Available online at www.sciencerepository.org

Science Repository

Research Article

Identification of BAP1-associated MicroRNAs and Implications in Cancer Development

Tikam Chand Dakal*

Genome and Computational Biology Lab, Department of Biotechnology, Mohanlal Sukhadia University, Udaipur-313001, Rajasthan, India

ARTICLEINFO

Article history:
Received: 25 August, 2019
Accepted: 8 October, 2019
Published: 9 November, 2019

ABSTRACT

Having role in gene regulation and silencing, miRNAs have been implicated in development and progression of a number of diseases, including cancer. Herein, I present potential miRNAs associated with BAP1 gene identified using *in-silico* tools such as TargetScan and Exiqon miRNA Target Prediction. I identified fifteen highly conserved miRNA (hsa-miR-423-5p, hsa-miR-3184-5p, hsa-miR-4319, hsa-miR-125b-5p, hsa-miR-125a-5p, hsa-miR-6893-3p, hsa-miR-200b-3p, hsa-miR-200c-3p, hsa-miR-505-3p.1, hsa-miR-429, hsa-miR-370-3p, hsa-miR-125a-5p, hsa-miR-141-3p, hsa-miR-200a-3p, and hsa-miR-429) associated with BAP1 gene. We also predicted the differential regulation of these twelve miRNAs in different cancer types.

Introduction

MicroRNAs (miRNAs) are endogenous produced small non-coding RNAs having role in post-transcriptional gene silencing, and thus, are considered as important regulators of eukaryotic gene expression. The human genome encodes for approximately 1800 microRNAs (miRNAs), that function to regulate gene expression post-transcriptionally. miRNAs are characterized by a growing class of ~22 nt long non-protein coding RNAs [1, 2]. Due to the potential for one miRNA to target multiple gene transcripts, miRNAs are recognized as a major mechanism to regulate gene expression and mRNA translation. While gene expressions can be influenced by many factors, post-transcriptional gene regulation involving microRNAs (miRNAs) is particularly fascinating because of the breadth of their interactions facilitated by their synergistic/combinatorial relationships with target genes. Nowadays, identification of miRNAs and their targets have been an important way to unravel the role of miRNAs in the development and progression of any disease.

Materials & Methods

MicroRNA associated with human BAP1 was predicted using TargetScan Human (Release 7.2), miRSearch ver 3.0 (http://www.exiqon.com/microrna-target-prediction) and miRDB (http://mirdb.org/) [3]. TargetScan employs the seed region of the miRNA and searches conserved 6mer, 7mer and 8mer sites in its biological targets [4]. TargetScan also predicts additional sites with lesser degree of conservation as an option. Besides this, sites that have mismatch with the seed region but are well compensated by conserved 3' pairing and centered sites are also predicted. For human targets, TargetScan take into consideration gene orthologs and 3' UTRs of the human [5, 6]. TargetScan calculates the cumulative weighted context ++ score for each sites and predictions are then ranked based on this efficacy of targeting [3]. Besides this, predictions are also ranked based on the probability score [5].

MicroRNA prediction using miRSearch ver 3.0 (http://www.exiqon.com/microrna-target-prediction) considers an advanced cross-referencing system that predicts miRNAs validated using high throughput experiments. miRSearch also includes some latest implications for the interaction between the miRNA and the target gene in question such as information about disease, tissue etc. miRDB is a web-based tool and database resource for the prediction miRNA targets as well as functional annotations. miRDB employs MirTarget for prediction which contains several miRNA-target interactions from

**Correspondence to: Tikam Chand Dakal, Genome and Computational Biology Lab, Department of Biotechnology, Mohanlal Sukhadia University, Udaipur-313001, Rajasthan, India; Tel: +91-294-2470071; E-mail: tikam260707@gmail.com*

http://dx.doi.org/10.31487/j.IJCST.2019.01.01

validated and predicted results/experiments.

Results

Based on the percent context ++ score, we found seventy one miRNAs (Supplemental Table 1) and out of which twelve miRNAs were predicted to be targeting BAP1 with higher context ++ score (>90%) (Table 1). These miRNAs were hsa-miR-423-5p, hsa-miR-3184-5p, hsa-miR-4319, hsa-miR-125b-5p, hsa-miR-125a-5p, hsa-miR-6893-3p, hsa-miR-200b-3p, hsa-miR-200c-3p, hsa-miR-505-3p.1, hsa-miR-429, hsa-miR-370-3p, and hsa-miR-125a-5p.

Supplemental Table 1: BAP1 is predicted to be targeted by 71 miRNAs in miRDB.

Target Rank	miRNA Name	Target Score
1	hsa-miR-200c-3p	98
2	hsa-miR-4319	98
3	hsa-miR-200b-3p	98
4	hsa-miR-429	98
5	hsa-miR-593-3p	96
6	hsa-miR-125b-5p	94
7	hsa-miR-125a-5p	94
8	hsa-let-7a-2-3p	92
9	hsa-let-7g-3p	92
10	hsa-miR-4646-5p	87
11	hsa-miR-204-3p	87
12	hsa-miR-7162-5p	86
13	hsa-miR-516a-3p	86
14	hsa-miR-516b-3p	86
15	hsa-miR-4283	84
16	hsa-miR-6813-5p	84
17	hsa-miR-6085	83
18	hsa-miR-6764-5p	83
19	hsa-miR-185-3p	82
20	hsa-miR-3918	82
21	hsa-miR-3184-5p	81
22	hsa-miR-4533	81
23	hsa-miR-423-5p	81
24	hsa-miR-1915-3p	79
25	hsa-miR-1277-5p	78
26	hsa-miR-7847-3p	77
27	hsa-miR-6882-3p	76
28	hsa-miR-640	76
29	hsa-miR-4489	75
30	hsa-miR-6895-5p	75
31	hsa-miR-545-5p	73
32	hsa-miR-6893-3p	73
33	hsa-miR-370-3p	73
34	hsa-miR-8084	73
35	hsa-miR-4306	72
36	hsa-miR-6829-5p	71
37	hsa-miR-664a-3p	70
38	hsa-miR-10526-3p	70
39	hsa-miR-2467-3p	70
40	hsa-miR-1909-5p	69
41	hsa-miR-2861	68
42	hsa-miR-6837-5p	67
43	hsa-miR-4264	66
44	hsa-miR-4685-5p	65
45	hsa-miR-4492	65
46	hsa-miR-6845-3p	64

47	hsa-miR-4704-3p	64
48	hsa-miR-6734-5p	63
49	hsa-miR-3127-5p	62
50	hsa-miR-6165	62
51	hsa-miR-31-5p	62
52	hsa-miR-1972	61
53	hsa-miR-12129	61
54	hsa-miR-12123	60
55	hsa-miR-6773-5p	60
56	hsa-miR-6724-5p	59
57	hsa-miR-132-5p	58
58	hsa-miR-3664-3p	57
59	hsa-miR-6895-3p	56
60	hsa-miR-5192	56
61	hsa-miR-4481	56
62	hsa-miR-185-5p	55
63	hsa-miR-4644	55
64	hsa-miR-7160-3p	55
65	hsa-miR-5194	54
66	hsa-miR-939-3p	54
67	hsa-miR-9900	53
68	hsa-miR-4768-3p	52
69	hsa-miR-5011-5p	51
70	hsa-miR-3622b-5p	51
71	hsa-miR-4721	50

Table 1: Context ++ score for the MicroRNA prediction using TargetScane for *BAP1* gene.

miRNA	Seed match	Context++ score	Context++ score percentile	Weighted context++ score
hsa-miR-423-5p	8mer	-0.43	98	-0.41
hsa-miR-3184-5p	8mer	-0.44	98	-0.41
hsa-miR-4319	8mer	-0.29	95	-0.28
hsa-miR-125b-5p	8mer	-0.29	95	-0.28
hsa-miR-125a-5p	8mer	-0.28	95	-0.27
hsa-miR-6893-3p	8mer	-0.28	95	-0.27
hsa-miR-200b-3p	8mer	-0.19	94	-0.19
hsa-miR-200c-3p	8mer	-0.19	94	-0.19
hsa-miR-505-3p.1	8mer	-0.34	94	-0.34
hsa-miR-429	8mer	-0.19	93	-0.19
hsa-miR-370-3p	8mer	-0.17	92	-0.16
hsa-miR-125a-5p	7mer-m8	-0.21	90	-0.2

Since, looking at the Pct score has an advantage of predicting the target sites with more effective likelihood of interaction with miRNAs, I predicted the target miRNAs associated with BAP1 based on the Pct score also. I found that 3 miRNAs namely, hsa-miR-200b-3p, hsa-miR-200c-3p, and hsa-miR-429 (Table 2).

Table 2: Pct score for the MicroRNA prediction using TargetScane for *BAP1* gene.

miRNA	Conserved branch length	Pct
hsa-miR-200b-3p	5.132	0.88
hsa-miR-200c-3p	5.132	0.88
hsa-miR-429	5.132	0.88
hsa-miR-200c-3p	4.381	0.85
hsa-miR-429	4.381	0.85
hsa-miR-200b-3p	4.381	0.85

I also subjected the BAP1 genomic data for miRNAs prediction using miRSearch ver 3.0 and found three additional miRNAs namely hsa-miR-

141-3p, hsa-miR-200a-3p, and hsa-miR-429 that are found to be inhibiting the product formation (Table 3).

Table 3: MicroRNA prediction using miRSearch for *BAP1* gene.

microRNA	Accession	Products
hsa-miR-141-3p	MIMAT0000432	Inhibit
hsa-miR-200a-3p	MIMAT0000682	Inhibit
hsa-miR-200b-3p	MIMAT0000318	Inhibit
hsa-miR-200c-3p	MIMAT0000617	Inhibit
hsa-miR-429	MIMAT0001536	Inhibit

Conclusion

The online webtools available for miRNA target prediction rely on different computational approaches and algorithms, including biophysics and machine learning. With reference to the current study, I found that in all the miRNA target prediction tools, four primarily important features to be taken into consideration are: seed match, context ++ score, conservation branch length, and Pct score. In total, I found fifteen miRNAs that potentially target BAP1 and regulate its expression differentially in a variety of cancers.

References

1. Bartel D (2004) Micrornas: Genomics, Biogenesis, Mechanism, And Function. *Cell* 116: 281-297. [Crossref]
2. Zhao T, Li G, Mi S, Li S, Qi Y et al. (2007) A Complex System of Small RNAs In the Unicellular Green Alga Chlamydomonas reinhardtii. *Genes Dev* 21: 1190-1203. [Crossref]
3. Agarwal V, Bell GW, Nam JW, Bartel DP (2015) Predicting Effective Microrna Target Sites In Mammalian Mrnas. *Elife* 4. [Crossref]
4. Lewis BP, Burge CB, Bartel DP (2005) Conserved Seed Pairing, Often Flanked by Adenosines, Indicates That Thousands of Human Genes Are Microrna Targets. *Cell* 120: 15-20. [Crossref]
5. Friedman RC, Farh KK, Burge CB, Bartel DP (2009) Most Mammalian Mrnas Are Conserved Targets of Microrna. *Genome Res* 19: 92-105. [Crossref]
6. Shin C, Nam JW, Farh KK, Chiang HR, Shkumatava A et al. (2010) Expanding the Microrna Targeting Code: Functional Sites with Centered Pairing. *Mole Cell* 38: 789-802. [Crossref]