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Profiling circulating microRNA and regulatory pathways in transfusion-dependent thalassemia and thalassemia trait compared to healthy controls: a preliminary study

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Table S1. Functional analysis alterations significant microRNAs that have role on biological process and diseases in thalassemia patients.

No.	KEGG pathway	p-value	Genes	miRNAs	Function
1	Prion Disease	1.93×10^{-1}	EGR1, HSPA1A, HSPA5, NOTCH1, PRNP, LAMC1, IL1A, IL6, MAPK1	has-miR-3065-3p, has-miR-338-5p, has-miR-708-5p, has-let-7e-5p, has-miR-1303, has-miR-450a-5p, has-miR-149-5p, has-miR-548h-5p, and has-miR-744-5p	Cell adhesion regulation, protection against oxidative stress, protection against anisomycin-induced apoptosis, apoptosis, cell survival, proliferation, neurotic outgrowth, oxidative stress, regulation of autophagy, and neuronal apoptosis autophagy
2	ECM-receptor interaction	1.93×10^{-1}	LAMB2, ITGB1, ITGB8, THBS1, THBS2, AGRN, COL3A1, HSPG2, COL6A1, LAMC3, ITGAV, COL4A2, COL6A2, COL5A1, COL1A1, DAG1, COL1A2, LAMC1, FN1, TNC, SDC4, LAMC2, COL5A2, CD44, CD47, and COL4A1.	hsa-miR-708-5p, hsa-let-7e-5p, hsa-miR-1303, hsa-miR-450a-5p, hsa-miR-199b-5p, hsa-miR-338-5p, hsa-miR-149-5p, hsa-miR-744-5p, hsa-miR-485-5p, hsa-miR-3065-3p, and hsa-miR-548h-5p	Focal adhesion, glycoprotein, and leukocytes proteins

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
3	Cell cycle	2.77×10^{-1}	ESPL1, GSK3B, RBL2, CDKN2C, PCNA, E2F1, SMC1A, YWHAH, CCNB1, CDK4, SMAD2, E2F2, YWHAE, CCNA2, CDC25B, MCM6, YWHAG, CDK2, CCND2, SMAD3, SMC3, CDKN1B, CUL1, STAG2, YWHAB, WEE1, ANAPC1, CDK6, SKP1, YWHAQ, TP53, GADD45B, ATM, MCM2, ANAPC10, CCND1, CCNE2, E2F5, SKP2, E2F3, MYC, TTK, RB1, MAD2L2, YWHAZ, ANAPC7, HDAC2, MAD2L1, TFDP1, MAD1L1, CDC27, RBX1, CDKN1A, PRKDC, E2F4, ANAPC13, CREBBP, RAD21, MDM2,A and CDC25A	hsa-miR-708-5p, hsa-miR-1303, hsa-let-7e-5p, hsa-miR-744-5p, hsa-miR-548h-5p, hsa-miR-3065-3p, hsa-miR-338-5p, hsa-miR-149-5p, hsa-miR-182-3p, hsa-miR-199b-5p, hsa-miR-450a-5p, hsa-miR-566, and hsa-miR-485-5p	DNA biosynthesis, apoptosis, DNA damage checkpoint, ubiquitin mediated proteolysis, and cell cycle
4	Adherents junction	3.92×10^{-1}	ACTB, CSNK2A2, TGFBR1, WASL, SMAD2, TCF7L2, ACTG1, IQGAP1, SNAI2, SMAD3, PTPN1, IGF1R, VCL, MLLT4, NLK, CTNNB1, PVRL4, CTNNA1, ACTN1, WASF2, CSNK2A1, FARP2, PTPRJ, RAC1, INSR, SRC, SSX2IP, ACTN4, RAC3, YES1, TCF7, FGFR1, MAPK1, MAP3K7, CREBBP, TGFBR2, and PVRL1	hsa-miR-744-5p, hsa-miR-338-5p, hsa-let-7e-5p, hsa-miR-182-3p, hsa-miR-199b-5p, hsa-miR-149-5p, hsa-miR-3065-3p, hsa-miR-485-5p, hsa-miR-708-5p, hsa-miR-1303, hsa-miR-566, and hsa-miR-450a-5p	Tight Junction, regulation of actin cytoskeleton, cell growth, differentiation, and gene expression
5	Fatty acid biosynthesis	5.24×10^{-2}	FASN, MCAT, ACSL4, ACACA	hsa-miR-548h-5p, hsa-miR-1303, hsa-miR-149-5p, hsa-miR-744-5p, hsa-miR-3065-3p, hsa-let-7e-5p, and hsa-miR-182-3p	Lipoic acid metabolism, fatty acid degradation, glycolipid metabolism, glycerophospholipid metabolism, fatty acid elongation, citrate cycle, pyruvate metabolism, B-alanine metabolism
6	Oocyte meiosis	1.09×10^{-3}	ESPL1, PPP1CA, FBXO5, CAMK2D, SMC1A, YWHAH, ADCY1, CCNB1, CAMK2G, YWHAE, BTRC, CALM3, CALM1, PPP2CA, CPEB4, YWHAG, PPP1CC CDK2, SMC3, CUL1, PPP2R5D, YWHAB, IGF1R, PPP2R5C, ANAPC2, ANAPC1, SKP1, YWHAQ, PPP2R5A, ANAPC10, PPP3CB, CCNE2, CPEB2, MAD2L2, YWHAZ, ANAPC7, MAD2L1, RPS6KA3, CDC27, RBX1, AURKA, SGOL1, ANAPC13, CPEB3, MAPK1, ITPR2, FBXW11, ADCY9, PPP1CB	hsa-miR-3065-3p, hsa-miR-338-5p, hsa-miR-708-5p, hsa-let-7e-5p, hsa-miR-548h-5p, hsa-miR-149-5p, hsa-miR-485-5p, hsa-miR-744-5p, hsa-miR-1303, hsa-miR-182-3p, hsa-miR-566, hsa-miR-450a-5p, hsa-miR-199b-5p	Progesterone-mediated oocyte maturation, ubiquitin mediated proteolysis, fertilization, and prevent DNA replication bipolar spindle formation meiosis I progression

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
7	Hippo signalling pathway	2.73×10^{-3}	PPP1CA, ACTB, GSK3B, DVL3, TGFBR1, YWHAH, YAP1, SMAD2, YWHAE, BTRC, APC, PPP2CA, WNT5A, YWHAG, PPP1CC, CCND2, ACTG1, GLI2, SNAI2, SMAD3, BIRC5, AXIN1, YWHAB, WNT5B, FZD3, BMP8B, LIMD1, YWHAQ, MPP5, CSNK1D, CCND1, CTNNB1, CTNNA1, PPP2R2A, MYC, CDS, FRMD6, ID1, FZD2, TEAD1, YWHAZ, STK3, BMP2, CSNK1E, TEAD4, SMAD7, MOB1A, TCF7, FBXW11, PARD6B, DVL2, TGFBR2, WNT9A, BMP4, BMPR2, CTGF, PPP1CB, and SCRIB	hsa-miR-149-5p, hsa-miR-566, hsa-miR-708-5p, hsa-miR-744-5p, hsa-miR-3065-3p, hsa-miR-1303, hsa-let-7e-5p, hsa-miR-450a-5p, hsa-miR-199b-5p, hsa-miR-338-5p, hsa-miR-485-5p, hsa-miR-182-3p	Cytoplastic retention, cell contact inhibition organ size control, Ubiquitin mediated proteolysis, and Cellular stress
8	Hepatitis B	6.59×10^{-5}	FOS, PRKCA, PCNA, STAT3, ATP6AP1, E2F1, TGFBR1, CDK4 , CXCL8, ATF2, E2F2, NRAS, CCNA2, ATF6B, CDK2, SMAD3, CHUK, BCL2, CDKN1B, BIRC5, YWHAB, MAP3K1, TLR4, KRAS, CDK6, DDX3X, YWHAQ, TP53, HSPG2, CREB1, APAF1, AKT2, MAVS, CASP3, JUN, CCND1, CCNE2, E2F3, MAPK8, MYC, NFKBIA, PIK3R1, RB1, YWHAZ, TBK1, SRC, FAS, CREB3L2, CREB3L1, CDKN1A, MAP2K4, PTEN, NFATC3, IL6, MAPK1, CREBBP, NFATC1, JAK1, and ATF4	hsa-miR-708-5p, hsa-miR-548h-5p, hsa-let-7e-5p, hsa-miR-338-5p, hsa-miR-149-5p, hsa-miR-3065-3p, hsa-miR-744-5p, hsa-miR-1303, hsa-miR-199b-5p, hsa-miR-450a-5p, hsa-miR-566, hsa-miR-485-5p, hsa-miR-182-3p	Inhibition of transcription of ISGs, Inhibition of HBV genome replication, shift from tumor suppression to oncogenesis, relief of HBx stability and viral replication, HCC invasion and metastasis, antiapoptotic, tumor suppression, deregulation of early cell cycle checkpoints, Hepatocyte proliferation, HCC invasion and metastasis, and Cell proliferation and differentiation
9	Lysine degradation	1.67×10^{-6}	WHSC1L1, SETD7, SETD1B, NSD1, ASH1L, KMT2D, SUV420H1, DOT1L, WHSC1, SUV420H2, KMT2A, SUV39H2, KMT2E, SETD1A, ALDH2, EHMT1, KMT2B	hsa-miR-708-5p, hsa-miR-3065-3p, hsa-miR-744-5p, hsa-let-7e-5p, hsa-miR-182-3p, hsa-miR-485-5p, hsa-miR-1303, hsa-miR-338-5p, hsa-miR-149-5p	Penicillin and cephalosporins biosynthesis, and citrate cycle
10	FoxO signalling pathway	1.67×10^{-6}	IRS2, RBL2, STAT3, TGFBR1, FBXO32, CCNB1, SOS2, SMAD2, NRAS, STK4, SIRT1, SETD7, KLF2, MAPK14, CDK2, CCND2, SMAD3, CHUK, CDKN1B, IGF1R, TNFSF10, KRAS, HOMER2, GADD45B, G6PC3, AKT2, ATM, NLK, CCND1, SKP2, MAPK8, IRS4, PLK2, AGAP2, GABARAPL1, MAPK11, PIK3R1, IRS1, INSR, PRKAA1, BCL6, PRKAB2, CSNK1E, SOD2, HOMER1, FOXO3, CDKN1A, PTEN, SGK3, FOXO1, IL6, MAPK1, CREBBP, TGFBR2, and MDM2	hsa-miR-485-5p, hsa-let-7e-5p, hsa-miR-744-5p, hsa-miR-708-5p, hsa-miR-149-5p, hsa-miR-338-5p, hsa-miR-548h-5p, hsa-miR-3065-3p, hsa-miR-199b-5p, hsa-miR-1303, hsa-miR-182-3p, hsa-miR-450a-5p	DNA damage, muscle atrophy, immuno-regulation, metabolism (glycolysis/gluconeogenesis), oxidative stress resistance & DNA repair, autophagy (regulation of autophagy), Apoptosis, cell cycle regulation, and ubiquitin-mediated proteolysis

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
11	Thyroid hormone signalling pathway	4.27×10^{-6}	ESR1, ACTB, GSK3B, PRKCA, MED13L, NRAS, MED14, MED12, PLCD3, DIO2, ACTG1, MED13, SLC16A10, THRA, NOTCH2, KRAS, RHEB, NCOA3, TP53, MED1, AKT2, MED16, ITGAV, MED24, TBC1D4, NOTCH1, PLCG1, CCND1, CTNNB1, HIF1A, MYC, NCOR1, NCOA2, PIK3R1, HDAC2, SRC, NOTCH3, SLC2A1, PFKFB2, ATP2A2, ATP1A1, FOXO1, MAPK1, CREBBP, MDM2, BMP4, and SIN3A	hsa-miR-338-5p, hsa-let-7e-5p, hsa-miR-3065-3p, hsa-miR-199b-5p, hsa-miR-485-5p, hsa-miR-708-5p, hsa-miR-1303, hsa-miR-744-5p, hsa-miR-548h-5p, hsa-miR-450a-5p, hsa-miR-149-5p	Calcium signalling pathway, Regulation of actin cytoskeleton, Cell cycle metabolism, Cell cycle arrest apoptosis translation, Glucose transport, Glucose metabolism, Survival, Glucose metabolism, Terminal differentiation, Contractility, Angiogenesis Glycolysis, Gene transcription cell proliferation, Enhanced cytokine and growth factor action and p53 signalling pathway
12	Proteoglycans in cancer	5.49×10^{-6}	ESR1, PPP1CA, CAMK2D, ACTB, PRKCA, STAT3, PDCD4, ITGB1, EZR, SOS2, SMAD2, CBL, CAMK2G, NRAS, THBS1, CAV1, WNT5A, ARHGEF12, PPP1CC, MAPK14, ACTG1, FRS2, RDX, IQGAP1, TIAM1, IGF1R, TLR4, WNT5B, RPS6, KRAS, FZD3, MSN, RPS6KB2, TP53, HSPG2, VAV2, AKT2, PTK2, ITGAV, NUDT16L1, PPP1R12A, DROSHA, MMP2, PLCG1, CASP3, CCND1, CTNNB1, HIF1A, MYC, IGF2, MAPK11, FLNA, FZD2, PIK3R1, RAC1, SRC, FAS, GAB1, HOXD10, FN1, CDKN1A, SDC4, FGFR1, MAPK1, ITPR2, MDM2, WNT9A, RPS6KB1, CD44, and PPP1CB	hsa-miR-708-5p, hsa-let-7e-5p, hsa-miR-548h-5p, hsa-miR-338-5p, hsa-miR-199b-5p, hsa-miR-3065-3p, hsa-miR-485-5p, hsa-miR-744-5p, hsa-miR-1303, hsa-miR-450a-5p, and hsa-miR-149-5p	Cytoskeleton activation. Cell growth and survival, cell migration and invasion, oncogenic signalling, ECM degradation enzyme activation, cell adhesion, Proliferation and survival, Growth suppression, Apoptosis, Inhibition of tumor angiogenesis, Growth suppression and inhibition of cell adhesion
13	Pathways in cancer	6.91×10^{-5}	LAMB2, FOS, GSK3B, PRKCA, DVL3, STAT3, PDGFRA, E2F1, TGFBR1, ADCY1, ITGB1, GNA12, SOS2, CDK4, CXCL8, SMAD2, CBL, E2F2, NRAS, CRKL, STK4, APC, CRK, RUNX1, CUL2, TCF7L2, WNT5A, ARHGEF12, CDK2, HSP90AA1, GLI2, GNG12, SMAD3, CHUK, BCL2, CDKN1B, BIRC5, AXIN1, CXCL12, IGF1R, GNB1, PTCH2, TRAF5, WNT5B , KRAS, CDK6, FZD3, VHL, EPAS1, MLH1, TP53, AKT2, PTK2, LAMC3, ITGAV, MMP2, ARNT2, GNB2, PLCG1, CASP3, JUN, CCND1, CTNNB1, LPAR1, MSH6, CTNNA1, CCNE2, SKP2, COL4A2, HIF1A, E2F3, MAPK8, F2R, MYC, PDGFB, NFKBIA, KIT, VEGFC, GNG2, PTGS2, FZD2, PIK3R1, RB1, HSP90B1, HDAC2, RAC1, BMP2, EGLN2, MAX, FAS, LAMC1, GNAQ, NKX3-1, RBX1, FN1, CDKN1A, BIRC3, SLC2A1, RAC3, LAMC2, TCF7, PTEN, FGFR1, FOXO1, CSF1R, IL6, MAPK1, CREBBP, GNG5, ADCY9, DVL2, TGFBR2, TFG, PPARD, JAK1, MDM2, WNT9A, BMP4, PDGFRB, XIAP, EGLN1, COL4A1, NCOA4, and RASSF5	hsa-miR-708-5p, hsa-miR-3065-3p, hsa-miR-744-5p, hsa-miR-338-5p, hsa-miR-1303, hsa-miR-450a-5p, hsa-let-7e-5p, hsa-miR-199b-5p, hsa-miR-485-5p, hsa-miR-182-3p, hsa-miR-149-5p, and hsa-miR-548h-5p	Apoptosis, Sustained angiogenesis, Failed repair of genes, Insensitivity to anti-growth signals, Genomic damage, Resistance to chemotherapy, Block of differentiation, Proliferation, Evading apoptosis, and ECM-receptor interaction

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
14	Transcriptional misregulation in cancer	8.60×10^{-6}	BMI1, CCNT2, TCF3, CDKN2C, NFKBIZ, FUS, CXCL8, LMO2, ELK4, RUNX1, HMGA2, DUSP6, CCND2, HOXA9, PBX1, CDKN1B, IGF1R, NUPR1, TP53, ETV5, UTY, CCNT1, PTK2, ATM, ARNT2, PBX3, MYC, HIST1H3D, KLF3, BMP2K, FLT1, NCOR1, JMJD1C, HDAC2, H3F3A, H3F3C, KDM6A, HIST1H3H, SP1, BCL6, MAX, DOT1L, WHSC1, H3F3B, SPINT1, KMT2A, MYCN, CDKN1A, BIRC3, EWSR1, FOXO1, CSF1R, IL6, HOXA10, GOLPH3, TGFBR2, MDM2, SIN3A, PAX3, TAF15	hsa-miR-744-5p, hsa-let-7e-5p, hsa-miR-149-5p, hsa-miR-450a-5p, hsa-miR-338-5p, hsa-miR-199b-5p, hsa-miR-485-5p, hsa-miR-1303, hsa-miR-3065-3p, hsa-miR-708-5p, hsa-miR-182-3p, and hsa-miR-548h-5p	Differentiation resistance, proliferation, Cell survival, Resistance to chemotherapy, Cellular invasion, Cellular migration, invasion, Cell cycle progression, Self-renewal of T cells, Inhibition of apoptosis, Cell survival, Repression of tumor suppressors, Escape from growth inhibition, senescence, apoptosis, tumor cell growth, and interaction with ECM
15	Colorectal cancer	1.21×10^{-4}	FOS, GSK3B, TGFBR1, SMAD2, APC, TCF7L2, SMAD3, BCL2, BIRC5, AXIN1, KRAS, MLH1, TP53, AKT2, CASP3, JUN, CCND1, CTNNB1, MSH6, MAPK8, MYC, PIK3R1, RAC1, RAC3, TCF7, MAPK1, TGFBR2	hsa-let-7e-5p, hsa-miR-182-3p, hsa-miR-1303, hsa-miR-708-5p, hsa-miR-149-5p, hsa-miR-338-5p, hsa-miR-199b-5p, hsa-miR-485-5p, hsa-miR-744-5p, hsa-miR-3065-3p	Apoptosis, survival, Suppressed apoptosis, Karyotypic instability impaired G1 Cycle arrest Reduced apoptosis, Loss of growth inhibitory effect of TGFb, Proliferation, Cell Cycle, Apoptosis, and Anti-apoptosis
16	TGF-Beta Signalling pathway	1.29×10^{-4}	FST, TGFBR1, SMAD2, THBS1, PPP2CA, ACVR1B, SMURF2, SMAD3, CUL1, INHBA, BMP8B, SKP1, RPS6KB2, ACVR2B, ZFYVE16, E2F5, MYC, SMAD5, ID1, BMP2, TFDP1, SP1, RBX1, LTBP1, SMAD7, E2F4, MAPK1, CREBBP, TGFBR2, BMP4, BMPR2, and RPS6KB1	hsa-miR-338-5p, hsa-miR-182-3p, hsa-let-7e-5p, hsa-miR-744-5p, hsa-miR-548h-5p, hsa-miR-149-5p, hsa-miR-708-5p, hsa-miR-3065-3p, hsa-miR-199b-5p, hsa-miR-450a-5p, and hsa-miR-485-5p	Osteoblast differentiation, neurogenesis, ventral mesoderm specification, angiogenesis, Extracellular matrix neogenesis, immunosuppression, apoptosis induction, Cell cycle (G1 arrest), Gonadal growth, Embryo differentiation, Placenta formation, and Left-right determination Mesoderm and Endoderm.

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
17	Viral carcinogenesis	1.29×10^{-4}	RBL2, STAT3, C3, YWHAH, RANBP1, CDK4, ATF2, NRAS, IRF9, YWHAE, CCNA2, ATF6B, YWHAG, HIST1H2BC, CDK2, CCND2, HIST1H4C, CDKN1B, HLA-C, HLA-B, YWHAB, GTF2B, TRAF5, KRAS, CDK6, DDX3X, CHD4, YWHAQ, TP53, CREB1, PMAIP1, CASP3, JUN, CCND1, CCNE2, SKP2, ACTN1, DNAJA3, NFKBIA, HIST1H2BG, PIK3R1, RB1, YWHAZ, HDAC2, RAC1, SRC, RBPJ, MAD1L1, ACTN4, HIST1H2BL, CREB3L2, CREB3L1, IL6ST, CDKN1A, HIST2H2BE, HIST2H2BF, GTF2A1, MAPK1, SRF, CREBBP, LYN, TBPL1, JAK1, MDM2, ATF4, UBR4, and SCRIB	hsa-miR-548h-5p, hsa-miR-3065-3p, hsa-let-7e-5p, hsa-miR-708-5p, hsa-miR-199b-5p, hsa-miR-338-5p, hsa-miR-1303, hsa-miR-485-5p, hsa-miR-450a-5p, hsa-miR-182-3p, hsa-miR-149-5p, hsa-miR-566, and hsa-miR-4435	Proliferation, Viral infectivity and replication, Inhibition of apoptosis, Proliferation survival, Inhibition of p53-mediated apoptosis inhibition of nucleotide excision repair, Mitochondrial dysfunction, Stimulation/inhibition of cell proliferation, Alteration of host cellular gene expression, Growth retardation, Cell cycle, Transformation Anchorage-independent cell proliferation, Suppression of immunoresponse, Immortalization transformation, DNA damages, Cell cycle, Survival Growth Proliferation, Regulation of actin cytoskeleton,
18	Prostate cancer	1.69×10^{-4}	GSK3B, PDGFRA, E2F1, SOS2, E2F2, NRAS, TCF7L2, CDK2, HSP90AA1, CHUK, BCL2, CDKN1B, IGF1R, KRAS, TP53, CREB1, AKT2, CCND1, CTNNB1, CCNE2, E2F3, PDGFB, NFKBIA, PIK3R1, RB1, HSP90B1, NKX3-1, PDGFC, CREB3L2, CREB3L1, CDKN1A, TCF7, PTEN, FGFR1, FOXO1, MAPK1, CREBBP, MDM2, ATF4, PDGFRB	hsa-let-7e-5p, hsa-miR-3065-3p, hsa-miR-548h-5p, hsa-miR-1303, hsa-miR-450a-5p, hsa-miR-338-5p, hsa-miR-744-5p, hsa-miR-182-3p, hsa-miR-485-5p, hsa-miR-149-5p, hsa-miR-199b-5p, hsa-miR-708-5p	Genomic damage, G1/S progression, Impaired G1 and G2 arrest Reduced apoptosis Genomic instability, Cell proliferation, Cell Survival and Cell proliferation survival
19	Glioma	3.01×10^{-4}	CAMK2D, PRKCA, PDGFRA, E2F1, SOS2, CDK4, CAMK2G, E2F2, NRAS, CALM3, CALM1, IGF1R, KRAS, CDK6, TP53, AKT2, PLCG1, CCND1, E2F3, PDGFB, PIK3R1, RB1, CDKN1A, PTEN, MAPK1, MDM2, PDGFRB	hsa-miR-199b-5p, hsa-miR-338-5p, hsa-miR-485-5p, hsa-let-7e-5p, hsa-miR-3065-3p, hsa-miR-182-3p, hsa-miR-744-5p, hsa-miR-1303, hsa-miR-708-5p, hsa-miR-149-5p, hsa-miR-548h-5p	Cell migration and mitosis, Cell survival, Cell growth and proliferation, G1/S progression DNA, Impaired G1 and G2 arrest reduced apoptosis genomic instability, Cell cycle,

Table S1. *Cont.*

No.	KEGG pathway	p-value	Genes	miRNAs	Function
20	Endocytosis	4.81×10^{-4}	RNF41, VPS4A, HSPA2, RAB4A, PDGFRA, HSPA1A, TGFBR1, CHMP7, ADRBK1, SMAD2, CBL, DNM2, AGAP3, ARF3, DAB2, PDCD6IP, CAV1, SMURF2, CHMP1B, EEA1, EHD4, SMAD3, VPS36, HLA-C, HLA-B, SH3GL1, AGAP1, ADRB2, IGF1R, CLTC, ARFGEF2, SH3GLB1, MVB12B, RAB11FIP4, CYTH3, ASAP1, ZFYVE16, RAB11FIP2, GIT1, GIT2, F2R, AGAP2, SMAP1, TFRC, SH3GLB2, FLT1, ARRB2, KIT, RAB11FIP5, STAM2, PIP5K1A, SRC, AP2A1, HSPA8, NEDD4, GRK6, ZFYVE20, STAMBP, CYTH1, ARF6, LDLR, VPS28, SMAD7 , EHD2, RAB5C, RAB11FIP1, AP2S1, CSF1R, PARD6B, TGFBR2, MDM2, ASAP2	hsa-miR-548h-5p, hsa-let-7e-5p, hsa-miR-744-5p, hsa-miR-3065-3p, hsa-miR-708-5p, hsa-miR-450a-5p, hsa-miR-338-5p, hsa-miR-149-5p, hsa-miR-1303, hsa-miR-182-3p, hsa-miR-485-5p, hsa-miR-199b-5p	TGF-Beta signalling pathways, cytokine-cytokine receptor interaction. Phosphatidylinositol signalling system,

Table S2. Functional analysis microRNAs dysregulation correlated with thalassemia patients.

No.	Pathways	micrroRNAs	Gene targets	mRNA targets
1	HIF-1 signaling pathway (hsa04066)	hsa-let-7e-5p	18	CAMK2D, CUL2, GAPDH, EIF4EBP1, IGF1R, RPS6KB2, PLCG1, INSR, EGLN2, EIF4E2, CDKN1A, PFKFB2, EDN1, ALDOA, MAPK1, PDHB, PFKFB3, IL6R
		hsa-miR-3065-3p	10	STAT3, CDKN1B, IGF1R, VHL, AKT2, INSR, SLC2A1, PFKFB2, PDHB, IL6R
		hsa-miR-338-5p	7	CDKN1B, TLR4, PIK3R1, INSR, RBX1, CREBBP, EGLN1
		hsa-miR-485-5p	6	CAMK2G, ENO1, HIF1A, PIK3R1, CDKN1A, PFKFB2
		hsa-miR-744-5p	2	CAMK2G, CREBBP
		hsa-miR-149-5p	6	GAPDH, IFNGR2, EIF4EBP1, IL6, PGK1, RPS6KB1
		hsa-miR-708-5p	2	IGF1R, FLT1
		hsa-miR-182-3p	3	VHL, HK1, ENO2
		hsa-miR-199b-5p	2	PRKCA, INSR
		hsa-miR-1303	3	BCL2, CDKN1B, RPS6
		hsa-miR-450a-5p	2	CDKN1B, TFRC

Table S2. *Cont.*

No.	Pathways	micrroRNAs	Gene targets	mRNA targets
2	Wnt signaling pathway (hsa04310)	hsa-let-7e-5p	22	CAMK2D, BTRC, TCF7L2, CHD8, CCND2, CUL1, WNT5B, FZD3, TP53, NLK, GPC4, CCND1, MAPK8, MYC, FZD2, CSNK2A1, RAC1, PSEN1, FOSL1, NFATC3, MAP3K7, WNT9A
		hsa-miR-485-5p	6	LRP6, CAMK2G, FOSL1, FBXW11, DVL2, PPARD
		hsa-miR-3065-3p	10	DVL3, LRP6, APC, CCND2, FRAT2, SENP2, CTNNB1, RAC1, CSNK1E, WNT9A
		hsa-miR-338-5p	4	TCF7L2, SKP1, RBX1, CREBBP
		hsa-miR-149-5p	11	DAAM2, TBL1X, BTRC, CHD8, CCND2, CUL1, AXIN1, CSNK1E, TCF7, NFATC1, TBL1XR1
		hsa-miR-199b-5p	4	PRKCA, CCND2, JUN, MYC
		hsa-miR-182-3p	3	TCF7L2, MAPK8, RAC3
		hsa-miR-1303	2	GSK3B, CTNNB1
		hsa-miR-744-5p	8	CSNK2A2, CAMKS2, WNT5A, SMAD3, JUN, CTNNB1, CSNK2A1, CREBBP
		hsa-miR-548h-5p	2	PPP3CB, DAAM1
		hsa-miR-708-5p	2	CCND2, CTNNB1

Table S2. *Cont.*

No.	Pathways	micrroRNAs	Gene targets	mRNA targets
3	PI3K-Akt signaling pathway (hsa04151)	hsa-let-7e-5p	57	PRLR, RBL2, TSC1, ITGB8, CDK4, ATF2, NRAS, YWHAE, THBS1, ATF6B, THBS2, PPP2CA, YWHAG, CDK2, CCND2, CHUK, PPP2R5D, EIF4EBP1, IGF1R, CDK6, COL3A1, YWHAQ, RPS6KB2, TP53, CREB1, PTK2, LAMC3, ITGAV, CRTC2, CCND1, LPAR1, CCNE2, COL4A2, F2R, MYC, PDGFB, HSP90B1, YWHAZ, RAC1, INSR, PRKAA1, COL1A2, LAMC1, EIF4E2, CREB3L2, FN1, PKN2, CDKN1A, PTEN, FGFR1, MAPK1, GNG5, MDM2, COL4A1, IL6R, EFNA1, NR4A1
		hsa-miR-199b-5p	13	LAMB2, PRKCA, THBS1, CCND2, KRAS, RHEB, COL6A1, MYC, COL5A1, INSR, FN1, LAMC2, CSF3
		hsa-miR-744-5p	13	GNB1, CDK6, G6PC3, DDIT4, GNB2, COL4A2, F2R, RPTOR, EPHA2, IRS1, COL1A2, TNC, PDGFRB
		hsa-miR-149-5p	10	ITGB1, YWHAE, MCL1, CCND2, EIF4EBP1, DDIT4, VEGFC, IL6, COL5A2, RPS6KB1
		hsa-miR-3065-3p	19	YWHAE, YWHAG, CCND2, CDKN1B, IGF1R, YWHAQ, AKT2, GNG2, HSP90B1, YWHAZ, RAC1, INSR, CREB3L2, FOXO3, CSF1R, COL5A2, JAK1, ATF4, IL6R
		hsa-miR-338-5p	18	PRLR, SOS2, CDKN1B, YWHAB, TLR4, KRAS, PPP2R5A, ITGAV, F2R, COL5A1, KIT, PIK3R1, EPHA2, INSR, CREB3L1, SGK3, JAK1, MDM2
		hsa-miR-1303	9	GSK3B, TSC1, MCL1, BCL2, CDKN1B, RPS6, CDK6, YWHAZ, LAMC1
		hsa-miR-450a-5p	5	HSP90AA1, CDKN1B, PPP2R2A, LAMC1, PKN2
		hsa-miR-708-5p	18	YWHAH, CDK4, YWHAE, CCND2, GNG12, IGF1R, GNB1, PPP2R5C, EFNA5, IFNAR2, COL6A1, COL6A2, COL1A1, FLT1, GNG2, PRKAA1, LAMC1, CSF3
		hsa-miR-182-3p	5	PDGFRA, YWHAE, MCL1, CDK6, PDGFC
		hsa-miR-566	1	YWHAB
		hsa-miR-548h-5p	6	CDK4, MCL1, ITGAV, DDIT4, CCNE2, PTEN
		hsa-miR-485-5p	2	PI3KR1, CDKN1A
		hsa-miR-4435	1	CDC37

Table S2. *Cont.*

No.	Pathways	micrroRNAs	Gene targets	mRNA targets
4	MAPK signaling pathway (hsa04010)	hsa-let-7e-5p	41	DUSP4, TGFBR1, ATF2, NRAS, DUSP2, CRKL, STK4, CRK, MAP2K7, CHUK, MAP4K3, MAP3K1, TAB2, RPS6KA5, TP53, NLK, CASP3, RAPGEF2, MAPK8, MYC, PDGFB, FLNA, RAC1, HSPA8, NF1, FAS, RPS6KA3, MAP3K2, DUSP5, IL1A, MAP2K4, RPS6KA4, NFATC3, FGFR1, DUSP16, MAPK1, MAP3K7, SRF, DUSP1, TGFBR2, NR4A1
		hsa-miR-338-5p	10	HSPA2, FOS, IL1R1, SOS2, DUSP2, MAP4K3, KRAS, TAOK1, RAPGEF2, HSPA8
		hsa-miR-182-3p	5	PDGFRA, GADD45B, MAPK8, RAC3, PTPN5
		hsa-miR-708-5p	9	GNA12, CRKL, CDC25B, TAOK2, GNG12, TAOK1, DUSP8, STK3, NF1
		hsa-miR-450a-5p	1	TAOK1
		hsa-miR-485-5p	4	MAP3K13, HSPB1, NF1, DUSP7
		hsa-miR-3065-3p	10	HSPA1A, MAP3K1, AKT2, RASA1, CACNA1B, MAPK11, FLNA, RAC1, MAP3K2, ATF4
		hsa-miR-744-5p	11	CACNG8, GNA12, DUSP2, MAPK7, PAK2, HSPB1, JUN, ARRB2, MAX, DUSP5, PDGFRB
		hsa-miR-199b-5p	4	PRKCA, KRAS, JUN, MYC
		hsa-miR-1303	4	PAK2, RAP1A, TAB2, MAP3K5
		hsa-miR-548h-5p	3	PAK2, RPS6KA5, PPP3CB
		hsa-miR-149-5p	11	ELK4, DUSP6, MAPK14, MAP3K4, FLNA, CACNG4, HSPA8, NF1, DUSP7, SRF, NFATC1
		hsa-miR-4707-3p	1	HSPB1