extensive isolation measures and quarantine are considered important factors in controlling the SARS pandemic and successfully ending its worldwide epidemic [11].

In June 2012, 10 years after the emergence of SARS-CoV, a novel coronavirus, MERS-CoV, was isolated from the sputum of a Saudi Arabian man who died of acute pneumonia and renal failure [12]. Like SARS, patient outcomes are affected by age and previous medical history [13]. Still, as a betacoronavirus strain, it has a much higher mortality rate than SARS at more than 35% [14].

As the seventh known coronavirus strain, the COVID-19 outbreak caused by SARS-CoV-2 is thought to have originated in a seafood market in Wuhan, China, in December 2019 [15]. It shares similar symptoms of infection as SARS and MARS [16] but is more contagious [17], making it more difficult to isolate and contain [18].

2.2. Structure of COVID-19

The SARS-CoV-2 strain, the MERS-CoV strain and the SARS-CoV-1 strain belong to the Betacoronavirus genus of the family Coronaviridae [15].

The genome of SARS-CoV-2 is a positive-stranded single-stranded RNA [(+) ssRNA] with a 5'-cap, 3'-UTR poly (A) tail [15]. Viral particles are spherical or pleomorphic, with a diameter of about 60 - 140 nm [19]. As shown in **Figure 1**, structural proteins include spike (S), envelope (E), membrane/matrix (M) and nucleocapsid (N), as well as accessory proteins [20]. The S, E, and M proteins form the virus's membrane, while the N protein forms the capsid to package the

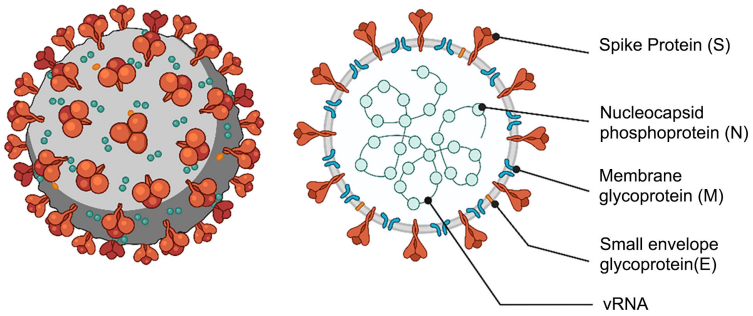

Figure 1. A rough schematic diagram of the structure of SARS-CoV-2.

genomic RNA [9] [21] [22]. In more detail, the S protein is responsible for mediating the attachment of the virus to the cell membrane receptor, membrane fusion, and finally entering the host cell; the M protein, as the most abundant membrane protein, is responsible for the membrane structure of the coronavirus together with the E protein [23]. In addition, the new coronavirus has evolved into different branches and lineages and has another naming system [15].

2.3. Health Problems Led by COVID-19

At present, virus-containing droplets are considered the main route of SARS-CoV-2 transmission, and this medium is widely present in human sneezing, coughing, and mucosal secretions. Confined spaces (BE) will significantly affect this. Virus transmission effect [24]. Under experimental conditions, the virus can persist in the air as an aerosol for 3 hours. It can be transmitted mediated by pollutants ranging from a few hours to 3 days from cardboard to stainless steel, depending on the material. Surfaces of contaminated materials have proven to be contagious [25]. In addition, SARS-CoV-2 has asymptomatic infected individuals, and although they do not have the typical onset characteristics of infected individuals, they can still transmit the virus [26].

Most COVID-19 patients have a fever, cough, and shortness of breath [27]. In addition, smell and taste dysfunction, sudden sensorineural hearing loss (SSHNL), and blood clots may also occur in patients with COVID-19 [28] [29] [30]. COVI-19 has also been associated with comorbidities, including hypertension, diabetes, cardiovascular disease, and respiratory disease [31]. Patients with these comorbidities have a higher risk of infection and a higher rate of severe illness; some patients with comorbidities have a higher mortality rate after infection with COVID-19, which makes these comorbidities a risk for the severity of COVID-19 factor [32]. Moreover, age is essential in contracting COVID-19 and its severe adverse health consequences [33].

3. Telomere

3.1. Structure of Telomeres

A telomere is a protein-DNA complex. It has repetitive tandem TTAGG sequences (DNA) and is associated with many proteins. These proteins eventually

form protein complexes with DNA-remodeling activity called "shelterins". This protein complex helps stabilise a type of telomeric ring structure (T-loop) developed by telomeric DNA [34]. Telomeres contain a C-rich lagging strand and a G-rich leading strand followed by a terminal 3' G-rich single-stranded overhang; the 3' G-strand overhang invades double-stranded DNA and forms a D-loop while promoting the Formation of T-loops [35] [36], as **Figure 2** showed. To balance the loss of DNA at the ends of chromosomes, telomerase—a ribonucleoprotein (RNP) reverse transcriptase enzyme that adds telomeric single-stranded DNA (*i.e.*, ssDNA) repeats by repeating the reverse-transcribed template sequence in its intrinsic RNA is used sequence, under the condition that telomeric DNA is still a suitable substrate. The conformation of single-stranded 3' overhangs of telomeres and their folding into secondary structures form a poor substrate, the G-quadruplex. G-quadruplexes are formed from G-rich nucleic acids and have a secondary structure. G-quadruplexes mainly inhibit telomere elongation controlled by telomerase but are also involved in telomere protection and recombination inhibition [37]-[42].

3.2. The Function of Telomeres

Telomeres are thought to be protective structures at the ends of linear chromosomes that play an essential role in preventing genomic instability. However, as cells replicate, telomeres shorten and lead to a permanent cell cycle arrest known as "replicative senescence" [43]. Senescence (Aging) is considered a progressive and irreversible loss of the proliferative potential of human somatic cells [44]. Furthermore, it is thought to be an advanced and phenotypically diverse set of cellular states acquired after an initial growth arrest and act on several complex biological processes, including development, tissue repair, ageing and age-related diseases [45]. While the best explanation for replicative senescence is the shortening of telomeres, Harley *et al.* found that the telomere region gradually shortens as cells divide—this is thought to be an inducer of cellular senescence [46]. Later in 1998, in experiments where telomerase was introduced into normal cells, telomere length was the limiting factor in senescence arrest, and here the theory of causality was confirmed [47].

In addition, telomeres are thought to protect the ends of chromosome arms from inappropriate DNA repair mechanisms and to prevent the degradation of genes near the ends of chromosome arms due to incomplete DNA replication. As a "buffer system", telomeres avoid the loss of critical DNA. However, as multiple mechanisms cause wear and tear, telomeres shorten. The proteins that form the Shelterin complex fail to bind to telomere sequences and eventually lose their role in capping at the ends of chromosomes [48].

Related diseases with Telomeres:

As an inducer of senescence, future research publications on telomeres will further demonstrate the link between telomeres and ageing-related diseases and genetics-related diseases. Therefore, this article extracts some of the known telomere-related diseases for presentation.

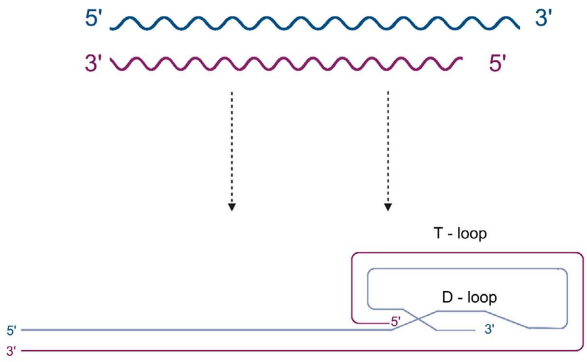

Figure 2. A simple schematic diagram of T-loop and D-loop. The 3' end of the G-rich strand protrudes as a single-stranded telomere extension and curls back into a T-loop, then invades the 5' double-stranded telomeric duplex, forming a D-loop.

3.2.1. Cancer

Cancer is considered an age-related disease because the risk of cancer increases as age increases [49]. Cells with malignant potential can adapt and evade replicating senescence by inhibiting DNA damage response mechanisms or over-activating telomere maintenance pathways, avoiding apoptosis and becoming tumour cells [50]. Telomere length measured in some cancer tissues is shorter than telomeres from healthy tissues from the same organ and patient [51] [52] [53]. In addition, telomeres in healthy tissues adjacent to cancer cell tissue are shorter than telomeres in cells far away from cancer cell tissue [54]. Thus, shortened and dysfunctional telomeres can lead to genetic instability and tumorigenesis [49] [55] [56].

3.2.2. Coronary Heart Disease

Coronary heart disease is one of the most common causes of human mortality worldwide [57], with complex pathogenesis, hypertension, hyperlipidemia, smoking, obesity, and a family history of coronary heart disease are all risk factors for coronary heart disease [58]. A standard view is that inflammatory responses and oxidative stress reactions may occur in lesion sites such as coronary atherosclerotic plaques in patients with coronary heart disease; As a response, the proliferation of hematopoietic stem cells will accelerate and directly lead to faster shortening of telomeres [59] [60]. In addition, risk factors for coronary heart disease, such as obesity, can directly shorten telomere length by increasing systemic inflammation and oxidative stress. Inflammation and oxidative stress play an important role in regulating telomere length has also been demonstrated by studies that can delay telomere shortening at low levels of plasma trans fatty acid concentrations or high levels of serum lipophilic antioxidants [61] [62]. Therefore, telomere length predicts that mortality in patients with stable coronary heart disease will be possible [63].

In addition, telomeres have also been shown to be associated with many chronic diseases, such as stroke [64], high blood pressure [65], atherosclerosis [66], dyslipidemia [67], etc. As more research is conducted, more diseases

caused or affected by telomeres will likely be detected.

3.3. COVID-19 and Telomeres' Link

Immune response patterns are highly dependent on age, so age-related changes in immune cells can affect the efficiency of the immune response [68]. Again, ageing is a set of progressive and phenotypically diverse cellular states acquired after initial growth arrest and acts on many complex biological processes, including development, tissue repair, ageing, and age-related diseases [45]. However, the solid age alone is insufficient to reflect the physiological data state. Biological age is more strongly associated with all-cause mortality than actual age, and genetic and epigenetic changes over life can affect the biological ageing process. They may also increase vulnerability to multiple diseases, such as infectious diseases [69]. Currently, adults over 65 and people with comorbidities are at the most significant risk of death and morbidity from COVID-19 [70]. It is worth noting that the causal role of DNA damage accumulation in ageing cannot be ignored, and several descriptions of genetic defects accelerate ageing in organisms [71]. Telomeres, in turn, are protective structures at the ends of linear chromosomes. Therefore, telomere length and epigenetic characteristics may have a specific correlation with susceptibility to viral infection; that is, the host's telomere length and epigenetic features affect the likelihood of infection with the virus [72] [73]. As a result, cellular senescence is likely to be a key pathological mechanism of susceptibility to SARS-CoV-2 infection [74].

4. Conclusion and Future Direction

As one of the most severe public health crises worldwide, the SARS-CoV-2 virus has several different variants. Although vaccines are available for common strains, further research is needed on the source of the virus and its pathological effects on humans. In the COVID-19 outbreak, the elderly and young people have been judged to be high-risk susceptible groups, among which some comorbidities common to the elderly group are considered common factors in aggravating SARS-CoV-2 infection that has a great relationship with cellular ageing and telomere wear.

Further research on telomeres and SARS-CoV-2 strains will help provide new treatment options for comorbid populations, such as immunotherapy, anti-ageing therapy, and stem cell therapy, and better understand the long-term impact of the COVID-19 pandemic on humans.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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