



microRNA-Based Vaccination and Treatment for COVID-19

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Abstract

Coronavirus disease (Coronavirus Disease 2019, COVID-19) is an emerging transmissible disease that was first reported in Wuhan, China, in December 2019 as beta coronavirus. As of April 9, 2020, about 1,569,849 confirmed cases have been documented globally with over 92,191 deaths. COVID-19 is communicated by inhalation or contact with respiratory droplets of infected individuals. Generally, COVID-19 is mild in most cases, even though it might worsen to pneumonia, acute respiratory distress syndrome (ARDS), and multi organ dysfunction in the elderly people. COVID-19 has become a global life-threatening disease. We propose a novel approach to control SARS-CoV-2 viral infection which is based on miRNA.

Keywords

SARS-CoV-2; Coronavirus; vaccine; Therapeutic treatment, rAAV

Introduction

Similar to SARS-CoV, COVID-19 uses the angiotensin-converting enzyme 2 (ACE2) as a cell entry receptor to enter the cells by endocytosis, while other CoVs such as MERS-CoV uses the dipeptidyl peptidase 4 (DPP4) host cell receptor as an entry point [1]. A recent molecular dynamics simulation revealed that compared to other CoVs (SARS-CoV and HCoV-NL63), the spike protein-ACE2 receptor interaction contains a higher number of contacts, a larger interface area, and decreased interface residue fluctuations in COVID-19 [2]. ACE2 plays a critical role in the renin angiotensin system (RAS), and the discrepancy of ACE/Ang II/AT1R and ACE2/Ang (1-7)/Mas receptor may lead to develop inflammatory response. In addition, elevated ACE and Ang II are bad prognosis for severe pneumonia [3]. Whether COVID-19 can attack neurological tissues expressing ACE2 still needs intensive research [4]. Currently there are little data on the availability of approved therapeutics option for the recently emerged COVID-19. This situation presses researchers over the globe to develop new vaccines or therapeutic molecules to combat this severe virus. For the sake of developing novel drugs, the COVID-19 main protease was made publicly available to facilitate attaining this goal.

miRNA MicroRNAs (miRNAs) are short non-coding RNA fragments involved in post-transcriptional regulation of gene expression [5-7]. In physiological conditions, miRNAs regulate a kaleidoscope of biological pathways including cell differentiation, proliferation and survival [8-10]. miRNA is a regulatory mechanism by which cells can eliminate undesired or malformed mRNA.

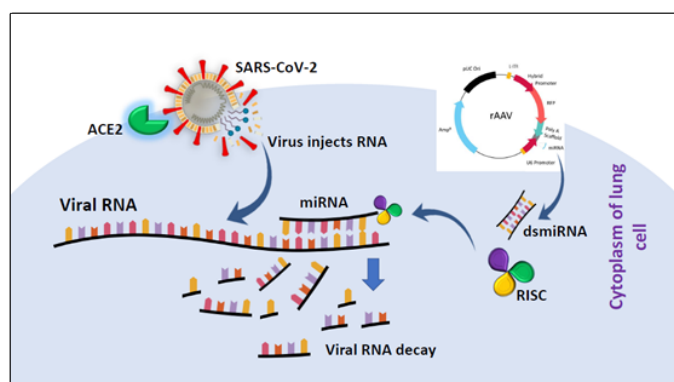


Figure 1: Graphical representation of the idea

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Based on this phenomenon, we propose that using *in vitro*-constructed miRNA specific to SARS-CoV-2 RNA genome will destroy the viral RNA and protect lung cells from being inflamed. Establishing a vaccine and/or therapeutic intervention for this virus is an international goal.

Discussion and Conclusion

Human adeno-associated virus (AAV) are a frequent cause of upper respiratory infections, and therefore, it can be used as delivery vehicles for several lung diseases. It has a single-stranded approximately 4.7kb genome. Recombinant AAV (rAAV) is constructed by replacing the viral cap and rep genes with the desired transgene along with promoter and polyadenylation sequences [11]. These rAAV are extensively characterized as molecular tools with a high safety profile. Generally, rAAV-mediated miRNA inhibition or overexpression of target mRNA provides a simple, efficient way to control the subsequent processing of such mRNA [12]. Long term expression of the cassette harbored by AAV has been reported in several studies on pigs [13], sheep [14], mice [15,16], and human [17,18].

We postulate constructing an AAV with an insert that encodes for miRNA (20-22 nt) specific to a conserved region of the SARS-CoV-19 genome in the 3' end. This region (about 10,000 kb) is encoding for the S, E, M, and N functional proteins of the virus. Specific miRNA(s) can be designed to attack one or all of these segments and, using the host cell's RISC machinery, the target sequence will be destroyed.

This approach enables us to design either a vaccine, with long term expression, or a therapeutic treatment that can be used for patients already contacted the infection. Furthermore, given this approach is successful, it could be employed to future RNA viral attacks (Figure 1).

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