The effect of COVID-19 on micro RNA and therefore gene expression

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Abstract---After the scourge of the coronavirus invaded almost all of the world, they were infected with this epidemic, and therefore this has caused changes and variations within the corridors of living cells, which have transgressed to some organs and even systems, which were not spared most of the vital pathways and the natural interdependence that regulates natural activities. Some studies also indicate that the family of The coronavirus reached its claws to the skin of genes and gene expression, thus opening the doors of genetics and molecular bio to study and investigate everything that this nano creature might affect. Which has been used by many vaccines that did not intercede to withdraw terror from those who hear the term Covid 19. This study sheds light on the effect of Covid 19 on the microRNA, which shows the extent of the disease's impact on this indicator that regulates gene expression, which consequently causes an imbalance in gene expression.we will review research that examined the relationship between covid 19 and its effect on the micro RNA and findings of it.

Keywords---SARS-CoV-2, human ACE2, vaccination, micro RNA.

Introduction

SARS-CoV-2

Before 2003, only 2 human coronaviruses—Human Coronavirus (HCoV)-229E and HCoV-OC43, causing mild illness—were known. However, the emergence of Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) changed the view worldwide

because coronaviruses can cause life threatening infections. The ongoing pandemic of a novel strain of coronavirus, Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is posing an unforeseen public health and economic threats worldwide(Mittal et al. 2020). Cases of a novel coronavirus were frst reported in Wuhan, Hubei province, China, in December 2019 and have since spread across the world. Epidemiological studies have indicated human-to-human transmission in China and elsewhere (Xu et al. 2020). coronavirus disease 2019 (COVID-19).

These cases showed symptoms such as fever and dyspnea and were diagnosed as viral pneumonia . Whole-genome sequencing results showed that the causative agent was a novel coronavirus that was initially named 2019-nCoV by the World Health Organization (WHO) (Wang et al. 2020). The global pandemic of novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) , and has since spread worldwide.As of April 5, 2020, there have been more than 1.2 million reported cases and 69 000 deaths in more than 200 countries. This novel Betacoronavirus is similar to severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV); based on its genetic proximity, it likely originated from bat-derived coronaviruses with spread via an unknown intermediate mammal host to humans. The viral genome of SARS-CoV-2 was rapidly sequenced to enable diagnostic testing, epidemiologic tracking, and development of prevention and therapeutic strategies (Sanders et al. 2020). SARS-CoV-2 which is genetically similar to SARS-CoV and Middle East respiratory syndrome coronavirus (MERS-CoV) is an enveloped, single and positive-stranded RNA virus with a genome comprising 29,891 nucleotides, which encode the 12 putative open reading frames responsible for the synthesis of viral structural and nonstructural proteins which are very similar to SARS-CoV and MERS-CoV proteins (Pandey et al. 2020). COVID-19 has radically transformed many aspects of human life and global society both now and for many years to come (Barnes 2020).

Human ACE2

A novel severe acute respiratory syndrome (SARS)-like coronavirus (SARS-CoV-2) is causing the global coronavirus disease 2019 (COVID-19) pandemic. Understanding how SARS-CoV-2 enters human cells is a high priority for deciphering its mystery and curbing its spread. A virus surface spike protein mediates SARS-CoV-2 entry into cells. To fulfill its function, SARS-CoV-2 spike binds to its receptor human ACE2 (hACE2) through its receptor-binding domain (RBD) and is proteolytically activated by human proteases (Shang et al. 2020). Viral entry into the host cell is a multistep process in which SARS-CoV-2 utilizes the receptor-binding domain (RBD) of the spike (S) glycoprotein to recognize angiotensin-converting enzyme 2 (ACE2) receptors on the human cells; this initiates host-cell entry by promoting viral–host cell membrane fusion through large-scale conformational changes in the S protein. Receptor recognition and fusion are critical and essential steps of viral infections and are key determinants of the viral host range and cross-species transmission (Mittal et al. 2020). Several structures of SARS-CoV-2-S were observed in multiple states (the prefusion, closed, and partially open conformations and in complex with hACE2 receptor)

with the RBDs either in an "up" or "down" conformation . Of note, to engage the hACE2 receptor, the RBDs of S1 undergo hinge-like movements that either expose or hide the receptor-binding regions and these conformations are referred to as "up" (receptor-accessible) or "down" (receptor-inaccessible) conformations, respectively. SARS-CoV-2-S structures show that the protein adopts a clover-shaped homotrimeric structure, with 3 S1 heads that recognize a cognate cell-surface receptor and a membrane-anchored trimeric S2 stalk that contains the fusion machinery and is primarily α-helical . In the prefusion conformation of SARS-CoV-2-S protein, the RBDs rest above the trimeric S2 stalk, exhibiting protomers in the "down" conformation and 1 protomer in the "up" conformation, which is a receptor-accessible state required for binding to an hACE2 receptor (Mittal et al. 2020).

Vaccination

2020 has been a difficult year for all, but has seen 58 vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) be developed and in clinical trials (Knoll and Wonodi 2021).

Development of Vaccine

Rapid development of a vaccine to prevent coronavirus disease 19 (COVID-19) is a global imperative, and defining the stakes and potential hurdles is critical because regulatory and medical decisions are based on benefit: risk calculations. The ability of viruses to achieve pandemic spread is diminished by establishing higher levels of community (herd) immunity, and a key question is whether protection against severe acute respiratory syndrome–coronavirus 2 (SARS-CoV-2) will happen by widespread deployment of an effective vaccine or by repeated waves of infection over the next few years until ~60 to 70% of people develop immunity (Graham 2020).Vaccine development is usually measured in decades, so having access to approved vaccines available for large-scale distribution before the end of 2020 or even 2021 would be unprecedented. However, new manufacturing platforms, structure-based antigen design, computational biology, protein engineering, and gene synthesis have provided the tools to now make vaccines with speed and precision. Antiviral vaccines can be classified into two broad   categories. Gene based vaccines deliver gene sequences that encode protein antigens that are produced by host cells. These include live virus vaccines, recombinant vaccine vectors, or nucleic acid vaccines .Protein-based vaccines include whole-inactivated virus, individual viral proteins or subdomains, or viral proteins assembled as particles, all of which are manufactured in vitro. Recombinant vaccine vectors and nucleic acid vaccines are best suited for speed because they can be more easily adapted to platform manufacturing technologies in which upstream supply chains and downstream processes are the same for each product. Precision is achieved by knowing the atomic structure of the vaccine antigen and that the targeted epitopes are preserved in the vaccine (Graham 2020).

Vaccine Challenge

The COVID-19 pandemic can be considered a global unifer, with countries worldwide all challenged to contain the spread of SARS-CoV-2. The World Health Organization (WHO) is currently orchestrating a global campaign of prevention, early diagnosis, and medical treatment. Parallel to ongoing eforts to fatten the infection curve, the development of a COVID-19 vaccine represents the holy grail for global health organizations. With numerous clinical vaccine trials in progress, the timeline for public distribution of a safe and efective vaccine is estimated to be between late 2020 and 2022 (Dror et al. 2020). The COVID-19 outbreak has demonstrated the diverse challenges that supply chains face to significant disruptions. Vaccine supply chains are no exception. Therefore, it is elemental that challenges to the COVID-19 vaccine supply chain (VSC) are identified and prioritized to pave the way out of this pandemic, The COVID-19 outbreak has posed a significant danger to the lives and well-being of billions of citizens around the world .The pandemic has implied huge changes in the way administration associations work . In the current scenario, a shortfall of vaccines due to failure of the vaccine supply chain (VSC) will make circumstances more confounded. A pandemic VSC is different than that of a traditional VSC because governments are directly procuring vaccines from the manufacturers bypassing the traditional chains of wholesalers and distributors. Hence, healthcare experts and VSC analysts are looking for proper policies and adequate strategies for appropriate vaccine manufacturing and distribution to fight against the COVID-19 pandemic. It is fundamental to look closely into pandemic VSCs and comprehend the challenges within to put an end to the devastating effects of the pandemic (Alam et al. 2021).

Types of Vaccine

Messenger RNA (mRNA) Vaccines

The Moderna mRNA- and Pfizer/BioNtech BNT162b2 (also known by brand name Comirnaty or by generic name tozinameran.

Viral Vector-Based (Non-Replicating) Vaccines

Four groups (Astra Zeneca/University of Oxford (AZ/Ox), CanSino Biologics, Gamaleya Research Institute and Johnson & Johnson/Janssen (J&J).

Recombinant Protein-Based Vaccines

The protein subunit Novavax candidate NVX-CoV2373 uses the recombinant, properly folded, full-length SARS-CoV-2 spike glycoprotein in the pre-fusion state engineered from insect cells in a nanoparticle formulation along with their proprietary saponinbased Matrix-M adjuvant.

Inactivated Virus

Three Chinese conglomerates and one Indian company have used the tried-and-true method of viral inactivation by β-propriolactone treatment, along with

various alum adjuvants for generation of their SARS-CoV-2 vaccine candidates (Funk, Laferrière, and Ardakani 2021).

Side Effect of Vaccine

The study of the efficacy and side effects of different vaccines among different populations is necessary. In addition, fear of side effects is the most important reason for reduced vaccine readiness. Clinical trial studies of the AZD- 1222 and Sputnik V have shown that the injection of these vaccines has no serious side effects. In a clinical trial related to the AZD-1222, pain, fever, chills, muscle pain, headache and fatigue were the most common side effects of the vaccine (Zhu et al. 2020).

Micro RNA

Over the past decade, it has become progressively more clear that a large class of small noncoding RNAs, known as microRNAs (miRNAs), function as important regulators of a wide range of cellular processes by modulating gene expression. Within 10 years of research, we have gone from discovering the existence of miRNAs in mammals to exploring their therapeutic applications in numerous diseases. Inherent to the rapid advancements and general excitement surrounding miRNA discoveries is the growing need for applicable and validated experimental tools to enable researchers to accurately study the expression and biological function of miRNAs (Jansson and Lund 2012). Since the discovery of the founding members of the microRNA (miRNA) family, , lin4 and let-7 , hundreds of miRNAs have been identified in plants, animals, and viruses by molecular cloning and bioinformatic approaches . miRNAs were found to downregulate gene expression by base-pairing with the 3 untranslated regions (3 UTRs) of target messenger RNAs (mRNAs) . These discoveries indicated that this class of noncoding RNA molecules may constitute a new layer of regulatory control over gene expression programs in many organisms. More than 500 different miRNAs have been identified in animals and plants, where the number of miRNA genes is expected to increase to 500–1000 per species, which would comprise w2–3% of protein-coding genes (Kim and Nam 2006).

Genomic of Micro RNA

miRNA genes are scattered in all chromosomes in humans except for the Y chromosome. Approximately 50% of known miRNAs are found in clusters and they are transcribed as polycistronic primary transcripts The miRNAs in a given cluster are often related to each other, suggesting that the gene cluster is a result of gene duplication. A miRNA gene cluster also often contains unrelated miRNAs. A plausible but yet-to-be validated possibility is that the clustered miRNAs are functionally related by virtue of targeting the same gene or different genes in the same pathway (Kim and Nam 2006).

Catecorization of Micro RNA

miRNA genes can be categorized based on their genomic locations: intronic miRNA in protein coding TU; intronic miRNA in noncoding TU; and exonic miRNA

in noncoding TU . 'Mixed' miRNA genes can be assigned to one of the above groups depending on the given splicing pattern. Unexpectedly, a large number of miRNAs are found in introns of protein-coding genes (90 out of 161 miRNAs) (Kim and Nam 2006).

Methods

This research presented electronic database , Medline, PubMed , SweetSereach , web of science ,an additional manual search using research word including the effect of covid 19 disease on the biomarker miRNA and therefore the relationship with gene expression . This article includes several study that said MiRNAs play very important roles in modulating the immune response during viral infections. MiRNAs can repress gene expression by targeting host cellular RNAs or viral RNAs during infection (Li et al. 2020). That's means there is a controversial aspect between covid 19 and miRNA.

Results

Despite the lack of experiments in this field, it indicated the clear impact of the coronavirus on this indicator, through which we can say ,This research examines the harmful effect of covid 19 on miRNA and therefore gene expression.

Discussion

As we mentioned above, the experiments in this field are few, so the results are limited to a narrow path according to the experiments, so from our study we found. MiRNAs play very important roles in modulating the immune response during viral infections. MiRNAs can repress gene expression by targeting host cellular RNAs or viral RNAs during infection.Furthermore, miRNAs have essential functions in a number of immune-related diseases. For example, mechanistically, aberrant expression of miRNAs can contribute to the Th17/Treg imbalance in immune thrombocytopenic purpura patients; this finding may offer clues regarding potential targets for novel treatments. The association between miRNAs and COVID-19 remains to be investigated. Our data suggest that miR-16-2-3p, miR-6501-5p, and miR-618 were more highly expressed in COVID-19 patients than in healthy controls and that miR-183-5p, miR-627-5p, and miR-144-3p were less expressed in COVID-19 patients than in healthy controls (Li et al. 2020).

Conclusion

Several studies have found that miRNA-618 differentially expressed, which was similar in our study, is related to dysregulation of immune function and thereforethe dysregulated expression of miRNAs in the COVID-19 patients (Li et al. 2020).

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