

A Review On: The Potential of Mirna- Based Therapeutics in Severe Acute Respiratory Syndrome Coronavirus 2 (Sars-Cov-2) Infection

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ABSTRACT

Since the WORLD HEALTH ORGANIZATION (WHO) declared COVID – 19, the disease caused by severe acute respiratory syndrome corona virus 2 (SARS- CoV-2), a disease that spread in world in March 2020, and more than 117 million people worldwide have been confirmed to have been infected. However no drug with high efficacy to treat SARS – CoV-2 infection has been approved. With the increase popularity scientists have explored the act of using small RNAs such as microRNAs (miRNAs) as therapeutics. As per World Health Organization on 11 February 2020 more than 43000 confirmed cases have been identified in 28 countries over world wide. SARS-CoV-2 spread by human- to- human transmission via droplet or direct contact. Among the confirmed cases most infected people where of ages 30-79 years and the percentage was 86.6%.

KEYWORDS: microRNA, SARS-CoV-2, RNAs, targeted therapy.

I. INTRODUCTION

The lockdown of Wuhan that was the heart in china has altered people everywhere the globe of a unique corona virus that was creating major public health on 23 Feb 2020. The current name given for novel virus was severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). On 27 Feb, approximately 47 Countries were infected by this virus over 82,294 infected with 2,804 death are recorded.

First MiRNAs patient was observed in phenotype variants of *Caenorhabditis elegant*; through some experimental approaches a negative regulatory element located at the 3'-UTR of the line 14 gene was found to be responsible for the observed abnormal morphology and it was that the element produced small RNA molecules. However the level of protein were not affected.

Typically Corona Virus present with respiratory symptoms. Some people do get infected but do not show any symptoms and the ones who get infected may have mild to moderate but self limiting diseases with symptoms similar to seasonal cold.

Symptoms may include:

- Respiratory symptoms
- Fever
- Sore throat
- Cough
- Shortness of breath
- Fatigue

A minority group of people will present with severe symptoms and will need to be hospitalized it is more often with pneumonia and in some cases the illness can include ARDS means Respiratory distress syndrome it's the condition during which fluid collects in the air sacs of the lungs.

ROLES OF MIRNAS IN VIRAL INFECTION

Immunity is a compound or complex process. During an immune several molecular pathway which include miRNAs have been known to moderate the process of inflammation primarily via immune cell modulation. Most pathogens or pyrogens such as viruses also encode miRNAs to encourage or promote their survival condition. Due to their small size, and excellent function flexibility miRNAs are capable to host miRNA co-modulation expression during infection. To ensure their survival viruses must replicate their genetic material by using the host cellular machinery. During this process unwanted transfer can occur between host miRNAs and the viral genome. However viruses can also mediated changes in cellular miRNAs prior of infection to create an advantageous environment for pathogenesis. In some studies it has suggested that the host miRNA

– viral genome interaction are beneficial for virus sustainability.

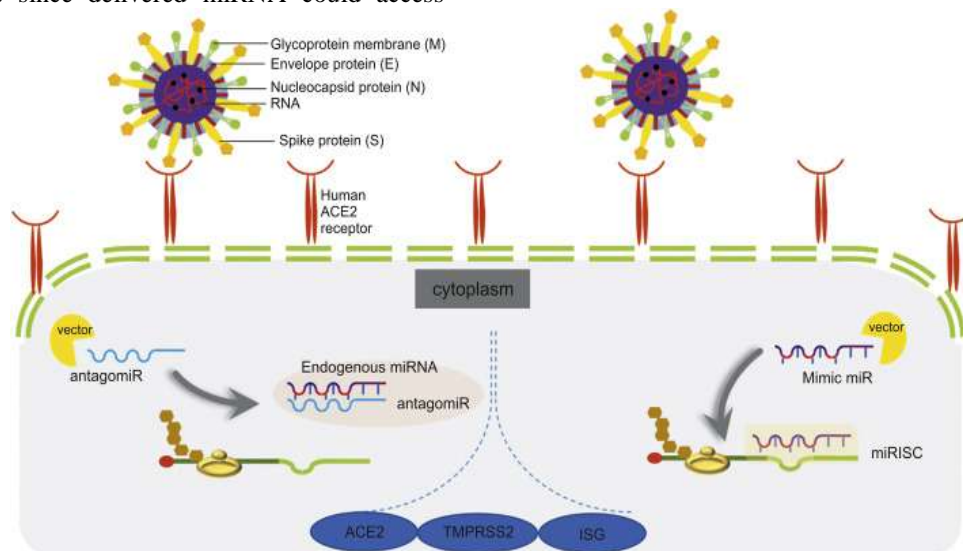
The Poxvirus that causes smallpox in human has been reported to facilitate the degradation of the host miRNA. Cell degradation after viral infection was also shown after miRNA from influenza gene coding region bound to the host miRNA. The increasing interest miRNA related studies is due to part to its role in resolve the mysteries of RNA and because they can be used as a tool to determine targets for alternative therapies for various diseases such as COVID-19 the disease caused by Severe Acute Respiratory Syndrome - Corona virus-2. The latest update from the SARS-CoV-2 has been spread to more than 200 countries and has affected over 65.8 million people out coming in almost 1.5 million deaths worldwide reported by WHO. SARS-CoV-2 which like SARS-CoV and Middle East Respiratory Syndrome Corona virus (MERS-CoV) belongs to family Coronaviridae but has the lower rates that the pervious viruses.

miRNA DELIVERY SYSTEM

Systemic miRNA delivery still noticeably challenges since delivered miRNA could access

many cytosolic mRNAs. In infection immunity acts as a double edged blade and it has been reported that miRNA may activate the innate immune response or even be rejected by cellular immunity. The physiological characteristic of miRNA such as their short half life makes them difficult to handle. Before a miRNA reaches its target it may be degraded and delivery of naked miRNA is impossible. Therefore each miRNA required to be conjugated to a unique vehicle. Sever deterrent points must be considered when constructing vectors for miRNA delivery including possible toxicity and formulation of the effective dose to maximize the potency of dose or bioavailability.

Recently well developed nanocarries based on organic, inorganic, lipid, or and liposome based, nanocrystal based and iron carbohydrate complex based nanocarries. Nanocarries are often chemically modified with peptide like antibodies, proteins, or small molecular to ensure high transfixion through cells. Possible toxicity and immunogenicity risk of viral vector, nanocarries may be the answer is reduced or minimized. Nucleic acid delivery systems usually require nanocarries or vector.



When do people infected with SARS-CoV infect others?

Knowing when an infected person can spread SARS-CoV-2 is just an important as how the virus spreads. WHO has recently published a scientific brief outlining what is known about when a person may be able to spread based on severity of their illness.

It is known that SARS-CoV-2 RNA can be detected in people 1-3 days before their

symptom onset .In duration of RT-PCR positivity appears to be 1-2 weeks for asymptomatic person and up to 1-2 weeks or more for the patients with mild to moderate diseases. It can be much severe in patients with COVID-19 diseases. The finding of viral RNA does not essentially mean that a person is transmittable and able to transmit the virus to a different person. The studies determine the using of viral culture of patients samples to assess the presence of infectious SARS-CoV-2 are currently

limited. The viable virus has been isolated from an asymptomatic case from patients with mild to moderated diseases up to 8-9 days after symptom onset and for longer from severely ill patients.

SIGNS AND SYMPTOMS OF PATIENTS INFECTED BY SARS-COV-2

Pneumonia which is now recast as Corona virus Diseases 2019 has general characteristic for SARS-CoV-2 patients. It had been indicated by computer tomographic (CT) scan or chest X-ray. China Novel Corona virus Investigation Research Team had reported that the three patients developed severe pneumonia and two of them showed common fever and cough. The study had exposed that the chest X-ray and CT-scan shows that 75% patients indicate bilateral pneumonia and 25% patients as unilateral pneumonia over 14% of the patients showed multiple mottling and ground-glass opacity. Ground-glass opacity is define as the radiological finding in computer tomography that is CT scan consisting of a hazy opacity that does not obscure the underlying bronchial structures or pulmonary vessels. On the 10 day of the illness the patients was detected by pneumonia.

It has been observed that one patient among the family failed to present the other common signs and symptoms of patients are fever and cough. Fatigue complaints are observed in approximately 96% of Patients. Analysis has been determine that the signs and symptoms of the reported cases found

that fever was observed around 90% in infected patients. The quantity of patients with cough is a smaller amount than 68% as compared to fever. In some patients shortness of breathing, muscle ache, headache, chest pain, nausea and vomiting were also observed. A common feature of patients of SARS, MERS or COVID-19 is observed that the presence of sever acute respiratory syndrome. However the estimated fatal accident rate of COVID-19 was 2.3% is much lower than SARS and MERS.

PREVENTING TRANSMISSION

The WHO suggests the following fundamental preventative measures to protect from corona virus, SARS-CoV 2

1. Perform hand cleanliness regularly with an alcohol-based hand sanitizer.
2. Avoid touching your eyes, nose and mouth.
3. Practice respiratory cleanliness by coughing or sneezing into a twisted elbow or tissue and then instantaneously disposing of the tissue.
4. Where a medical mask if you have respiratory symptoms and performing hand hygiene after disposing of the mask.
5. Approximately 2 meters social distance are maintain from individuals with respiratory symptoms.
6. If you have fever, cough, and difficulty breathing seek health care.



TESTING FOR SARS-COV-2 INFECTION

Many tests are used to detect SARS-CoV-2 and their performance characteristic varies:

1. Some tests carry outcome quickly that is within a minutes and others requires time for processing.
2. Some can be performed in laboratory by the skilled person, and some can be performed at the point-of-care.

3. Some tests can be performed persistently because they are cheap easier to use and supplies are quickly existing.
4. Some tests are extremely sensitive that is few false – negative outcome or few are missed finding of SARS-CoV-2 and by the ways others are very particular that is few- positive outcome or few tests wrongly identifying SARS-CoV-2 when the virus is absent, and some are both sensitive and particular.



TEST TYPES

Viral tests, including NAATs means Nucleic Acid Amplification Test. Nucleic acid is the genetic substance detector for NAAT's. NAAT's and antigen test are used as diagnostic tests to identify infection with SARS-CoV-2 and to inform an individual's medical care. Viral tests can also be used to screening test to trim down the spreading of SARS-CoV-2 by identifying affected human being who required dividing or isolated from others healthy persons.

For the diagnosing SARS-CoV-2 infection NAATs are high-sensitivity, high-specificity tests. NAATs detect one or more viral RNA ribonucleic acid genes and indicate a current infection or a recent infection but due to prolonged viral RNA detection is not always direct evidence for the presence of virus capable of replacing or being transmitted to others. Most NAATs need to be processed in a laboratory and the time for the outcome can vary to 1-3 days, but some NAATs are point of care tests with outcome are available in 15-45 minutes. NAATs can be performed on superior respiratory specimens such as

nasopharyngeal, nasal mid-turbinate, anterior nasal or saliva.

Antigen tests are immunoassays that diagnose the reality of a particular viral antigen. Antigens test normally have like specificity, but are less susceptible than NAATs. Most are cheap than NAATs and can be processed at the point of care with no outcome is available in minutes. Because of the antigen test it may be necessary to authenticate some antigen test out comes a negative test in person with symptoms or a positive test in person with no symptoms with a laboratory based NAAT.

CLINICAL CHARACTERISTICS

The fever, fatigue, and dry cough are typical medical symptoms are observed of SARS-CoV-2. Atypical medical symptoms it includes following symptoms such as expectoration, headache, hemoptysis, nausea, vomiting and diarrhea. Other symptom such as loss of smell and taste is also closely associated with SARS-CoV-2 infection. Some confirmed patients are asymptomatic or have low fever, mild fatigue, or other symptoms without presenting with

pneumonia and mostly patients recover after 1 week. 72.9% of lung damage by pneumonia was observed in X-ray chest examination. Which was mainly characterized by ground glass opacities that 68.5%. CT imaging that was analysis by patients showed that their distribution centered in the sub pleural and lobular zone with the two possible fused into a succeeding into bimodal diffuse opacities in severe cases. During the recovery period the margins of consolidation opacities contract the bronchi enlarge and sub pleural linear or fibrous opacities are main characteristic. The lung lesion in recovered pneumonia patients disappears totally on CT and there are no symptoms of fibrosis.

- Following are the hindrance and self-care on should take while suffering from SARS-CoV-2 contamination:
1. Separate yourself in a well ventilated room.
 2. Use a triple medical mask, throw away mask after 8 hours of use or earlier if they become wet or visibly soiled.
 3. If the caregiver toward the inside room, both caregiver and patient may consider using N95 mask.
 4. Take rest and drink a lot of fluids to uphold sufficient hydration
 5. Follow respiratory protocol at all the time.
 6. Regular hand washing with soap or water for at least 40 second or sanitary with alcohol based sanitizer.
 7. Make sure cleaning of exterior in the room that is touched often for example tabletop, doorknobs, handles, etc. with 1% hypochlorite solution.
 8. Check temperature every day.
 9. Check oxygen saturation with plus oximeter every day.
 10. In Contact with the medical doctor promptly if any deterioration of symptoms is noticed.

II. CONCLUSIONS

Understanding the role of miRNA in SARS-CoV-2 pathobiology has been a great interest. Although the overall mechanism of viral infection for SARS-CoV-2 has been well clarified based on those of the related viruses, SARS-CoV and MERS-CoV many question remain regarding the exact molecular signaling pathway involved. The ineffective drug available for the treatment at the instant is an emerging pathogen for SARS-CoV-2. It suffusion very quickly and might end in death of the infection patients. The rate of the

despite fatality was 2.3%. The emergence of huge number of infected patients without short period of time could out comes in the collapse of health care system and thus the mortality rate might be elevated. Adequately precautions must be provided to manage it from global spreading. For the development of vaccine and antiviral drug furthermore efforts should be made. In the further consideration intermediated host and molecular mechanism of its species should be spread. Legislation should be employed to ban the trade of untamed animals, the potential intermediated hosts of assorted viruses to stop the outbreak of this and other novel viruses in future.

REFERENCE

- [1]. Cui, J., Li, F, and Shi, Z. L. Origin and evolution of pathogenic corona viruses. *Nat. Rev. Microbiol.* 17, 181-192(2019).
- [2]. Zhu N, Zhang D, Wang W, et al; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020; 382(8):727-733.doi:10.1056/NEJMoa2001017.
- [3]. Aboobaker, A.A., and M. L. Blaxter. 2003. RNA interference to investigate gene function in the human filarial nematode parasite *Brugia malayi*. *Mol. Biochem. Parasitol.*129:41-51.
- [4]. Akhtar, A., D. Zinc, and P.B. Becker. 2000. Chromodomains are protein-RNA interaction modules. *Nature* 407:405.
- [5]. Liu J, Liao X , Qian S, Yuan J, Wang F, Liu Y, et al. Community Transmission of Severe Acute Respiratory Syndrome Coronavirus 2, Shenzhen, China,2020. *Emerg Infect Dis.* 2020;26; 1320-3.
- [6]. Ambros V, Horvitz HR. Heterochronic mutants of the nematode *Caenorhabditis elegans*. *Science.* 1984; 226:409-416.
- [7]. Wu, J., Leung, K, and Leung, G.M. Nowcasting and forecasting the potential the potential domestic and international and spread of the 2019-nCoV outbreak originating in Wuhan, China: a modeling study. *Lancet*395, 181-192(2019)
- [8]. Lee RC, Feinbaum RL, Ambros V. The *C. elegans* heterochronic gene *lin-4* encodes small RNAs with antisense complementarity to *lin-14*. *Cell.*1993; 75:843-854.

- [9]. Molyneaux K, Wylie C. Primordial germ cell migration. *Int J Dev Biol.*2004; 48(5-6):537-44. 10.1387//ijdb.041833km.
- [10]. Z. Bai, J. Wei, C. Yu, et al., Non-viral nanocarriers for intercellular delivery of microRNA therapeutics, *J. Mater. Chem, B.* 7 (2019) 1209-1225.
- [11]. V. Chaudhary, S. Jangra, N.R. Yadav, Nanotechnology based approaches for detection and delivery of microRNA in healthcare and crop protection, *J. Nanobiotechnology.* 16 (2018), 40.
- [12]. Drosten C, Gunther S, Preiser W, Van der Werf S, Brodt HR, Becker S. et al. Identification of a novel coronavirus in patients with severe acute respiratory syndrome. *N Engl J Med.* 2003; 348:1967-76.
- [13]. Sun, S. H. et al. A mouse model of SARS-CoV-2 infection and pathogenesis. *Cell host microbe* 28, 124-133.
- [14]. G. Tan, X. Tang, F. Tang, and The role of microRNAs in nasopharyngeal carcinoma, *Tumor Biol.* 36 (2014)69-79.
- [15]. D.W. Trobaugh, W.B. Klimstra, Micro RNA Regulation of RNA virus Replication and Pathogenesis, *Trends Mol. Med.* 23(2017)80-93.
- [16]. World Health Organization, Weekly epidemiological update -8 December 2020, <https://www.who.int/publication/m/item/weekly-epidemiological-update-8-december-2020>,
- [17]. K. Dhama, S. Khan, R. Tiwari, et al., Coronavirus Disease 2019-COVID19, *Clin. Microbiol, Rev.*33
- [18]. F.K. Yoshimoto, The Protein of Severe Acute Respiratory Syndrome Coronavirus-2, the Causes of COVID-19, *Protein J.* 39 (2020)198-216.
- [19]. S. Kannan, P.S.S. Ali, A. Sheeza, et al., COVID-19- recent trends, *Eur. Rev. Med. Pharmacol. Sci.*24 (2020) 2006-2011.
- [20]. S.O. Aftab, M.Z. Ghouri, M.U. Masood, et al., Analysis of SARS-CoV-2 RNA-dependent RNA polymerase as a potential therapeutic drug target using a computational approach, *J. Transl. Med.* 18 (2020).
- [21]. J. Paces, Z. Strizova, D. Smrz, et al., COVID-19 nad immune system, *Physiol. Res.* 69 (2020) 379-388.
- [22]. C. Liu, X. Yu, C. Gao, et al., Characterization of antibody responses to SARS-CoV-2 in convalescent COVID-19 patients, *J. Med. Virol.* (2020) 1-7.
- [23]. P.K. Mishra, R. Tandon, S.N. Byrareddy, Diabetes and COVID-19 risk; an miRNA perspective, *Am. J. Physiol,- Hear. Circ. Physiol.*319 H604-H609.
- [24]. Q. Liu, J. Du, X1. Yu, et al., MiRNA-200c- 3p is crucial in acute respiratory distress syndrome, *Cell Discov.* 3(2017) 1-7.
- [25]. J.T.-S. Chow, I. Salmena, Prediction and Analysis of SARS-CoV-2- Targeting microRNA in Human Lung Epithelium, *Genes (Basel).* 11(2020)1-12.