The potential role of miRNAs in SARS-CoV-2 infection prognosis: an in-silico approach

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Objective:

Utilize existing data on the role of the non-coding genome to determine possible functional relationships between microRNAs, their target genes, and COVID-19.

Introduction:

SARS-CoV-2 is a novel coronavirus that is responsible for COVID-19. The infection results in a wide range of symptoms affecting the respiratory and cardiovascular systems that have been noted to differ across race, age, and sex. Because of the differing outcomes of infection between groups, it is critical that biomarkers are identified to determine the aggressiveness of the infection prior to the onset of clinical symptoms.

Single nucleotide polymorphisms (SNPs), which are genetic variations of a single nucleotide amongst people, have been associated with the prognosis of COVID-19 infection. Evidence of SNPs, mostly part of non-coding genome, having an impact on the progression and outcome of COVID-19 infections[1], suggests that they may be involved in the regulation of the expression of genes controlling critical biological functions of physiological responses to viral infections.

MicroRNAs (miRNAs) are short non-coding RNAs involved in the post-transcriptional gene regulation by binding to target mRNA sequences and effectively silencing gene expression. They are involved in the regulation of gene controlling many biological functions including immune responses. MiRNAs can be easily detected and quantified in the blood; therefore they can works as circulating biomarkers[2], including COVID-19.

HYPOTHESIS

We hypothesized that SNPs from genomic regions linked to COVID-19 aggressivity contains microRNAs that can be used as early biomarkers (through their expression) for the evolution of the disease.

Methods:

PubMed searches using "SNP" and "COVID-19" revealed X papers on the significance of specific SNPs on the prognosis of patients with COVID-19. The positions of the collected SNPs were compared to the positions of human miRNAs from miRBase using the hg38 reference genome. SNPs were assigned to a miRNA if less than 100 kb or 1Mb away from the start of the miRNA sequence (**Figure 1**). MiRNA target genes were identified using miRWalk 2.0, miRTarBase, miRecords, and Tarbase V8. These targets were compared across miRNAs to identify similarities using RStudio, an open source software for statistical analysis.
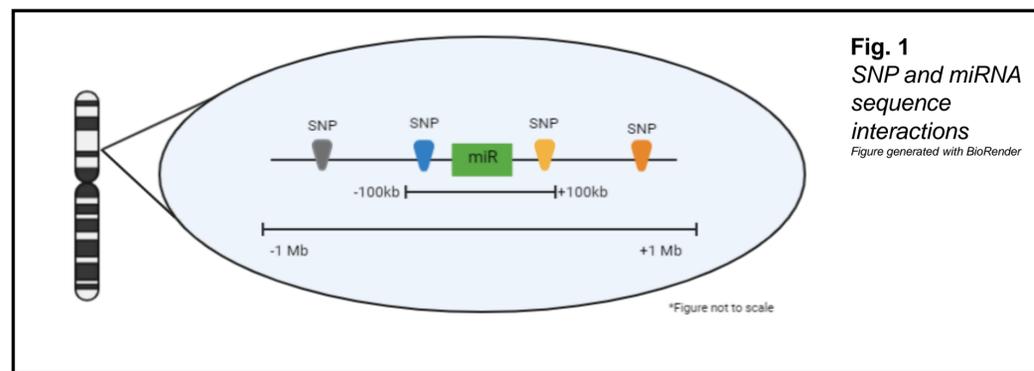

Fig. 1
SNP and miRNA sequence interactions
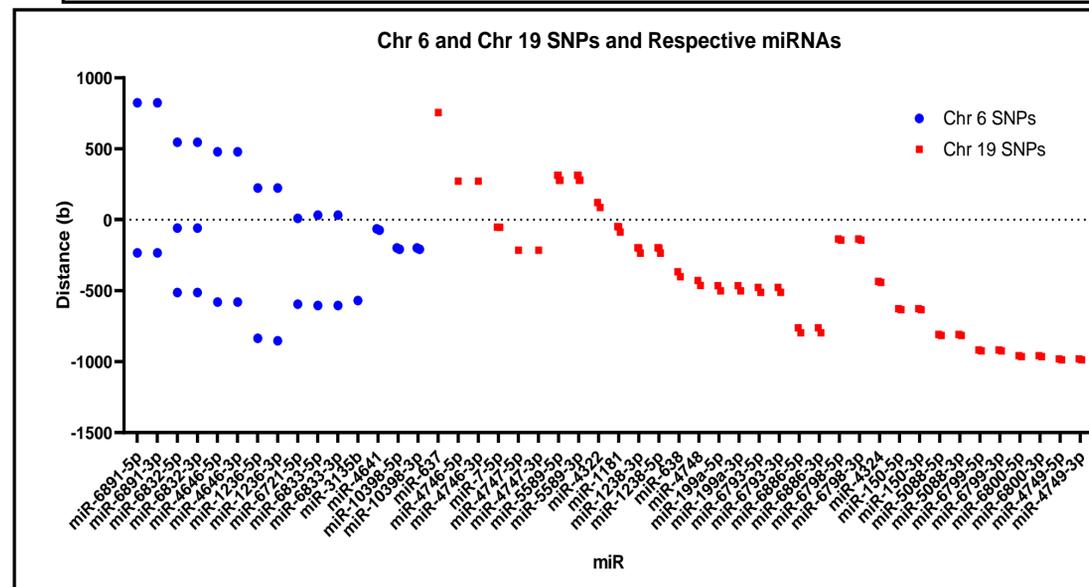Figure generated with BioRender

Fig. 2: *The distance of SNPs from the start position of miRNAs. The start of a miRNA is denoted as 0 b.*
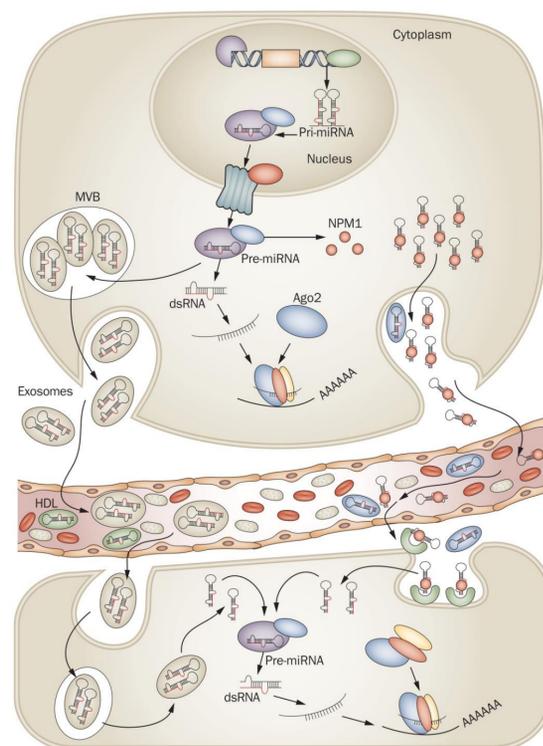

Fig 3. In the process of miRNA maturation, miRNA sequences go through processing in the nucleus and transported in the cytoplasm. From there, mature miRNAs can be excreted from the cell through exosomes into the extracellular environment (serum, plasma, etc.). The concentration of miRNAs in these environments can be measured and quantified utilizing amplification techniques.

From reference 8.

Results:

Final results are pending. Preliminary results revealed 115 human miRNAs in close proximity to the studied SNPs with notable clusters in chromosomes 6 and 19 (**Figure 2**).

For these miRNAs we are now analyzing the known target messenger RNAs and identify common signaling pathway. We expect to discover an enrichment in immune related signaling targets.

Conclusions:

The confirmed target genes for the identified miRNAs will be studied using available databases to identify their biological significance and possible relation to COVID-19. A target gene's biological significance and possible relation to COVID-19 will be defined as having involvement in lung structure and function, cardiopulmonary function, immune response, and cytokine release. In order to confidently determine whether or not the miRNAs could serve as potential biomarkers for the prognosis and severity of COVID-19 infection, further wet-lab analysis of the miRNA concentrations in control, surviving patient, and deceased patient plasma samples is required. Plasma samples are key samples for miRNA analysis because miRNAs can be released into the bloodstream through exosomes, where miRNAs can be transported to other cells as shown by Cortez et al's diagram[8] (**Figure 3**). A statistically significant difference between the concentrations of miRNAs in control, surviving patient, and deceased patient samples would be considered evidence to support the classification of a microRNA as a biomarker for SARS-CoV-2 infection prognosis.

References

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