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Original Article

BINDING SITE ANALYSIS OF MICRORNAS TARGET INTERACTION FROM GENOME WIDE ASSOCIATION STUDIES

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ABSTRACT

Objective: Identification of micro RNAs (miRNAs) as a biomarker to diagnose and treat auto immune diseases is a challenge in the era of post genomics and the ability to apply an accurate computational approach leads to the initiation of discovering novel biomarkers.

Methods: Initially we have identified the list of genes from a database which contain a catalog of Genome Wide Association Study (GWAS) and then we have identified the predicted miRNAs from TargetScan. Finally we have found the connectivity map between the gene and validated miRNA target from miRmap and the number of binding sites were analyzed for each pair (gene-miRNA).

Results: We have applied the above mentioned approach to Psoriasis. In case of Psoriasis, 15 distinct genes are present in GWAS and among them; TRAF3IP2, KCNH7, CAST, NOS2, STAT2, IL23R and CoG6 contain predicted miRNAs in TargetScan. Finally, the number of mRNA binding sites were analyzed for miRNAs obtained from TargetScan and it has been found that the binding of hsa-miR-520d-5p and hsa-miR-524-5p with the mRNA of TRAF3IP2 is more stable than the binding of other miRNAs with their respective genes on the basis of binding site analysis and hence there is a maximum probability for the utilization of hsa-miR-520d-5p and hsa-miR-524-5p as a biomarker for Psoriasis.

Conclusion: At present we have applied our model for Psoriasis. In future, we will be applying our methodology to other auto immune diseases for identifying a miRNA based biomarker.

Keywords: miRNAs, auto immune diseases, post genomics, GWAS, TargetScan and miRmap

INTRODUCTION

Micro RNA is a small nucleotide sequence of non coding RNA molecules with a sequence length of 22-24 nucleotides found in plants, virus, animals and humans which help in the process of transcriptional and post transcriptional repression of gene expression [1].Majority of miRNA are intragenic [2].Micro RNAs are initially transcribed as part of an RNA stem-loop that in turn forms part of a several hundred nucleotides long miRNA precursor miRNA (pri-miRNA) [3]. Mature miRNA is a part of an RNA-induced silencing complex (RISC) which contains Dicer and many associated proteins [4].Since miRNA is involved in the functioning of eukaryotic cells, dysregulation of miRNA been associated with disease and a miR2Disease database contain documents with known relationships between miRNA dysregulation and human disease [5]. Micro RNAs can bind to target messenger RNA (mRNA) transcripts of protein-coding genes and negatively control their translation or cause mRNA degradation and the key factor is to identify the importance miRNA target with accuracy. A detailed review for the advances in the miRNA target identification methods and available resources has been published by Zheng et.al. [6].Several other methodologies were also proposed on the basis of tertiary structure of precursor miRNA by Hin et.al. [7], system biology by Manczinger et.al. [8],SNPs by Marcin et.al.[9],molecular dynamic simulations by Yonghua et.al.[10].

MATERIALS AND METHODS

Genome Wide Association Study (GWAS)

A genome-wide association study is an examination of common genetic variants in different individuals to identify the association of a variant with its trait [11]. GWAS typically focus on associations between single-nucleotide polymorphisms (SNPs) and traits involved in major diseases [12].

`Target Scan

Target Scan predicts biological targets of miRNAs by searching the presence of conserved sites (7mer and 8mer) in the seed region of each miRNA [13]. In Humans, TargetScan considers the match to annotate human UTRs (Untranslated regions) and their orthologs, as defined by whole-genome alignments from UCSC browser [14].

Mapping of gene and miRNA: Mapping of gene (mRNA) and miRNA is done by MiRmap software. This software allows us to examine feature correlations a using high throughput experimental data from immunopurification, transcriptomics and proteomics experiments [15]. Overall, accessibility of target site appears to be the most predictive feature of miRmap.

RESULTS AND DISCUSSION

Associated genes of Psoriasis are identified from GWAS and their corresponding miRNAs are identified from Target Scan and the number of miRNA binding sites in the mRNA of its corresponding gene is identified from miRmap. The complete list of miRNAs related to GWAS of Psoriasis is given in Table 1.

CONCLUSION

Based on our analysis it has been found that the binding of hsa-miR-520d-5p and hsa-miR-524-5p with the mRNA of TRAF3IP2 is more stable than the binding of other miRNAs and hence there exist a maximum chance for the above mentioned miRNAs to become a biomarker for Psoriasis. Since other miRNAs contain only one or two binding site, it was not consider for selection. Further understanding of the complete mechanism involved in miRNA dynamics require simulation methods like monte-carlo and constrained dynamics but those methodologies are beyond the scope of our investigation. In future our methodology can also be utilized for identifying novel miRNAs which could be a probable therapeutic target for auto immune diseases.

Table 1: Micro RNAs related to GWAS of Psoriasis

Genes (GWAS)	Predicted miRNAs (TargetScan)	Number of mRNA Binding Sites (miRmap)
TRAF3IP2	**hsa-miR-520d-5p**	**6**
	hsa-miR-524-5p	**6**
	hsa-miR-548n	3
	hsa-miR-4795-3p	2
KCNH7	hsa-miR-1297	1
	hsa-miR-4465	1
CAST	hsa-miR-375	2
NOS2	hsa-miR-485-3p	1
	hsa-miR-4456	1
	hsa-miR-4797-5p	1
STAT2	hsa-miR-761	1
	hsa-miR-3619-5p	1
IL23R	hsa-miR-4729	1
CoG6	hsa-miR-2909	2
	hsa-miR-4682	1

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