In Silico Identification Of Human Mir-26a-1 From Hypertension Genome Sequence

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ABSTRACT

Background: Hypertension is a non-communicable condition that affects about half of the world's adult population. MicroRNAs (miRNAs), also known as non-coding RNAs, govern biological processes such as Proliferation and apoptosis are two processes that can be employed as treatment targets in the treating of diseases like hypertension. The current study aims in identifying miRNAs in hypertension from genome sequences found in public genomic databases.

Materials and methods: In this study, we have used the National Centre for Biotechnology Information (NCBI) web portal to identify miR-26a for hypertension using a bioinformatics approach and RNA fold was used to create the secondary structure.

Results and discussion: Careful evaluation of secondary structure results showed that hsa-

miR-26a-1 with the minimum free energy of - 37.30 kcal for hypertension genome sequence was identified.

Conclusion: These computational approaches have concluded that miR-26a-1 can be used as a diagnosis, prognosis and as an effective therapeutic target for treating hypertension.

Keywords: Hypertension; miRNAs; biomarkers; therapeutic target; hsa-miR-26a-1; Innovative technique.

Running title: Human miR-26a-1 from hypertension genome

Introduction

High blood pressure, often known as hypertension, is a major problem that affects nearly half of the world's adult population. Hypertension has lately been discovered to have reached epidemic proportions. (1) According to the cause of hypertension, it can be classified as primary or secondary. Essential hypertension (EH), pulmonary hypertension (PH), pulmonary arterial hypertension (PAH), white coat hypertension, nocturnal hypertension, portal hypertension, and other kinds of hypertension exist .(2) Clinical management of hypertension needs novel biomarkers in order to come up with a cure. The human DNA may be the most important component in understanding the complex multifactorial nature of hypertension. Although it was previously assumed that each of the human genes would code for proteins, it has recently been shown that the majority of these genes are unable to do so. These genes are transcribed into non-coding RNA molecules, which regulate the protein-coding genes in a variety of ways. Because of their widespread expression, RNAs can control widely parameters(3)

MicroRNAs (miRNAs) are a type of non-coding RNA molecule with a measurement of 19-25 nucleotides that control various processess including cell proliferation, differentiation, and programmed cell demise (4) MicroRNAs (miRNAs) are important regulators of post-transcriptional alterations and have a important role in research like gene expression.(5) miRNAs biogenesis is divided There are two types of pathways: canonical and non-canonical. Drosha and Dicer, two RNase III enzymes that catalyse two successive processing processes, one in nucleus and cytoplasm, are involved in miRNA production.(6) The microprocessor complex, which includes the enzymes namely Drosha and DGCR8 and other proteins, catalyzes the nuclear event.(7) MiRNA precursors (pre-miRNAs) are produced in the nucleus and then exported to the cytoplasm via the exportin-5/Ran-GTP complex. (8) In the cytoplasm, Dicer processes pre-miRNAs to form miRNA duplexes. (8) They're then combined with an argonaute (AGO) protein and introduced to the RISC (RNA induced silencing complex), where one of the strands is chosen to generate the mature miRNA. (10) Individual miRNAs have the capacity to affect a large number of genes at the similar time due to their coordinated action in diverse pathways and networks. MiRNA expression and function abnormalities have been linked to the pathophysiology or target organ damage of hypertension, according to research. They're quite stable and found in blood, serum, and urine. (11) Because of the existence of miRNAs in body fluids and their changed expression

levels in people with high blood pressure, they've been considered as potential biomarkers for treating various kinds of hypertension..(12) Studies at molecular levels were performed by our team of researches which insisted us to proceed this study (13–20),(21),(22),(23),(24,25),(26),(27),(28–32). From the above concept, it has been understood that there are no valid biomarkers for treating hypertension, Hence this study uses hypertensive genome sequences to identify the miRNAs.

Materials and methods

In this study we used the bioinformatics approach to identify the miRNA in the hypertension genome sequence, where the data was collected from publicly accessible databases.

Computational method

The National Center for Biotechnology Information (NCBI) web page for the International Nucleotide Sequence Database Consortium was used to get human genome sequence data. Using this free search engine, the hypertension genome sequence was extracted using the query "Hypertension genome sequence in Homo sapiens." Human mature miRNAs were chosen from a large number of entries in the miRbase database. (http://www.mirbase.org/). A nucleotide database for hypertension-specific genome sequences was created after the low-quality and repetitive sequences were removed. The nucleotide data collection given before was used to find homologs in the miRNA dataset. The mature miRNAs were utilised as a starting point for searching for similar hypertension genome sequences. All sequences were processed in FASTA format, and mature miRNA sequences were compared to genome sequences that were unique. As a baseline, genome sequences were compared to pre-miRNA sequences and expessed as pre-miRNA sequence. The secondary structure was then obtained using RNAfold which provided the miRNA expressed in the hypertension genome sequence which helped in target prediction, which was done using target scan.

Results

The miRNA identification was performed through computational approach and it is more economical than other methods. In the hypertension genome sequences, one miRNA, hsa-miR-26a-1, was found after collecting databases from NCBI and carefully evaluating the secondary structure. The mature sequence found using RNAfold is-GUGGCCUCGUUCAAGUAAUCCAGGAUAGGCUGUGCAGGUCCCAAUGGGCCUAUUCUUGGUUACUUGCACGGGGACGC. And the minimum free energy was found to be -37.30 kcal. Figure 1 represents the secondary structure of hsa-miR-26a-1. Based on target scan analysis, we identified other important transcripts that are targeted by miR-26a-1 are zinc finger protein 568, HCG2038717, dCTP pyrophosphatase 1, ephrin-A5, zinc finger protein 630 etc. Table 1 representing the target genes of hsa-miR-26a-1.

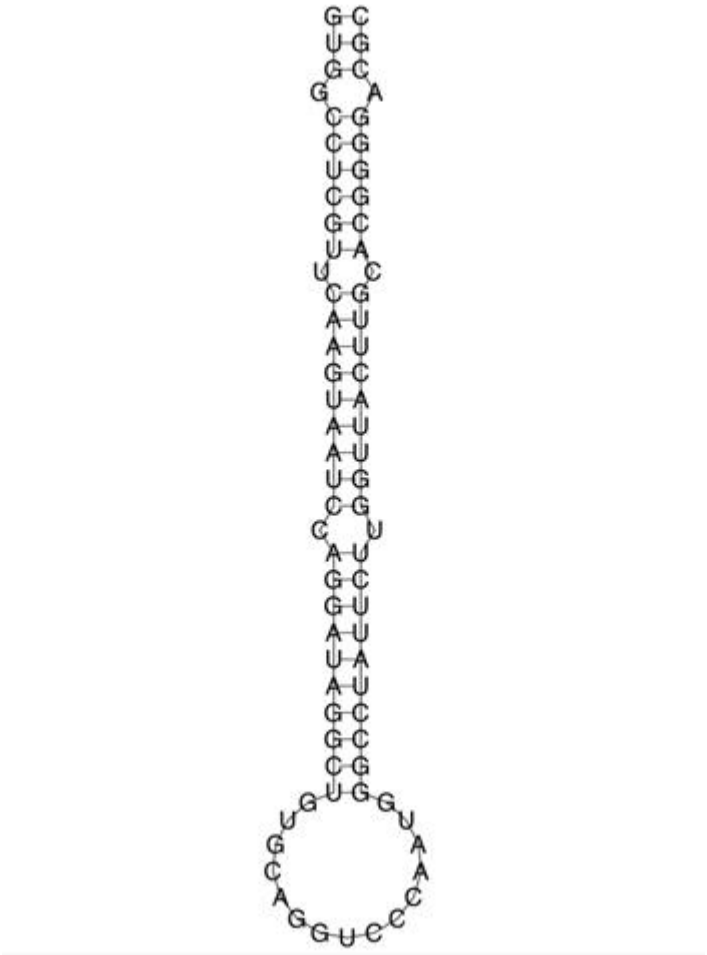
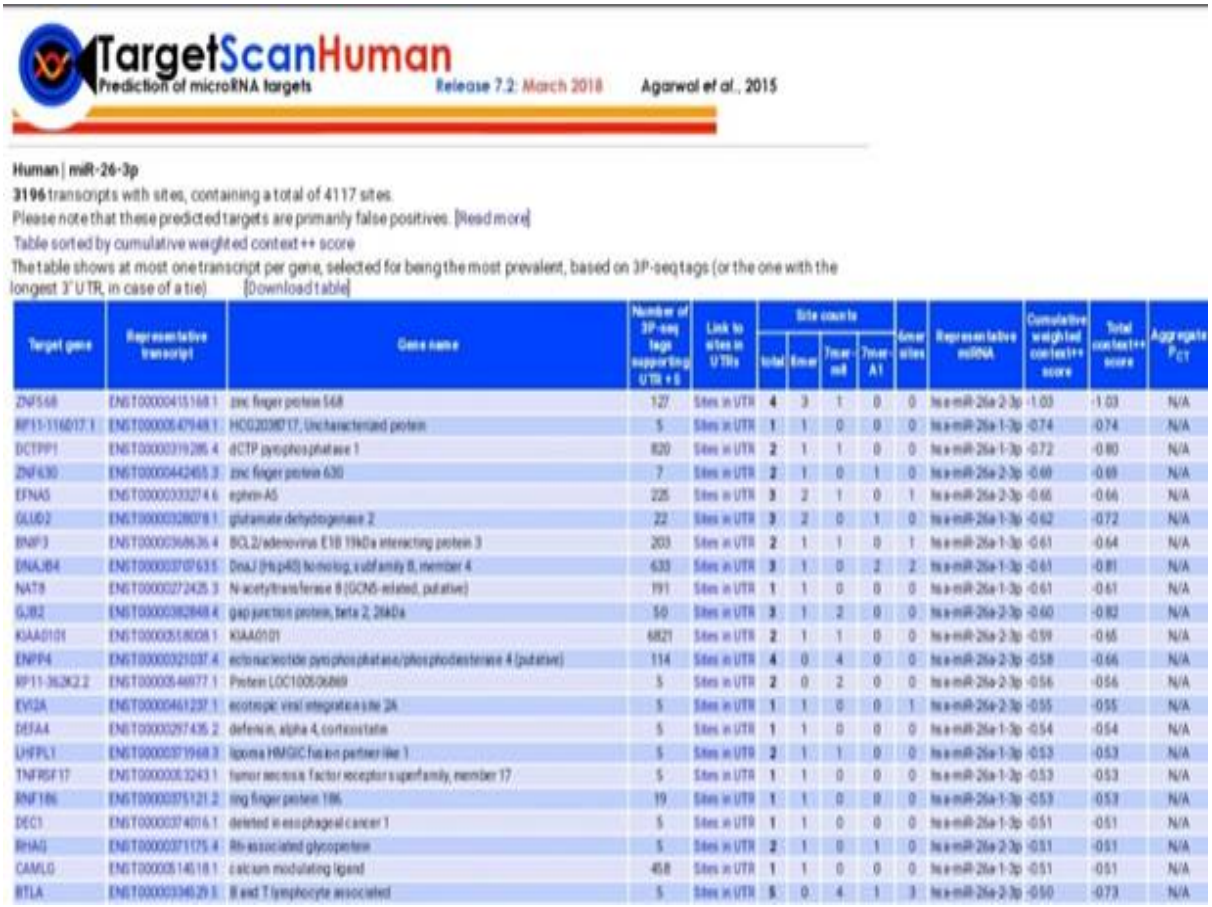


Figure 1 represents the secondary structure of hsa-miR-26a-1

Table 1 representing the target genes of hsa-miR-26a-1.



TargetScanHuman
Prediction of microRNA targets Release 7.2: March 2018 Agarwal et al., 2015

Human | miR-26-3p
3196 transcripts with sites, containing a total of 4117 sites
Please note that these predicted targets are primarily false positives. [Read more]
Table sorted by cumulative weighted context++ score
The table shows at most one transcript per gene, selected for being the most prevalent, based on 3P-seq tags (or the one with the longest 3' UTR, in case of a tie) [Download table]

Target gene	Representative transcript	Gene name	Number of 3P-seq tags supporting UTR	Link to sites in UTRs	Site counts				6mer sites	Representative miRNA	Cumulative weighted context++ score	Total context++ score	Aggregate P_{CT}
					total	8mer	7mer-m8	7mer-A1					
ZNF568	ENST00000415168.1	zinc finger protein 568	127	Sites in UTR	4	3	1	0	0	hsa-miR-26a-2-3p	-1.03	-1.03	N/A
RP11-116D17.1	ENST00000547948.1	HCG2039817, Uncharacterized protein	5	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.74	-0.74	N/A
DCTPP1	ENST00000319285.4	dCTP pyrophosphatase 1	820	Sites in UTR	2	1	1	0	0	hsa-miR-26a-1-3p	-0.72	-0.80	N/A
ZNF630	ENST00000442465.3	zinc finger protein 630	7	Sites in UTR	2	1	0	1	0	hsa-miR-26a-2-3p	-0.69	-0.69	N/A
EFNA5	ENST00000333274.6	ephrin-A5	225	Sites in UTR	3	2	1	0	1	hsa-miR-26a-2-3p	-0.66	-0.66	N/A
GLUD2	ENST00000328078.1	glutamate dehydrogenase 2	22	Sites in UTR	3	2	0	1	0	hsa-miR-26a-1-3p	-0.62	-0.72	N/A
BNIP3	ENST00000368636.4	BCL2/adenovirus E1B 19kDa interacting protein 3	203	Sites in UTR	2	1	1	0	1	hsa-miR-26a-1-3p	-0.61	-0.64	N/A
DNAJB4	ENST00000370763.5	DnaJ (Hsp40) homolog, subfamily B, member 4	633	Sites in UTR	3	1	0	2	2	hsa-miR-26a-1-3p	-0.61	-0.81	N/A
NAT8	ENST00000272425.3	N-acetyltransferase 8 (GCN5-related, putative)	191	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.61	-0.61	N/A
GJB2	ENST00000382848.4	gap junction protein, beta 2, 26kDa	50	Sites in UTR	3	1	2	0	0	hsa-miR-26a-2-3p	-0.60	-0.82	N/A
KIAA0101	ENST00000518008.1	KIAA0101	6821	Sites in UTR	2	1	1	0	0	hsa-miR-26a-2-3p	-0.59	-0.65	N/A
ENPP4	ENST00000321037.4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	114	Sites in UTR	4	0	4	0	0	hsa-miR-26a-2-3p	-0.58	-0.66	N/A
RP11-362K2.2	ENST00000544977.1	Protein LOC100506869	5	Sites in UTR	2	0	2	0	0	hsa-miR-26a-2-3p	-0.56	-0.56	N/A
EVI2A	ENST00000461237.1	ecotropic viral integration site 2A	5	Sites in UTR	1	1	0	0	1	hsa-miR-26a-2-3p	-0.55	-0.55	N/A
DEFA4	ENST00000297435.2	defensin, alpha 4, corticostatin	5	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.54	-0.54	N/A
LHFPL1	ENST00000371968.3	lipoma HMGIC fusion partner-like 1	5	Sites in UTR	2	1	1	0	0	hsa-miR-26a-1-3p	-0.53	-0.53	N/A
TNFRSF17	ENST00000353243.1	tumor necrosis factor receptor superfamily, member 17	5	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.53	-0.53	N/A
RNF186	ENST00000375121.2	ring finger protein 186	19	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.53	-0.53	N/A
DEC1	ENST00000374016.1	deleted in esophageal cancer 1	5	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.51	-0.51	N/A
RHAG	ENST00000371175.4	Rh-associated glycoprotein	5	Sites in UTR	2	1	0	1	0	hsa-miR-26a-2-3p	-0.51	-0.51	N/A
CAMLG	ENST00000514518.1	calcium modulating ligand	458	Sites in UTR	1	1	0	0	0	hsa-miR-26a-1-3p	-0.51	-0.51	N/A
BTLA	ENST00000346293.5	B and T lymphocyte associated	5	Sites in UTR	5	0	4	1	3	hsa-miR-26a-2-3p	-0.50	-0.73	N/A

Discussion

Hypertension is a non-communicable disease affecting almost 1.13 billion people around the globe. Despite the fact that the cause of hypertension is unknown, environmental and genetic factors may play a significant role in the pathophysiologic mechanism in modern societies .(33) Many biological processes are regulated by miRNAs, and their levels of expression are affected in many human diseases, including hypertension. Although our knowledge of miRNAs' role in hypertension biology has advanced greatly, further research is needed to study and validate miRNAs as biomarkers for illness diagnosis and prognosis. We used a cost-effective computational strategy in our research. The presence of miR-26a-1 in the hypertension genome sequence was discovered after rigorous examination of the secondary structure.

MiR-34b levels were shown to be higher in spontaneously hypertensive rats (SHR) than in Wistar Kyoto (WKY) rats in prior investigations. The target genes of miR34b in the database were predicted using online target prediction algorithms, which indicated cyclin G1 (CCNG1) and cyclin dependent kinase 6 (CDK6) as plausible targets. MiR34b's direct target gene was eventually determined to be CDK6. MiR34b and CDK6 were later discovered to have a potential negative regulatory interaction, suggesting that they could be used as a new therapeutic target in the treatment of hypertension. (34) According to a study by Li, H et al.,

human PAH may be linked to circulating miR-17 levels (2020). (35) (36) Many other miRNAs, on the other hand, need to be explored further in order to understand their functions in signalling pathways..

Conclusion

Finally, a computational technique was used to identify miR-26a-1, a new miRNA, from hypertension genomic sequences. However, more research on miR-26a-1 is needed to uncover the underlying mechanisms that control the suppression or advancement of hypertension. At the moment, hypertension management and treatment options remain tricky, and the specific molecular process is still unknown. There is also an urgent need for further development of miRNAs for the treatment of hypertension in both animal models and human clinical trials. This computational approach helps in understanding the role of miRNAs as biomarkers and how they can be used for diagnosis, prognosis and as an effective therapeutic target.

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Conflict of Interest: The authors declare no conflict of interest.

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