RESEARCH ARTICLE

Computational Analysis of Expression Based Regulation in Psoriasis: An Approach of Systems Biology to Understand Disease Pathology and Predict Potential Regulators

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Abstract

In the era of post genomics, computational analysis of expression based regulation in Psoriasis by the approach of Systems Biology to understand the pathology of disease and predicting a potential regulator is a challenging task to execute. The challenge was approached on the context of bottom-up approach [Expression analysis of Psoriasis associated genes from RNA Seq data with text mining of regulators (microRNAs and Transcription Factors)] to construct and analyze the network by the approach of Systems Biology for understanding the disease pathology and predict potential regulators to enhance the discovery of biomarker for Psoriasis in future.

Introduction

Psoriasis is considered as an autoimmune disease because both genetic and environmental factors play a significant role in cause. The name "Psoriasis" was derived from Greek word "psora" which means "itch". Psoriasis is non-contagious and dry inflammatory disorder with ugly skin; it involves the entire system of person [1]. In most cases, it is inherited and characterized by marginated scaly and erythematous plaques that develop in a relatively symmetrical distribution. The most affected sites were the scalp, palms, soles, umbilicus, gluteus, under the breasts and genitals, elbows, knees, tips of fingers and toes [2]. In nature, this disease is chronic with a tendency to relapse. In this disease, the skin keeps peeling to create a scaling as flakes and it is termed as "Psoriatic Plaques" due to excessive multiplication of epidermis cells to create fishy skin. Psoriasis can affect both male and female. It can occur at any age, though the common appearance for the first time is generally between ages 15-25 years. In western population, the prevalence of psoriasis was estimated to be around 2-3%. The prevalence of psoriasis in the United Kingdom was found to be 1.5% [3]. In Americans, the prevalence of psoriasis was found to be 2.1% among adults. The results from case studies found that around 25% of people with psoriasis could be classified from moderate to severe psoriasis [4]. Around one-third of people with psoriasis were reported with a family history and researchers have identified the association of genetic loci with the diseased condition [5]. Studies on monozygotic twins suggest 70% chance for a twin to develop psoriasis, if the other is affected. The rate of concordance was around 20% for dizygotic twins. The finding suggests that both predisposition in genetics and response in environment were involved in the development of psoriasis. Early onset before 4 years indicates a greater susceptibility in genetics of psoriasis [6].

Psoriasis is a disorder mediated by immune system by making certain faulty signals in the human body. It's still a belief that psoriasis can be developed under the specified condition i.e. "when the immune system signals the body to accelerate the growth of skin cells. Normally, skin cells get matured from the surface of the skin on every 28-30 days [7]. In case of psoriasis, the skin cells mature in 3-6 days. Instead of being in shed, the cells in skin get pile up to cause the visible lesions. It was also found that the genes that cause psoriasis can determine the reaction of a person's immune system. These genes can either cause psoriasis or other conditions which are immune-mediated like Type-I Diabetes or rheumatoid arthritis. Pathophysiology of psoriasis involves the understanding of the occurrence of prominent pathologies in the major components of skin i.e. the epidermis and the dermis. There are two well established hypotheses about the process that occurs in the development of the disease. The first hypothesis considers psoriasis as a disorder with excessive growth and reproduction of skin cells. Here, the problem is viewed as a fault of the epidermis and its keratinocytes [8]. In second hypothesis, the disease is viewed as an immune-mediated disorder. Here, the excessive reproduction of skin cells is secondary to the factors produced by the immune system [9,10]. In Current research, the inflammatory mechanisms are immune based and

maintained by T cells in dermis. Antigen-presenting cells in skin like Langerhans cells were believed to migrate from skin to the regional lymph nodes to interact with T cells. Presentation of an unidentified antigen to the T cells along with various co-stimulatory signals triggers an immune response to lead to the activation of T cells and release of cytokines. Co-stimulatory signals were initiated by the interaction of adhesion molecules on the antigen-presenting cells like lymphocyte function-associated antigen (LFA)-3 and the intercellular adhesion of molecules with their respective receptors (CD2 and LFA-1) on T cells. These T cells are released into the circulation.

Reactivation of T cells in dermis and epidermis with local effects of cytokines like tumor necrosis factor (TNF) to lead to the cell mediated immune responses, inflammation and epidermal hyper proliferation in persons with psoriasis. The immune based model of psoriasis was supported on the basis of the observation that the immunosuppressant medications can clear plaques in psoriasis. However, the complete role of the immune system needs refinement in understanding. It was recently reported that an animal model of psoriasis can be triggered in mice without T cells. This concept is a paradox to researchers because the reduction in the count of T-cell causes psoriasis but the count of CD4-T-cell decreases with the progression of HIV in psoriasis [11]. As an additive, HIV is characterized by a strong profile of Th2 cytokine but psoriasis vulgaris is characterized with a strong secretion pattern of Th1. It was also hypothesized that the presence of diminished CD4-T-cell can cause an over-activation in CD8-T-cells to exacerbate the cause of psoriasis in patients with HIV positive [10].

Materials and Methods

GEO

Gene Expression Omnibus (GEO) is an open access public repository for next-generation sequencing, RNA Seq, microarray and other forms of high-throughput functional genomics data submitted by the research community. It provides a robust database to store the high-throughput functional data in genomics with a simple procedure and format for submission.

Array Express

Array Express is an archive of functional genomics; in which the data from high-throughput experiments on functional genomics were stored for reusability in the research community.

Target Scan

Target Scan is a web server to predict the biological targets of miRNAs by searching for the presence of target sites that matches with the seed region of each miRNA. The target predictions of each miRNA are updated regularly [12].

miRTar Base

miRTar Base is a curated database of miRNA based target interactions. At present, miRTar Base has accumulated more than fifty thousand interactions of miRNA with target (MTIs); the interactions were manually collected by surveying the literature after the processing of data mining of the text to filter

research articles to functional studies of miRNAs in a systematic method [13]. In general, the MTIs were also experimentally validated by a reporter assay, western blot, microarray and experiments on next-generation sequencing. The miRTar Base provides the most updated collection by comparing with the previously developed databases.

Reg Networks

Reg Network is a data base that contains five types (Transcription Factor-Transcription factor, Transcription Factor-Gene, Transcription Factor-microRNA, microRNA-Transcription Factor) of transcriptional and posttranscriptional regulatory relationships for human and mouse [14]. RegNetwork integrates the curated regulations from various databases and the potential regulations were inferred on the basis of transcription factor binding sites (TFBSs). Transcription factor (TF) and microRNA (miRNA) in gene regulations. Recently, more regulatory relationships in databases and literatures are available and it's valuable for studying the system of gene regulation by integrating the prior knowledge of the transcriptional regulations between TF and target genes along with the posttranscriptional regulations between miRNA and targets. The conservation of knowledge about the binding site of transcription factor (TFBS) can also be implemented to couple the potential regulation between regulators and their targets.

Cytoscape

Cytoscape software is used for network construction, visualization and analysis in bioinformatics with an open source platform for visualizing the interactions in molecular networks and integrating them with the profiles of gene expression [15]. Additional features in cytoscape are available as plugins for network and molecular profiling. Plugins may be developed using the Cytoscape.

Method (Bottom-Up Approach)

- Obtain the list of genes associated with psoriasis from GEO/Array Express (RNAseq).

- Analyze the list of up-regulated and down-regulated genes on the basis of statistical deviation between lesional and non-lesional expression.

- Obtain the list of miRNA associated with the differently expressed genes of psoriasis from miRTarbase and TargetScan.

- Obtain the list of transcription factors associated with psoriasis related genes from RegNetworks.

- Construct and analyze the network in Cytoscape.

Results and Discussion

Expression Analysis (RNA Seq)

In case of gene identification from RNA seq data, the genes associated with psoriasis were retrieved from GEO/Array Express. Psoriasis associated gene search in GEO/Array Express resulted in 2 identifiers (E-GEOD-4175, E-GEOD-54456) with 200 genes that are differentially expressed (Table 1).

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In order to proceed to the bottom-up approach, the expressed genes were subjected to the regulatory analysis and it was observed that only 118 genes among 200 contain sites for regulation.

Bottom-Up Approach

In case of bottom up approach in regulatory analysis of genes associated with psoriasis; the genes are paired with the associated miRNAs and Transcription Factors (Table 2)

Further the genes, miRNAs and proteins in bottom-up approach were subjected to network analysis and the further details about the statistical methods were given below.

Table 1: Expression Analysis of Psoriasis associated genes

E-GEOD-4175		E-GEOD-54456	
Genes (RNA seq)	Fold Change (lesional vs non lesional)	Genes (RNA seq)	Fold Change (lesional vs non lesional)
SERPINB4	6.3	IL36A	10.9
SERPINB3	5.2	DEFB4A	10.2
S100A12	5.1	IL19	9.8
SPRR2C	4.8	SPRR2C	9.8
TCN1	4.7	HSPD1P3	9.4
PI3	4.7	PI3	9
S100A9	4.4	CLEC3A	8.5
CH507-513H4.4	4.4	SPRR2F	8.4
KRT6C	4.2	VNN3	8.3
KRT6A	4.1	S100A12	8.1
KRT16	4.1	CXCL8	8
TMPRSS11D	4.1	TCN1	7.8
LTF	3.8	HSPD1P2	7.7
GJB2	3.7	TMPRSS11D	7.6
PLA2G4D	3.6	IL17A	7.6
TNIP3	3.6	SPRR2B	7.5
VNN3	3.4	DEFB4B	7.4
S100A8	3.4	SERPINB4	7.2
ACP7	3.3	LCE3A	7.1
OASL	3.3	TNIP3	7.1
HEPHL1	3.3	TMPRSS11A	7.1
SLC6A14	3.1	SPRR3	7
AKR1B10	3.1	KRT6C	6.9
RHCG	3.1	SPRR2A	6.9
SPRR1A	3	KRT24	6.9
TYMP	3	S100A7	6.8
SPRR2A	3	S100A9	6.8
ARSF	2.9	S100A7A	6.8
ADAMDEC1	2.9	S100A8	6.7
NOS2	2.9	SERPINB3	6.6
CNFN	2.7	IL17F	6.5
RP4-529N6.2	2.7	LCE3B	6.5
KCNK10	2.7	CXCL1	6.4
LINC01206	2.7	AKR1B10	6.2
S100A7A	2.7	HEPHL1	6.2
KLK13	2.6	LCE3C	6
TGM1	2.6	CXCL13	5.9
SLC26A9	2.6	SPRR2D	5.9
HSPD1P3	2.6	C12orf74	5.9
FABP5	2.5	CTC-490G23.2	5.8
IFI27	2.5	CLDN17	5.7
SPRR1B	2.5	GDA	5.7
IL36A	2.5	LTF	5.7
GJB6	2.4	IL22	5.7
HAL	2.4	IL20	5.6
UPP1	2.4	IL36G	5.6
ZC3H12A	2.4	AL591704.7	5.6
ADGRF1	2.4	CASP5	5.5
FUT3	2.4	C10orf99	5.4
SERPINB13	2.3	NOS2	5.4
WIF1	-2.6	AGR3	-6.8
RP11-1008C21.1	-2.4	AC092635.1	-5.1
UGT3A2	-2.4	SOHLH1	-4.8
AWAT2	-2.3	CYP1A2	-4.7
RP11-517M22.1	-2.3	CYP2W1	-4.6
CDH12	-2.2	CDK8P2	-4.6
DDX25	-2.1	UGT3A2	-4.5
KRT28	-2.1	RP1-97J1.2	-4.3
GAL	-2.1	BTC	-4.2
GPR12	-2	DDC	-4.2
ROS1	-2	RP11-438F14.3	-4.2
AXDND1	-2	RP11-98L5.5	-4.1
SLC14A1	-1.9	KB-1410C5.3	-4.1
MYEOV	-1.9	AC016730.1	-4.1
TPPP	-1.8	RP13-392I16.1	-4.1
MUC16	-1.8	AC008268.1	-4.1
WDR72	-1.8	CHRM4	-4
HMGCS2	-1.8	RP11-407H12.8	-4
TNNI2	-1.8	ASNSP1	-4
CNTNAP3B	-1.7	SYT9	-3.9
ANKRD18A	-1.7	SLC26A3	-3.9
ANKRD33B	-1.7	RP11-350F16.2	-3.9
ERBB4	-1.7	SPINK1	-3.8
KRT77	-1.7	CILP2	-3.8
ZDHHC11B	-1.7	LINC02169	-3.8
IGFL2	-1.6	PRB1	-3.8
TMEM132B	-1.6	RP11-508M8.1	-3.8
CNTNAP3	-1.6	RP11-3N13.2	-3.8
CNKSR2	-1.6	SPINT3	-3.8
RAB3B	-1.6	EEF1GP2	-3.7
RP11-53O19.1	-1.6	AADACL3	-3.7
FREM2	-1.6	KRT77	-3.6
ACADL	-1.6	HSD3B1	-3.6
CYP4A11	-1.6	RP11-350F16.1	-3.6
BTBD16	-1.6	AC138647.1	-3.6
SLC26A5	-1.6	HSD3BP2	-3.5
WFDC3	-1.6	AP003025.2	-3.5
ACTC1	-1.6	GJB4	-3.4
LHCGR	-1.6	AP000439.3	-3.4
FADS2	-1.6	LINC01300	-3.4
CLEC2A	-1.5	FADS2	-3.4
ATP6V0A4	-1.5	ELOVL3	-3.4
GRIN2A	-1.5	HAO2	-3.4
SYT17	-1.5	THRSP	-3.4
RORC	-1.5	LINC01497	-3.4
KB-1460A1.5	-1.5	RP11-257I8.2	-3.4
CA1	-1.5	AC000111.6	-3.4
CHRM3	-1.5	NAT16	-3.4
FPGT-TNNI3K	-1.5	SPATA31D1	-3.4
ADAM1B	-1.5	LINC01164	-3.4

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Table 2: Associated genes, miRNAs and Transcription factors of Psoriasis (Bottom-Up Approach)

Genes (RNA Seq.- GEO/Array Express)	miRNAs (miRtarbase / Target Scan)	Transcription Factor (RegNetworks)
WIF1	hsa-miR-127-5p; hsa-miR-129-5p; hsa-miR-137; hsa-miR-140-3p; hsa-miR-144; hsa-miR-15a; hsa-miR-15b; hsa-miR-16; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d hsa-miR-194; hsa-miR-195; hsa-miR-200b; hsa-miR-200c; hsa-miR-216b hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-330-3p; hsa-miR-335; hsa-miR-33a; hsa-miR-33b; hsa-miR-424; hsa-miR-429; hsa-miR-450b-5p hsa-miR-485-3p; hsa-miR-497; hsa-miR-498; hsa-miR-556-5p; hsa-miR-578; hsa-miR-586; hsa-miR-603; hsa-miR-654-3p; hsa-miR-656; hsa-miR-889	CTCF; CUX1
AWAT2	hsa-let-7d; hsa-let-7g; hsa-let-7i; hsa-miR-185; hsa-miR-34b; hsa-miR-361-5p; hsa-miR-518a-5p; hsa-miR-768-3p hsa-miR-802; hsa-miR-922	FOXJ2
CDH12	hsa-miR-137; hsa-miR-383; hsa-miR-453; hsa-miR-499-3p; hsa-miR-511; hsa-miR-519a; hsa-miR-548a-3p; hsa-miR-548c-3p; hsa-miR-648; hsa-miR-922	FOXO4; HSF2
DDX25	hsa-miR-142-5p; hsa-miR-32	REST; USF1
KRT28	hsa-miR-105; hsa-miR-130a; hsa-miR-143; hsa-miR-301a; hsa-miR-338-5p hsa-miR-495; hsa-miR-501-5p; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-567; hsa-miR-570; hsa-miR-574-5p; hsa-miR-595; hsa-miR-7; hsa-miR-944	CTCF; PAX6; POU2F1; POU3F2
GAL	hsa-miR-154; hsa-miR-338-5p; hsa-miR-345; hsa-miR-376c; hsa-miR-548a-5p; hsa-miR-548c-5p; hsa-miR-665; hsa-miR-888	MAX; MYC; TAL1; TCF4 TFAP2A; TFAP2C
GPR12	hsa-miR-302a; hsa-miR-302b; hsa-miR-302c; hsa-miR-302d; hsa-miR-372; hsa-miR-373; hsa-miR-520a-3p hsa-miR-520b; hsa-miR-520c-3p hsa-miR-520d-3p; hsa-miR-520e	Nil
ROS1	hsa-miR-325; hsa-miR-33a; hsa-miR-33b; hsa-miR-586; hsa-miR-606; hsa-miR-609; hsa-miR-613	ABL1
AXDND1	hsa-miR-506; hsa-miR-509-5p; hsa-miR-557; hsa-miR-890	GABPA; SPI1; YY1
SLC14A1	hsa-miR-100; hsa-miR-200b; hsa-miR-200c; hsa-miR-429; hsa-miR-496; hsa-miR-500; hsa-miR-501-5p; hsa-miR-575; hsa-miR-586; hsa-miR-591; hsa-miR-768-5p; hsa-miR-99a; hsa-miR-99b	CREB1; CTCF; GATA1; HNF4A; NFE2; TAL1::GATA1; TBP
MYEOV	hsa-miR-105; hsa-miR-214; hsa-miR-365; hsa-miR-610; hsa-miR-650	CTCF; NFYA; NFYB; NFYC
TPPP	hsa-miR-1; hsa-miR-206	Nil
WDR72	hsa-miR-186; hsa-miR-576-5p; hsa-miR-599	Nil
HMGCS2	hsa-miR-490-5p	AR; CEBPA; NFIC; PPARA; RXRA; RXRB; RXRG; TFAP2A
TNNI2	Nil	CTCF; CUX1; ELK1; POU2F1; RORA; SPI1; TFAP2A; TFAP2C
CNTNAP3B	Nil	HLF; STAT5A
ANKRD18A	hsa-miR-203; hsa-miR-518a-5p; hsa-miR-520g; hsa-miR-520h; hsa-miR-671-5p	Nil
ANKRD33B	Nil	EBF1; NFKB1; NFKB2; RELA; RELB; SPI1; TFAP2A; TFAP2C; USF1
ERBB4	hsa-miR-101; hsa-miR-106a; hsa-miR-125a-5p; hsa-miR-125b; hsa-miR-130a; hsa-miR-130b; hsa-miR-135a; hsa-miR-135b; hsa-miR-137; hsa-miR-144; hsa-miR-145; hsa-miR-146a; hsa-miR-146b-5p; hsa-miR-17; hsa-miR-184; hsa-miR-186; hsa-miR-199a-3p; hsa-miR-199b-3p; hsa-miR-19a; hsa-miR-19b; hsa-miR-200b; hsa-miR-200c; hsa-miR-205; hsa-miR-219-1-3p; hsa-miR-22; hsa-miR-221; hsa-miR-222; hsa-miR-23a; hsa-miR-23b hsa-miR-26a; hsa-miR-26b; hsa-miR-300; hsa-miR-301; hsa-miR-301a; hsa-miR-301b; hsa-miR-302d; hsa-miR-323-3p; hsa-miR-330-3p; hsa-miR-335 hsa-miR-339-5p; hsa-miR-340; hsa-miR-342-3p; hsa-miR-342-5p; hsa-miR-372; hsa-miR-377; hsa-miR-378 hsa-miR-383; hsa-miR-410; hsa-miR-422a; hsa-miR-429; hsa-miR-432; hsa-miR-433; hsa-miR-454; hsa-miR-495; hsa-miR-507; hsa-miR-508-3p; hsa-miR-518a-5p; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-519d; hsa-miR-520g; hsa-miR-520h; hsa-miR-527; hsa-miR-539; hsa-miR-548c-3p; hsa-miR-548d-3p; hsa-miR-571; hsa-miR-576-5p; hsa-miR-578; hsa-miR-579; hsa-miR-583; hsa-miR-584; hsa-miR-590-3p; hsa-miR-606; hsa-miR-653; hsa-miR-7; hsa-miR-876-5p; hsa-miR-93; hsa-miR-940; hsa-miR-944; hsa-miR-96	CEBPB; EP300; MEF2A; MEIS1; SMURF2; STAT5A; STAT5B; WWP1
TMEM132B	hsa-miR-10a; hsa-miR-10b; hsa-miR-137; hsa-miR-143; hsa-miR-148b; hsa-miR-152; hsa-miR-199a-5p; hsa-miR-19a; hsa-miR-19b; hsa-miR-218; hsa-miR-221; hsa-miR-222; hsa-miR-224; hsa-miR-297; hsa-miR-298; hsa-miR-338-3p; hsa-miR-377; hsa-miR-433; hsa-miR-548c-3p; hsa-miR-590-3p; hsa-miR-653; hsa-miR-766	Nil

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Gene	miRNAs	Transcription Factors
CNTNAP3	hsa-miR-22; hsa-miR-26a; hsa-miR-26b; hsa-miR-9	HLF; STAT5A
CNKSR2	hsa-miR-144; hsa-miR-199b-5p; hsa-miR-21; hsa-miR-25; hsa-miR-28-3p; hsa-miR-29b; hsa-miR-30c; hsa-miR-32; hsa-miR-363; hsa-miR-374a; hsa-miR-374b; hsa-miR-450b-5p; hsa-miR-491-3p; hsa-miR-516b; hsa-miR-542-3p; hsa-miR-554; hsa-miR-627; hsa-miR-643; hsa-miR-942; hsa-miR-944	BACH2; NFE2
RAB3B	hsa-miR-194	SMAD1; SMAD4; TLX2
FREM2	hsa-miR-142-3p; hsa-miR-142-5p; hsa-miR-147; hsa-miR-150; hsa-miR-200b; hsa-miR-200c; hsa-miR-24; hsa-miR-299-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-30b; hsa-miR-32; hsa-miR-363; hsa-miR-367; hsa-miR-412; hsa-miR-429; hsa-miR-494; hsa-miR-509-3p; hsa-miR-544; hsa-miR-548c-3p; hsa-miR-556-3p; hsa-miR-568; hsa-miR-580; hsa-miR-590-3p; hsa-miR-607; hsa-miR-628-3p hsa-miR-633; hsa-miR-802; hsa-miR-885-5p; hsa-miR-9	CTCF; EGR3; SP1; TBP; ZEB1
ACADL	hsa-miR-142-3p; hsa-miR-299-3p; hsa-miR-518a-5p; hsa-miR-641	PPARD; RXRA; RXRB RXRG
CYP4A11	hsa-miR-150	AR; HNF4A; PPARA; PPARD; PPARG; RXRA; RXRB; RXRG
BTBD16	hsa-miR-204; hsa-miR-211; hsa-miR-337-3p; hsa-miR-491-3p; hsa-miR-548c-3p; hsa-miR-599; hsa-miR-605; hsa-miR-625; hsa-miR-875-3p	CTCF; ELK1; TFAP2C; TLX2
WFDC3	hsa-miR-185; hsa-miR-28-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-329; hsa-miR-331-3p; hsa-miR-361-3p; hsa-miR-362-3p; hsa-miR-455-3p; hsa-miR-619; hsa-miR-657; hsa-miR-765; hsa-miR-875-3p; hsa-miR-923	ATF1; ATF2; ATF3; ATF4; ATF5; ATF6; ATF7; CTCF; E2F1; ELK1; GABPA; JUN; NR3C1; RFX1; SP1; SPI1
ACTC1	hsa-miR-142-5p; hsa-miR-185; hsa-miR-195; hsa-miR-200b; hsa-miR-200c; hsa-miR-25; hsa-miR-30a; hsa-miR-30a-5p; hsa-miR-30b; hsa-miR-30c; hsa-miR-30d; hsa-miR-30e; hsa-miR-32; hsa-miR-324-3p; hsa-miR-340; hsa-miR-363; hsa-miR-367; hsa-miR-369-3p; hsa-miR-429; hsa-miR-495; hsa-miR-508-5p; hsa-miR-608; hsa-miR-7; hsa-miR-768-5p; hsa-miR-876-3p; hsa-miR-92a; hsa-miR-92b	BACH1; CUX1; IRF1; MEF2A; SRF; TFAP2A; TFAP2C; TGIF1; ZEB1
LHCGR	hsa-miR-148b; hsa-miR-545	NFIC; SP1; TFAP2A
FADS2	hsa-let-7b	AR; CEBPA; CTCF; CUX1; DDIT3; HNF4A; MYC; PPARA; RXRA; RXRB; RXRG
GRIN2A	hsa-miR-101; hsa-miR-125a-5p; hsa-miR-125b; hsa-miR-137; hsa-miR-139-5p; hsa-miR-194; hsa-miR-19a; hsa-miR-19b; hsa-miR-206; hsa-miR-216b; hsa-miR-220b; hsa-miR-299-5p; hsa-miR-325; hsa-miR-329; hsa-miR-330-5p; hsa-miR-331-5p; hsa-miR-362-3p; hsa-miR-376a; hsa-miR-376b; hsa-miR-451; hsa-miR-454; hsa-miR-510; hsa-miR-519d; hsa-miR-520h; hsa-miR-525-5p; hsa-miR-574-3p; hsa-miR-576-5p; hsa-miR-577; hsa-miR-584; hsa-miR-593; hsa-miR-598; hsa-miR-603; hsa-miR-628-5p; hsa-miR-630; hsa-miR-656; hsa-miR-765 hsa-miR-767-5p; hsa-miR-9; hsa-miR-939	AHR; ARNT; CTCF; PAX5; REST; USF1
SYT17	hsa-miR-22; hsa-miR-297; hsa-miR-380; hsa-miR-574-5p; hsa-miR-633	CTCF; MYC; PAX5; RREB1; TSC22D4
RORC	hsa-let-7a; hsa-let-7b; hsa-let-7c; hsa-let-7e; hsa-let-7f; hsa-let-7g; hsa-let-7i hsa-miR-106b; hsa-miR-202; hsa-miR-205; hsa-miR-20a; hsa-miR-298; hsa-miR-485-5p; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-593; hsa-miR-605; hsa-miR-608; hsa-miR-766; hsa-miR-93; hsa-miR-98	ARNT; ARNTL; CEBPA; CHD4; CLOCK; CTCF; FOXO4; LMO2; MAX; MXI1::CLEC5A; NCOA6 NKX2-2; NPAS2; PPARG SREBF1; SREBF2; TAL1 TCF3; USF1; ZEB1
CA1	hsa-miR-944	TBP
CHRM3	hsa-miR-30c; hsa-miR-629	TFAP2A
FPGT-TNNI3K	Nil	AHR; ARNT; E2F1; E2F2 E2F3; E2F4; E2F5; E2F6 E2F7; EGR1; YY1
AGR3	hsa-miR-32; hsa-miR-367; hsa-miR-448; hsa-miR-455-5p; hsa-miR-507; hsa-miR-548a-3p; hsa-miR-548c-3p; hsa-miR-557; hsa-miR-573; hsa-miR-656; hsa-miR-876-5p	Nil
SOHLH1	hsa-miR-132; hsa-miR-220c; hsa-miR-484; hsa-miR-504; hsa-miR-516a-3p; hsa-miR-520a-5p; hsa-miR-525-5p; hsa-miR-600	CTCF; USF1
CYP1A2	Nil	CUX1; NFIC;NKX6-1; TAL1; TCF4; USF1; USF2 YY1
CYP2W1	hsa-miR-423-3p; hsa-miR-608; hsa-miR-637	ZIC2
BTC	hsa-miR-490-3p	CTCF; FOXC1; TFAP2A USF1

Gene	miRNA	TF
DDC	Nil	AR; HNF1A; RORA
CHRM4	Nil	ARID5B; E2F1; E2F2; E2F3; E2F4; E2F5; E2F6 E2F7; FOXO4; GATA1
SYT9	hsa-miR-1271; hsa-miR-196a; hsa-miR-196b; hsa-miR-19a; hsa-miR-19b; hsa-miR-205; hsa-miR-29b; hsa-miR-326; hsa-miR-330-5p; hsa-miR-34a; hsa-miR-34c-5p; hsa-miR-448; hsa-miR-485-5p; hsa-miR-619; hsa-miR-671-5p; hsa-miR-9; hsa-miR-96	PATZ1; PAX5
SLC26A3	hsa-let-7a; hsa-let-7b; hsa-let-7c; hsa-let-7d; hsa-let-7f; hsa-miR-125a-3p; hsa-miR-137; hsa-miR-142-5p; hsa-miR-190; hsa-miR-190b; hsa-miR-20b; hsa-miR-21; hsa-miR-28-3p; hsa-miR-340; hsa-miR-382; hsa-miR-494 hsa-miR-556-5p; hsa-miR-561; hsa-miR-568; hsa-miR-576-3p; hsa-miR-590-5p; hsa-miR-592; hsa-miR-620 hsa-miR-624; hsa-miR-649; hsa-miR-652; hsa-miR-93; hsa-miR-98	ETS1; GATA1; HNF1A; PPARG; TBP
SPINK1	hsa-miR-659; hsa-miR-876-5p	CEBPB; FOXA2; FOXD1 FOXF2; HNF1A; RXRA
CILP2	Nil	CREB1; LMO2
SPINT3	Nil	REST
AADACL3	hsa-miR-32; hsa-miR-520a-5p; hsa-miR-525-5p	Nil
HSD3B1	hsa-let-7b; hsa-let-7c; hsa-miR-181a; hsa-miR-181c; hsa-miR-371-5p; hsa-miR-492; hsa-miR-543; hsa-miR-571; hsa-miR-578; hsa-miR-608; hsa-miR-650; hsa-miR-665; hsa-miR-885-3p	Nil
GJB4	Nil	NR2F2; PAX2; STAT5A; TCF3; TFAP2A; TFAP2C
ELOVL3	hsa-miR-150; hsa-miR-191; hsa-miR-194; hsa-miR-23a; hsa-miR-23b; hsa-miR-326; hsa-miR-491-5p; hsa-miR-494; hsa-miR-516b; hsa-miR-532-3p; hsa-miR-548a-5p; hsa-miR-559; hsa-miR-578; hsa-miR-653; hsa-miR-671-5p; hsa-miR-802; hsa-miR-874	ARNT; NFYA
HAO2	Nil	POU2F1
THRSP	hsa-let-7a; hsa-let-7c; hsa-let-7f; hsa-let-7g; hsa-let-7i; hsa-miR-98	CUX1; RXRA; SREBF1; SREBF2;TP53
NAT16	Nil	SP1
SERPINB4	Nil	FOXD1; CEBPA; FOXD1
S100A12	hsa-miR-185; hsa-miR-574-5p; hsa-miR-602; hsa-miR-921	Nil
SPRR2C	hsa-miR-196a	RORA; SRF
TCN1	hsa-miR-154; hsa-miR-185; hsa-miR-30a; hsa-miR-421; hsa-miR-491-3p; hsa-miR-502-3p; hsa-miR-549; hsa-miR-95	CTCF
PI3	hsa-miR-214; hsa-miR-298; hsa-miR-299-3p; hsa-miR-383; hsa-miR-422a; hsa-miR-552; hsa-miR-564; hsa-miR-675; hsa-miR-768-5p; hsa-miR-885-3p; hsa-miR-892b; hsa-miR-922	MXI1::CLEC5A
S100A9	hsa-miR-196a	AR; CTCF; MYB; RARA; RARB; RARG; SPI1; TBP; TFAP2A; TP53
KRT6C	Nil	PPARG; E2F1; FOS; TBP; AHR; ARNT; BACH1; FOS; FOSB; FOSL1; JUN; JUNB; JUND; RREB1; SP1; SP3; TFAP2; TOPORS
TMPRSS11D	hsa-miR-590-3p	HLF; IRF1
LTF	hsa-miR-214	CEBPA; CEBPE; ESR1; ETS1; SP1; SPI1
GJB2	hsa-miR-323-3p; hsa-miR-944	E2F4; ETV4; HNF1A; JUN
PLA2G4D	Nil	POU2F1; POU2F2; POU3F1; POU3F2; POU3F3; POU5F1; RFX1
TNIP3	hsa-miR-338-5p	CEBPB; SPI1; TGIF1
VNN3	hsa-miR-135a; hsa-miR-135b; hsa-miR-199a-3p; hsa-miR-345; hsa-miR-371-5p; hsa-miR-421; hsa-miR-455-3p; hsa-miR-455-5p; hsa-miR-505; hsa-miR-514; hsa-miR-744	CTCF; FOXA2; NFKB1; NFKB2; REL; RELA; STAT5B
S100A8	hsa-miR-135a; hsa-miR-135b; hsa-miR-202; hsa-miR-326; hsa-miR-330-5p; hsa-miR-544	AR; FOS; FOSB; JUN; JUND; PDCD11; RARA; RARB; RARG; TBP; TP53

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OASL	hsa-miR-1; hsa-miR-184; hsa-miR-206 hsa-miR-298; hsa-miR-516b	MBD1; THRA
HEPHL1	hsa-miR-1297; hsa-miR-145; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d; hsa-miR-195; hsa-miR-26a; hsa-miR-26b; hsa-miR-30a; hsa-miR-30b; hsa-miR-30c; hsa-miR-30d; hsa-miR-30e; hsa-miR-424; hsa-miR-494; hsa-miR-543; hsa-miR-573	STAT3
SLC6A14	hsa-miR-23a; hsa-miR-23b; hsa-miR-299-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-340; hsa-miR-367; hsa-miR-374b; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-3p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-576-5p	CEBPA; NFKB1; NFKB2 NR2F2; REL; RELA; TCF3; TLX2
AKR1B10	hsa-let-7a; hsa-let-7c; hsa-let-7d; hsa-let-7f; hsa-let-7g; hsa-let-7i; hsa-miR-196a; hsa-miR-196b; hsa-miR-923; hsa-miR-98	MYC
RHCG	Nil	CTCF; EGR1; EGR2; EGR3; GATA1; SREBF1 SREBF2; USF1
SPRR1A	hsa-miR-105; hsa-miR-24; hsa-miR-382; hsa-miR-423-3p; hsa-miR-484; hsa-miR-501-3p; hsa-miR-502-3p; hsa-miR-509-3-5p; hsa-miR-509-5p; hsa-miR-518a-5p; hsa-miR-542-3p; hsa-miR-555; hsa-miR-609; hsa-miR-7; hsa-miR-768-5p	BACH1; BACH2; FOS; FOSB; FOSL1; JUN; JUNB; JUND
TYMP	Nil	ATF1; ATF2; ATF3; ATF4; ATF5; ATF6; ATF7; E2F1; E2F2; E2F3; E2F4; E2F5; E2F6; E2F7; EGR1; FOXI1; FOXO3; FOXO3B; GABPA; HNF4A; LMO2; MAX; MYC; PPARG; SRF; STAT1; USF1
SPRR2A	hsa-miR-127-5p; hsa-miR-133a; hsa-miR-133b; hsa-miR-185; hsa-miR-28-5p; hsa-miR-383; hsa-miR-610; hsa-miR-920	FOS; JUN; MEF2A; NFKB1; POU2F1; POU2F3; TAL1::GATA1
ARSF	Nil	CTCF; FOXA1; FOXA2; HNF4A; PPARG::RXRA; RXRA
NOS2	Nil	CEBPA; CEBPB; CEBPD; ESR1; HIF1A; JUN; NFIL3; NFKB1; NFKB2; NR2F2; RELA; STAT1; STAT3; TP53; USF1
CNFN	Nil	POU2F1; REST
KCNK10	hsa-miR-101; hsa-miR-124; hsa-miR-128; hsa-miR-128a; hsa-miR-128b; hsa-miR-181b; hsa-miR-182; hsa-miR-183; hsa-miR-22; hsa-miR-25; hsa-miR-32; hsa-miR-329; hsa-miR-331-5p; hsa-miR-362-3p; hsa-miR-363; hsa-miR-367; hsa-miR-455-3p; hsa-miR-485-5p; hsa-miR-498; hsa-miR-506; hsa-miR-507; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-579; hsa-miR-649; hsa-miR-92a; hsa-miR-92b; hsa-miR-96	E2F1; EGR3; FOS; FOSB; FOSL1; FOXO4; JUN; JUNB; JUND; MEF2A; MIF; TLX2
S100A7A	hsa-miR-128a; hsa-miR-27a; hsa-miR-27b; hsa-miR-504; hsa-miR-613; hsa-miR-625	TGIF1
KLK13	hsa-miR-455-5p; hsa-miR-542-3p; hsa-miR-591; hsa-miR-620; hsa-miR-654-5p	CREB1; EGR1; KLF12; MZF1; PPARG
TGM1	hsa-miR-130a; hsa-miR-130b; hsa-miR-142-3p; hsa-miR-148a; hsa-miR-148b; hsa-miR-149; hsa-miR-152; hsa-miR-301a; hsa-miR-301b; hsa-miR-345; hsa-miR-34a; hsa-miR-34c-5p; hsa-miR-361-3p; hsa-miR-378; hsa-miR-422a; hsa-miR-449a; hsa-miR-449b; hsa-miR-454; hsa-miR-502-5p; hsa-miR-508-5p; hsa-miR-558; hsa-miR-564; hsa-miR-617; hsa-miR-648; hsa-miR-920; hsa-miR-939	AR; ESR1; HOXA7; RARA; RARB; RARG; TGIF1; TP5
SLC26A9	hsa-miR-1271; hsa-miR-181a; hsa-miR-181c; hsa-miR-181d; hsa-miR-22; hsa-miR-34c-3p; hsa-miR-378; hsa-miR-453; hsa-miR-532-3p; hsa-miR-543; hsa-miR-607; hsa-miR-645; hsa-miR-659; hsa-miR-760; hsa-miR-890; hsa-miR-96	ESR1; FOXI1; JUN; NFYA; NFYB; NFYC; POU3F2; RREB1
FABP5	hsa-miR-144; hsa-miR-198; hsa-miR-203; hsa-miR-525-5p; hsa-miR-553; hsa-miR-562; hsa-miR-576-5p; hsa-miR-603; hsa-miR-616; hsa-miR-620	CTCF; E2F1; MAX; MYC
SPRR1B	Nil	JUN
IL36A	Nil	SRF; TBP
GJB6	hsa-miR-203; hsa-miR-21; hsa-miR-628-3p	AHR; ARNT; RORA
HAL	Nil	CEBPB; SREBF1; SREBF2; TFAP2A
UPP1	hsa-miR-301a; hsa-miR-301b; hsa-miR-384; hsa-miR-539; hsa-miR-561	EBF1; FLI1; HNF4A; MAX; MXI1::CLEC5A; MYC; TFAP2A; USF1

ZC3H12A	hsa-let-7i; hsa-miR-139-5p; hsa-miR-144; hsa-miR-192; hsa-miR-193a-3p; hsa-miR-193b; hsa-miR-369-5p; hsa-miR-421; hsa-miR-431; hsa-miR-432; hsa-miR-449b; hsa-miR-486-3p; hsa-miR-768-5p; hsa-miR-885-3p; hsa-miR-9	CEBPA; EGR1; FOS; FOSB; FOSL1; JUN; JUNB; JUND; PAX6; RFX1; SREBF1; SREBF2; SRF
FUT3	hsa-miR-125a-3p	Nil
DEFB4A	hsa-miR-129-3p; hsa-miR-299-5p; hsa-miR-593; hsa-miR-646	CDC5L
IL19	Nil	CEBPA; CEBPB; CTCF NFKB1; NFKB2; REL; RELA; TCF3
CLEC3A	hsa-miR-363; hsa-miR-383; hsa-miR-624	SRF
SPRR2F	hsa-miR-127-5p; hsa-miR-18b; hsa-miR-383; hsa-miR-501-5p; hsa-miR-920	Nil
IL17A	hsa-miR-520f; hsa-miR-875-5p	BACH1; HOXA9; MEIS1; RORA; TBP
LCE3A	Nil	CTCF; FOS; FOSB; FOSL1; HNF1A; JUN JUNB; JUND
ZBTB17	Nil	TMPRSS11A
SPRR3	hsa-miR-338-3p; hsa-miR-641; hsa-miR-921	ATF1; FOS; JUN; POU2F1
KRT24	hsa-miR-127-5p; hsa-miR-198; hsa-miR-335; hsa-miR-378; hsa-miR-382 hsa-miR-422a; hsa-miR-488; hsa-miR-525-5p; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-559; hsa-miR-576-3p; hsa-miR-576-5p; hsa-miR-581; hsa-miR-599; hsa-miR-630; hsa-miR-640; hsa-miR-921	TFAP4
S100A7A	hsa-miR-128a; hsa-miR-27a; hsa-miR-27b; hsa-miR-504; hsa-miR-613; hsa-miR-625	TGIF1
IL17F	hsa-miR-501-3p; hsa-miR-502-3p; hsa-miR-544; hsa-miR-555; hsa-miR-573; hsa-miR-590-3p; hsa-miR-608; hsa-miR-924; hsa-miR-944; hsa-miR-96	CEBPB; JUN; RORA; TBP
CXCL1	Nil	JUN; MAPK11; MAPK12; MAPK13; MAPK14; NFKB1; PATZ1; REL; RELA; SP1; SP3
LCE3C	Nil	PAX6
CXCL13	hsa-miR-153; hsa-miR-186; hsa-miR-198; hsa-miR-340; hsa-miR-452; hsa-miR-590-3p	GATA1; GATA2; GATA3; POU2F1
C12orf74	Nil	POU2F1; SPI1
CLDN17	Nil	ARID5B
GDA	hsa-miR-106a; hsa-miR-106b; hsa-miR-10a; hsa-miR-10b; hsa-miR-130a; hsa-miR-130b; hsa-miR-139-5p; hsa-miR-140-5p; hsa-miR-146a; hsa-miR-146b-5p; hsa-miR-17; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d; hsa-miR-182; hsa-miR-183 hsa-miR-186; hsa-miR-19a; hsa-miR-19b; hsa-miR-206; hsa-miR-20a; hsa-miR-20b; hsa-miR-212; hsa-miR-221; hsa-miR-222; hsa-miR-23a; hsa-miR-28-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-301; hsa-miR-301a; hsa-miR-301b; hsa-miR-30a; hsa-miR-30b; hsa-miR-330-3p; hsa-miR-330-5p; hsa-miR-342-3p; hsa-miR-384; hsa-miR-409-5p; hsa-miR-454; hsa-miR-455-5p; hsa-miR-485-3p hsa-miR-485-5p; hsa-miR-487a; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-519d; hsa-miR-519e; hsa-miR-520d-3p; hsa-miR-520g; hsa-miR-520h; hsa-miR-539; hsa-miR-543; hsa-miR-548a-3p; hsa-miR-559; hsa-miR-561; hsa-miR-563; hsa-miR-579; hsa-miR-580; hsa-miR-582-5p; hsa-miR-589; hsa-miR-613; hsa-miR-617; hsa-miR-620; hsa-miR-624; hsa-miR-767-5p; hsa-miR-885-3p; hsa-miR-891b; hsa-miR-93	CDC5L; RFX1
IL22	hsa-miR-1; hsa-miR-127-5p; hsa-miR-135b; hsa-miR-203; hsa-miR-29b; hsa-miR-29c; hsa-miR-335; hsa-miR-340; hsa-miR-409-3p; hsa-miR-422a; hsa-miR-433; hsa-miR-493; hsa-miR-548b-5p; hsa-miR-548d-5p; hsa-miR-562; hsa-miR-579; hsa-miR-875-3p; hsa-miR-935; hsa-miR-944	BPTF; GATA1; TBP
IL20	hsa-miR-103; hsa-miR-107; hsa-miR-151-3p; hsa-miR-153; hsa-miR-154; hsa-miR-15a; hsa-miR-15b; hsa-miR-16; hsa-miR-195; hsa-miR-19a; hsa-miR-19b; hsa-miR-26a; hsa-miR-26b; hsa-miR-300; hsa-miR-301a; hsa-miR-301b; hsa-miR-331-3p; hsa-miR-338-3p; hsa-miR-381; hsa-miR-424; hsa-miR-491-3p; hsa-miR-497; hsa-miR-499-5p; hsa-miR-503; hsa-miR-518a-5p; hsa-miR-532-5p; hsa-miR-548c-3p hsa-miR-551a; hsa-miR-551b; hsa-miR-561; hsa-miR-568; hsa-miR-590-5p; hsa-miR-616; hsa-miR-634; hsa-miR-655; hsa-miR-659; hsa-miR-7; hsa-miR-876-3p; hsa-miR-936	CTCF
IL36G	hsa-miR-143; hsa-miR-208b; hsa-miR-22; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-548c-5p	Nil
CASP5	Nil	MAX; POU2F1
USF1	Nil	USF1

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Genes (RNA Seq.-GEO/Array Express)	miRNAs (miRtarbase / Target Scan)	Transcription Factor (RegNetworks)
WIF1	hsa-miR-127-5p; hsa-miR-129-5p; hsa-miR-137; hsa-miR-140-3p; hsa-miR-144; hsa-miR-15a; hsa-miR-15b; hsa-miR-16; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d hsa-miR-194; hsa-miR-195; hsa-miR-200b; hsa-miR-200c; hsa-miR-216b hsa-miR-29a; hsa-miR-29c; hsa-miR-29c; hsa-miR-330-3p; hsa-miR-335; hsa-miR-33a; hsa-miR-33b; hsa-miR-424; hsa-miR-429; hsa-miR-450b-5p hsa-miR-485-3p; hsa-miR-497; hsa-miR-498; hsa-miR-556-5p; hsa-miR-578; hsa-miR-586; hsa-miR-603; hsa-miR-654-3p; hsa-miR-656; hsa-miR-889	CTCF; CUX1
AWAT2	hsa-let-7d; hsa-let-7g; hsa-let-7i; hsa-miR-185; hsa-miR-34b; hsa-miR-361-5p; hsa-miR-518a-5p; hsa-miR-768-3p hsa-miR-802; hsa-miR-922	FOXJ2
CDH12	hsa-miR-137; hsa-miR-383; hsa-miR-453; hsa-miR-499-3p; hsa-miR-511; hsa-miR-519a; hsa-miR-548a-3p; hsa-miR-548c-3p; hsa-miR-648; hsa-miR-922	FOXO4; HSF2
DDX25	hsa-miR-142-5p; hsa-miR-32	REST; USF1
KRT28	hsa-miR-105; hsa-miR-130a; hsa-miR-143; hsa-miR-301a; hsa-miR-338-5p hsa-miR-495; hsa-miR-501-5p; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-567; hsa-miR-570; hsa-miR-574-5p; hsa-miR-595; hsa-miR-7; hsa-miR-944	CTCF; PAX6; POU2F1; POU3F2
GAL	hsa-miR-154; hsa-miR-338-5p; hsa-miR-345; hsa-miR-376c; hsa-miR-548a-5p; hsa-miR-548c-5p; hsa-miR-665; hsa-miR-888	MAX; MYC; TAL1; TCF4 TFAP2A; TFAP2C
GPR12	hsa-miR-302a; hsa-miR-302b; hsa-miR-302c; hsa-miR-302d; hsa-miR-372; hsa-miR-373; hsa-miR-520a-3p hsa-miR-520b; hsa-miR-520c-3p hsa-miR-520d-3p; hsa-miR-520e	Nil
ROS1	hsa-miR-325; hsa-miR-33a; hsa-miR-33b; hsa-miR-586; hsa-miR-606; hsa-miR-609; hsa-miR-613	ABL1
AXDND1	hsa-miR-506; hsa-miR-509-5p; hsa-miR-557; hsa-miR-890	GABPA; SPI1; YY1
SLC14A1	hsa-miR-100; hsa-miR-200b; hsa-miR-200c; hsa-miR-429; hsa-miR-496; hsa-miR-500; hsa-miR-501-5p; hsa-miR-575; hsa-miR-586; hsa-miR-591; hsa-miR-768-5p; hsa-miR-99a; hsa-miR-99b	CREB1; CTCF; GATA1; HNF4A; NFE2; TAL1::GATA1; TBP
MYEOV	hsa-miR-105; hsa-miR-214; hsa-miR-365; hsa-miR-610; hsa-miR-650	CTCF; NFYA; NFYB; NFYC
TPPP	hsa-miR-1; hsa-miR-206	Nil
WDR72	hsa-miR-186; hsa-miR-576-5p; hsa-miR-599	Nil
HMGCS2	hsa-miR-490-5p	AR; CEBPA; NFIC; PPARA; RXRA; RXRB; RXRG; TFAP2A
TNNI2	Nil	CTCF; CUX1; ELK1; POU2F1; RORA; SPI1; TFAP2A; TFAP2C
CNTNAP3B	Nil	HLF; STAT5A
ANKRD18A	hsa-miR-203; hsa-miR-518a-5p; hsa-miR-520g; hsa-miR-520h; hsa-miR-671-5p	Nil
ANKRD33B	Nil	EBF1; NFKB1; NFKB2; RELA; RELB; SPI1; TFAP2A; TFAP2C; USF1
ERBB4	hsa-miR-101; hsa-miR-106a; hsa-miR-125a-5p; hsa-miR-125b; hsa-miR-130a; hsa-miR-130b; hsa-miR-135a; hsa-miR-135b; hsa-miR-137; hsa-miR-144; hsa-miR-145; hsa-miR-146a; hsa-miR-146b-5p; hsa-miR-17; hsa-miR-184; hsa-miR-186; hsa-miR-199a-3p; hsa-miR-199b-3p; hsa-miR-19a; hsa-miR-19b; hsa-miR-200b; hsa-miR-200c; hsa-miR-205; hsa-miR-219-1-3p; hsa-miR-22; hsa-miR-221; hsa-miR-222; hsa-miR-23a; hsa-miR-23b hsa-miR-26a; hsa-miR-26b; hsa-miR-300; hsa-miR-301; hsa-miR-301a; hsa-miR-301b; hsa-miR-302d; hsa-miR-323-3p; hsa-miR-330-3p; hsa-miR-335 hsa-miR-339-5p; hsa-miR-340; hsa-miR-342-3p; hsa-miR-342-5p; hsa-miR-372; hsa-miR-377; hsa-miR-378 hsa-miR-383; hsa-miR-410; hsa-miR-422a; hsa-miR-429; hsa-miR-432; hsa-miR-433; hsa-miR-454; hsa-miR-495; hsa-miR-507; hsa-miR-508-3p; hsa-miR-518a-5p; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-519d; hsa-miR-520g; hsa-miR-520h; hsa-miR-527; hsa-miR-539; hsa-miR-548c-3p; hsa-miR-548d-3p; hsa-miR-571; hsa-miR-576-5p; hsa-miR-578; hsa-miR-579; hsa-miR-583; hsa-miR-584; hsa-miR-590-3p; hsa-miR-606; hsa-miR-653; hsa-miR-7; hsa-miR-876-5p; hsa-miR-93; hsa-miR-940; hsa-miR-944; hsa-miR-96	CEBPB; EP300; MEF2A; MEIS1; SMURF2; STAT5A; STAT5B; WWP1
TMEM132B	hsa-miR-10a; hsa-miR-10b; hsa-miR-137; hsa-miR-143; hsa-miR-148b; hsa-miR-152; hsa-miR-199a-5p; hsa-miR-19a; hsa-miR-19b; hsa-miR-218; hsa-miR-221; hsa-miR-222; hsa-miR-224; hsa-miR-297; hsa-miR-298; hsa-miR-338-3p; hsa-miR-377; hsa-miR-433; hsa-miR-548c-3p; hsa-miR-590-3p; hsa-miR-653; hsa-miR-766	Nil

CNTNAP3	hsa-miR-22; hsa-miR-26a; hsa-miR-26b; hsa-miR-9	HLF; STAT5A
CNKSR2	hsa-miR-144; hsa-miR-199b-5p; hsa-miR-21; hsa-miR-25; hsa-miR-28-3p; hsa-miR-29b; hsa-miR-30c; hsa-miR-32; hsa-miR-363; hsa-miR-374a; hsa-miR-374b; hsa-miR-450b-5p; hsa-miR-491-3p; hsa-miR-516b; hsa-miR-542-3p; hsa-miR-554; hsa-miR-627; hsa-miR-643; hsa-miR-942; hsa-miR-944	BACH2; NFE2
RAB3B	hsa-miR-194	SMAD1; SMAD4; TLX2
FREM2	hsa-miR-142-3p; hsa-miR-142-5p; hsa-miR-147; hsa-miR-150; hsa-miR-200b; hsa-miR-200c; hsa-miR-24; hsa-miR-299-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-30b; hsa-miR-32; hsa-miR-363; hsa-miR-367; hsa-miR-412; hsa-miR-429; hsa-miR-494; hsa-miR-509-3p; hsa-miR-544; hsa-miR-548c-3p; hsa-miR-556-3p; hsa-miR-568; hsa-miR-580; hsa-miR-590-3p; hsa-miR-607; hsa-miR-628-3p; hsa-miR-633; hsa-miR-802; hsa-miR-885-5p; hsa-miR-9	CTCF; EGR3; SP1; TBP; ZEB1
ACADL	hsa-miR-142-3p; hsa-miR-299-3p; hsa-miR-518a-5p; hsa-miR-641	PPARD; RXRA; RXRB RXRG
CYP4A11	hsa-miR-150	AR; HNF4A; PPARA; PPARD; PPARG; RXRA; RXRB; RXRG
BTBD16	hsa-miR-204; hsa-miR-211; hsa-miR-337-3p; hsa-miR-491-3p; hsa-miR-548c-3p; hsa-miR-599; hsa-miR-605; hsa-miR-625; hsa-miR-875-3p	CTCF; ELK1; TFAP2C; TLX2
WFDC3	hsa-miR-185; hsa-miR-28-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-329; hsa-miR-331-3p; hsa-miR-361-3p; hsa-miR-362-3p; hsa-miR-455-3p; hsa-miR-619; hsa-miR-657; hsa-miR-765; hsa-miR-875-3p; hsa-miR-923	ATF1; ATF2; ATF3; ATF4; ATF5; ATF6; ATF7; CTCF; E2F1; ELK1; GABPA; JUN; NR3C1; RFX1; SP1; SPI1
ACTC1	hsa-miR-142-5p; hsa-miR-185; hsa-miR-195; hsa-miR-200b; hsa-miR-200c; hsa-miR-25; hsa-miR-30a; hsa-miR-30a-5p; hsa-miR-30b; hsa-miR-30c; hsa-miR-30d; hsa-miR-30e; hsa-miR-32; hsa-miR-324-3p; hsa-miR-340; hsa-miR-363; hsa-miR-367; hsa-miR-369-3p; hsa-miR-429; hsa-miR-495; hsa-miR-508-5p; hsa-miR-608; hsa-miR-7; hsa-miR-768-5p; hsa-miR-876-3p; hsa-miR-92a; hsa-miR-92b	BACH1; CUX1; IRF1; MEF2A; SRF; TFAP2A; TFAP2C; TGIF1; ZEB1
LHCGR	hsa-miR-148b; hsa-miR-545	NFIC; SP1; TFAP2A
FADS2	hsa-let-7b	AR; CEBPA; CTCF; CUX1; DDIT3; HNF4A; MYC; PPARA; RXRA; RXRB; RXRG
GRIN2A	hsa-miR-101; hsa-miR-125a-5p; hsa-miR-125b; hsa-miR-137; hsa-miR-139-5p; hsa-miR-194; hsa-miR-19a; hsa-miR-19b; hsa-miR-206; hsa-miR-216b; hsa-miR-220b; hsa-miR-299-5p; hsa-miR-325; hsa-miR-329; hsa-miR-330-5p; hsa-miR-331-5p; hsa-miR-362-3p; hsa-miR-376a; hsa-miR-376b; hsa-miR-451; hsa-miR-454; hsa-miR-510; hsa-miR-519d; hsa-miR-520h; hsa-miR-525-5p; hsa-miR-574-3p; hsa-miR-576-5p; hsa-miR-577; hsa-miR-584; hsa-miR-593; hsa-miR-598; hsa-miR-603; hsa-miR-628-5p; hsa-miR-630; hsa-miR-656; hsa-miR-765 hsa-miR-767-5p; hsa-miR-9; hsa-miR-939	AHR; ARNT; CTCF; PAX5; REST; USF1
SYT17	hsa-miR-22; hsa-miR-297; hsa-miR-380; hsa-miR-574-5p; hsa-miR-633	CTCF; MYC; PAX5; RREB1; TSC22D4
RORC	hsa-let-7a; hsa-let-7b; hsa-let-7c; hsa-let-7e; hsa-let-7f; hsa-let-7g; hsa-let-7i hsa-miR-106b; hsa-miR-202; hsa-miR-205; hsa-miR-20a; hsa-miR-298; hsa-miR-485-5p; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-593; hsa-miR-605; hsa-miR-608; hsa-miR-766; hsa-miR-93; hsa-miR-98	ARNT; ARNTL; CEBPA; CHD4; CLOCK; CTCF; FOXO4; LMO2; MAX; MXI1::CLEC5A; NCOA6 NKX2-2; NPAS2; PPARG SREBF1; SREBF2; TAL1 TCF3; USF1; ZEB1
CA1	hsa-miR-944	TBP
CHRM3	hsa-miR-30c; hsa-miR-629	TFAP2A
F P G T - TNNI3K	Nil	AHR; ARNT; E2F1; E2F2 E2F3; E2F4; E2F5; E2F6 E2F7; EGR1; YY1
AGR3	hsa-miR-32; hsa-miR-367; hsa-miR-448; hsa-miR-455-5p; hsa-miR-507; hsa-miR-548a-3p; hsa-miR-548c-3p; hsa-miR-557; hsa-miR-573; hsa-miR-656; hsa-miR-876-5p	Nil
SOHLH1	hsa-miR-132; hsa-miR-220c; hsa-miR-484; hsa-miR-504; hsa-miR-516a-3p; hsa-miR-520a-5p; hsa-miR-525-5p; hsa-miR-600	CTCF; USF1
CYP1A2	Nil	CUX1; NFIC;NKX6-1; TAL1; TCF4; USF1; USF2 YY1
CYP2W1	hsa-miR-423-3p; hsa-miR-608; hsa-miR-637	ZIC2

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BTC	hsa-miR-490-3p	CTCF; FOXC1; TFAP2A USF1
DDC	Nil	AR; HNF1A; RORA
CHRM4	Nil	ARID5B; E2F1; E2F2; E2F3; E2F4; E2F5; E2F6 E2F7; FOXO4; GATA1
SYT9	hsa-miR-1271; hsa-miR-196a; hsa-miR-196b; hsa-miR-19a; hsa-miR-19b; hsa-miR-205; hsa-miR-29b; hsa-miR-326; hsa-miR-330-5p; hsa-miR-34a; hsa-miR-34c-5p; hsa-miR-448; hsa-miR-485-5p; hsa-miR-619; hsa-miR-671-5p; hsa-miR-9; hsa-miR-96	PATZ1; PAX5
SLC26A3	hsa-let-7a; hsa-let-7b; hsa-let-7c; hsa-let-7d; hsa-let-7f; hsa-miR-125a-3p; hsa-miR-137; hsa-miR-142-5p; hsa-miR-190; hsa-miR-190b; hsa-miR-20b; hsa-miR-21; hsa-miR-28-3p; hsa-miR-340; hsa-miR-382; hsa-miR-494 hsa-miR-556-5p; hsa-miR-561; hsa-miR-568; hsa-miR-576-3p; hsa-miR-590-5p; hsa-miR-592; hsa-miR-620 hsa-miR-624; hsa-miR-649; hsa-miR-652; hsa-miR-93; hsa-miR-98	ETS1; GATA1; HNF1A; PPARG; TBP
SPINK1	hsa-miR-659; hsa-miR-876-5p	CEBPB; FOXA2; FOXD1 FOXF2; HNF1A; RXRA
CILP2	Nil	CREB1; LMO2
SPINT3	Nil	REST
AADACL3	hsa-miR-32; hsa-miR-520a-5p; hsa-miR-525-5p	Nil
HSD3B1	hsa-let-7b; hsa-let-7c; hsa-miR-181a; hsa-miR-181c; hsa-miR-371-5p; hsa-miR-492; hsa-miR-543; hsa-miR-571; hsa-miR-578; hsa-miR-608; hsa-miR-650; hsa-miR-665; hsa-miR-885-3p	Nil
GJB4	Nil	NR2F2; PAX2; STAT5A; TCF3; TFAP2A; TFAP2C
ELOVL3	hsa-miR-150; hsa-miR-191; hsa-miR-194; hsa-miR-23a; hsa-miR-23b; hsa-miR-326; hsa-miR-491-5p; hsa-miR-494; hsa-miR-516b; hsa-miR-532-3p; hsa-miR-548a-5p; hsa-miR-559; hsa-miR-578; hsa-miR-653; hsa-miR-671-5p; hsa-miR-802; hsa-miR-874	ARNT; NFYA
HAO2	Nil	POU2F1
THRSP	hsa-let-7a; hsa-let-7c; hsa-let-7f; hsa-let-7g; hsa-let-7i; hsa-miR-98	CUX1; RXRA; SREBF1; SREBF2;TP53
NAT16	Nil	SP1
SERPINB4	Nil	FOXD1; CEBPA; FOXD1
S100A12	hsa-miR-185; hsa-miR-574-5p; hsa-miR-602; hsa-miR-921	Nil
SPRR2C	hsa-miR-196a	RORA; SRF
TCN1	hsa-miR-154; hsa-miR-185; hsa-miR-30a; hsa-miR-421; hsa-miR-491-3p; hsa-miR-502-3p; hsa-miR-549; hsa-miR-95	CTCF
PI3	hsa-miR-214; hsa-miR-298; hsa-miR-299-3p; hsa-miR-383; hsa-miR-422a; hsa-miR-552; hsa-miR-564; hsa-miR-675; hsa-miR-768-5p; hsa-miR-885-3p; hsa-miR-892b; hsa-miR-922	MXI1::CLEC5A
S100A9	hsa-miR-196a	AR; CTCF; MYB; RARA; RARB; RARG; SPI1; TBP; TFAP2A; TP53
KRT6C	Nil	PPARG; E2F1; FOS; TBP; AHR; ARNT; BACH1; FOS; FOSB; FOSL1; JUN; JUNB; JUND; RREB1; SP1; SP3; TFAP2; TOPORS
TMPRSS11D	hsa-miR-590-3p	HLF; IRF1
LTF	hsa-miR-214	CEBPA; CEBPE; ESR1; ETS1; SP1; SPI1
GJB2	hsa-miR-323-3p; hsa-miR-944	E2F4; ETV4; HNF1A; JUN
PLA2G4D	Nil	POU2F1; POU2F2; POU3F1; POU3F2; POU3F3; POU5F1; RFX1
TNIP3	hsa-miR-338-5p	CEBPB; SPI1; TGIF1
VNN3	hsa-miR-135a; hsa-miR-135b; hsa-miR-199a-3p; hsa-miR-345; hsa-miR-371-5p; hsa-miR-421; hsa-miR-455-3p; hsa-miR-455-5p; hsa-miR-505; hsa-miR-514; hsa-miR-744	CTCF; FOXA2; NFKB1; NFKB2; REL; RELA; STAT5B

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Gene	miRNAs	Transcription Factors
S100A8	hsa-miR-135a; hsa-miR-135b; hsa-miR-202; hsa-miR-326; hsa-miR-330-5p; hsa-miR-544	AR; FOS; FOSB; JUN; JUND; PDCD11; RARA; RARB; RARG; TBP; TP53
OASL	hsa-miR-1; hsa-miR-184; hsa-miR-206 hsa-miR-298; hsa-miR-516b	MBD1; THRA
HEPHL1	hsa-miR-1297; hsa-miR-145; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d; hsa-miR-195; hsa-miR-26a; hsa-miR-26b; hsa-miR-30a; hsa-miR-30b; hsa-miR-30c; hsa-miR-30d; hsa-miR-30e; hsa-miR-424; hsa-miR-494; hsa-miR-543; hsa-miR-573	STAT3
SLC6A14	hsa-miR-23a; hsa-miR-23b; hsa-miR-299-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-340; hsa-miR-367; hsa-miR-374b; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-3p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-576-5p	CEBPA; NFKB1; NFKB2 NR2F2; REL; RELA; TCF3; TLX2
AKR1B10	hsa-let-7a; hsa-let-7c; hsa-let-7d; hsa-let-7f; hsa-let-7g; hsa-let-7i; hsa-miR-196a; hsa-miR-196b; hsa-miR-923; hsa-miR-98	MYC
RHCG	Nil	CTCF; EGR1; EGR2; EGR3; GATA1; SREBF1 SREBF2; USF1
SPRR1A	hsa-miR-105; hsa-miR-24; hsa-miR-382; hsa-miR-423-3p; hsa-miR-484; hsa-miR-501-3p; hsa-miR-502-3p; hsa-miR-509-3-5p; hsa-miR-509-5p; hsa-miR-518a-5p; hsa-miR-542-3p; hsa-miR-555; hsa-miR-609; hsa-miR-7; hsa-miR-768-5p	BACH1; BACH2; FOS; FOSB; FOSL1; JUN; JUNB; JUND
TYMP	Nil	ATF1; ATF2; ATF3; ATF4; ATF5; ATF6; ATF7; E2F1; E2F2; E2F3; E2F4; E2F5; E2F6; E2F7; EGR1; FOXI1; FOXO3; FOXO3B; GABPA; HNF4A; LMO2; MAX; MYC; PPARG; SRF; STAT1; USF1
SPRR2A	hsa-miR-127-5p; hsa-miR-133a; hsa-miR-133b; hsa-miR-185; hsa-miR-28-5p; hsa-miR-383; hsa-miR-610; hsa-miR-920	FOS; JUN; MEF2A; NFKB1; POU2F1; POU2F3; TAL1::GATA1
ARSF	Nil	CTCF; FOXA1; FOXA2; HNF4A; PPARG::RXRA; RXRA
NOS2	Nil	CEBPA; CEBPB; CEBPD; ESR1; HIF1A; JUN; NFIL3; NFKB1; NFKB2; NR2F2; RELA; STAT1; STAT3; TP53; USF1
CNFN	Nil	POU2F1; REST
KCNK10	hsa-miR-101; hsa-miR-124; hsa-miR-128; hsa-miR-128a; hsa-miR-128b; hsa-miR-181b; hsa-miR-182; hsa-miR-183; hsa-miR-22; hsa-miR-25; hsa-miR-32; hsa-miR-329; hsa-miR-331-5p; hsa-miR-362-3p; hsa-miR-363; hsa-miR-367; hsa-miR-455-3p; hsa-miR-485-5p; hsa-miR-498; hsa-miR-506; hsa-miR-507; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-579; hsa-miR-649; hsa-miR-92a; hsa-miR-92b; hsa-miR-96	E2F1; EGR3; FOS; FOSB; FOSL1; FOXO4; JUN; JUNB; JUND; MEF2A; MIF; TLX2
S100A7A	hsa-miR-128a; hsa-miR-27a; hsa-miR-27b; hsa-miR-504; hsa-miR-613; hsa-miR-625	TGIF1
KLK13	hsa-miR-455-5p; hsa-miR-542-3p; hsa-miR-591; hsa-miR-620; hsa-miR-654-5p	CREB1; EGR1; KLF12; MZF1; PPARG
TGM1	hsa-miR-130a; hsa-miR-130b; hsa-miR-142-3p; hsa-miR-148a; hsa-miR-148b; hsa-miR-149; hsa-miR-152; hsa-miR-301a; hsa-miR-301b; hsa-miR-345; hsa-miR-34a; hsa-miR-34c-5p; hsa-miR-361-3p; hsa-miR-378; hsa-miR-422a; hsa-miR-449a; hsa-miR-449b; hsa-miR-454; hsa-miR-502-5p; hsa-miR-508-5p; hsa-miR-558; hsa-miR-564; hsa-miR-617; hsa-miR-648; hsa-miR-920; hsa-miR-939	AR; ESR1; HOXA7; RARA; RARB; RARG; TGIF1; TP53
SLC26A9	hsa-miR-1271; hsa-miR-181a; hsa-miR-181c; hsa-miR-181d; hsa-miR-22; hsa-miR-34c-3p; hsa-miR-378; hsa-miR-453; hsa-miR-532-3p; hsa-miR-543; hsa-miR-607; hsa-miR-645; hsa-miR-659; hsa-miR-760; hsa-miR-890; hsa-miR-96	ESR1; FOXI1; JUN; NFYA; NFYB; NFYC; POU3F2; RREB1
FABP5	hsa-miR-144; hsa-miR-198; hsa-miR-203; hsa-miR-525-5p; hsa-miR-553; hsa-miR-562; hsa-miR-576-5p; hsa-miR-603; hsa-miR-616; hsa-miR-620	CTCF; E2F1; MAX; MYC
SPRR1B	Nil	JUN
IL36A	Nil	SRF; TBP
GJB6	hsa-miR-203; hsa-miR-21; hsa-miR-628-3p	AHR; ARNT; RORA
HAL	Nil	CEBPB; SREBF1; SREBF2; TFAP2A
UPP1	hsa-miR-301a; hsa-miR-301b; hsa-miR-384; hsa-miR-539; hsa-miR-561	EBF1; FLI1; HNF4A; MAX; MXI1::CLEC5A; MYC; TFAP2A; USF1

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ZC3H12A	hsa-let-7i; hsa-miR-139-5p; hsa-miR-144; hsa-miR-192; hsa-miR-193a-3p; hsa-miR-193b; hsa-miR-369-5p; hsa-miR-421; hsa-miR-431; hsa-miR-432; hsa-miR-449b; hsa-miR-486-3p; hsa-miR-768-5p; hsa-miR-885-3p; hsa-miR-9	CEBPA; EGR1; FOS; FOSB; FOSL1; JUN; JUNB; JUND; PAX6; RFX1; SREBF1; SREBF2; SRF
FUT3	hsa-miR-125a-3p	Nil
DEFB4A	hsa-miR-129-3p; hsa-miR-299-5p; hsa-miR-593; hsa-miR-646	CDC5L
IL19	Nil	CEBPA; CEBPB; CTCF NFKB1; NFKB2; REL; RELA; TCF3
CLEC3A	hsa-miR-363; hsa-miR-383; hsa-miR-624	SRF
SPRR2F	hsa-miR-127-5p; hsa-miR-18b; hsa-miR-383; hsa-miR-501-5p; hsa-miR-920	Nil
IL17A	hsa-miR-520f; hsa-miR-875-5p	BACH1; HOXA9; MEIS1; RORA; TBP
LCE3A	Nil	CTCF; FOS; FOSB; FOSL1; HNF1A; JUN JUNB; JUND
ZBTB17	Nil	TMPRSS11A
SPRR3	hsa-miR-338-3p; hsa-miR-641; hsa-miR-921	ATF1; FOS; JUN; POU2F1
KRT24	hsa-miR-127-5p; hsa-miR-198; hsa-miR-335; hsa-miR-378; hsa-miR-382 hsa-miR-422a; hsa-miR-488; hsa-miR-525-5p; hsa-miR-548a-5p; hsa-miR-548b-5p; hsa-miR-548c-5p; hsa-miR-548d-5p; hsa-miR-559; hsa-miR-576-3p; hsa-miR-576-5p; hsa-miR-581; hsa-miR-599; hsa-miR-630; hsa-miR-640; hsa-miR-921	TFAP4
S100A7A	hsa-miR-128a; hsa-miR-27a; hsa-miR-27b; hsa-miR-504; hsa-miR-613; hsa-miR-625	TGIF1
IL17F	hsa-miR-501-3p; hsa-miR-502-3p; hsa-miR-544; hsa-miR-555; hsa-miR-573; hsa-miR-590-3p; hsa-miR-608; hsa-miR-924; hsa-miR-944; hsa-miR-96	CEBPB; JUN; RORA; TBP
CXCL1	Nil	JUN; MAPK11; MAPK12; MAPK13; MAPK14; NFKB1; PATZ1; REL; RELA; SP1; SP3
LCE3C	Nil	PAX6
CXCL13	hsa-miR-153; hsa-miR-186; hsa-miR-198; hsa-miR-340; hsa-miR-452; hsa-miR-590-3p	GATA1; GATA2; GATA3; POU2F1
C12orf74	Nil	POU2F1; SPI1
CLDN17	Nil	ARID5B
GDA	hsa-miR-106a; hsa-miR-106b; hsa-miR-10a; hsa-miR-10b; hsa-miR-130a; hsa-miR-130b; hsa-miR-139-5p; hsa-miR-140-5p; hsa-miR-146a; hsa-miR-146b-5p; hsa-miR-17; hsa-miR-181a; hsa-miR-181b; hsa-miR-181c; hsa-miR-181d; hsa-miR-182; hsa-miR-183 hsa-miR-186; hsa-miR-19a; hsa-miR-19b; hsa-miR-206; hsa-miR-20a; hsa-miR-20b; hsa-miR-212; hsa-miR-221; hsa-miR-222; hsa-miR-23a; hsa-miR-28-5p; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-301; hsa-miR-301a; hsa-miR-301b; hsa-miR-30a; hsa-miR-30b; hsa-miR-330-3p; hsa-miR-330-5p; hsa-miR-342-3p; hsa-miR-384; hsa-miR-409-5p; hsa-miR-454; hsa-miR-455-5p; hsa-miR-485-3p hsa-miR-485-5p; hsa-miR-487a; hsa-miR-519a; hsa-miR-519b-3p; hsa-miR-519c-3p; hsa-miR-519d; hsa-miR-519e; hsa-miR-520d-3p; hsa-miR-520g; hsa-miR-520h; hsa-miR-539; hsa-miR-543; hsa-miR-548a-3p; hsa-miR-559; hsa-miR-561; hsa-miR-563; hsa-miR-579; hsa-miR-580; hsa-miR-582-5p; hsa-miR-589; hsa-miR-613; hsa-miR-617; hsa-miR-620; hsa-miR-624; hsa-miR-767-5p; hsa-miR-885-3p; hsa-miR-891b; hsa-miR-93	CDC5L; RFX1
IL22	hsa-miR-1; hsa-miR-127-5p; hsa-miR-135b; hsa-miR-203; hsa-miR-29b; hsa-miR-29c; hsa-miR-335; hsa-miR-340; hsa-miR-409-3p; hsa-miR-422a; hsa-miR-433; hsa-miR-493; hsa-miR-548b-5p; hsa-miR-548d-5p; hsa-miR-562; hsa-miR-579; hsa-miR-875-3p; hsa-miR-935; hsa-miR-944	BPTF; GATA1; TBP
IL20	hsa-miR-103; hsa-miR-107; hsa-miR-151-3p; hsa-miR-153; hsa-miR-154; hsa-miR-15a; hsa-miR-15b; hsa-miR-16; hsa-miR-195; hsa-miR-19a; hsa-miR-19b; hsa-miR-26a; hsa-miR-26b; hsa-miR-300; hsa-miR-301a; hsa-miR-301b; hsa-miR-331-3p; hsa-miR-338-3p; hsa-miR-381; hsa-miR-424; hsa-miR-491-3p; hsa-miR-497; hsa-miR-499-5p; hsa-miR-503; hsa-miR-518a-5p; hsa-miR-532-5p; hsa-miR-548c-3p hsa-miR-551a; hsa-miR-551b; hsa-miR-561; hsa-miR-568; hsa-miR-590-5p; hsa-miR-616; hsa-miR-634; hsa-miR-655; hsa-miR-659; hsa-miR-7; hsa-miR-876-3p; hsa-miR-936	CTCF
IL36G	hsa-miR-143; hsa-miR-208b; hsa-miR-22; hsa-miR-29a; hsa-miR-29b; hsa-miR-29c; hsa-miR-548c-5p	Nil
CASP5	Nil	MAX; POU2F1
USF1	Nil	USF1

Network Analysis of Bottom-Up Approach (Cytohubba)

Genes and their regulators in Top-down approach were subjected to the analysis by various statistical methods (Degree, Edge Percolated Component, Maximum Neighborhood Component, Density of Maximum Neighborhood Component, and Maximal Clique Centrality with six centralities Bottleneck, Ec Centricity, Closeness, Radiality, Betweenness and Stress) to identify the their connectivity.

In case of MCC analysis in Bottom-Up approach, ERBB4, GDA, GRIN2A were ranked from 1 to 3 respectively. Then; RORC, KCNK10 were ranked 4 and IL20, WIF1, FREM2, ACTC1 and TGM1 were ranked from 6 to 10 respectively. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 1).

In case of DMNC analysis in Bottom-Up approach; hsa-miR-130a, hsa-miR-130b, ETS1, MAX, ESR1, TGM1,

ETV4, AR, HOXA7 and MXI1::CLEC5A were ranked 1 (Figure 2).

In case of MNC analysis in Bottom-Up approach hsa-miR-130a, hsa-miR-130b, ETS1, MAX, ESR1, TGM1, ETV4, AR, HOXA7 and MXI1::CLEC5A were ranked 1 (Figure 3).

In case of degree analysis in Bottom-Up approach; ERBB4, GDA and GRIN2A were ranked from 1 to 3 respectively. Then RORC and KCNK10 were ranked 4. Further; IL20 and WIF1 wed re ranked 6 and 7 respectively. Finally; FREM2 and ACTC1 were ranked 8 and TGM1 was ranked 10. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 4).

In case of EPC analysis in Bottom-Up approach; ERBB4, GDA, CTCF, FREM2, WIF1, KCNK10, ACTC1, GRIN2A, RORC and IL20 were ranked from 1 to 10 respectively. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 5).

In case of Bottleneck analysis in Bottom-Up approach; GDA, IL20, TGM1 and KCNK10 were ranked from 1 to 4 respectively. Then, ERBB4 and ZC3H12A were ranked 5.Further; CTCF and TYMP were ranked 7 and 8 respectively. Finally, GRIN2A and RORC were ranked 9 (Figure 6).
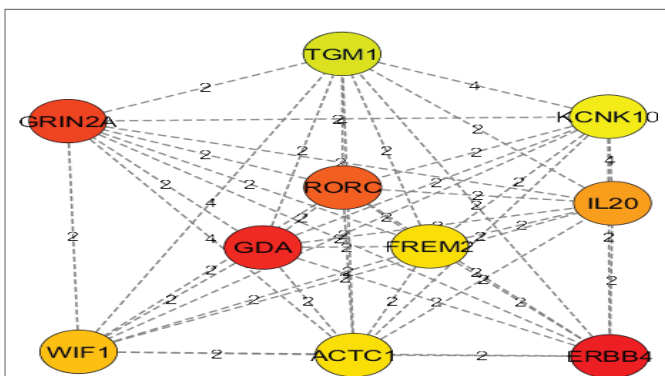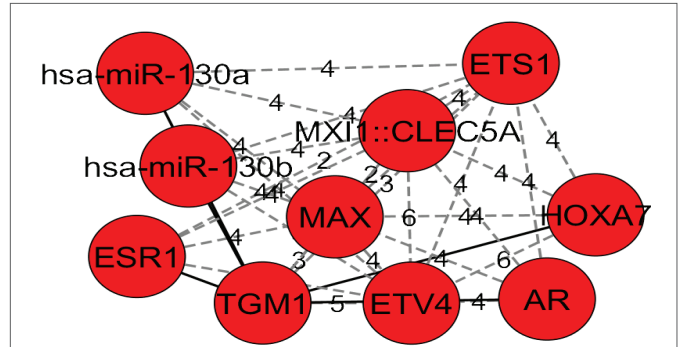

Figure 2: DMNC Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

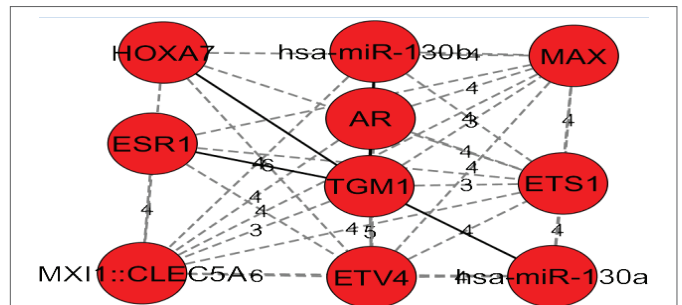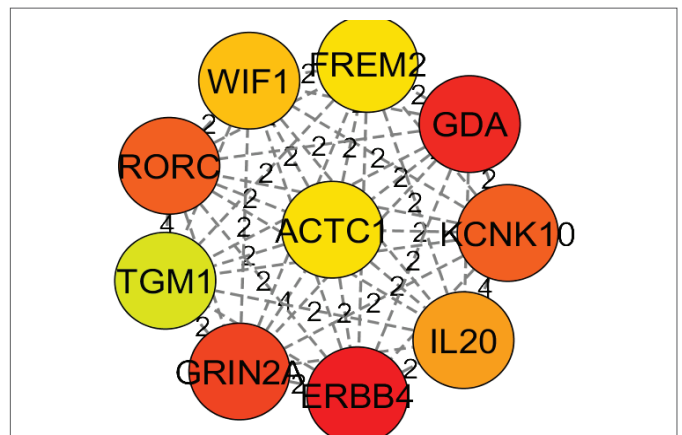**Figure 3:** MNC Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

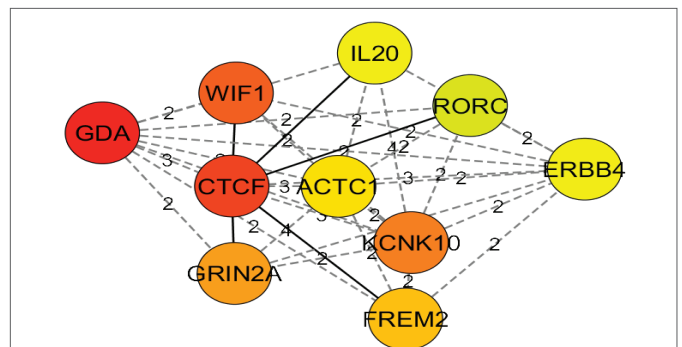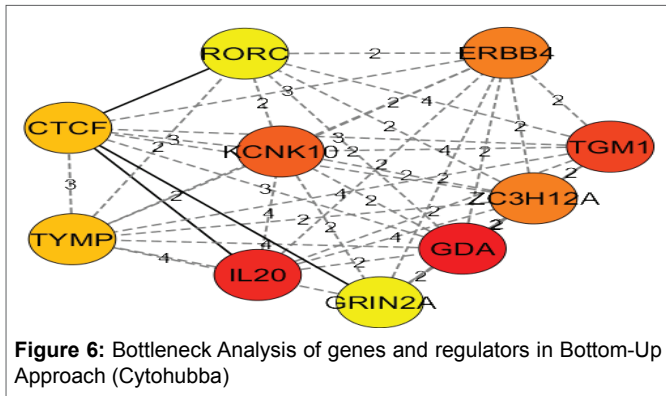**Figure 4:** **Degree** Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Figure 5: EPC Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Figure 1: MCC Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

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Figure 6: Bottleneck Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Conclusion

Overall network analysis of Bottom-up approach resulted in identifying 25 potential regulators of Psoriasis [20 Transcription Factors (MTHFR, AHR, ARNT, CUX1, E2F1, EP300, VDR, GSTP1, MAX, CYP1A2, ABCC1, HLA-B, MYC, SLC19A1,

In case of Eccentricity analysis in Bottom-Up approach, RORC was ranked 1 and CTCF, WIF1, hsa-miR-137 hsa-miR-144, hsa-miR-200b, hsa-miR-200c, hsa-miR-29a, hsa-miR-29b and hsa-miR-29c were ranked 2. RORC is involved in the inflammatory pathways associated with Psoriasis (Figure 7).

Figure 7: Eccentricity Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

In case of Closeness analysis in Bottom-Up approach, ERBB4, CTCF, GDA, RORC, GRIN2A, FREM2, KCNK10, WIF1, IL20 and ACTC1 were ranked from 1 to 10 respectively. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 8).

In case of Radiality analysis in Bottom-Up approach, CTCF, ERBB4 and RORC were ranked from 1 to 3 respectively. Then; FREM2 and DGA were ranked 4. Further; GRIN2A, WIF1, WFDC3, ACTC1 and IL20 were ranked from 6 to 10. CTCF is associated with Psoriasis because it activates the differentiation of B lymphocytes (Figure 9).

Figure 8: Closeness Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

In case of Betweenness analysis in Bottom-Up approach; ERBB4, GDA, CTCF, RORC, GRIN2A, IL20, KCNK10

FREM2, ACTC1 and WIF1 were ranked from 1 to 10 respectively. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 10).
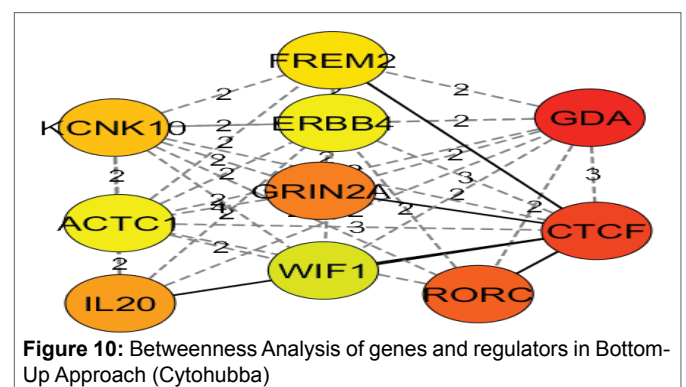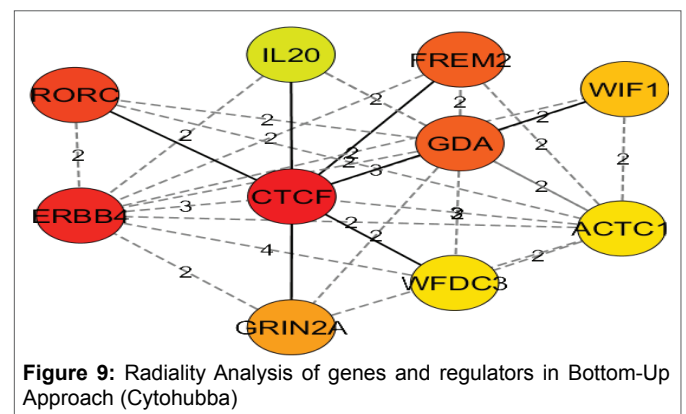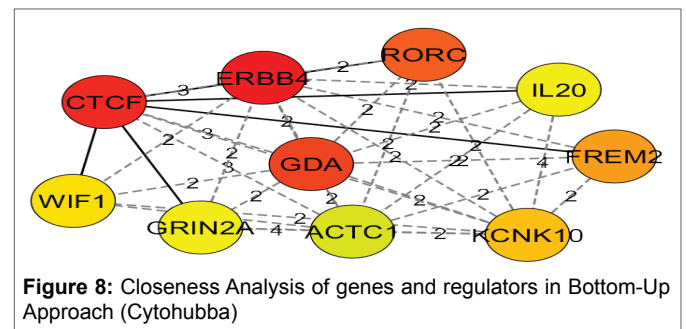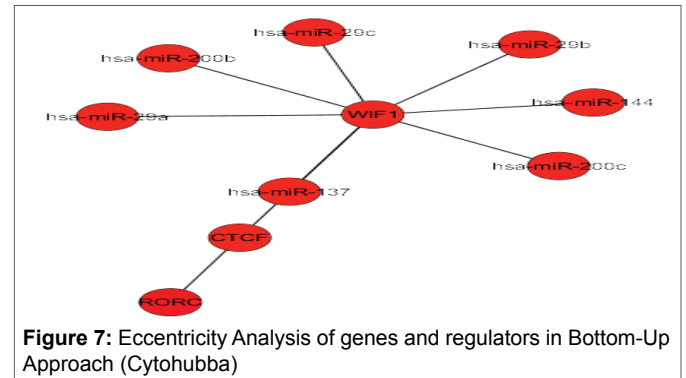
In case of Stress analysis in Bottom-Up approach; ERBB4, GDA, CTCF, GRIN2A, RORC, KCNK10, WFDC3, WIF1, ACTC1 and IL20 were ranked from 1 to 10. Signaling of ERBB4 is involved in the disease pathology of Psoriasis (Figure 11).

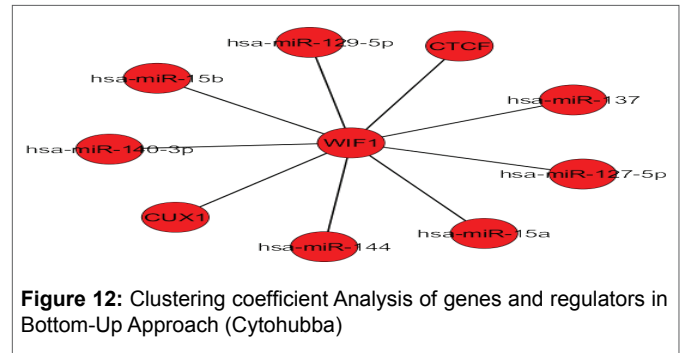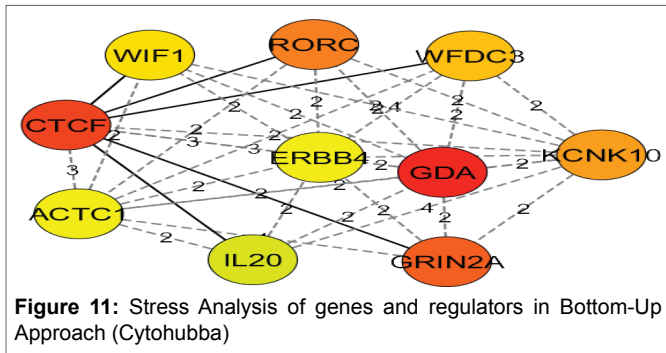**Figure 9:** Radiality Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

In case of clustering coefficient analysis in Bottom-Up approach WIF1, CTCF, CUX1, hsa-miR-127-5p, hsa-miR-129-5p, hsa-miR-137, hsa-miR-140-3p, hsa-miR-144, hsa-miR-15a and hsa-miR-15b were ranked 1. WIF1 is associated with Psoriasis because it down regulates the WNT proteins in lesions (Figure 12).

In case of overall network analysis of Bottom-up approach, 25 potential regulators of Psoriasis [20 Transcription Factors (MTHFR, AHR, ARNT, CUX1, E2F1, EP300, VDR, GSTP1, MAX, CYP1A2, ABCC1, HLA-B, MYC, SLC19A1, TYMS, JUN, CREB1, STAT1, YY1 and USF1) and 5 miRNAs (hsa-miR-103, hsa-miR-107, hsa-miR-125a-3p, hsa-miR-138 and hsa-miR-24)] were retrieved (Table 3).

Figure 10: Betweenness Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Figure 11: Stress Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Figure 12: Clustering coefficient Analysis of genes and regulators in Bottom-Up Approach (Cytohubba)

Table 3: Network Analysis (Bottom-Up Approach)

	Methods for Analysis of Shortest Path of Regulators in BottomUp Approach (Cytohubba)											
Rank	MCC	DMNC	MNC	Degree	EPC	Bottle Neck	Eccentricity	Closeness	Radiality	Betweenness	Stress	Clustering coefficient
1	ERBB4	hsa-miR-130a hsa-miR-130b ETS1 MAX Nil ESR1 TGM1 ETV4 AR HOXA7 MXI1::CLEC5A Nil	hsa-miR-130a hsa-miR-130b ETS1 MAX ESR1 TGM1 ETV4 AR HOXA7 MXI1::CLEC5A	ERBB4	ERBB4	GDA	RORC	ERBB4	CTCF	ERBB4	ERBB4	WIF1 CTCF CUX1 hsa-miR-127-5p hsa-miR-129-5p hsa-miR-137 hsa-miR-140-3p hsa-miR-144 hsa-miR-15a hsa-miR-15b
2	GDA	Nil	Nil	GDA	GDA	IL20	CTCF WIF1 hsa-miR-137 hsa-miR-144 hsa-miR-200b hsa-miR-200c hsa-miR-29a hsa-miR-29b hsa-miR-29c	CTCF	ERBB4	GDA	GDA	Nil
3	GRIN2A	Nil	Nil	GRIN2A	CTCF	TGM1	Nil	GDA	RORC	CTCF	CTCF	Nil
4	RORC KCNK10	Nil	Nil	RORC KCNK10	FREM2	KCNK10	Nil	RORC	FREM2 DGA	RORC	GRIN2A	Nil
5	Nil	Nil	Nil	Nil	WIF1	ERBB4 ZC3H12A	Nil	GRIN2A	Nil	GRIN2A	RORC	Nil
6	IL20	Nil	Nil	IL20	KCNK10	Nil	Nil	FREM2	GRIN2A	IL20	KCNK10	Nil
7	WIF1	Nil	Nil	WIF1	ACTC1	CTCF TYMP	Nil	KCNK10	WIF1	KCNK10	WFDC3	Nil
8	FREM2	Nil	Nil	FREM2 ACTC1	GRIN2A	Nil	Nil	WIF1	WFDC3	FREM2	WIF1	Nil
9	ACTC1	Nil	Nil	Nil	RORC	GRIN2A RORC	Nil	IL20	ACTC1	ACTC1	ACTC1	Nil
10	TGM1	Nil	Nil	TGM1	IL20	Nil	Nil	ACTC1	IL20	WIF1	IL20	Nil

TYMS, JUN, CREB1, STAT1, YY1 and USF1) and 5 miRNAs (hsa-miR-103, hsa-miR-107, hsa-miR-125a-3p, hsa-miR-138 and hsa-miR-24)]. In case of Annotation analysis, it is evident that these regulators play a vital role in the pathways (Apoptosis Signaling pathway, CCKR Signaling, Gonadotropin releasing hormone receptor pathway, Interleukin Signaling pathway, JAK/STAT signaling pathway, Oxidative Stress response and PDGF signaling pathway) associated with Psoriasis and it was also clear from studies of text mining in Pubmed; has-miR-103 and has-miR-107 is associated with the 3' UTR region of CDK5R1, hsa-miR-125a-3p is associated with the clinical implication of inflammatory skin and hsa-miR-138 is responsible for inhibiting the expression of RUNX3 in Psoriasis but till date there is no experimental evidence in Pubmed to illustrate the role of hsa-miR-24 in Psoriasis. In biological context, the potential regulators of psoriasis have a maximum probability to become a potential biomarker for Psoriasis and the identical pattern between the comparative-network analysis of bottom-up and direct approach illustrate the fact that there is a maximum probability for those potential regulators to be considered to treat psoriasis in future.

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