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A Computational approach for identifying novel micro RNAs from Genome Wide Association Studies of Psoriasis

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Abstract: **Identification of micro RNAs (miRNAs) as a biomarker to diagnose and treat auto immune diseases is a great challenge in the era of post genomics and the ability to apply an accurate computational approach leads to the initiation of discovering novel biomarkers. 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 validated miRNAs from miRTarBase. Finally we have found the connectivity map between the gene and validated miRNA target from miRmap and the binding energies were analyzed for each pair (gene-miRNA). We have applied the above mentioned approach to Psoriasis. In case of Psoriasis, 15 distinct genes are present in GWAS and among them; NOS2, IL13, TNFAIP3 and TSC1 contain validated miRNAs in miRTarBase. Finally, binding energies were analyzed for the obtained miRNAs and it has been found that the binding of hsa-miR-26a-5p with the mRNA of NOS2 is more stable than the binding of other miRNAs with their respective genes on the basis of binding energy and hence there is a maximum probability for the utilization of hsa-miR-26a-5p as a biomarker for Psoriasis. At present we have applied this model for Psoriasis and in future we will be applying this model to other auto immune diseases and the above mentioned methodology can also be applied to predict miRNA based biomarkers in a disease.**

Keywords: miRNAs, miRTarBase, binding energy, biomarker and auto immune diseases.

I. 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].

II. GENOME WIDE ASSOCIATION STUDIES

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].

III. MIR-TAR-BASE

miRTarBase has accumulated more than fifty thousand interactions of miRNAs with its target (MTIs).Those datas are manually surveyed from pertinent literature after performing the data mining of the text in a systematic procedure for filtering research articles related to functional studies of miRNAs. Generally, the collected MTIs are validated experimentally by reporter assay, western blot, microarray and next-generation sequencing experiments. While containing the largest amount of validated MTIs, the miRTarBase provides the most updated collection by comparing with other similar, previously developed databases [13].

IV. 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 [14]. Overall, accessibility of target site appears to be the most predictive feature of miRmap.

V. EXPERIMENTAL RESULTS

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 and the interaction of a miRNA target within a specific gene position is given in Figure 1.

Table 1: Micro RNAs and mRNA associated with GWAS of Psoriasis

Genes **(GWAS)**	Validated miRNAs **(miRTarBase)**	Binding Energies Predicted by miRmap **(Kcal/mol)**
NOS2	**hsa-miR-26a-5p**	45.75
IL13	hsa-miR-98-5p	79.14
	hsa-let-7d-5p	80.10
	hsa-let-7g-5p	96.15
	hsa-let-7f-5p	94.38
	hsa-let-7i-5p	90.76
TNFAIP3	hsa-miR-21-5p	60.67
	hsa-miR-29a-3p	81.96
	hsa-miR-125a-5p	83.04
	hsa-miR-125b-5p	86.36
TSC1	hsa-miR-32-5p	47.98

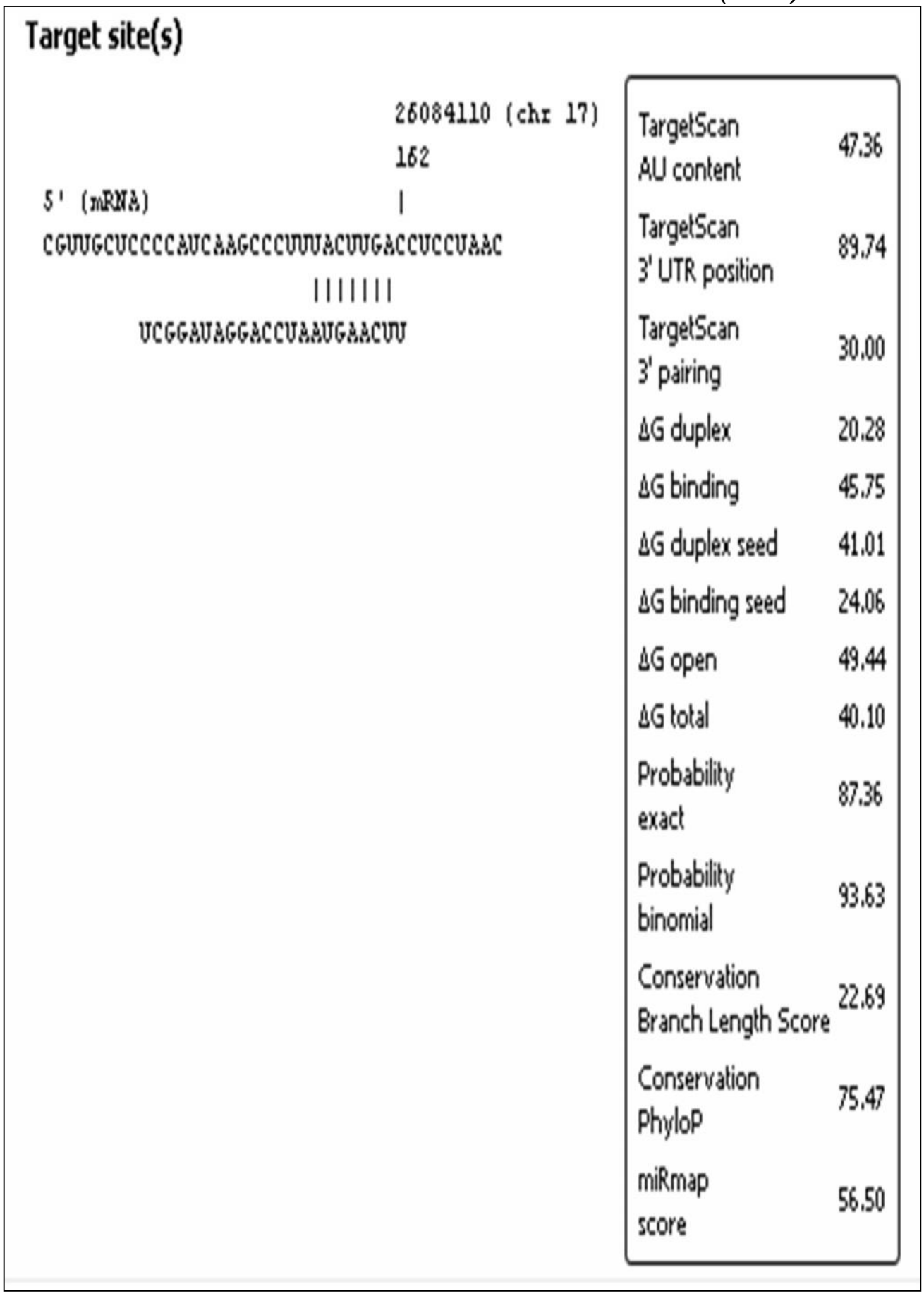

Fig.1 Interaction of hsa-miR-26a with NOS2

VI. CONCLUSION

Based on our analysis it has been found that the binding of **hsa-miR-26a-5p** with the mRNA of **NOS2** 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 a maximum binding energy for miRNA-gen pair, it was not considered 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.

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