Research Article

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A computational approach to identify microRNA (miRNA) based biomarker of Pharmacovariant from the regulation of disease pathology

Abstract

In the post genomic era, identification of a potential miRNA in a computational approach for the significance of a discovery of systemic biomarker with respect to pharmacovarient studies to treat diseases is a challenging task to execute. The challenge was addressed by identifying the Pharmacovarient based associate genes from Verse and it was followed by identifying the associated miRNAs from PharmacomiR and finally the transcription factors(TFs) of associate target genes were identified from RegNetworks. In the next step, a miRNA based regulatory network was constructed on the basis of association between genes, miRNAs and TFs. Finally, the network was analyzed on the basis of statistical studies and miRNA based compatibility to identify a potential miRNA to be utilized as a biomarker of Pharmacovarient to treat diseases in future. In this article, the computational approach was used for the identification of a miRNA based systemic biomarker in association with the pharmacovaience of Psoriasis and in future this approach can also be used for other diseases.

Keywords: pharmacovarience; transcription factors; post genomic era; RegNetworks; miRNA; biomarker.

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Introduction

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. In case of psoriasis, the skin cells mature in 3-6days. 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. 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.[1,2]

Micro RNA is a family of non coding RNA (ncRNA) which was discovered in 1993, it consist of 19-25 nucleotides and regulates the expression of approximately 30% of protein-coding miRNAs in humans.[3] Base pairing at the position of 2-8 nucleotides were relative to the 5′ end of the small RNA to be termed as the "seed" region and it appears to be important for target recognition.[3] Maturation of miRNAs involves multiple steps and initially two intermediate forms of miRNAs, namely primary (pri-) and precursor (pre-) miRNAs, were produced sequentially. In this process, Drosha (RNase III enzyme) and the double-stranded RNA (dsRNA) binding protein Dgcr8 cleaves the pri-miRNAs to produce a hairpin-shaped pre-

miRNAs that are recognized by Exportin5 and they are subsequently transported from the nucleus to cytoplasm. There is another RNase III enzyme called Dicer which cleaves the pre-miRNAs to release ~22-nt double-stranded RNA duplexes (namely miRNA/miRNA* duplexes) with ~2-nt 3' overhangs.[4] One strand of a RNA duplex is termed as a mature miRNA which is further loaded into an Argonaute protein in the RNA-induced silencing complex (RISC) to exert its regulatory function on the basis of its binding with the target transcripts.[5]

A unique miRNA can regulate the expression of hundreds of proteins and the expression of a specific protein may be controlled by several miRNAs.[6] The sequence conservation of most miRNAs lies between the distantly related organisms to suggest the impact of a strong evolutionary pressure[7] and they have been shown to participate in many fundamental life processes like development, differentiation, organogenesis, growth control and apoptosis. Accordingly, deregulation of miRNA expression has been shown to contribute to cancer, heart diseases, infectious diseases, inflammatory diseases and other medical conditions, making them potential targets for medical diagnosis and therapy.[8] Initially, Lee had found lin-4 as a regulator of developmental timing in nematode Caenorhabditis elegans.[9] After several years, Reinhart had discovered lethal-7 (let-7) gene in Caenorhabditis elegans.[10] At present, 2500 miRNAs are in the human genome. Majority of miRNA are intragenic.[11] Micro RNAs are initially transcribed as a part of an RNA stem-loop that in turn forms part of a several hundred nucleotides long miRNA precursor miRNA (pri-miRNA).[12]

Results

Text mining of Genes from Pharmacogenomics and clinical varients were analyzed along with the associated miRNAs from PharmacomiR and transcription factors from Regnetworks and the

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analysis of interaction resulted in the pairing of 101 genes with 576 miRNAs and 638 transcription factors and the results were given in Table 1. A regulatory network was constructed in Cytoscape and the properties of the network were analyzed in the Network Analyzer.

Finally, the hub genes were identified from cytohubba and the miRNA based regulation was analyzed on the basis of seed pairing in miRmap and triplex miRNA along with the experimental evidences from the previous literature.

Table 1 Psoriasis associated genes, miRNAs and transcription factors with respect to Pharmacovarience from Pharmacogenomics and Clinical varients.

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
1	ABCB1	hsa-miR-222, hsa-miR-338-5p & hsa-miR-451	AR, CEBPA, CEBPB, EGR1, EGR2, ETS1, HAX1, HIF1A, JUN, NFKB1 RARA, RNF2, SP1, TFAP2A, TP53 & WT1
2	CYP3A4	hsa-miR-221	SP1 & TFAP2A
3	CTLA4	hsa-miR-200C, hsa-miR-101, hsa-miR-105, hsa-miR-155, hsa-miR-205, hsa-miR-380, hsa-miR-384, hsa-miR-429, hsa-miR-432, hsa-miR-449b, hsa-miR-451, hsa-miR-496, hsa-miR-516a-3p, hsa-miR-517a, hsa-miR-651 & hsa-miR-656	BPTF, STAT5A & STAT5B
4	TNF	hsa-miR-27a, hsa-miR-130a, hsa-miR-130b, hsa-miR-149, hsa-miR-187, hsa-miR-19a, hsa-miR-296-3p, hsa-miR-409-5p, hsa-miR-454 hsa-miR-516a-5p, hsa-miR-516b, hsa-miR-519b-3p, hsa-miR-542-3p, hsa-miR-581, hsa-miR-592, hsa-miR-599, hsa-miR-654-3p, hsa-miR-770-5p, hsa-miR-875-3p, hsa-miR-875-5p & hsa-miR-939	AHR, ARNT, ATF1, ATF2, CEBPB, CEBPD, CREB1, EBF1, EGR1, EGR4, ELK1, ETS1, ETV4, FOS, IKBKB, IRF5, JUN, NFAT5, NFATC1, NFATC2, NFATC3, NFATC4, NFE2L1, NFKB1, NFKB1, NFKB2, POU2F1, RELA, RELA, SMAD6, SMAD7, SP1, SP3, SPI1, STAT1, STAT2, STAT3, STAT4, STAT5A, STAT5B, STAT6, TBP, TFAP2A & TP53
5	MTHFR	hsa-miR-331-5p, hsa-miR-103, hsa-miR-107, hsa-miR-125a-3p, hsa-miR-138, hsa-miR-16, hsa-miR-195, hsa-miR-214, hsa-miR-22, hsa-miR-220b, hsa-miR-24, hsa-miR-424, hsa-miR-486-3p, hsa-miR-497, hsa-miR-516a-5p, hsa-miR-565, hsa-miR-642 & hsa-miR-646	AHR, ARNT, CUX1, E2F1, EP300, JUN, MAX, MXI1::CLEC5A, MYC, REST, SP1, SREBF1, SREBF2, TFAP2A, USF1, XBP1 & YY1
6	VDR	hsa-miR-451, hsa-miR-124 hsa-miR-125b, hsa-miR-506 & hsa-miR-544	BACH2, CREBBP, CTCF, FOS, FOSB, FOSL1, GTF2B, HMGN3, HNF4A, HR, JUN, JUNB, JUND, KDM5A, LMO2, MAX, MED1, NCOA1, NCOA2, NCOA6, NR0B2, NR1H2, NRIP1, RXRA, RXRB, RXRG, SMAD3, SNW1, STAT1 & TRIM24
7	CREBBP	hsa-miR-27b	AIRE, ALX1, AR, ATF1, ATF4, BCL3, BRCA1, CALCOCO1, CDX2, CEBPA, CEBPB, CEBPD, CITED1, CITED2, CNOT3, CREB1, CREB3, CREB3L1, CREB3L3, CREB3L4 & CREB5
8	ABCC2	hsa-miR-155, hsa-miR-339-5p	CEBPB, HNF4A, PPARG::RXRA, RXRA & TP53
9	UGT1A8	hsa-miR-181a	MYB & SRF
10	UGT1A9	hsa-miR-181c	CUX1, MYB & SRF
11	NR1I2	hsa-miR-181d, hsa-miR-148a & hsa-miR-148a	NCOA1, NCOA3, NCOR2, POU1F1, PPARGC1A, RXRA, RXRB & RXRG
12	AKT1	hsa-miR-181b, hsa-miR-125b, hsa-miR-149*, hsa-miR-185, hsa-miR-409-3p, hsa-miR-451& hsa-miR-625	AR, BRCA1, CREB1, EGR1 EP300, ESR1, ESR2, EZH2 FOXO1, FOXO3, FOXO4 GATA1, GATA2, HIST2, H2BE, HTT, IKBKB, IKBKG, MDM4 NFKB1, NFKBIA, NFKBIB NKX3-1, NR4A1, PATZ1 PHB2, PPARA, PPARG, PPARGC1B, RELA, SMAD2 SMAD3, SMAD4, SMAD7 SP1, STAT1, STAT5A, TP53, TRIB3, XBP1, YBX1 & YY1

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
13	MAP2K1	hsa-miR-19a, hsa-miR-103, hsa-miR-107, hsa-miR-1271, hsa-miR-130a, hsa-miR-130b, hsa-miR-144, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-181a, hsa-miR-181c, hsa-miR-195, hsa-miR-301a hsa-miR-335, hsa-miR-34a, hsa-miR-34c, hsa-miR-34c-5p, hsa-miR-411, hsa-miR-424, hsa-miR-449a, hsa-miR-497, hsa-miR-501-5p, hsa-miR-506, hsa-miR-516a-3p, hsa-miR-545, hsa-miR-575, hsa-miR-620, hsa-miR-889 & hsa-miR-96	ATF1, ATF2, ATF3, ATF4, ATF5 ATF6, ATF7, CREB1, ELK1, EP300, MYC, POU3F2 & SP1
14	PIK3CA	hsa-miR-19b, hsa-miR-10a, hsa-miR-10b, hsa-miR-124, hsa-miR-135a, hsa-miR-135b, hsa-miR-148a, hsa-miR-148b, hsa-miR-152, hsa-miR-155, hsa-miR-193a-5p, hsa-miR-19a, hsa-miR-19b, hsa-miR-203, hsa-miR-302a, hsa-miR-302b, hsa-miR-302c, hsa-miR-302d, hsa-miR-370, hsa-miR-372, hsa-miR-373, hsa-miR-422a, hsa-miR-490-5p, hsa-miR-506, hsa-miR-512-3p, hsa-miR-520a-3p, hsa-miR-520a-5p, hsa-miR-520b, hsa-miR-520d-3p, hsa-miR-520e, hsa-miR-525-5p, hsa-miR-561, hsa-miR-576-5p & hsa-miR-942	CTCF, ESR1, FOXI1, FOXO1, FOXO3, FOXO3B, FOXO4, PGR & TP53
15	BCL2	hsa-miR-301b, hsa-let-7a, hsa-miR-1, hsa-miR-103, hsa-miR-106a, hsa-miR-107, hsa-miR-125a-5p, hsa-miR-125b, hsa-miR-139-5p, hsa-miR-140-3p, hsa-miR-143, hsa-miR-153, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-17, hsa-miR-181a, hsa-miR-181b, hsa-miR-181c hsa-miR-181d, hsa-miR-182, hsa-miR-192, hsa-miR-195, hsa-miR-204, hsa-miR-20a, hsa-miR-21, hsa-miR-211, hsa-miR-217, hsa-miR-23a, hsa-miR-23b, hsa-miR-296-5p, hsa-miR-29a, hsa-miR-29b hsa-miR-29c, hsa-miR-30a, hsa-miR-30b, hsa-miR-30c, hsa-miR-338-5p, hsa-miR-34a, hsa-miR-34b, hsa-miR-34b*, hsa-miR-34c, hsa-miR-34c-5p, hsa-miR-365, hsa-miR-424, hsa-miR-429, hsa-miR-448, hsa-miR-451, hsa-miR-495, hsa-miR-497, hsa-miR-503, hsa-miR-504, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-548b-5p, hsa-miR-548c-3p, hsa-miR-548c-5p, hsa-miR-548d-5p, hsa-miR-587, hsa-miR-630, hsa-miR-641, hsa-miR-646 & hsa-miR-96	AR, ATF1, BCLAF1, BRCA1, CEBPA, CREB1, CTCF, CUX1, DDIT3, EGR1, ETS1, GLI1, GLI2 MYB, MYBL1, MYC, NFKB1, NFKB2, NR4A1, PARP1, PML PPARG, RARA, RARB, RARG RELA, SF1, SP1, STAT3, STAT5A TP53 & WT1
16	SLC30A8	hsa-miR-454, hsa-miR-143, hsa-miR-183, hsa-miR-186, hsa-miR-194, hsa-miR-205, hsa-miR-25 hsa-miR-298, hsa-miR-378, hsa-miR-422a, hsa-miR-501-3p, hsa-miR-502-3p, hsa-miR-543, hsa-miR-563, hsa-miR-577, hsa-miR-874 & hsa-miR-9	CEBPB, FOXO3, FOXO3B & HNF1A
17	CD3G	hsa-miR-301a, hsa-miR-136, hsa-miR-28-5p, hsa-miR-33b & hsa-miR-619	JUN
18	CD4	hsa-miR-130a, hsa-miR-181c hsa-miR-181d, hsa-miR-221 hsa-miR-222 & hsa-miR-765	CREB1, ETS1, ETS2 & MYB
19	CHN1	hsa-miR-130b, hsa-miR-194, hsa-miR-205, hsa-miR-210, hsa-miR-224, hsa-miR-300, hsa-miR-30a, hsa-miR-30d, hsa-miR-30e, hsa-miR-335, hsa-miR-452, hsa-miR-494, hsa-miR-502-5p, hsa-miR-543, hsa-miR-570 & hsa-miR-802	CUX1, FOXO3, FOXO3B, FOXO4 GTF3C1, NKX6-1, POU3F1, POU3F2, SREBF1, SREBF2 SRY & TCF3
20	ELK1	hsa-miR-24, hsa-miR-135a, hsa-miR-135b, hsa-miR-136, hsa-miR-150, hsa-miR-185, hsa-miR-205, hsa-miR-326, hsa-miR-330-5p, hsa-miR-34b, hsa-miR-34c-3p hsa-miR-361-3p, hsa-miR-495 hsa-miR-498, hsa-miR-539, hsa-miR-542-5p, hsa-miR-626, hsa-miR-660 & hsa-miR-873	AR, ARNT, BRCA1, BRCA1, CEBPA, CEBPB, CREBBP, CUX1, EGR1, EP300, FOS, ID1, ID2, ID3, KLF4, MAX, MXI1::CLEC5A, MYB, MYC, NFKB1, NFYA, PIAS2, SP1, SRF, STAT1, STAT2, TFAP2A, TFAP2C & USF1

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
21	FYN	hsa-miR-15b, hsa-miR-125a-3p, hsa-miR-1271, hsa-miR-183, hsa-miR-326, hsa-miR-330-5p, hsa-miR-369-3p, hsa-miR-370, hsa-miR-376a hsa-miR-376b, hsa-miR-380, hsa-miR-452, hsa-miR-486-3p, hsa-miR-489, hsa-miR-569, hsa-miR-583 hsa-miR-586, hsa-miR-604, hsa-miR-624, hsa-miR-639, hsa-miR-646, hsa-miR-889, hsa-miR-921 hsa-miR-939, hsa-miR-944& hsa-miR-96	ALX1, BCL3, CREB1, CTNNB1 EGR1, HLF, HNRNPK, KHDRBS1 NFIL3, NFKB1, NKX2-2, NR3C1 PAX5, RFX1, RREB1, SP1, STAT1 VSX2 & YTHDC1
22	LAT	hsa-miR-497, hsa-miR-216b, hsa-miR-296-3p, hsa-miR-376c, hsa-miR-574-3p, hsa-miR-602, hsa-miR-604, hsa-miR-608, hsa-miR-631 & hsa-miR-941	CTCF, PAX2, PPARG, TFAP4 & YY1
23	LCK	hsa-miR-424 & hsa-miR-202	ARNT, CTCF, EBF1, ELK1 ESR1, ESR2, ETS1, HNF4A KHDRBS1, MIF, MYB, NFKBIA NR3C1, RXRA, SP1, STAT1, STAT3, STAT5A, TAL1, TCF3 & USF1
24	MAP2K4	hsa-miR-16, hsa-miR-124, hsa-miR-128, hsa-miR-128a, hsa-miR-128b hsa-miR-136, hsa-miR-137, hsa-miR-141, hsa-miR-15b, hsa-miR-16 hsa-miR-195, hsa-miR-200a, hsa-miR-218, hsa-miR-22, hsa-miR-24 hsa-miR-25, hsa-miR-27a, hsa-miR-27b, hsa-miR-29a, hsa-miR-29b, hsa-miR-29c, hsa-miR-30b, hsa-miR-30d, hsa-miR-30e, hsa-miR-32 hsa-miR-363, hsa-miR-367, has-miR-374a, hsa-miR-424, hsa-miR-487b, hsa-miR-497, hsa-miR-503, hsa-miR-505, hsa-miR-506, hsa-miR-580, hsa-miR-892a, hsa-miR-92, hsa-miR-92a, hsa-miR-92b & hsa-miR-938	AHR, ARID5B, ARNT, PAX5 & YY1
25	MAP3K1	hsa-miR-195, hsa-let-7a, hsa-let-7b, hsa-let-7c, hsa-let-7d, hsa-let-7e, hsa-let-7f, hsa-let-7g, hsa-let-7i, hsa-miR-1, hsa-miR-106a, hsa-miR-106b, hsa-miR-124, hsa-miR-129-3p hsa-miR-129-5p, hsa-miR-136, hsa-miR-137, hsa-miR-17, hsa-miR-18a, hsa-miR-18b, hsa-miR-190, hsa-miR-192, hsa-miR-193a-3p, hsa-miR-193b, hsa-miR-19a, hsa-miR-19b, hsa-miR-200b, hsa-miR-200c, hsa-miR-203, hsa-miR-206, hsa-miR-20a, hsa-miR-20b, hsa-miR-21, hsa-miR-23a, hsa-miR-23b hsa-miR-30a, hsa-miR-31, hsa-miR-340, hsa-miR-371-5p, hsa-miR-372 hsa-miR-411, hsa-miR-429, hsa-miR-433, hsa-miR-488, hsa-miR-495, hsa-miR-499-3p, hsa-miR-506 hsa-miR-517b, hsa-miR-519d, hsa-miR-520d-5p, hsa-miR-524-5p, hsa-miR-544, hsa-miR-548c-3p, hsa-miR-557, hsa-miR-582-5p, hsa-miR-590-5p, hsa-miR-607, hsa-miR-613, hsa-miR-643, hsa-miR-892b, hsa-miR-9, hsa-miR-93 & hsa-miR-98	CEBPB, EGR1, IKBKB, IKBKG NFKB1, RELA & SPI1
26	PTPN7	hsa-miR-15a & hsa-miR-126	E2F1, EGR1, GATA1 & MXI1::CLEC5A
27	RAC1	hsa-miR-214, hsa-miR-101, hsa-miR-122, hsa-miR-137, hsa-miR-142-3p, hsa-miR-144, hsa-miR-155, hsa-miR-182, hsa-miR-194 hsa-miR-200c, hsa-miR-217 hsa-miR-299-5p, hsa-miR-300 hsa-miR-320, hsa-miR-361-5p hsa-miR-369-3p, hsa-miR-374a hsa-miR-429, hsa-miR-485-3p hsa-miR-518f, hsa-miR-655 & hsa-miR-96	ABL1, E2F1, EIF2AK2, ELK1, GABPA, NFKB1, RELA, STAT1 STAT3 & YY1

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
28	RAF1	hsa-miR-22, hsa-miR-125b, hsa-miR-135a, hsa-miR-135b, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-195, hsa-miR-19a, hsa-miR-19b, hsa-miR-424, hsa-miR-497, hsa-miR-516a-3p, hsa-miR-516b, hsa-miR-634, hsa-miR-646, hsa-miR-649 & hsa-miR-7	AR, MYC, NR3C1, RB1, RBL2, RFXANK, TSC22D3 & YY1
29	RELA	hsa-miR-544, hsa-miR-124, hsa-miR-138, hsa-miR-22, hsa-miR-302a, hsa-miR-302b, hsa-miR-302c hsa-miR-302d, hsa-miR-329, hsa-miR-362-3p, hsa-miR-371-5p, hsa-miR-373, hsa-miR-506, hsa-miR-512-3p, hsa-miR-520f, hsa-miR-569 hsa-miR-596, hsa-miR-7, hsa-miR-769-5p & hsa-miR-891b	AATF, AES, AHR, AR, BRCA1, CEBPB, CEBPD, CREBBP, EGR1, EGR1, EP300, ESR1, FOS, FUS, GTF2B, HDAC1, HDAC2, HDAC3, HEXIM1, HMGA2, IKBKB, IKBKG, ING4, IRF1, IRF2, IRF3, JUN, KAT2B, MEN1, MYC, NCOA3, NCOR2, NFKB1, NFKB2, NFKB2, NFKBIA, NFKBIB, NKRF, NKX2-1, NR3C1, PARP1, PAX6, PDCD11, PGR, PIAS1, PIAS3, PML, POU2F1, PPARA, PPARD, REL, RELB, RFC1, RXRA, SIN3A, SIRT1, SNIP1, SP1, SRF, STAT1, STAT3, STAT6, TAF1, TAF11, TAF4B, TAF6, TBP, TP53, TP53BP1, TRIB3, TRIP4, TSC22D3 & TWIST1
30	CLAR	hsa-miR-302e, hsa-miR-324-3p, hsa-miR-361-3p, hsa-miR-450b-3p, hsa-miR-516a-5p, hsa-miR-627, hsa-miR-660 & hsa-miR-768-5p	AR, E2F1, E2F4, GABPA, MYC NFYA, NKX2-1, NR3C1, RREB1 SP1, TFAP2A, TFAP2C, USF1 VSX2 & YY1
31	CAMK4	hsa-miR-302d, hsa-miR-106a, hsa-miR-129-5p, hsa-miR-17, hsa-miR-187, hsa-miR-191, hsa-miR-20a hsa-miR-299-3p, hsa-miR-30a hsa-miR-30b, hsa-miR-30c, hsa-miR-33a & hsa-miR-33b, hsa-miR-34b, hsa-miR-34c-3p, hsa-miR-455-5p, hsa-miR-507, hsa-miR-511, hsa-miR-567, hsa-miR-586, hsa-miR-885-5p & hsa-miR-96	ATF4, BACH1, BACH2, CREBBP EP300, HDAC4, MAX, MEF2A MYC, PPARG & RELA
32	CA1KK1	hsa-miR-302b, hsa-miR-103, hsa-miR-107, hsa-miR-145, hsa-miR-221, hsa-miR-222, hsa-miR-361-3p, hsa-miR-515-5p, hsa-miR-574-5p, hsa-miR-596, hsa-miR-619, hsa-miR-631, hsa-miR-634, hsa-miR-671-5p, hsa-miR-769-5p, hsa-miR-921 & hsa-miR-943	ARNT, BACH1, BACH2, E2F1, MAX, MXI1::CLEC5A, MYC, NFYA, PAX6, PPARG, TFAP2A TFAP2C & USF1
33	EDN1	hsa-miR-302a, hsa-let-7b, hsa-let-7c, hsa-miR-1, hsa-miR-147, hsa-miR-155, hsa-miR-185, hsa-miR-199a-5p, hsa-miR-203, hsa-miR-206, hsa-miR-220c, hsa-miR-454, hsa-miR-517b, hsa-miR-574-5p, hsa-miR-613 hsa-miR-648, hsa-miR-892a & hsa-miR-935	AR, CEBPA, CREB1, E2F1, FOXJ2 FOXO1, HIF1A, HLF, JUN, MEF2A, NFIC, NFKB1, PPARA, PPARG, SMAD1, SMAD3, SMAD4, TCF3 & ZEB1
34	GATA4	hsa-miR-302c, hsa-miR-1, hsa-miR-200b, hsa-miR-200c, hsa-miR-208b & hsa-miR-429	ATF1, ATF2, ATF3, ATF4, ATF5 ATF6, ATF7, CEBPA, CREB1, CUX1, EP300, FOS, FOSB, HAND2, JARID2, JUN, JUNB JUND, MED1, MEF2C, NFATC4 NFKB1, NFKB2, NKX2-5 NR5A1, PIAS1, RELA, SRF, TBX5 USF1& ZFPM2
35	GSK3B	hsa-miR-181d, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-224, hsa-miR-26a, hsa-miR-26b, hsa-miR-548a-5p, hsa-miR-548b-5p, hsa-miR-548c-5p, hsa-miR-548d-5p, hsa-miR-582-3p, hsa-miR-647 & hsa-miR-876-3p	APC, AR, ARNT, ATF4, BCL3, CDX2, CEBPA, CEBPA, CREB1, CREB3, CREB3L1, CREB3L3, CREB3L4, CREB5, CREM, CSDA, CTNNB1, CUX1, E2F1, E2F1, FOXO1, GLI1, GLI2, GLI3, HNRNPD, HOXA9, IKBKG, MEIS1, MITF, MYC, MYOCD, NFAT5, NFATC1 NFATC2, NFATC3, NFATC4 NFKB1, NFYA, NFYB, NFYC NKX2-2, NOTCH2, PAX5, POU2F1, PPARGC1A, SNAI1 SOX9, SPI1, STAT5A, TP53 & YBX1

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
36	HAND1	hsa-miR-520a-3p, hsa-let-7a, hsa-let-7b, hsa-let-7c, hsa-let-7d, hsa-let-7e, hsa-let-7f, hsa-let-7g, hsa-let-7i hsa-miR-196a, hsa-miR-196b, hsa-miR-25, hsa-miR-32, hsa-miR-335, hsa-miR-363, hsa-miR-367, hsa-miR-92, hsa-miR-92a, hsa-miR-98	FHL2, FOXD1, FOXF2, HEY2, HEYL, HOXA9, MEIS1, MYOD1, POU3F1, RORA, TCF12 & TCF3
37	HAND2	hsa-miR-520e, hsa-miR-1, hsa-miR-128, hsa-miR-135b, hsa-miR-140-5p, hsa-miR-181a, hsa-miR-181b, hsa-miR-181c, hsa-miR-181d, hsa-miR-202, hsa-miR-206, hsa-miR-25 hsa-miR-296-5p, hsa-miR-32, hsa-miR-363, hsa-miR-367, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-543, hsa-miR-566 hsa-miR-615-5p, hsa-miR-661, hsa-miR-767-3p, hsa-miR-876-3p, hsa-miR-92, hsa-miR-92a & hsa-miR-92b	AHR, ARNT, BPTF, CENPB, COPS5, EP300, FOXD3, GATA4 HEY2, HEYL, NPM1, PHOX2A SRY, TCF3 & VSX2
38	HDAC5	hsa-miR-373, hsa-miR-124, hsa-miR-128, hsa-miR-134, hsa-miR-30a, hsa-miR-30b, hsa-miR-506, hsa-miR-589, hsa-miR-629, hsa-miR-653, hsa-miR-765, hsa-miR-768-3p & hsa-miR-9	ANKRA2, BCL6, BCOR, CIITA, HR, KLF4, MAX, MEF2A, MEF2C MEF2D, NCOR1, NCOR2, NFKB2 NRIP1, PHB2, RFXANK, RUNX3 USF1 & ZBTB16
39	HDAC9	hsa-miR-520c-3p, hsa-miR-124, hsa-miR-147, hsa-miR-182, hsa-miR-190b, hsa-miR-199b-5p, hsa-miR-19a, hsa-miR-26a, hsa-miR-26b, hsa-miR-27a, hsa-miR-27b, hsa-miR-299-5p, hsa-miR-302b, hsa-miR-302c, hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d, hsa-miR-30e, hsa-miR-32, hsa-miR-338-5p, hsa-miR-365, hsa-miR-377, hsa-miR-383, hsa-miR-409-5p, hsa-miR-452, hsa-miR-506, hsa-miR-514, hsa-miR-515-5p, hsa-miR-542-5p, hsa-miR-558, hsa-miR-768-3p, hsa-miR-891a & hsa-miR-96	KLF12, MEF2A, MEF2A, NCOR1 REST, SIN3A, SIN3B, USF1, ZBTB16 & ZEB1
40	LIF	hsa-miR-520b, hsa-miR-125a-5p, hsa-miR-125b, hsa-miR-1297, hsa-miR-181b, hsa-miR-181d, hsa-miR-199a, hsa-miR-199a-5p, hsa-miR-26a, hsa-miR-28-5p, hsa-miR-29a, hsa-miR-29b, hsa-miR-29c, hsa-miR-328, hsa-miR-331-3p, hsa-miR-346, hsa-miR-494, hsa-miR-504, hsa-miR-654-5p, hsa-miR-874 & hsa-miR-93	CTCF, EGR3, ETS1, ETS2, MZF1 NFKB1, PBX1, RREB1, STAT1 STAT2 & TBP
41	MEF2C	hsa-miR-520d-3p, hsa-miR-135a, hsa-miR-135b, hsa-miR-137, hsa-miR-153, hsa-miR-182, hsa-miR-183, hsa-miR-18a, hsa-miR-18b, hsa-miR-190, hsa-miR-190b, hsa-miR-194, hsa-miR-19a, hsa-miR-19b, hsa-miR-203, hsa-miR-21, hsa-miR-223, hsa-miR-23a, hsa-miR-23b, hsa-miR-27b, hsa-miR-302a, hsa-miR-302b, hsa-miR-302c, hsa-miR-302d, hsa-miR-330-3p, hsa-miR-331-5p, hsa-miR-33a, hsa-miR-340, hsa-miR-372, hsa-miR-421, hsa-miR-448, hsa-miR-450b-5p, hsa-miR-520a-3p, hsa-miR-520b, hsa-miR-520c-3p, hsa-miR-520d-3p, hsa-miR-520d-5p, hsa-miR-520e, hsa-miR-520f, hsa-miR-524-5p, hsa-miR-556-3p, hsa-miR-603, hsa-miR-621 & hsa-miR-656	ATF2, BPTF, CDC5L, CREB1, CUX1, EP300, ESR1, FOXD3, FOXI1, FOXJ2, GATA4, HDAC4, HDAC5, HLF, IRF1, KLF12, MEF2A, MEF2D, NCOA2, NKX2-2 NKX3-1, PAX6, PBX1, POU2F1, POU2F2, POU3F1, POU3F2, POU3F3 POU5F1, SMAD2, SP1, SPI1, STAT5A, STAT5B, TCF3, TEAD1 TFAP4, TGIF1, TWIST2 & VGLL2
42	MYL2	hsa-miR-124, hsa-miR-490-5p hsa-miR-593 & hsa-miR-876-5p	HNF1A & MEF2A
43	ACTA1	hsa-miR-506, hsa-let-7a, hsa-let-7b hsa-let-7c, hsa-let-7d, hsa-let-7e, hsa-let-7f, hsa-let-7g, hsa-let-7i, hsa-miR-122, hsa-miR-155, hsa-miR-21 hsa-miR-220c, hsa-miR-569, hsa-miR-574-5p & hsa-miR-98	ABL1, E2F4, ELK1, HCLS1, MEF2A, NR3C2, REST, SRF, TBP TP53 & ZEB1
44	PDPK1	hsa-miR-23a, hsa-miR-147, hsa-miR-181a, hsa-miR-181c, hsa-miR-214, hsa-miR-27a, hsa-miR-27b, hsa-miR-323-5p, hsa-miR-374b, hsa-miR-375, hsa-miR-382, hsa-miR-410, hsa-miR-486-3p, hsa-miR-499-3p, hsa-miR-504, hsa-miR-885-3p & hsa-miR-944	EGR1, EGR3, GABPA, PPARD RXRA, RXRB, RXRG & SP1

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
45	RPS6KB1	hsa-miR-23b, hsa-miR-103, hsa-miR-107, hsa-miR-124, hsa-miR-128, hsa-miR-129-5p, hsa-miR-130a hsa-miR-130b, hsa-miR-135a, hsa-miR-135b, hsa-miR-137, hsa-miR-142-5p, hsa-miR-145, hsa-miR-153 hsa-miR-155, hsa-miR-181a, hsa-miR-181b, hsa-miR-181c, hsa-miR-181d, hsa-miR-186, hsa-miR-200b hsa-miR-200c, hsa-miR-218, hsa-miR-223, hsa-miR-27a, hsa-miR-27b, hsa-miR-301a, hsa-miR-301b hsa-miR-340, hsa-miR-369-3p, hsa-miR-377, hsa-miR-429, hsa-miR-506, hsa-miR-507, hsa-miR-548c-3p, hsa-miR-557, hsa-miR-561, hsa-miR-568, hsa-miR-579, hsa-miR-590-3p, hsa-miR-605, hsa-miR-607, hsa-miR-641, hsa-miR-655, hsa-miR-7 & hsa-miR-944	E2F1, E2F2 & LMO2
46	YWHAH	hsa-miR-125b, hsa-miR-103, has-miR-107, hsa-miR-137, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-195, hsa-miR-25, hsa-miR-28-3p, hsa-miR-33, hsa-miR-33a, hsa-miR-33b, hsa-miR-361-5p, hsa-miR-365, hsa-miR-381, hsa-miR-421, hsa-miR-424, hsa-miR-490-5p, hsa-miR-497, hsa-miR-519d, hsa-miR-521, hsa-miR-523,hsa-miR-563, hsa-miR-576-5p,hsa-miR-583, hsa-miR-584, hsa-miR-586, hsa-miR-598, hsa-miR-652, hsa-miR-660, hsa-miR-708, hsa-miR-885-5p, hsa-miR-888, hsa-miR-95& hsa-miR-96	ABL1,ATF2, CREB1, CREBBP, E2F4, EGR3, ESR1, ESR2, ING1, JUN, MDM4, MED1, MEF2A, MYC, NCOA1, NCOA2, NCOA3, NR3C1, NRIP1, TFAP2A,THRA,TLX2,TNFAIP3,YY1 & ZFP36
47	ADSS	hsa-miR-125a-5p, hsa-miR-1, hsa-miR-16, hsa-miR-182, hsa-miR-19a hsa-miR-19b, hsa-miR-206, hsa-miR-28-3p, hsa-miR-383, hsa-miR-503, hsa-miR-514, hsa-miR-548a-3p hsa-miR-548a-5p, hsa-miR-548b-5p hsa-miR-548c-5p, hsa-miR-548d-5p hsa-miR-561, hsa-miR-609, hsa-miR-642, hsa-miR-922, hsa-miR-923 & hsa-miR-96	CTCF, EGR1, EGR2, EGR3 KLF12, SP1,TFAP2A & TFAP2C
48	CDKN1A	hsa-miR-590-3p, hsa-miR-449a, hsa-miR-449b, hsa-let-7a, hsa-let-7e, hsa-let-7f, hsa-miR-106a, hsa-miR-106b, hsa-miR-125a-5p, hsa-miR-130a, hsa-miR-130b, hsa-miR-132, hsa-miR-145, hsa-miR-146a, hsa-miR-146b-5p, hsa-miR-17, hsa-miR-17-5p,hsa-miR-182, hsa-miR-193a-5p,hsa-miR-20, hsa-miR-208a hsa-miR-208b, hsa-miR-20a, hsa-miR-20b, hsa-miR-21, hsa-miR-212, hsa-miR-22, hsa-miR-224, hsa-miR-28-5p, hsa-miR-298, hsa-miR-299-5p, hsa-miR-301a, hsa-miR-301b hsa-miR-302a, hsa-miR-345, hsa-miR-363, hsa-miR-370, hsa-miR-372, hsa-miR-423-3p, hsa-miR-454, hsa-miR-503, hsa-miR-509-3-5p, hsa-miR-515-3p, hsa-miR-516a-3p, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-519d, hsa-miR-519e, hsa-miR-520a-3p, hsa-miR-520b, hsa-miR-520g, hsa-miR-520h, hsa-miR-572, hsa-miR-608, hsa-miR-639, hsa-miR-641, hsa-miR-654-3p, hsa-miR-657, hsa-miR-93, hsa-miR-939 hsa-miR-942 & hsa-miR-96	AR,ATF2, CDC5L, CEBPA, CEBPA, ESR1, ESR1, ETS1, FLI1, FOS, FOXC1, FOXD1, FOXF2, FOXJ2, HDAC11, HIF1A, HNF4A, JUN, PARP1, PPARG, RARA, RB1, RELB, SMAD1, SMAD2, SMAD3, SMAD4, SP1, SP3, SP4, SRF, STAT1, STAT3,TFAP2A, TP53,TP53,TP63,TP73,TSG101,WT1&XRCC6
49	GNAQ	hsa-miR-381, hsa-miR-142-3p, hsa-miR-182, hsa-miR-423-5p, hsa-miR-491-3p, hsa-miR-574-3p, hsa-miR-581, hsa-miR-587, hsa-miR-642, hsa-miR-886-3p & hsa-miR-96	CTCF, CUX1, EGR1, MEF2A & PPARG
50	MARCKS	hsa-miR-300, hsa-miR-1, hsa-miR-128a, hsa-miR-128b, hsa-miR-138, hsa-miR-142-3p, hsa-miR-143, hsa-miR-144, hsa-miR-182, hsa-miR-200b, hsa-miR-200c, hsa-miR-205, hsa-miR-206, hsa-miR-21, hsa-miR-216a, hsa-miR-218, hsa-miR-222, hsa-miR-23a, hsa-miR-25, hsa-miR-27a, hsa-miR-27b, hsa-miR-300, hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d, hsa-miR-30e, hsa-miR-370, hsa-miR-429, hsa-miR-491-5p, hsa-miR-495, hsa-miR-499-5p, hsa-miR-561, hsa-miR-655, hsa-miR-770-5p & hsa-miR-876-3p	AHR,ALX1,ARNT, HNF1A MZF1, NFKB1, PAX6, POU2F1 TOB1 &YY1

A computational approach to identify microRNA (miRNA) based biomarker of Pharmacovariant from the regulation of disease pathology

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
51	SP1	hsa-miR-153, hsa-miR-1, hsa-miR-105, hsa-miR-124, hsa-miR-128, hsa-miR-128a, hsa-miR-128b, hsa-miR-135a, hsa-miR-135b, hsa-miR-137, hsa-miR-138, hsa-miR-149, hsa-miR-150, hsa-miR-155, hsa-miR-203, hsa-miR-204, hsa-miR-206, hsa-miR-211, hsa-miR-216a, hsa-miR-218, hsa-miR-22, hsa-miR-223, hsa-miR-24, hsa-miR-27a, hsa-miR-27b, hsa-miR-29a, hsa-miR-29b, hsa-miR-29c, hsa-miR-300, hsa-miR-32, hsa-miR-320, hsa-miR-324-5p, hsa-miR-335, hsa-miR-361-5p, hsa-miR-362-3p, hsa-miR-374b, hsa-miR-375, hsa-miR-377, hsa-miR-381, hsa-miR-384, hsa-miR-410, hsa-miR-429 hsa-miR-487a, hsa-miR-488, hsa-miR-495, hsa-miR-506, hsa-miR-539, hsa-miR-548a-5p, hsa-miR-548b-3p, hsa-miR-548c-5p, hsa-miR-548d-5p, hsa-miR-570, hsa-miR-590-3p, hsa-miR-603, hsa-miR-607, hsa-miR-613, hsa-miR-625 & hsa-miR-7	AATF, AHR, AR, ARNT, ATF7IP BCL6, BCOR, BRCA1, CEBPA, CEBPB, E2F1, E2F2, E2F3, E2F4, EGR1, EGR1, EGR3, ELF1, EP300, ESR1, ESR2, ETS1, GABPA, GATA1, HCFC1, HDAC1, HDAC2, HIF1A, HMGA1, HNF4A, HTT, JUN, KLF10, KLF4, KLF6, MEF2A, MEF2C, MEF2D, MIS18BP1, MSX1, MYB, MYC, MYOD1, MYOG, NCOR1, NCOR2, NFYA, NFYB, NR2F1, NR5A1, PAX6, PER3, PML, POU2F1, POU2F1, PURA, RARA, RB1, RBBP4, RBL1, REL, RELA, RREB1, RXRA, SMAD2, SMAD3 SMAD4, SOX10 & SOX8
52	SP3	hsa-miR-361-5p, hsa-miR-105, hsa-miR-124, hsa-miR-133a, hsa-miR-133b, hsa-miR-135a, hsa-miR-135b hsa-miR-145, hsa-miR-153, hsa-miR-155, hsa-miR-182, hsa-miR-223, hsa-miR-27a, hsa-miR-338-5p hsa-miR-369-3p, hsa-miR-374a hsa-miR-374b, hsa-miR-410, hsa-miR-421, hsa-miR-448, hsa-miR-487a, hsa-miR-487b, hsa-miR-506 hsa-miR-507, hsa-miR-520d-5p, hsa-miR-522, hsa-miR-524-5p, hsa-miR-548a-5p, hsa-miR-548b-5p hsa-miR-548c-5p, hsa-miR-548d-5p hsa-miR-568, hsa-miR-580, hsa-miR-590-3p, hsa-miR-634, hsa-miR-655, hsa-miR-889 & hsa-miR-96	E2F1, E2F2, E2F3, E2F4, E2F5, E2F6, E2F7, EGR1, EP300, ESR1 GABPA, HDAC1, HDAC2, MEF2A NFYA, PAX6, PBX1, PIAS1, RB1, RBBP4 & SP1
53	MAPK3	hsa-miR-429, hsa-miR-132, hsa-miR-212, hsa-miR-497 & hsa-miR-613	AR, BCL3, CEBPB, ELK1, ELK4, ESR1, ETS1, ETS2, ETV6, ETV7, FOS, GATA1, GATA4, GTF2I, HDAC4, HIF1A, HSF1, HSF4, JUN, JUND, MAX, MITF, MYC, NR3C1, PPARA, SMAD1, SMAD2, SMAD3, SMAD4, SMAD5, SMAD9, SNAI2, SP1, SPIB, SREBF1, SREBF2, STAT3, STAT5A, TAL1, TAL2, TCF3, TGIF1, TOP2B, TP53, UBTF, USF1, YY1 & ZNF7
54	PRKCA	hsa-miR-200b, hsa-miR-147, hsa-miR-183, hsa-miR-186, hsa-miR-200c, hsa-miR-203, hsa-miR-205, hsa-miR-25, hsa-miR-340, hsa-miR-362-5p, hsa-miR-495, hsa-miR-522 hsa-miR-545, hsa-miR-548a-5p, hsa-miR-548b-5p, hsa-miR-548c-5p hsa-miR-548d-5p, hsa-miR-590-3p hsa-miR-603, hsa-miR-9 & hsa-miR-15a	AR, BTG2, CREM, DDX5, DLX3, EDF1, EWSR1, HABP4, HAND1 HAND2, HES1, HMGN1, HMGN2 MAX, MXI1::CLEC5A, MYOD1 NFATC1, NFKB1, PA2G4, PPARA RARA, RARA, SP1, TFAP2A TP53, TRIM29 & USF1
55	FOS	hsa-miR-340, hsa-miR-345-3p, hsa-miR-4771, hsa-miR-4765, hsa-miR-4749-5p, hsa-miR-4749-3p, hsa-miR-4742-5p, hsa-miR-4742-3p, hsa-miR-4732-5p, hsa-miR-4732-3p hsa-miR-4692, hsa-miR-4659b-5p hsa-miR-4659b-3p, hsa-miR-4657 hsa-miR-4645-5p, hsa-miR-4645-3p, hsa-miR-4534, hsa-miR-4533, hsa-miR-4522, hsa-miR-4521, hsa-miR-451a, hsa-miR-4519, hsa-miR-4518, hsa-miR-449c-5p, hsa-miR-449c-3p, hsa-miR-449b-5p, hsa-miR-449b-3p hsa-miR-449a, hsa-miR-4484, hsa-miR-4479, hsa-miR-4457, hsa-miR-4425, hsa-miR-4419a, hsa-miR-4317, hsa-miR-4310, hsa-miR-4292 hsa-miR-4288, hsa-miR-4282, hsa-miR-4274, hsa-miR-4258, hsa-miR-4256, hsa-miR-383, hsa-miR-3690, hsa-miR-3676-5p, hsa-miR-3676-3p, hsa-miR-3670, hsa-miR-3616-5p, hsa-miR-3616-3p, hsa-miR-3179, hsa-miR-3117-5p, hsa-miR-3117-3p, hsa-miR-30a-5p, hsa-miR-30a-3p, hsa-miR-301b, hsa-miR-29b-3p, hsa-miR-22-5p, hsa-miR-22-3p, hsa-miR-212-5p, hsa-miR-212-3p, hsa-miR-2116-5p, hsa-miR-2116-3p, hsa-miR-1827, hsa-miR-1470, hsa-miR-144-5p, hsa-miR-144-3p, hsa-miR-139-5p, hsa-miR-139-3p, hsa-miR-132-5p, hsa-miR-132-3p, hsa-miR-130b-5p, hsa-miR-130b-3p, hsa-miR-130a-5p, hsa-miR-130a-3p, hsa-miR-1302, hsa-miR-1283, hsa-miR-1269a, hsa-miR-125b-5p, hsa-miR-1255b-5p hsa-miR-1252, hsa-miR-1249 hsa-miR-1227 & hsa-let-7a-5p	ATF1, ATF2, ATF7, BACH2, BATF, BCL3, CEBPB, CEBPG, COBRA1, CREB1, DDIT3, EGR1 EGR2, ELK1, ELK3, ELK4, ESR1 ESR2, ETS1, ETS2, ETV4 & FLI1

A computational approach to identify microRNA (miRNA) based biomarker of Pharmacovariant from the regulation of disease pathology

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
56	JUN	hsa-miR-324-3p, hsa-miR-139-5p, hsa-miR-141, hsa-miR-15a, hsa-miR-16, hsa-miR-200a, hsa-miR-200b, hsa-miR-200c, hsa-miR-216b, hsa-miR-297, hsa-miR-30a, hsa-miR-340, hsa-miR-429, hsa-miR-495, hsa-miR-496, hsa-miR-517c, hsa-miR-520d-5p, hsa-miR-522, hsa-miR-524-5p, hsa-miR-612, hsa-miR-642, hsa-miR-758, hsa-miR-890, hsa-miR-889, hsa-miR-802, hsa-miR-766-5p, hsa-miR-766-3p, hsa-miR-661, hsa-miR-645, hsa-miR-614, hsa-miR-5706, hsa-miR-5684, hsa-miR-5587-5p, hsa-miR-5587-3p, hsa-miR-5586-5p, hsa-miR-5586-3p, hsa-miR-553, hsa-miR-548z, hsa-miR-548ao-3p, hsa-miR-548aj-3p, hsa-miR-544a, hsa-miR-539-3p, hsa-miR-520b, hsa-miR-519a-3p, hsa-miR-518e-5p, hsa-miR-518e-3p, hsa-miR-518a-5p, hsa-miR-518a-3p, hsa-miR-516a-5p, hsa-miR-516a-3p, hsa-miR-5008-5p, hsa-miR-5008-3p, hsa-miR-5000-5p, hsa-miR-5000-3p, hsa-miR-487b, hsa-miR-487a, hsa-miR-4792, hsa-miR-4784, hsa-miR-4771, hsa-miR-4763-5p, hsa-miR-4763-3p, hsa-miR-4732-5p, hsa-miR-4732-3p hsa-miR-4716-5p, hsa-miR-4716-3p hsa-miR-4696, hsa-miR-4692 hsa-miR-4687-5p, hsa-miR-4687-3p hsa-miR-4683, hsa-miR-4665-5p hsa-miR-4665-3p, hsa-miR-4659b-5p, hsa-miR-4659b-3p, hsa-miR-4640-5p, hsa-miR-4640-3p, hsa-miR-4534, hsa-miR-4521, hsa-miR-451a, hsa-miR-4519, hsa-miR-449c-5p, hsa-miR-449c-3p, hsa-miR-449b-5p, hsa-miR-449b-3p, hsa-miR-449a, hsa-miR-4457, hsa-miR-4434 & hsa-miR-4425	ABL1, AR, ATF1, ATF2, ATF3, ATF4, BATF, BCL3, BCL6, BRCA1, COBRA1, COPS5, CREB1, CREB5 CREBBP, DDIT3, E2F1, E2F4, EGR1, ELF3, EN1, EP300, ERG, ESR1, ESR2, ETS1, ETS2, FOS FOSL1, FOSL2, GATA1, GATA2 GATA3, GTF2B, GTF2F2, HCFC1 HDAC3, HHEX, HIF1A, HMGA1 HOXA9, HOXC8, LEF1, MAF MAFB, MEF2A, MYBBP1A MYC, MYOD1, NCOA1, NCOA2 NCOA3, NFE2L1, NFE2L2, NFIC NFYA, NR3C1, NR5A1, NRIP1 PGR, PIAS1, POU1F1, RARA, RARB, RARG, RB1, RBM39 REL, RELA, RUNX1, RUNX2 SKI, SMAD2, SMAD3, SMAD4 SMARCD1, SMARCD3, SNAPC5 SOX10, SOX8, SP1, SPI1, SPIB SREBF1, SREBF2, STAT1, STAT2 STAT3, STAT4, STAT5A, STAT6 TAF1, TBP, TCF20, TCF4, TCF7 TCF7L1, TCF7L2, TGIF1, TRIP4 TSC22D3, VDR, HSF2 & JDP2
57	MAPK8	hsa-miR-26a, hsa-miR-103, hsa-miR-107, hsa-miR-196b, hsa-miR-214, hsa-miR-548c-3p & hsa-miR-641	ATF2, COPS2, ELK1, ELK3, FOS HSF1, HSF4, JDP2, JUN, JUNB, JUND, IL8, MECOM, MYC, NFATC2, NFATC4, NR3C1, PAX2 PGR, PPARG, REL, SMAD2, SMAD3, SPIB, STAT3, TP53, TP73 & XRCC6
58	SRC	hsa-miR-1297, hsa-miR-137, hsa-miR-141, hsa-miR-144, hsa-miR-149, hsa-miR-153, hsa-miR-200a, hsa-miR-203, hsa-miR-220c, hsa-miR-31, hsa-miR-34a, hsa-miR-34c-5p, hsa-miR-449a, hsa-miR-449b, hsa-miR-9, hsa-miR-940, hsa-miR-145 & hsa-miR-143	ABL1, AR, ARHGAP35, CTNNB1, DAB2, ESR1, ESR2, ETS1, ETS2, FOXO1, GTF2I, HCLS1, HNF1A, HNRNPK, IKBKB, KHDRBS1, MAX, MXI1::CLEC5A, MYC, NFKBIA, NR1I2, PAX5, PGR, PPARD, RXRA, SMARCB1, SMARCE1, SP1, SRF, STAT1, STAT3, STAT5A, STAT5B, STAT6, TFAP2A, THRA, TRIP6 WBP11 & YTHDC1
59	GRB2	hsa-miR-26b, hsa-miR-124, hsa-miR-128a, hsa-miR-128b, hsa-miR-141, hsa-miR-153, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-182, hsa-miR-195, hsa-miR-200a hsa-miR-208b, hsa-miR-220c, hsa-miR-27a, hsa-miR-27b, hsa-miR-320, hsa-miR-329, hsa-miR-376c hsa-miR-424, hsa-miR-433, hsa-miR-497, hsa-miR-506, hsa-miR-520g, hsa-miR-520h, hsa-miR-532-3p, hsa-miR-941 & hsa-miR-96	ABL1, DAB2, DTX1, EGR1, ELK1, ESR1, FOXA2, FOXO1, FOXO3, FOXO3B, GABPA, HTT, KHDRBS1, KHDRBS2, MTA1 MTA3, NPM1, PAX5 & TP63
60	PIK3R1	hsa-miR-376c, hsa-miR-103, hsa-miR-107, hsa-miR-128, hsa-miR-132, hsa-miR-136, hsa-miR-150, hsa-miR-153, hsa-miR-155, hsa-miR-15a, hsa-miR-15b, hsa-miR-16 hsa-miR-186, hsa-miR-195, hsa-miR-21, hsa-miR-212, hsa-miR-218 hsa-miR-221, hsa-miR-222, hsa-miR-29a, hsa-miR-29b, hsa-miR-29c, hsa-miR-361-5p, hsa-miR-424 hsa-miR-448, hsa-miR-455-3p, hsa-miR-486-5p, hsa-miR-488, hsa-miR-495, hsa-miR-497, hsa-miR-503, hsa-miR-520a-5p, hsa-miR-525-5p, hsa-miR-532-3p, hsa-miR-542-3p, hsa-miR-545, hsa-miR-548a-3p, hsa-miR-548c-3p, hsa-miR-579, hsa-miR-590-5p, hsa-miR-603, hsa-miR-630, hsa-miR-655, hsa-miR-656, hsa-miR-767-5p, hsa-miR-891b hsa-miR-93 & hsa-miR-96	ABL1, CTCF, CTNNB1, EBF1, EGR1, EGR2, EGR3, ELK1, ESR1, GABPA, GATA3, GTF2H1, HNF1A, HOXA9, IRF1, KHDRBS1 KLF12, MEF2A, MEIS1, NFE2L1 NFIL3, NFKBIA, NFYA, NFYB NFYC, NR2F2, PBX1, PGR, POU3F1, POU3F2, RB1, SP1, USF1 & WBP11

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
61	ABCG2	hsa-miR-496, hsa-miR-192, hsa-mir-328, hsa-miR-328, hsa-miR-519c-3p hsa-miR-519d, hsa-miR-520a-3p hsa-miR-520b, hsa-miR-520c-3p hsa-miR-520d-3p, hsa-miR-520e hsa-miR-520f, hsa-miR-520g & hsa-miR-520h	FOS, JUN, MAX & USF1
62	SHC1	hsa-miR-186, hsa-miR-124, hsa-miR-1271, hsa-miR-127-5p, hsa-miR-140-3p, hsa-miR-140-5p, hsa-miR-198, hsa-miR-204, hsa-miR-211, hsa-miR-219, hsa-miR-219-5p hsa-miR-330-5p, hsa-miR-452, hsa-miR-506, hsa-miR-518e, hsa-miR-568, hsa-miR-572, hsa-miR-650, hsa-miR-9 & hsa-miR-96	ABL1, BCL3, ELK1, EP300, ESR1 ESR1, FOS, GABPA, JUN, NPM1 POU2F1, REL, RELA, SP1, STAT5A, STAT5B, TOPORS & TP53
63	SOS1	hsa-miR-495, hsa-miR-124, hsa-miR-132, hsa-miR-148b, hsa-miR-152, hsa-miR-155, hsa-miR-181a, hsa-miR-181b, hsa-miR-181d, hsa-miR-204, hsa-miR-211, hsa-miR-212, hsa-miR-217, hsa-miR-302c, hsa-miR-30a, hsa-miR-30b, hsa-miR-30d, hsa-miR-30e, hsa-miR-506, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-520a-3p, hsa-miR-520b, hsa-miR-520c-3p, hsa-miR-520d-3p, hsa-miR-520e, hsa-miR-520f, hsa-miR-9 & hsa-miR-96	AR, BIN1, CTCF, EGR1, ESR1, NFIC, RARA, SP1, STAT3, TFAP2A, USF1, NFIC, RARA, SPRY1, SPRY2, CCND1, SPRY4 SPRY3, BCL2L1, CCND2, CCND3 MYC, SPRED1 & SPRED2
64	CREB1	hsa-miR-653, hsa-miR-103, hsa-miR-124, hsa-miR-128a, hsa-miR-128b, hsa-miR-141, hsa-miR-181a hsa-miR-181b, hsa-miR-181c hsa-miR-181d, hsa-miR-182, hsa-miR-200a, hsa-miR-223, hsa-miR-25, hsa-miR-27a, hsa-miR-27b, hsa-miR-32, hsa-miR-34b*, hsa-miR-363, hsa-miR-367, hsa-miR-433, hsa-miR-519b-3p, hsa-miR-526b hsa-miR-543, hsa-miR-552, hsa-miR-576-5p, hsa-miR-92a, hsa-miR-92b, hsa-miR-944 & hsa-miR-96	ABL1, AHR, ARNT, ATF1, ATM, CEBPA, CEBPB, CIITA, CREBBP, CREM, EDF1, EGR1, EP300, FHL5, GLI2, GTF2F2, KAT5, KCNIP3, MYC, NFKB1, NFKB2, NR3C1, PDX1, REL, RELA, RELB, SMARCA4, SMARCA5, SOX9, SRF, STAT3, THRA & TLX2
65	PLCG1	hsa-miR-543, hsa-miR-101, hsa-miR-129, hsa-miR-129-5p, hsa-miR-149, hsa-miR-182, hsa-miR-200b, hsa-miR-218, hsa-miR-221, hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d hsa-miR-30e, hsa-miR-34a, hsa-miR-429, hsa-miR-455-5p, hsa-miR-874 & hsa-miR-96	ABL1, ATF2, CREB1, CTCF, E2F4 EEF1A1, EGR1, ESR1, GTF2H1 KHDRBS1, NFYA, SREBF1, SREBF2, TOPORS, USF1 & YY1
66	CD247	hsa-miR-410, hsa-miR-214 & hsa-miR-346	EP300, FOS, JUN, SLA2, STAT5A STAT5B & YY1
67	ZAP70	hsa-miR-297, hsa-miR-331-3p, hsa-miR-34a, hsa-miR-34b, hsa-miR-34c-5p, hsa-miR-484, hsa-miR-629 hsa-miR-885-3p & hsa-miR-939	ABL1, ATF6, CTCF, HNF4A, NFYA, NR2F1, NR2F2, SLA2, USF1 & XBP1
68	CSNK2A1	hsa-miR-520h, hsa-miR-125b hsa-miR-141, hsa-miR-186, hsa-miR-200a, hsa-miR-216b & hsa-miR-221	AIP, APEX1, ARNT, ATF1, ATF2, BDP1, BRCA1, BRF1, CREBBP, CREM, CTDP1, CTNNB1, CUX2, DDIT3, EGR1, ETS1, FOS, GTF2A1, GTF2A1L, HCLS1, HDAC1, HDAC2, HDAC3, HES6, HIF1A, HMGA1, HMGA2, HOXB7 HSF1, IFI16, IRF2, JUN, KLF1, MAX, MAZ, MEF2C, MYB, MYC, MYCN, MYF5, NAP1L4, NFIC, NFKB1, NFKBIA, NKX2-5, PGR, PML, RELA, SHOX, SP1, SPIB, SRF, SSRP1, SUB1, TCF7L2, TOPORS, TP53, UBTF, VDR, YY1 & ZHX1
69	PTK2B	hsa-miR-519c-3p, hsa-miR-19a, hsa-miR-205, hsa-miR-23a, hsa-miR-23b, hsa-miR-345, hsa-miR-515-5p hsa-miR-647, hsa-miR-892b & hsa-miR-940	CTCF, EGR1, EWSR1, GABPA HNF4A, MYC, NFKB1, REST SP1, SPI1, SRF, STAT3, TGFB1I1 & TP53

Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
70	CAMK2B	hsa-miR-544	AHR, ARNT, ATF4, CTCF, E2F1 E2F2, E2F3, E2F4, E2F5, E2F6 E2F7, EGR1, EGR2, EGR3, ETS1 MEF2A, NFE2L1, PAX5, RORA RREB1, RXRG, SP1, THRB, USF1 & XBP1
71	HBXIP	hsa-miR-192, hsa-miR-106a, hsa-miR-106b, hsa-miR-140-5p, hsa-miR-145, hsa-miR-16, hsa-miR-17, hsa-miR-18a, hsa-miR-18b, hsa-miR-20a, hsa-miR-20b, hsa-miR-370, hsa-miR-378, hsa-miR-492, hsa-miR-496, hsa-miR-515-3p, hsa-miR-519d, hsa-miR-519e, hsa-miR-520d-5p, hsa-miR-520g, hsa-miR-520h, hsa-miR-524-5p, hsa-miR-545, hsa-miR-590-3p, hsa-miR-606, hsa-miR-619, hsa-miR-631, hsa-miR-876-3p & hsa-miR-93	EEF1A1, GABPA, HNF1A, HNF4A MAF1, MAX, POU2F1, USF1 & ZBTB16
72	PPP3CA	hsa-miR-328, hsa-let-7a, hsa-let-7b hsa-let-7c, hsa-let-7e, hsa-let-7f, hsa-let-7g, hsa-let-7i, hsa-miR-100, hsa-miR-106a, hsa-miR-106b, hsa-miR-142-3p, hsa-miR-145, hsa-miR-153, hsa-miR-17, hsa-miR-182, hsa-miR-20b, hsa-miR-21, hsa-miR-300 hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d, hsa-miR-30e, hsa-miR-31, hsa-miR-340, hsa-miR-34b, hsa-miR-372, hsa-miR-381, hsa-miR-410, hsa-miR-495, hsa-miR-499-5p, hsa-miR-501-3p, hsa-miR-502-3p, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-520d-3p, hsa-miR-520d-5p, hsa-miR-520e, hsa-miR-520g, hsa-miR-520h, hsa-miR-524-5p, hsa-miR-590-5p, hsa-miR-635, hsa-miR-93, hsa-miR-96 hsa-miR-98 & hsa-miR-99a	AHR, ARNT, CEBPB, CUX1, E2F1 E2F2, E2F3, E2F4, E2F5, E2F6, E2F7, EGR1, FOXC1, FOXJ2, NFAT5, NFATC1, NFATC2, NFATC3, NFATC4, NFYA, PPARG & ZBTB6
73	NFATC1	hsa-miR-519c, hsa-miR-122, hsa-miR-124, hsa-miR-137, hsa-miR-143, hsa-miR-155, hsa-miR-506 & hsa-miR-611	AHR, ARNT, ATF2, CDC5L, EP300, FOXC1, FOXF2, FOXI1, FOXO1, FOXO3, FOXO3B, FOXO4, NFKB1, PAX5, REL, RELA, SPI1, SRF & USF1
74	PPP3CB	hsa-miR-371-5p, hsa-miR-101, hsa-miR-103, hsa-miR-107, hsa-miR-1297, hsa-miR-137, hsa-miR-140-3p hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-192, hsa-miR-195 hsa-miR-196b, hsa-miR-19b, hsa-miR-215, hsa-miR-222, hsa-miR-26a, hsa-miR-26b, hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b, hsa-miR-30e, hsa-miR-326, hsa-miR-424, hsa-miR-506, hsa-miR-559, hsa-miR-613, hsa-miR-645, hsa-miR-646, hsa-miR-660, hsa-miR-768-3p & hsa-miR-802	CEBPA, CEBPB, DDIT3, EGR1, EP300, NFAT5, NFATC1, NFATC2 NFATC3, NFATC4, NR3C1 & PAX2
75	RCAN1	hsa-miR-148a, hsa-let-7b, hsa-miR -103, hsa-miR-107, hsa-miR-124, hsa-miR-323-3p, hsa-miR-34a, hsa-miR-34c-5p & hsa-miR-506	ALX1, CREB1, EBF1, EGR1, IRF1 JUN, MAX, POU3F1, SP1, SPI1 STAT5A, TGIF1, USF1 & VSX2
76	PPARG	hsa-miR-196a, hsa-miR-128a, hsa-miR-130a, hsa-miR-130b, hsa-miR-138, hsa-miR-144, hsa-miR-20b, hsa-miR-27a, hsa-miR-27b, hsa-miR-301, hsa-miR-338-5p, hsa-miR-34a, hsa-miR-409-3p, hsa-miR-449a, hsa-miR-520b, hsa-miR-520c-3p, hsa-miR-520d-3p, hsa-miR-548a-5p, hsa-miR-548b-5p, hsa-miR-548c-5p, hsa-miR-548d-5p & hsa-miR-559	AR, BRD8, CEBPA, CEBPB, COPS5, CREB1, EDF1, EGR1, ESR1, ESR2, FOXO1, GATA1, HDAC3, HMGA1, MED1, NCOA1 NCOA2, NCOA3, NCOA4, NCOA6 NCOR1, NCOR2, NFE2L1, NFE2L2, NR0B1 & NR0B2
77	NOS3	hsa-miR-10b	BACH1, CTCF, EPAS1, ERG, ESR1, ESR2, ETS1, ETV4, GABPA GATA1, GATA2, GATA3, JUN, NR2F2, RORA, SP1, SP1, SP3, SPI1, TAL1::GATA1, TFAP2A & TP53
78	ADRB2	hsa-miR-142-3p, hsa-let-7a, hsa-let-7b, hsa-let-7c, hsa-let-7d, hsa-let-7e hsa-let-7f, hsa-let-7g, hsa-let-7i, hsa-miR-155, hsa-miR-15a, hsa-miR-15b, hsa-miR-16, hsa-miR-195, hsa-miR-216b, hsa-miR-27a, hsa-miR-30a, hsa-miR-30a-5p, hsa-miR-30b hsa-miR-30d, hsa-miR-30e, hsa-miR-424, hsa-miR-497, hsa-miR-556-3p, hsa-miR-605, hsa-miR-607 hsa-miR-625, hsa-miR-634, hsa-miR-7, hsa-miR-888 & hsa-miR-98	CEBPA, CEBPB, CREB1, CUX1 ELK1, GATA1, HLF, NFIC, NFIL3 PBX1, RORA, STAT5A & TBP

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
79	CORIN	hsa-miR-873, hsa-miR-106a, hsa-miR-106b, hsa-miR-138, hsa-miR-148a, hsa-miR-152, hsa-miR-17, hsa-miR-20a, hsa-miR-20b, hsa-miR-302a, hsa-miR-302b, hsa-miR-302c, hsa-miR-302d, hsa-miR-373, hsa-miR-495, hsa-miR-520a-3p, hsa-miR-520b, hsa-miR-520c-3p hsa-miR-520d-3p, hsa-miR-520e hsa-miR-520f, hsa-miR-548a-3p, hsa-miR-561, hsa-miR-582-3p & hsa-miR-93	CTCF
80	GNAS	hsa-miR-139-5p, hsa-let-7i, hsa-miR-105, hsa-miR-136, hsa-miR-138, hsa-miR-143, hsa-miR-155, hsa-miR-15b, hsa-miR-18a, hsa-miR-205, hsa-miR-218, hsa-miR-219-2-3p, hsa-miR-219-5p, hsa-miR-221, hsa-miR-223, hsa-miR-338-3p, hsa-miR-34b, hsa-miR-361-3p, hsa-miR-361-5p, hsa-miR-362-5p, hsa-miR-452, hsa-miR-453, hsa-miR-489, hsa-miR-494, hsa-miR-502-5p, hsa-miR-512-3p, hsa-miR-532-5p, hsa-miR-582-3p, hsa-miR-588, hsa-miR-596, hsa-miR-624, hsa-miR-625, hsa-miR-629, hsa-miR-630, hsa-miR-660, hsa-miR-876-3p & hsa-miR-943	CEBPA, CTCF, CUX1, E2F2, E2F4 HSF1, NFIL3, REST, TFAP2A, TFAP2C, USF1, VSX2 & YY1
81	HSP90AA1	hsa-miR-133b	AHR, AIP, AR, ARNT, ARNTL, CREB1, CTCF, EGR1, EIF2AK2, ESR1, HIF1A, HSF1, HSF2, IKBKB, IKBKG, MAX, MXI1::CLEC5A, MYC, MYOD1, NPAS2, NR2C2, NR3C1, NR3C2, PPARA, REST, RUNX1T1, SRF, STAT1, STAT3, TFAP2A, TFAP2C, TP53, USF1 & YY1
82	GTF2A1	hsa-miR-9, hsa-miR-142-3p, hsa-miR-196a, hsa-miR-196b, hsa-miR-25, hsa-miR-32, hsa-miR-493 & hsa-miR-92a	ARNT, BACH2, BCL3, ELK1, EP300, ESR1, GTF2A2, GTF2E1, GTF2E2, GTF2F1, MAX, MXI1::CLEC5A, MYC, TAF1, TAF4, TBP, TBPL1, TRIP4 & USF1
83	GTF2E1	hsa-miR-145, hsa-miR-124, hsa-miR-155, hsa-miR-200b, hsa-miR-200c, hsa-miR-221, hsa-miR-222, hsa-miR-300, hsa-miR-361-5p, hsa-miR-381, hsa-miR-429, hsa-miR-494, hsa-miR-506, hsa-miR-654-5p & hsa-miR-944	AES, E2F2, ERCC3, GTF2A1, GTF2A2, GTF2B, GTF2E2, GTF2F2, GTF2H1, GTF2H4, NFYA SND1, SP1, TAF6, TBP, TCEA1, TRIM24, YY1 & ZEB1
84	NR3C1	hsa-miR-384, hsa-miR-1, hsa-miR-124, hsa-miR-137, hsa-miR-141, hsa-miR-142-3p, hsa-miR-144, hsa-miR-181a, hsa-miR-181b, hsa-miR-181c, hsa-miR-181d, hsa-miR-182, hsa-miR-183, hsa-miR-18a, hsa-miR-18b, hsa-miR-200a, hsa-miR-200b, hsa-miR-200c, hsa-miR-204 hsa-miR-206, hsa-miR-211, hsa-miR-22, hsa-miR-29a, hsa-miR-29b hsa-miR-29c, hsa-miR-300, hsa-miR-30a, hsa-miR-30b, hsa-miR-320, hsa-miR-328, hsa-miR-340, hsa-miR-377, hsa-miR-381, hsa-miR-410, hsa-miR-429, hsa-miR-506, hsa-miR-515-5p, hsa-miR-518d-5p, hsa-miR-543, hsa-miR-548c-3p, hsa-miR-582-5p, hsa-miR-603 & hsa-miR-889	AHR, AR, ARNT, ATF1, ATF2, ATF3, ATF4, ATF5, ATF6, ATF7, CEBPA, CEBPB, CREB1, CREBBP, CTCF, DDX54, E2F1, ECD, EGR1, EGR2, EGR3, ETS1, ETS2, HIF1A, JUN, KDM5A, MED14, NCOA1, NCOA2, NCOA6 NCOR1, NCOR2, NFIA, NFIC, NFKB1, NFKB2, NR2F2 & NR2F6
85	POLR2A	hsa-miR-28-5p , hsa-miR-214, hsa-miR-542-5p & hsa-miR-873	ABL1, ALX1, ATF2, BARD1, BRCA1, CREB1, CREBBP, CTCF, CTDP1, ELL, ERCC6, FUS, GTF2B, HTATSF1, KLF12, MCM3, MED21, NFIL3, NONO, NR3C1, POLR2C, POLR2D, POLR2E, POLR2F, POLR2G, POLR2H, POLR2L, POU2F1, PQBP1, SAFB, SND1, SP1, STAT1, STAT3, SUPT5H, TAF10, TBP, TCEA1, TCERG1, TFAP2A, UPF1, USF1 XAB2, XRCC5, YY1 & ZNF74
86	GNB1	hsa-let-7g, hsa-miR-101, hsa-miR-139-5p, hsa-miR-218, hsa-miR-570 & hsa-miR-598	CREB1, EGR1, EGR2, EP300, HDAC5, MZF1, NFKB1, PATZ1 RELA, SP1 & VSX2
87	RXRA	hsa-miR-98, hsa-miR-124, hsa-miR-219-5p, hsa-miR-27a, hsa-miR-27b, hsa-miR-506, hsa-miR-626, hsa-miR-876-5p & hsa-miR-9	BCL3, BRD8, COPS2, CTNNB1, EDF1, EGR1, ESR1, FOXO1, FUS, GATA2, HMGA1, JMJD1C, MED1, MYC, MYOD1, NCOA1, NCOA2, NCOA3, NCOA4, NCOA6, NCOR2, NFKB1, NFKBIB, NPAS2, NR0B2, NR1H2, NR1H3, NR1H4, NR1I2, NR1I3, NR2F1, NR4A2, NRBF2, NRIP1, NSD1, PARP1, PAX8, POU2F1, PPARA, PPARD, PPARG, PPARGC1A, RARA, RARB, RARG & RELA

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
88	SMARCD1	hsa-let-7c, hsa-miR-101, hsa-miR-127-5p, hsa-miR-133a, hsa-miR-133b, hsa-miR-141, hsa-miR-148a, hsa-miR-148b, hsa-miR-150, hsa-miR-152, hsa-miR-191, hsa-miR-200a, hsa-miR-21, hsa-miR-223, hsa-miR-324-5p, hsa-miR-325, hsa-miR-369-5p, hsa-miR-370, hsa-miR-421, hsa-miR-490-3p, hsa-miR-515-5p, hsa-miR-552, hsa-miR-556-3p, hsa-miR-590-5p, hsa-miR-624, hsa-miR-7 & hsa-miR-940	ATF1, ATF2, ATF3, ATF4, ATF5 ATF6, ATF7, CREB1, FOS, GATA1, JUN, MAX, MEIS1, MXI1::CLEC5A, MYC, NR3C1& REL
89	SMARCE1	hsa-let-7a, hsa-miR-103, hsa-miR-107, hsa-miR-134, hsa-miR-135a, hsa-miR-135b, hsa-miR-22, hsa-miR-485-3p, hsa-miR-494, hsa-miR-512-5p, hsa-miR-520a-5p, hsa-miR-548a-5p, hsa-miR-548b-5p, hsa-miR-548c-3p, hsa-miR-548c-5p, hsa-miR-548d-5p, hsa-miR-555, hsa-miR-603, hsa-miR-609, hsa-miR-760 & hsa-miR-9	BAZ1B, E2F1, E2F2, E2F3, E2F4, E2F5, E2F6, E2F7, ESR1, ESR2, IRF7, NCOA1, NCOA2, NCOA3, NR3C1, PAX5, RELB & SMAD1
90	ANXA1	hsa-let-7i , hsa-miR-196a, hsa-miR-221, hsa-miR-222, hsa-miR-376c, hsa-miR-598 & hsa-miR-758	FOS, FOXL1, POU3F1 & TBP
91	CAV1	hsa-let-7b, hsa-miR-106b, hsa-miR-124, hsa-miR-125a-3p, hsa-miR-203 hsa-miR-34b*, hsa-miR-34c-5p, hsa-miR-377, hsa-miR-409-3p, hsa-miR-494, hsa-miR-506, hsa-miR-548c-3p, hsa-miR-628-5p, hsa-miR-768-3p & hsa-miR-96	ABL1, AR, ATF6, E2F1, E2F4, EGR1, ESR1, NFIC, PAX2, RFX1 SP1, TFDP1, TP53 & XBP1
92	LPL	hsa-let-7e, hsa-miR-138, hsa-miR-155, hsa-miR-27a, hsa-miR-27b, hsa-miR-29a, hsa-miR-29b, hsa-miR-29c, hsa-miR-452, hsa-miR-588, hsa-miR-590-3p & hsa-miR-768-5p	AR, ARNT, ASCC2, E2F1, E2F2, E2F3, E2F4, E2F5, E2F6, E2F7, ESR1, POU2F1, POU2F2, POU3F1, POU3F2, POU3F3, POU5F1, PPARA, PPARD, PPARG, RXRA, RXRB & RXRG
93	ACTB	hsa-let-7d, hsa-miR-145, hsa-miR-216a, hsa-miR-221, hsa-miR-412, hsa-miR-582-3p, hsa-miR-647 & hsa-miR-648	ATF7IP, EEF1A1, EGR1, EGR3, ELK1, EP300, GABPA, HNF4A, HNRNPAB, NFKB1, NFKB2, NFYA, NFYB, NFYC, POLR2A, POU3F2, PPARG, REL, RELA, SMAD3, SMAD9, SMARCA4, SP1, SRF, STAT1, STAT3, TBP, TFAP2A & USF1
94	ARID1A	hsa-let-7f, hsa-miR-1, hsa-miR-101, hsa-miR-132, hsa-miR-144, hsa-miR-153, hsa-miR-185, hsa-miR-19a, hsa-miR-19b, hsa-miR-203, hsa-miR-212, hsa-miR-216, hsa-miR-216a, hsa-miR-221, hsa-miR-222, hsa-miR-223, hsa-miR-30a, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d, hsa-miR-30e, hsa-miR-31 hsa-miR-324-5p, hsa-miR-340, hsa-miR-377, hsa-miR-485-3p, hsa-miR-486-5p, hsa-miR-548c-3p, hsa-miR-555, hsa-miR-568, hsa-miR-576-5p, hsa-miR-583, hsa-miR-625, hsa-miR-765, hsa-miR-876-3p, hsa-miR-885-3p & hsa-miR-9	ARNT, CREB1, E2F1, E2F2, E2F3, E2F4, E2F5, E2F6, E2F7, FOXD3, FOXI1, GATA2, HNF4A, MAX, MLLT1, MXI1::CLEC5A, MYC, MZF1, PAX5, POU2F1, POU3F1, PPARG, SMARCA4, SOX9, SP1, SRF, TFAP2A, TFAP2C, TP53, USF1 & YY1
95	GTF2B	hsa-miR-202, hsa-miR-1, hsa-miR-103, hsa-miR-107, hsa-miR-122, hsa-miR-187, hsa-miR-190, hsa-miR-190b, hsa-miR-199a-3p, hsa-miR-206, hsa-miR-214, hsa-miR-22 hsa-miR-24, hsa-miR-26a, hsa-miR-26b, hsa-miR-338-3p, hsa-miR-384 hsa-miR-488, hsa-miR-511, hsa-miR-520d-5p, hsa-miR-524-5p, hsa-miR-561, hsa-miR-582-5p, hsa-miR-607 & hsa-miR-633	BCL3, CREBBP, EGR1, EP300, ESR1, ESRRA, FOXF2, GTF2E1, GTF2E2, GTF2F1, GTF2F2, HSF1, IKZF1, JUN, MAX, MCM2, MXI1::CLEC5A, MYC, NCOA1, NCOA3, NCOA4, NR2F1, NR5A1, POLR2A, POU2F1, POU2F2, POU3F2, REL, RELA, TAF9, TBP, TBPL1, TCEA2, THRA, USF1 & VDR
96	NF1	hsa-miR-30e , hsa-miR-103, has-miR-107, hsa-miR-10b, hsa-miR-125a-3p, hsa-miR-128, hsa-miR-135a, hsa-miR-135b, hsa-miR-137 hsa-miR-144, hsa-miR-153, hsa-miR-15a, hsa-miR-15b, hsa-miR-16 hsa-miR-182, hsa-miR-195, hsa-miR-19a, hsa-miR-19b, hsa-miR-200b, hsa-miR-200c, hsa-miR-217 hsa-miR-219-1-3p, hsa-miR-25, hsa-miR-27a, hsa-miR-27b, hsa-miR-30a, hsa-miR-30b, hsa-miR-30c, hsa-miR-30d, hsa-miR-30e, hsa-miR-338-5p, hsa-miR-340, hsa-miR-363, hsa-miR-369-3p, hsa-miR-370 hsa-miR-374a, hsa-miR-374b, hsa-miR-424, hsa-miR-448, hsa-miR-497, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-543, hsa-miR-548d-3p, hsa-miR-552, hsa-miR-561 hsa-miR-571, hsa-miR-582-5p, hsa-miR-590-3p, hsa-miR-617, hsa-miR-625, hsa-miR-655, hsa-miR-876-5p, hsa-miR-944 & hsa-miR-96	ATF2, CREB1, CTCF, JUN, PATZ1 PAX5, SP1, TBPL1 & TFAP2A

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Table Continued

S. No.	Genes (Varse)	miRNAs (pharmacomiR)	Transcription factor (RegNetworks)
97	SMARCA4	hsa-miR-30c, hsa-miR-1, hsa-miR-101, hsa-miR-132, hsa-miR-139-5p, hsa-miR-144, hsa-miR-155, hsa-miR-191, hsa-miR-206, hsa-miR-212, hsa-miR-221, hsa-miR-222, hsa-miR-296-5p, hsa-miR-301a, hsa-miR-30c, hsa-miR-452, hsa-miR-489, hsa-miR-495, hsa-miR-503, hsa-miR-508-5p, hsa-miR-512-3p, hsa-miR-517b, hsa-miR-568, hsa-miR-569, hsa-miR-574-3p, hsa-miR-582-5p, hsa-miR-613, hsa-miR-765 & hsa-miR-942	AHR, ARID1A, ARID1B, BRCA1, BRWD1, CEBPB, CHD4, CREB1, CTNNB1, E2F1, E2F4, EGR1, ESR1, ETS2, GABPA, HSF1, IKZF1, MYC, MZF1, NR3C1, PAX6, PBRM1, RB1, RELB, RFXAP, SMARCB1, SMARCC1, SMARCE1, STAT2, TMF1, TP53, YY1 & ZMYND11
98	SMARCB1	hsa-miR-30d, hsa-miR-1, hsa-miR-192, hsa-miR-206 & hsa-miR-300	CEBPB, E2F4, FOS, FOSB, FOSL1 HNF4A, JUN, JUNB, JUND, KLF1 MECP2, MYC, NR3C1, RB1, RELB SMARCA4, TCF3, TFAP2A, TP53 & YEATS4
99	SMARCC1	hsa-miR-30a, hsa-let-7a, hsa-let-7b, hsa-let-7c, hsa-let-7d, hsa-let-7e, hsa-let-7f, hsa-let-7g, hsa-let-7i, hsa-miR-1, hsa-miR-124, hsa-miR-129-5p, hsa-miR-144, hsa-miR-153, hsa-miR-196a, hsa-miR-196b, hsa-miR-202, hsa-miR-206, hsa-miR-208b, hsa-miR-214, hsa-miR-23a, hsa-miR-23b, hsa-miR-29b, hsa-miR-29c, hsa-miR-330-3p, hsa-miR-339-3p, hsa-miR-488, hsa-miR-506, hsa-miR-548d-3p, hsa-miR-567, hsa-miR-610, hsa-miR-641 & hsa-miR-98	CEBPB, FOXC1, GABPA, HOXA9 KLF1, MEIS1, NR3C1, RELB, SIN3A & SMARCA4
100	SMARCC2	hsa-miR-30b, hsa-miR-28-5p, hsa-miR-30a, hsa-miR-30b, hsa-miR-30c, hsa-miR-30e, hsa-miR-519a, hsa-miR-519b-3p, hsa-miR-519c-3p, hsa-miR-519d, hsa-miR-568, hsa-miR-608, hsa-miR-708 & hsa-miR-938	BAZ1B, CTCF, ESR1, GABPA POLR2C & RELB
101	HRH1	hsa-miR-196b, hsa-miR-192, hsa-miR-324-5p, hsa-miR-518a-5p, hsa-miR-527, hsa-miR-583	FOS, HNF4A, JUN, MAX, NR2F1, NR3C1, POU2F1, POU2F2, POU3F1, POU3F2, POU3F3, POU5F1 & TFAP2A

Construction of regulatory network (cytoscape)

The regulatory network was constructed with 101 genes, 576 miRNAs and 638 TFs. Network was initiated from the association of Pharmacogenomics and Clinical variants with the 1214 regulators (i.e. 638 TFs & 576 miRNAs) to interact with the 101 target genes in such a way to form 1316 nodes and 4174 edges.

Identification of hub genes in regulatory network in top-down approach (cytohubba)

The genes and their regulators (Micro RNAs & Transcription Factors) were subjected to the analysis in cytohubba by various global based statistical methods like Edge Percolated Component, Bottleneck, EcCentricity, Closeness, Radiality, Betweenness and Stress along with local based statistical methods like Maximal Clique Centrality, Density of Maximum Neighborhood Component, Maximum Neighborhood Component and degree to identify their connectivity. Among the various methods of analysis in top down approach only a global based statistics of EcCentricity method and the local based statistics of Maximal Clique Centrality along with Density of Maximum Neighborhood Component and Clustering coefficient methods in cytohubba resulted in obtaining a regulatory network of gene-miRNA-TFs in top-down approach. The details of regulatory network were given in Figure 1.
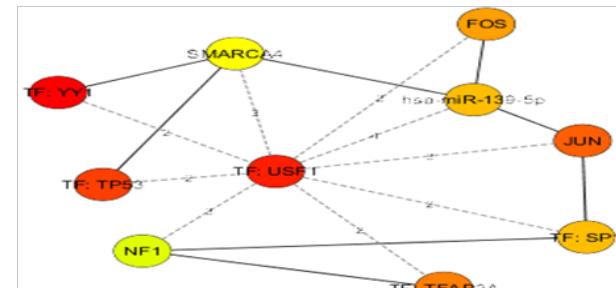
Figure1 Regulatory Network of SMARCA4, FOS, JUN & NF1 (Bottleneck method).

Implication of miRNAs in regulatory network

The implication of miRNAs in the regulatory network was analyzed on the basis of compatibility with respect to gene-miRNA seed pairing and gene-miRNA-miRNA triplex with respect to nature of binding and the details were given in Table 2.

Pathway analysis

The obtained genes from Varse data were subjected to pathway analysis in DAVID on the basis of P value and Benjamini statistic and the result is given in Table 3.

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Table 2 Implication of miRNA in regulatory network

S. No.	Genes	microRNA	No. of binding Sites (mIRmap)	Paired miRNA	Binding energy in Kcal/mol. (Triplex RNA)	Nature of binding (Triplex RNA)
I.	FOS		NIL	hsa-miR-543	-26.96	Canonical triplex
2.	JUN		NIL	NIL	NIL	NIL
3.	NF1	hsa-miR-139-5p	NIL	hsa-miR-590-3p	-22.46	Self complementary
4.	SMARCA4		NIL	hsa-miR-7	-21.16	Canonical triplex

Table 3 Annotation of Kegg Pathways in direct approach

S. No.	Pathway	P Value	Benjamini
1	T cell receptor signaling pathway	3.71E-27	7.08E-25
2	ErbB signaling pathway	1.03E-19	9.82E-18
3	Hepatitis B	4.00E-19	2.55E-17
4	Natural killer cell mediated cytotoxicity	4.20E-18	2.01E-16
5	Fc epsilon RI signaling pathway	2.93E-17	1.12E-15
6	Oxytocin signaling pathway	4.79E-17	1.53E-15
7	Neurotrophin signaling pathway	6.32E-17	3.00E-15
8	Osteoclast differentiation	3.45E-16	7.99E-15
9	Estrogen signaling pathway	7.95E-16	1.65E-14
10	B cell receptor signaling pathway	1.13E-15	2.12E-14
11	Focal adhesion	1.24E-14	2.14E-13
12	Choline metabolism in cancer	2.43E-14	3.87E-13
13	Prostate cancer	5.49E-14	8.06E-13
14	GnRH signaling pathway	9.23E-14	1.26E-12
15	MAPK signaling pathway	8.75E-13	1.11E-11
16	Proteoglycans in cancer	9.97E-13	1.19E-11
17	Prolactin signaling pathway	1.16E-12	1.30E-11
18	Thyroid hormone signaling pathway	2.84E-12	3.01E-11
19	VEGF signaling pathway	3.71E-12	3.73E-11
20	HIF-1 signaling pathway	5.14E-12	4.90E-11
21	Sphingolipid signaling pathway	6.09E-12	5.54E-11
22	Glioma	8.26E-12	7.17E-11
23	Pathways in cancer	1.01E-11	8.40E-11
24	Non-small cell lung cancer	3.19E-11	2.54E-10
25	Epstein-Barr virus infection	4.87E-11	3.72E-10
26	Ras signaling pathway	8.53E-11	6.26E-10
27	cAMP signaling pathway	9.40E-11	6.65E-10
28	Colorectal cancer	1.03E-10	7.02E-10
29	Chagas disease (American trypanosomiasis)	1.79E-10	1.18E-09
30	TNF signaling pathway	2.28E-10	1.45E-09
31	PI3K-Akt signaling pathway	2.84E-10	1.75E-09
32	Endometrial cancer	3.34E-10	1.99E-09
33	Cholinergic synapse	4.11E-10	2.38E-09
34	HTLV-I infection	6.66E-10	3.74E-09
35	Viral carcinogenesis	1.49E-09	8.13E-09
36	Fc gamma R-mediated phagocytosis	3.05E-09	1.62E-08

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Table Continued

S. No.	Pathway	P Value	Benjamini
37	Renal cell carcinoma	3.33E-09	1.72E-08
38	Hepatitis C	3.97E-09	2.00E-08
39	Insulin signaling pathway	6.27E-09	3.07E-08
40	cGMP-PKG signaling pathway	6.57E-09	3.14E-08
41	Chronic myeloid leukemia	9.34E-09	4.35E-08
42	Influenza A	1.21E-08	5.50E-08
43	Acute myeloid leukemia	1.44E-08	6.39E-08
44	Chemokine signaling pathway	2.85E-08	1.24E-07
45	Toll-like receptor signaling pathway	3.70E-08	1.57E-07
46	Long-term potentiation	6.38E-08	2.65E-07
47	Tuberculosis	1.26E-07	5.11E-07
48	Melanogenesis	2.31E-07	9.18E-07
49	Dopaminergic synapse	2.63E-07	1.02E-06
50	FoxO signaling pathway	4.19E-07	1.60E-06
51	Insulin resistance	4.78E-07	1.79E-06
52	Pancreatic cancer	8.12E-07	2.98E-06
53	Rap1 signaling pathway	9.13E-07	3.29E-06
54	Amphetamine addiction	9.15E-07	3.24E-06
55	Adrenergic signaling in cardiomyocytes	9.94E-07	3.45E-06
56	Inflammatory mediator regulation of TRP channels	2.00E-06	6.81E-06
57	Wnt signaling pathway	4.58E-06	1.53E-05
58	mTOR signaling pathway	4.72E-06	1.55E-05
59	Alcoholism	6.59E-06	2.13E-05
60	Calcium signaling pathway	7.34E-06	2.34E-05
61	Gap junction	8.29E-06	2.60E-05
62	Platelet activation	2.06E-05	6.33E-05
63	Signaling pathways regulating pluripotency of stem cells	3.71E-05	1.13E-04
64	Non-alcoholic fatty liver disease (NAFLD)	6.73E-05	2.01E-04
65	Progesterone-mediated oocyte maturation	6.96E-05	2.04E-04
66	NF-kappa B signaling pathway	6.96E-05	2.04E-04
67	Toxoplasmosis	7.08E-05	2.05E-04
68	Circadian entrainment	1.22E-04	3.48E-04
69	Epithelial cell signaling in Helicobacter pylori infection	1.30E-04	3.65E-04
70	Glucagon signaling pathway	1.58E-04	4.38E-04
71	Adherens junction	1.80E-04	4.90E-04
72	Melanoma	1.80E-04	4.90E-04
73	Bacterial invasion of epithelial cells	3.02E-04	8.12E-04
74	Salmonella infection	4.23E-04	0.001122189
75	Leukocyte transendothelial migration	4.68E-04	0.00122285
76	MicroRNAs in cancer	4.98E-04	0.001284737
77	Long-term depression	6.82E-04	0.001735164
78	Apoptosis	7.93E-04	0.001991496
79	Regulation of actin cytoskeleton	8.25E-04	0.002044609

Table Continued

S. No.	Pathway	P Value	Benjamini
80	Central carbon metabolism in cancer	9.17E-04	0.002244285
81	Shigellosis	9.17E-04	0.002244285
82	Renin secretion	9.17E-04	0.002244285
83	Measles	9.57E-04	0.002311316
84	Aldosterone-regulated sodium reabsorption	0.001105	0.002635727
85	Bladder cancer	0.001336	0.003147586
86	Leishmaniasis	0.001468	0.003416078
87	Amoebiasis	0.001541	0.003541751
88	Pertussis	0.001875	0.004259408
89	Serotonergic synapse	0.001951	0.00437895
90	Glutamatergic synapse	0.002234	0.004955541
91	Type II diabetes mellitus	0.002411	0.005284985
92	Aldosterone synthesis and secretion	0.002634	0.005708816
93	Amyotrophic lateral sclerosis (ALS)	0.002803	0.006004984
94	AMPK signaling pathway	0.003142	0.006655783
95	Small cell lung cancer	0.00325	0.00681028
96	Dorso-ventral axis formation	0.003837	0.007948938
97	NOD-like receptor signaling pathway	0.003969	0.008133865
98	Regulation of lipolysis in adipocytes	0.004236	0.008588374
99	Thyroid cancer	0.004712	0.009451116
100	Herpes simplex infection	0.005813	0.01153254
101	Prion diseases	0.006801	0.013346725
102	Jak-STAT signaling pathway	0.007286	0.01415115
103	Bile secretion	0.008878	0.017057979
104	Oocyte meiosis	0.009287	0.017662609
105	Adipocytokine signaling pathway	0.009333	0.017575749
106	Vascular smooth muscle contraction	0.013248	0.024664527
107	Alzheimer's disease	0.014431	0.026595965
108	Endocrine and other factor-regulated calcium reabsorption	0.015978	0.029148707
109	Axon guidance	0.017142	0.030963584
110	TGF-beta signaling pathway	0.017343	0.031033366
111	Insulin secretion	0.018039	0.031972854
112	Cocaine addiction	0.020058	0.035199369
113	Tight junction	0.022995	0.039944759
114	Vibrio cholerae infection	0.02466	0.042428996
115	Viral myocarditis	0.029784	0.050698785
116	Retrograde endocannabinoid signaling	0.031582	0.053257247
117	Inflammatory bowel disease (IBD)	0.039998	0.066669451
118	PPAR signaling pathway	0.044852	0.074003009
119	Transcriptional misregulation in cancer	0.048809	0.079750661
120	Thyroid hormone synthesis	0.049987	0.080967512
121	RIG-I-like receptor signaling pathway	0.049987	0.080967512
122	Gastric acid secretion	0.055396	0.08883728

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Table Continued

S. No.	Pathway	P Value	Benjamini
123	African trypanosomiasis	0.057954	0.092112284
124	Antigen processing and presentation	0.061074	0.096199891
125	Primary immunodeficiency	0.061114	0.095498989
126	Huntington's disease	0.077264	0.119205309
127	Dilated cardiomyopathy	0.077477	0.118607609
128	Salivary secretion	0.081853	0.124192439
129	Rheumatoid arthritis	0.086334	0.129837543
130	Carbohydrate digestion and absorption	0.088331	0.131776895
131	ABC transporters	0.095613	0.141305009
132	Pancreatic secretion	0.09798	0.143657121
133	Basal transcription factors	0.099317	0.144513494

Discussion

Combinatorial Analysis of miRNA based pharmacovarient association in regulatory network of Psoriasis indicate the fact that has-miR-139-5p was involved in the T cell receptor signaling pathway and contribute to the disease pathology of Psoriasis. In this article the significance of hsa-miR-139-5p was analysed for the pharmacologically associated genes of psoriasis and in the mere future the significance of miRNA association with Pharmacology will be analysed with respect to the associated genes of other diseases.

Materials and methods

PubMed

PubMed is an online search engine with open access facility to refer MEDLINE for identifying references and abstracts on topics in biomedical and life sciences. The United States National Library of Medicine (NLM) at the National Institutes of Health maintains the database as part of the Entrez system to retrieve information. Most of the records in PubMed contain links to the complete article, in PubMed Central.[13] Information regarding the indexed journals in MEDLINE can be found in the Catalog of NLM.

Varse and pharmacomiR

Pharmaco-miR Verified Sets (VerSe) databas[14] is generated from manual data mining of original research articles including the search terms 'miRNA' and 'drug' in the PubMed database.

Regnetwork

RegNetwork[15] 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.

Cytoscape

Cytoscape[16] 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. Additional features in cytoscape are available as plugins for network and molecular profiling.

Cytohubba

Cytohubba[17] is a cytoscape plugin for performing the analyses of gene regulation & protein-protein interaction involved in the process of cellular pathways in the process of signal transduction. Cytohubba ranks the nodes of network by topological methods like Radiality, Betweenness, Closeness, Bottleneck, EcCentricity and etc.

miRmap

miRmap[18] software addresses the challenges in post transcriptional repression of miRNAs in human genome by evolutionary, probabilistic thermodynamic and sequence-based features.

Triplex RNA

Triplex RNA[19] is a database of cooperating micrRNAs with their mutual targets. In this database miRNA target prediction is based on the analysis of predicted miRNA triplex with molecular dynamics simulations and differential modeling procedures in mathematics.

DAVID

The database for Annotation, Visualization and Integrated discovery (DAVID) contain complete information about functional annotation of genes. The current version of DAVID[20,21] is 6.8 and it provides a set of comprehensive tools for functional annotation of genes.

Methodology

(miRNA based association with pharmaco-clinical variants):

a. Identify the disease associated genes from Varse.

b. Obtain the associated list of miRNAs and transcription factors for the disease associated genes from PharmacomiR & Regnetworks.

c. Construct and analyze the network in Cytoscape.

d. Identify the miRNA based hub genes and transcription factors from cytohubba.

e. Identify the implication of miRNA in Regulatory network in miRmap & miRNA Triplex.

f. Identify and analyze the gene associated pathways in DAVID.

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None.

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Conflict of interest

Author declares there is no conflict of interest.

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