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Insilico analysis of micro RNA based target interaction: potential implication in the pharmacogenomics of psoriasis

Abstract

Identification of a therapeutic micro RNA (miRNA) with multiple gene targets is a major challenge in the era of post genomics and the ability to apply an accurate insilico approach leads to the initiation of discovering novel miRNAs. In order to identify a micro RNA (miRNA) based target interaction among the genes which are associated with pharmacology; we have taken a list of Psoriasis related genes from Pharmacogenomic database, and further identified the network of miRNAs which are significantly associated with the Pharmacogenomics of Psoriasis. Further, we performed an enrichment analysis for identifying a specific miRNA on the basis of statistical tests to predict the miRNA with pharmacological significance. Finally we have identified the binding of the selected miRNA with the genes which are related to Pharmacology of Psoriasis. While this protocol has presently been applied to Psoriasis, it can potentially be adopted for other diseases with the impact of recent advancements in modern science like nanotechnology on analyzing the pharmacological nature of miRNAs.

Keywords: micro RNA, gene targets, post genomics, insilico approach, psoriasis, pharmacogenomics, nanotechnology

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Introduction

Skin is the largest organ of the human body which regenerates throughout the entire life of every individual and serves as an outermost barrier for preventing internal organs from dehydration.[1–3] It has a system for maintaining the regulatory mechanism of mediators with local or systemic effects.[4–6] As a common skin disease, Psoriasis is chronic, auto immune and a complex genetic disorder which affects around 2% of world population. Psoriatic skin contains certain symptoms of inflammation which are raised as scaly lesions.[7–9] There are three types of cellular alterations in psoriatic skin i.e. abnormal differentiation of keratinocyte, hyper proliferation of keratinocyte and infiltration of immune cells.[10] Studies on molecular components and cellular pathways of inflammation serve as a major contribution to understand the pathogenesis of psoriasis.[11–13] The interplay between the genetic and environmental factors influence the onset and progression of psoriasis.[14,15] Recent studies on miRNAs, illustrate the fact that it is a novel regulator of gene expression and it plays a vital role in psoriasis.

Materials and methods

Pharmacogenomic database (*PharmG^{KB}*)

PharmG^{KB} is a knowledge based resource with clinical information about dosing guidelines and drug labels. This database summarizes the vital pharmacogenomics of various diseases. In our case, we have extracted the list of Pharmacogenomic genes associated with Psoriasis and cross validated with the published SNPs of Ryan et al.[16]

Enrichr

Enrichr is an interactive tool for enrichment analysis of gene list. Enrich R is one of the most powerful methods for analyzing the massive datasets and producing the results with the list of differentially expressed genes.[17,18] In Enrich R, Differentially expressed gene lists are extracted from RNA-seq or microarray studies; gene lists can be created from genes by analysing the mutations in cohorts of patients, or gene lists which can become a putative target of transcription factors or histone modifiers, as profiled by ChIP-seq.[19]

Mirmap

MiRmap software identifies the number of miRNA binding sites in a gene (mRNA).This software allows us to examines the feature correlation which is based on experimental data resulted from the high throughput techniques of immunopurification, transcriptomics and proteomics.[20]

Results and discussion

We have identified the list of Psoriasis related genes from *PharmG^{KB}* and identified the network of miRNAs associated with Psoriasis gene which is illustrated in Figure1 and enrichment analysis was performed for miRNA selection and the details are given in Table 1. Finally, binding analysis was performed for the selected miRNA to identifying its significance in therapy and the results are given in Tables 2 & 3.

Table 1 Enrichment analysis of miRNAs associated with pharmacogenomics of psoriasis

Micro RNAs	P-value	Z-score	Combined score
hsa-miR-18a	0.07204	-1.8	3.1
hsa-miR-34b	0.1132	-1.79	3.09
hsa-miR-149	0.07606	-1.76	3.04
hsa-miR-24	0.1185	-1.7	2.94
hsa-miR-125B	0.1651	-1.76	2.84
hsa-miR-29	0.2505	-1.88	2.61

Figure 1 Network of miRNAs associated with Psoriasis related genes in *PharmG*$_{KB}$.

Table 2 Binding of hsa-miR-18a-3p with pharmacologically significant genes of psoriasis

Genes (*PharmGKB*)	Number of binding sites (*miRmap*)
PSORS1C1	1
MTHFR	2
CLCN6	2
FCGR2A	1
FCGR3A	1
TNFAIP3	1

Table 3 Binding of hsa-miR-18a-5p with pharmacologically significant genes of psoriasis

Genes (*PharmGKB*)	Number of binding sites (*miRmap*)
PSORS1C2	1
ABCC1	1
MTHFR	9
CLCN6	1
SLC19A1	1
TNFRSF10A	2
VDR	4

According to the results Enrichr, it has been identified that has-miR-18a has the least ***p*** value of 0.07204 and hence we consider this miRNA for binding analysis to identify its compatibility in therapy.

Conclusion

Based on the binding analysis of miRmap, it has been identified that hsa-miR-18a-3p has a potential to become a therapeutic target for Psoriasis because it binds the mRNA of 7 genes (PSORS1C2, ABCC1, MTHFR, CLCN6, SLC19A1, TNFRSF10A and VDR) which are associated with the pharmacogenomics of Psoriasis. Whereas hsa-miR-18a-5p binds only with the mRNAs of 6 genes (PSORS1C1, MTHFR, CLCN6, FCGR2A, FCGR3A and TNFAIP3) which are associated with the pharmacogenomics of Psoriasis. Micro RNAs hsa-miR-18a-3p and hsa-miR-18a-5p bind with the mRNA of PSORS1C2 and PSORS1C1 respectively, which is a novel insight for associating the regulation of hsa-miR-18a-3p and hsa-miR-18a-5p in the signalling pathways of Psoriasis which involves the gene product of PSORS1C2 and PSORS1C1. hsa-miR-18a-3p contains 9 sites for mRNA binding in MTHFR and hence hsa-miR-18a-3p may also be used as a therapeutic target for diseases which contain MTHFR as a key component in their pathways.

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Conflict of interest

The author declares no conflict of interest.

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