Spike protein amino acid variants increased miRNA binding and hence reduced virulence of SARS-CoV-2 in Jordan, Middle East

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Abstract

Initial epidemiological studies inform the central COVID-19 disease prophet. Some papers have been studying miRNA and viral RNA interaction target predictions over the past few years. In this work, via the miRDB database, we determined the target scores of predicted miRNA to bind with the ss-RNA of SARS-CoV-2 in general and spike gene in specific. Our predicted miRNA targets of the ss-RNA of SARS-CoV-2 might destabilize and hence inhibit the ss-RNA translation of SARS-CoV-2 and prevent viral replication that has been established by more than 80% of asymptomatic infected cases in Jordan due to host miRNA interactions. In respiratory epithelial cells, the high scoring miRNAs prediction covers the RNA from 5' to 3' that explain successful antiviral defenses against ss-RNA of SARS-CoV-2 and lead to new nucleotide deletion mechanisms. The exciting finding here that the substitution 1841A>G at the viral genomic RNA level or the D614G at spike protein level showed a change in the predicted miRNA sequence and an increase in the target score (from 91 to 92) (hsa-miR-4793-5p to hsa-miR-3620-3p).

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused an outbreak in Wuhan city and characterized as a pandemic by the World Health Organization WHO [1]. The first case of SARS-CoV-2 was reported to the Jordanian Ministry of Health on March 2, 2020, for a Jordanian citizen who was in Italy. To the date of this report, there are 522 confirmed cases, 387 recovered and nine deaths of COVID-19 in Jordan, according to the Jordanian Ministry of Health official via its web site launched as a unified source of information about the preventive measurements and symptoms of corona virus-2019 (<https://corona.moh.gov.jo/en>).

In addition, 18 years ago, severe coronavirus acute breathing syndrome (SARS-CoV) appeared in China. It has spread to over 30 countries, infecting around 8,000 people, killing young people 10%, and aging 50%. No SARS CoV or other up-and-coming CoV vaccines or antivirals such as Middle East respiratory CoV (MERS-CoV) are approved to date [2]. The molecular mechanisms of viral pathogenesis will provide thoughtful help in the search for effective and secure therapeutic strategies against new and well-known human CoVs.

MicroRNAs (miRNAs) are non-coding RNAs that control many function targets within a cell by controlling protein levels through binding to mRNA translation process or mRNA abundance. Many evidence shows that miRNAs contain the RNA virus replication and pathogenesis through direct binding to the RNA virus-mediated and changes in the host transcriptome. Proof of host miRNAs can bind to a wide-ranging of RNA viruses, straight adaptable their pathogenesis through mimics' cellular mRNAs tolerating direct binding of the miRNA to the viral RNA. Theoretically, the regulation is analogous to that of host mRNAs [3,4].

Many miRNA targeted in Influenza viral RNA segments were linked with the activity of host miRNA-induced antiviral defense. This represents potential Treatment with a combination of the five miRNAs through agomir delivery to suppressed viral replication and effectively improved protection against lethal challenge with PR8 in mice [5].

In previous study, severe acute coronavirus syndrome (SARS-CoV) causes human fatal disease and reaction and extensive pulmonary disease. The significance of small non-coding RNAs for SARS-CoV pathologies, sequenced lung RNAs of infected mouse, and three 18 to 22nt small viral RNAs (svRNAs), were discovered. The three svRNAs originated from the SARS-CoV genomic regions nsp3 (svRNA-nsp3.1 and -nsp3.2), and N (svRNA-N). CoV svRNAs were autonomous, cell type and host species from RNase III; but the extent of viral replication was dependent. In vivo lung pathology and pro-inflammatory cytokine release, antagomir-mediated inhibition of svRNA-N significantly decreased. This indicates that SvRNAs contribute to the pathogenesis of SARS-CoV and demonstrates the potential for antagomers of svRNA-N as antivirals [6].

To understand the early steps of COVID-19 infection, we predicted miRNAs targeting the submitted 29903 bp ss-RNA of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 sequence), the isolate of Wuhan-Hu-1, complete genome. A predicted miRNAs targeting region at 3822 bp ss-RNA of the spike glycoprotein of SARS-CoV-2 was revealed. Also, we predicted miRNAs targeting a variable region of the ss-RNA spike glycoprotein of SARS-CoV-2 sequences from 20 positive nasopharyngeal specimens. These specimens were collected in Jordan and sequenced by Biolab Diagnostic Laboratories (Jordan) & Andersen lab at Scripps Research (USA), who deposited the sequences in GISAID, a maintained global database based in Germany. The perception in this work might help scientists to understand the molecular mechanisms of viral pathogenesis. In addition, it might support the research for effective, safe therapeutic strategies against known human CoVs and new emergent strains with a focus on miRNA-induced antiviral human body defense, which could be a potential treatment development for SARS-CoV-2.

Methods

The miRDB is an online <http://mirdb.org/custom.html> database for the target and working annotations of miRNA. All targets in miRDB were anticipated by MirTarget, a bioinformatics tool that was developed through the study of thousands of miRNA target interactions from high-performance research [7,8]. Using <http://biomodel.uah.es/en/lab/cybertory/analysis/trans.htm> to convert sequences from miRNA to DNA to demonstrate genome sequence alignment using ChromosPros Version 2.1.9. Wuhan-Hu-1, full NC 045512.2 accession genome sequence number and MIRNAs targeting area 3822 bp ss-RNA-spike SARS-CoV-2 Spike. We predicted miRNA targets 29903 bp ss-RNA (SARS-CoV-2 sequence) isolate Wuhan-Hu-1. In addition, miRNAs are predicted to target region on the SARS-CoV-2 sequence Accession no YP 009724390 ss-RNA spike glycoprotein variability from Jordanian positive nasopharyngeal specimens sequenced by Biolab Diagnostic Laboratories (Jordan) & Andersen lab at Scripps Research (USA) who published sequences retrieved from GISAID (<https://corona.moh.gov.jo/en>) (<https://gisaid.org>).

Results And Discussion

We predicted top ten score miRNAs targeting between (98-99) the submitted 29903 bp ss-RNA SARS-CoV-2 genome, accession number NC_045512.2, correspondingly, hsa-miR-4288, hsa-miR-195-5p, hsa-miR-16-5p, hsa-miR-15b-5p, hsa-miR-15a-5p, hsa-miR-6838-5p, hsa-miR-497-5p, hsa-miR-424-5p, hsa-miR-3133, hsa-miR-21-3p Table 1. These miRNAs are presented in miRDB, along with associated function annotations. As a recent update, miRDB displays expressions of hundreds of cell lines, and the user may limit their search for the cell line of interest miRNA targets. miRDB offers an integrative analysis of the target prediction and gene ontological data found in Tables 2,3,4,5,6,7,8,9,10 and 11, to promote the prediction of miRNA functions. In addition, we predicted only three miRNAs (hsa-miR-510-3p, hsa-miR-624-5p, hsa-miR-497-5p) with targeting scores of (92, 90 and 84) respectively for the submitted 3822 bp of the ss-RNA spike glycoprotein of SARS-CoV-2 sequence of Wuhan-Hu-1 (from the complete genome NCBI reference sequence: NC_045512.2 Region: 21563-25384) as shown in Table 13. These miRNAs, as well as associated functional annotations, presented in miRDB presents the expression profiles of hundreds of cell lines. To facilitate the prediction of miRNA functions, miRDB offers for integrative analysis of target prediction and Gene Ontology data found in Tables 14 and 15.

Moreover, in our study here we predicted the score of miRNAs targeting regions on many ss-RNA spike glycoprotein of SARS-CoV-2 sequence from Jordanian samples with amino acid substitutions (NCBI Reference Sequence: NC_045512.2 region: 21563-25384 and Nomenclature sequence, Amino Acid Variant (SAV) and annotation used the accession number YP_009724390.1).

The original sequence of the del 432TTA, and the del Y144 have the same miRNA with a target score of 91. The original 1841A target miRNA score (91, 64 and 56) for (hsa-miR-4793-5p, hsa-miR-143-5p and hsa-miR-3133) respectively. The interesting finding here that the 1841A>G, and D614G showed a change in the predicted miRNA and an increase in the target score (from 91 to 92) (hsa-miR-4793-5p to hsa-miR-3620-3p). However, the original and 3415G>T D1139Y showed the same sequence of the miRNA (hsa-miR-548g-3p) and an increase in the target score of 80 to 81. The last substitution of 3499 G>A G1167S showed the same the miRNA sequence of (hsa-miR-155-5p) and a decrease in the target score from 73 to 72. One of the record genomic changes observed in the severe acute respiratory syndrome coronavirus (SARS-CoV-1) isolated from humans after transmission human to human was the acquisition of a specific 29-nucleotide deletion occurred in open reading frame 8 (ORF8). Three top target score of miRNAs prediction (hsa-miR-497-5p, hsa-miR-195-5p and hsa-miR-21-3p) showed on Table 12, 16 and 24 have an expression in the respiratory epithelial cells and effective antiviral defenses against the ss-RNA of SARS-CoV-2 and lead to new mechanisms interaction binding miRNA and SARS-CoV-2 of nucleotide deletion [5-6]& [9].

Conclusion

Over the past few years, some articles studied the target prediction of miRNA and viral RNA interaction. In our predictions, more than 80% asymptomatic of the disease raised due to the host miRNA interactions, which have identified the target where the genome replication of the ss-RNA of SARS-CoV-2 has changed to inhibit the translation of the ss-RNA and hence preventing viral replication and stabilization by subsequent generations. The top target score of miRNAs prediction cover from 5' to 3' in the respiratory epithelial cells that might be the reason for an effective antiviral defense against the ss-RNA of SARS-CoV-2 and lead to new mechanisms of nucleotide deletion in the coding region of a protein. The miRNAs found in all tissues have target gene functions, which lead to an identification of novel cellular pathways to block RNA viral replication or even host cell-specific targeting the regulation for the ss-RNA of SARS-CoV-2.

Tables

Table 1: Predicted miRNAs targeting the submitted 29903 bp ss-RNA SARS-COV-2 genome, accession number NC_045512.2

Top of Form		
Bottom of Form		
Target Rank	Target Score	miRNA Name
1	99	hsa-miR-4288
2	99	hsa-miR-195-5p
3	99	hsa-miR-16-5p
4	99	hsa-miR-15b-5p
5	99	hsa-miR-15a-5p
6	99	hsa-miR-6838-5p
7	98	hsa-miR-497-5p
8	98	hsa-miR-424-5p
9	98	hsa-miR-3133
10	98	hsa-miR-21-3p

Table 2: Predicted targets function for hsa-miR-4288 on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	97	hsa-miR-4288	UIMC1	ubiquitin interaction motif containing 1
2	97	hsa-miR-4288	CC2D1A	coiled-coil and C2 domain containing 1A
3	96	hsa-miR-4288	ING3	inhibitor of growth family member 3
4	96	hsa-miR-4288	KCMF1	potassium channel modulatory factor 1
5	96	hsa-miR-4288	CAPZB	capping actin protein of muscle Z-line subunit beta
6	96	hsa-miR-4288	BCL11A	BCL11A, BAF complex component
7	96	hsa-miR-4288	AMELX	amelogenin X-linked
8	96	hsa-miR-4288	NTM	neurotrimin
9	95	hsa-miR-4288	LRRC4C	leucine rich repeat containing 4C
10	95	hsa-miR-4288	PSIP1	PC4 and SFRS1 interacting protein 1

Table 3: Predicted targets function for hsa-miR-195-5p on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-195-5p	PAPPA	pappalysin 1
2	100	hsa-miR-195-5p	FASN	fatty acid synthase
3	100	hsa-miR-195-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-195-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-195-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-195-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-195-5p	PHF19	PHD finger protein 19
8	100	hsa-miR-195-5p	DES1I	desumoylating isopeptidase 1
9	99	hsa-miR-195-5p	UBE2Q1	ubiquitin conjugating enzyme E2 Q1
10	99	hsa-miR-195-5p	LSM11	LSM11, U7 small nuclear RNA associated

Table 4: Predicted targets function for hsa-miR-16-5p on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-16-5p	PAPPA	pappalysin 1
2	100	hsa-miR-16-5p	FASN	fatty acid synthase
3	100	hsa-miR-16-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-16-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-16-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-16-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-16-5p	PHF19	PHD finger protein 19
8	100	hsa-miR-16-5p	DES1I	desumoylating isopeptidase 1
9	99	hsa-miR-16-5p	UBE2Q1	ubiquitin conjugating enzyme E2 Q1
10	99	hsa-miR-16-5p	LSM11	LSM11, U7 small nuclear RNA associated

Table 5: Predicted targets function for hsa-miR-15b-5p on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-15b-5p	PAPPA	pappalysin 1
2	100	hsa-miR-15b-5p	FASN	fatty acid synthase
3	100	hsa-miR-15b-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-15b-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-15b-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-15b-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-15b-5p	PHF19	PHD finger protein 19
8	100	hsa-miR-15b-5p	DESI1	desumoylating isopeptidase 1
9	99	hsa-miR-15b-5p	UBE2Q1	ubiquitin conjugating enzyme E2 Q1
10	99	hsa-miR-15b-5p	LSM11	LSM11, U7 small nuclear RNA associated

Table 6: Predicted targets function for hsa-miR-15a-5p on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-15a-5p	PAPPA	pappalysin 1
2	100	hsa-miR-15a-5p	FASN	fatty acid synthase
3	100	hsa-miR-15a-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-15a-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-15a-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-15a-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-15a-5p	PHF19	PHD finger protein 19
8	100	hsa-miR-15a-5p	DESI1	desumoylating isopeptidase 1
9	99	hsa-miR-15a-5p	UBE2Q1	ubiquitin conjugating enzyme E2 Q1
10	99	hsa-miR-15a-5p	LSM11	LSM11, U7 small nuclear RNA associated

Table 7: Predicted targets function for hsa-miR-6838-5p on 29903 bp ss-RNA SARS-COV-2 genome

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-6838-5p	PAPPA	pappalysin 1
2	100	hsa-miR-6838-5p	FASN	fatty acid synthase
3	100	hsa-miR-6838-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-6838-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-6838-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-6838-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-6838-5p	PHF19	PHD finger protein 19
8	99	hsa-miR-6838-5p	UBE2Q1	ubiquitin-conjugating enzyme E2 Q1
9	99	hsa-miR-6838-5p	LSM11	LSM11, U7 small nuclear RNA associated
10	99	hsa-miR-6838-5p	ANKUB1	ankyrin repeat and ubiquitin domain containing 1

Table 8: Predicted targets function for hsa-miR-497-5p on 29903 bp ss-RNA SARS-COV-2 genome.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-497-5p	PAPPA	pappalysin 1
2	100	hsa-miR-497-5p	FASN	fatty acid synthase
3	100	hsa-miR-497-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-497-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-497-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-497-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-497-5p	PHF19	PHD finger protein 19
8	99	hsa-miR-497-5p	UBE2Q1	ubiquitin conjugating enzyme E2 Q1
9	99	hsa-miR-497-5p	LSM11	LSM11, U7 small nuclear RNA associated
10	99	hsa-miR-497-5p	ANKUB1	ankyrin repeat and ubiquitin domain containing 1

Table 9: Predicted targets function for hsa-miR-424-5p on 29903 bp ss-RNA SARS-COV-2 genome.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-424-5p	PAPPA	pappalysin 1
2	100	hsa-miR-424-5p	FASN	fatty acid synthase
3	100	hsa-miR-424-5p	UNC80	unc-80 homolog, NALCN channel complex subunit
4	100	hsa-miR-424-5p	FGF2	fibroblast growth factor 2
5	100	hsa-miR-424-5p	TNRC6B	trinucleotide repeat containing 6B
6	100	hsa-miR-424-5p	PTPN4	protein tyrosine phosphatase, non-receptor type 4
7	100	hsa-miR-424-5p	PHF19	PHD finger protein 19
8	99	hsa-miR-424-5p	UBE2Q1	ubiquitin-conjugating enzyme E2 Q1
9	99	hsa-miR-424-5p	LSM11	LSM11, U7 small nuclear RNA associated
10	99	hsa-miR-424-5p	ANKUB1	ankyrin repeat and ubiquitin domain containing 1

Table 10: Predicted targets function for hsa-miR-3133 on 29903 bp ss-RNA SARS-COV-2 genome.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-3133	HOOK3	hook microtubule tethering protein 3
2	100	hsa-miR-3133	RIMS2	regulating synaptic membrane exocytosis 2
3	100	hsa-miR-3133	TGFBRAP1	transforming growth factor-beta receptor-associated protein 1
4	99	hsa-miR-3133	RPRD1A	regulation of nuclear pre-mRNA domain-containing 1A
5	99	hsa-miR-3133	TFAP2B	transcription factor AP-2 beta
6	99	hsa-miR-3133	PTPRK	protein tyrosine phosphatase, receptor type K
7	99	hsa-miR-3133	MAP2	microtubule-associated protein 2
8	99	hsa-miR-3133	NRF1	nuclear respiratory factor 1
9	99	hsa-miR-3133	KAT6A	lysine acetyltransferase 6A
10	99	hsa-miR-3133	URI1	URI1, prefoldin like chaperone

Table 11: Predicted targets function for hsa-miR-21-3p on 29903 bp ss-RNA SARS-COV-2 genome.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	99	hsa-miR-21-3p	STK38L	serine/threonine kinase 38 like
2	98	hsa-miR-21-3p	PCDH19	protocadherin 19
3	96	hsa-miR-21-3p	LAMP1	lysosomal associated membrane protein 1
4	96	hsa-miR-21-3p	GRIA2	glutamate ionotropic receptor AMPA type subunit 2
5	96	hsa-miR-21-3p	TOGARAM1	TOG array regulator of axonemal microtubules 1
6	96	hsa-miR-21-3p	ATP1B1	ATPase Na ⁺ /K ⁺ transporting subunit beta 1
7	96	hsa-miR-21-3p	TSC22D2	TSC22 domain family member 2
8	96	hsa-miR-21-3p	NAP1L5	nucleosome assembly protein 1 like 5
9	95	hsa-miR-21-3p	UBE4B	ubiquitination factor E4B
10	95	hsa-miR-21-3p	ZNF326	zinc finger protein 326

Table 12: Predicted miRNAs targeting region on 29903 nt SARS-COV-2 complete genome

Severe acute respiratory syndrome coronavirus 2 (SARS-COV-2 sequence) isolate Wuhan-Hu-1, complete genome NCBI Reference Sequence: NC_045512.2	miRNAs targeting the submitted 29903 nt SARS-COV-2 complete genome
181 ttctgcaggc tgcttacggt ttctccgtg ttgcagccga tcatcagcac atctaggttt 241 cgtccgggtg tgaccgaag gtaagatgga gagcctgtc cctggttca acgagaaac	<div>miRNA Name hsa-miR-15b-5p</div> <div>Previous Name hsa-miR-15b</div> <div>miRNA Sequence 5' - uagcagcacaucaugguuaca - 3' (length = 22)</div> <div>miRNA Name hsa-miR-497-5p</div> <div>Previous Name hsa-miR-497</div> <div>miRNA Sequence 5' - cagcagcacacuguguuugu - 3' (length = 21)</div>
4441 tgtggaact aaagcatag ttcaactat acagcgtaaa tataagggtta ttaaatata	<div>miRNA Name hsa-miR-16-5p</div> <div>Previous Name hsa-miR-16</div> <div>miRNA Sequence 5' - uagcagcacguaaaauuggcg - 3' (length = 22)</div>
6361 cgcgcaggga atggataatc ttgcctgcga agatctaaaa ccagtctctg aagaagtagt 6421 ggaaatcct accatacaga aagacgttct tgagtgtaat gtgaaaacta ccgaagtgt	<div>miRNA Name hsa-miR-6838-5p</div> <div>miRNA Sequence 5' - aagcagcaguggaagaccuccu - 3' (length = 22)</div>
8821 attgattgct gcagtcataa caagagaagt gggttttgtc gtgcctgggt tgcttgccac	<div>miRNA Name hsa-miR-4288</div> <div>miRNA Sequence 5' - uugucugcugaguuucc - 3' (length = 17)</div>
12421 aagagatggt tgtgtccct tgaacataat acctcttaca acagcagcca aactaatggt 12481 tgtcatacca gactataaca catataaaaa tacgtgtgat ggtacaacat ttacttatgc	<div>miRNA Name hsa-miR-497-5p</div> <div>Previous Name hsa-miR-497</div> <div>miRNA Sequence 5' - cagcagcacacuguguuugu - 3' (length = 21)</div>
14221 ttaacaaagc cttacattaa gtgggatttg taaatatg acttcacgga agagaggta 14281 aaactcttg accgttattt taaatttgg gatcagacat accacccaaa ttgtttaac	<div>miRNA Name hsa-miR-15a-5p</div> <div>Previous Name hsa-miR-15a</div> <div>miRNA Sequence 5' - uagcagcacauaugguuugug - 3' (length = 22)</div>
20161 aaagtgtatg gtgtgtgcc acaattacct gaaacttact ttactcagag tagaaattha 20221 caagaattha aaccaggag tcaaatggaa attgatttct tagaattagc tatggatgaa	<div>miRNA Name hsa-miR-3133</div> <div>miRNA Sequence 5' - uaaagaacucuuaaaacccaa - 3' (length = 22)</div>
21301 ccacgcgaac aaatagatgg ttatgtcatg catgcaaat acatatittg gaggaatata	<div>miRNA Name hsa-miR-424-5p</div> <div>Previous Name hsa-miR-424</div> <div>miRNA Sequence 5' - cagcagcaauucauguuugaa - 3' (length = 22)</div>
24841 tgtcttgggt tcaaatggca cacactggtt tgtaacacaa aggaatttt atgaaccaca	<div>miRNA Name hsa-miR-497-5p</div> <div>Previous Name hsa-miR-497</div> <div>miRNA Sequence 5' - cagcagcacacuguguuugu - 3' (length = 21)</div>
28501 caatagcagt ccagatgacc aaattggcta ctaccgaaga gctaccagac gaattcgtgg	<div>miRNA Name hsa-miR-195-5p</div> <div>Previous Name hsa-miR-195</div> <div>miRNA Sequence 5' - uagcagcacagaaaauuggc - 3' (length = 21)</div>
29521 aactcaggcc taaactcatg cagaccacac aaggcagatg ggctatataa acgttttcgc	<div>miRNA Name hsa-miR-21-3p</div> <div>Previous Name hsa-miR-21*</div> <div>miRNA Sequence 5' - caacaccagucgaugggcugu - 3' (length = 21)</div>

Table 13: Predicted miRNAs targeting the submitted 3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence, accession number NC_045512.2 REGION: 21563-25384.

Target Rank	Target Score	miRNA Name
1	92	hsa-miR-510-3p
2	90	hsa-miR-624-5p
14	84	hsa-miR-497-5p

Table 14: Predicted targets function for hsa-miR-510-3p on 3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence, accession number NC_045512.2 REGION: 21563-25384.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	100	hsa-miR-510-3p	CNOT6	CCR4-NOT transcription complex subunit 6
2	99	hsa-miR-510-3p	NEXMIF	neurite extension and migration factor
3	99	hsa-miR-510-3p	RBMS3	RNA binding motif single stranded interacting protein 3
4	99	hsa-miR-510-3p	DENND6A	DENN domain containing 6A
5	99	hsa-miR-510-3p	SNAP91	synaptosome associated protein 91
6	99	hsa-miR-510-3p	BCLAF1	BCL2 associated transcription factor 1
7	99	hsa-miR-510-3p	LATS2	large tumor suppressor kinase 2
8	99	hsa-miR-510-3p	ELOVL7	ELOVL fatty acid elongase 7
9	98	hsa-miR-510-3p	ZFXH3	zinc finger homeobox 3
10	98	hsa-miR-510-3p	FMR1	fragile X mental retardation 1

Table 15: Predicted targets function for hsa-miR-624-5p on 3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence, accession number NC_045512.2 REGION: 21563-25384.

Target Rank	Target Score	miRNA Name	Gene Symbol	Gene Description
1	96	hsa-miR-624-5p	ARL4A	ADP ribosylation factor like GTPase 4A
2	96	hsa-miR-624-5p	SOWAHC	sosondowah ankyrin repeat domain family member C
3	95	hsa-miR-624-5p	SYT1	synaptotagmin 1
4	95	hsa-miR-624-5p	CLOCK	clock circadian regulator
5	95	hsa-miR-624-5p	STK38	serine/threonine kinase 38
6	95	hsa-miR-624-5p	LCP1	lymphocyte cytosolic protein 1
7	95	hsa-miR-624-5p	ZNF800	zinc finger protein 800
8	95	hsa-miR-624-5p	DOCK11	dedicator of cytokinesis 11
9	94	hsa-miR-624-5p	UAP1	UDP-N-acetylglucosamine pyrophosphorylase 1
10	94	hsa-miR-624-5p	NFKBIA	NFKB inhibitor alpha

Table 16: Predicted miRNAs targeting region on 3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence

3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence isolate Wuhan-Hu-1, complete genome NCBI Reference Sequence: NC_045512.2	miRNAs targeting the submitted 3822 bp ss-RNA spike glycoprotein of SARS-COV-2 sequence
1 atgtttgttt ttctgtttt atfgccacta gtcctagtc agtgtgttaa tcttacaacc	miRNA Name hsa-miR-624-5p Previous Name hsa-miR-624;hsa-miR-624* miRNA Sequence 5' - uaguaccaguaccuuguguuca - 3' (length = 22)
2821 acagcaagtg cacttggaac acttcaagat gtggtcaacc aaaatgcaca agctttaaac	miRNA Name hsa-miR-510-3p miRNA Sequence 5' - auugaaacuccuaagagugga - 3' (length = 21)
3241 attgtcatg atggaaaagc acactttcct cgtgaagtg tctttgttc aaatggcaca 3301 cactggtttg taacacaaag gaattttat gaaccacaaa tcattactac agacaacaca	miRNA Name hsa-miR-497-5p Previous Name hsa-miR-497 miRNA Sequence 5' - cagcagcacacugugguuguu - 3' (length = 21)
3661 atagctggct tgattgcat agtaatgggtg acaattatgc ttgtctgtat gaccagttgc 3721 tgtagttgtc tcaaggcctg ttgtcttgtt ggatcctgct gcaaatttga tgaagacgac	miRNA Name hsa-miR-624-5p Previous Name hsa-miR-624;hsa-miR-624* miRNA Sequence 5' - uaguaccaguaccuuguguuca - 3' (length = 22)

Table 17: Original and del 432 TTAdel. Y144 have the same miRNA and target score

Target Rank	Target Score	miRNA Name
1	91	hsa-miR-196a-1-3p

Table 18: Original 1841 A target miRNA score

Target Rank	Target Score	miRNA Name
1	91	hsa-miR-4793-5p
2	64	hsa-miR-143-5p
3	56	hsa-miR-3133

Table 19: 1841A>G D614G showed a change in the sequence of the miRNA and increase in the target score from 90 to 91 on variable ss-RNA spike glycoprotein of SARS-COV-2 sequence from Jordanian samples

Target Rank	Target Score	miRNA Name
1	92	hsa-miR-3620-3p
2	55	hsa-miR-3133
3	54	hsa-miR-21-3p

Table 20: Original 3415G target miRNA score

Target Rank	Target Score	miRNA Name
1	80	hsa-miR-548g-3p
2	72	hsa-miR-627-5p
3	61	hsa-miR-506-5p

Table 21: 3415G>T D1139Y show same the miRNA and increase the target score 80 to 81 on variation ss-RNA spike glycoprotein of SARS-COV-2 sequence from Jordanian samples

Target Rank	Target Score	miRNA Name
1	81	hsa-miR-548g-3p
2	72	hsa-miR-627-5p
3	61	hsa-miR-506-5p

Table 22: Original 3499 G target miRNA score.

Target Rank	Target Score	miRNA Name
1	73	hsa-miR-155-5p
2	62	hsa-miR-6765-5p
3	53	hsa-miR-551b-5p

Table 23: 3499 G>A G1167S show same the miRNA and decrease the target score 73 to 72 on variation ss-RNA spike glycoprotein of SARS-COV-2 sequence from Jordanian samples

Target Rank	Target Score	miRNA Name
1	72	hsa-miR-155-5p
2	62	hsa-miR-6765-5p
3	51	hsa-miR-668-3p

Table 24: Predicted miRNAs targeting region on variation ss-RNA spike glycoprotein of SARS-COV-2 sequence from Jordanian samples

Sample number with accession on GISAID	Sequence variation ss-RNA spike glycoprotein of SARS-COV-2 sequence	Single Amino Acid Variation	miRNAs target submitted via spike glycoprotein SARS-COV-2 sequence
NCBI Reference Sequence: NC_045512.2	AATAACGCTACTAATGTTGTTATTAATCTGTGAATTTCAATTTTGAATGATCCATTTTGGGTGTTTATTACCAAAAAACAACAAAGTTGGATGGAAAGT	original	miRNA Name: 196a-1-3p miRNA Sequence: - caacaacauu 3' (length = 21)
Sample 23: hCoV-19/Jordan/SR-042/2020[EPI_ISL_430000/2020-03-30]	AATAACGCTACTAATGTTGTTATTAATCTGTGAATTTCAATTTTGAATGATCCATTTTGGGTGTTTACCACAAAAACAACAAAGTTGGATGGAAAGT	del 432 TTA del. Y144	miRNA Name: 196a-1-3p miRNA Sequence: - caacaacauu 3' (length = 21)
NCBI Reference Sequence: NC_045512.2	GGAACAAATACTTCTAACCAGGTTGCTGTTCTTTATCAGGATGTTAACTGCACAGAAGTCCTGTGCTATTTCATGCAGATCAACTTACTCCTACTTGGCGTGT	Original 1841A	miRNA Name: 4793-5p miRNA Sequence: - acauccugcuc 3' (length = 21)
Sample 3,5,7,8,9,10,11,12,13,15,18,20 and 21 Example: hCoV-19/Jordan/SR-036/2020[EPI_ISL_429996/2020-03-23]	GGAACAAATACTTCTAACCAGGTTGCTGTTCTTTATCAGGATGTTAACTGCACAGAAGTCCTGTGCTATTTCATGCAGATCAACTTACTCCTACTTGGCGTGT	1841A>G D614G	miRNA Name: 3620-3p Previous Name: 3620 miRNA Sequence: - ucaccugca 3' (length = 21)
NCBI Reference Sequence: NC_045512.2	ACTGTGATGTTGTAATAGGAATTGTCAACAACACAGTTTATGATCCTTTGCAACCTGAATTAGACTCATTCAAGGAGGAGTTAGATAAATATTTTAAGAATCATACA	Original 3415G	miRNA Name: 548g-3p Previous Name: 548g miRNA Sequence: - aaacuguaa 3' (length = 21)
Sample 21: hCoV-19/Jordan/SR-033/2020[EPI_ISL_429993/2020-03-16]	ACTGTGATGTTGTAATAGGAATTGTCAACAACACAGTTTATGATCCTTTGCAACCTGAATTAGACTCATTCAAGGAGGAGTTAGATAAATATTTTAAGAATCATACA	3415G>T D1139Y	miRNA Name: 548g-3p Previous Name: 548g miRNA Sequence: - aaacuguaa 3' (length = 21)
NCBI Reference Sequence: NC_045512.2	TCACCAGATGTTGATTTAGGTGACATCTCTGGCATTAAATGCTTCAGTTGTAACATTCAAAAAGAAATTGACCGCCTCAATGAGGTTGCCAAGAATTTAAATG	Original 3499 G	miRNA Name: 155-5p Previous Name: 155 miRNA Sequence: - uuaaugcuaau 3' (length = 21)
Sample 16: hCoV-19/Jordan/SR-039/2020[EPI_ISL_429998/2020-03-28]	TCACCAGATGTTGATTTAAGTGACATCTCTGGCATTAAATGCTTCAGTTGTAACATTCAAAAAGAAATTGACCGCCTCAATGAGGTTGCCAAGAATTTAAATG	3499 G>A G1167S	miRNA Name: 155-5p Previous Name: 155 miRNA Sequence: - uuaaugcuaau 3' (length = 21)

References

1. Wu F, Zhao S, Yu B, Chen YM, Wang W, Song ZG, et al. A new coronavirus associated with human respiratory disease in China. *Nature*. 2020 Mar 12;579(7798):265–9.
2. Perlman S, Netland J. Coronaviruses post-SARS: Update on replication and pathogenesis. Vol. 7, *Nature Reviews Microbiology*. Nature Publishing Group; 2009. p. 439–50.
3. Troughs DW, Gardner CL, Sun C, Haddow AD, Wang E, Chapnik E, et al. RNA viruses can hijack vertebrate microRNAs to suppress innate immunity. *Nature*. 2014 Dec 18;506(7487):245–8.
4. Troughs DW, Klimstra WB. MicroRNA Regulation of RNA Virus Replication and Pathogenesis. *Trends Mol Med*. 2017 Jan 1;23(1):80–93.

5. Peng S, Wang J, Wei S, Li C, Zhou K, Hu J, et al. Endogenous Cellular MicroRNAs Mediate Antiviral Defense against Influenza A Virus. *Mol Ther - Nucleic Acids*. 2018 Mar 2;10:361–75.
6. Morales L, Oliveros JC, Fernandez-Delgado R, tenOever BR, Enjuanes L, Sola I. SARS-CoV-Encoded Small RNAs Contribute to Infection-Associated Lung Pathology. *Cell Host Microbe*. 2017 Mar 8;21(3):344–55.
7. Chen Y, Wang X. miRDB: an online database for prediction of functional microRNA targets. *Nucleic Acids Res*. 2019;48:127–31.
8. Liu W, Wang X. Prediction of functional microRNA targets by integrative modeling of microRNA binding and target expression data. *Genome Biol*. 2019 Jan 22;20(1):18.
9. Oostra M, de Haan CAM, Rottier PJM. The 29-Nucleotide Deletion Present in Human but Not in Animal Severe Acute Respiratory Syndrome Coronaviruses Disrupts the Functional Expression of Open Reading Frame 8. *J Virol*. 2007 Dec 15;81(24):13876–88.

Declarations

The authors declare no competing interests.