Letter to the Editor

MicroRNA activation signature in patients with hemophagocytic lymphohistiocytosis and reversibility with disease-specific therapy

To the Editor:

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening immunoregulatory disorder occurring as either a familial or sporadic condition in association with a variety of triggers.[1] HLH is characterized by persistent immune activation, intrinsic imbalance in the innate and adaptive immune responses, abnormal immune-mediated pathologies, and breakdown of the natural termination of immune/inflammatory responses.[1] MicroRNAs (miRNAs) have diverse roles in the immune system, and their abnormal expression has been linked to multiple immune disorders.[2] To date, however, the expression of miRNAs in patients with HLH has not yet been reported.

We performed genome-wide miRNA sequencing on PBMCs obtained from patients with active untreated HLH (see Table E1 in this article's Online Repository at www.jaconline.org). Libraries were prepared, sequenced, mapped against the miRBase (version 20), and normalized to obtain relative miRNA expression levels (see the Methods section and Tables E2-E5 in this article's Online Repository at www.jaconline.org). The expression difference of 35 miRNAs was greater than 2 between

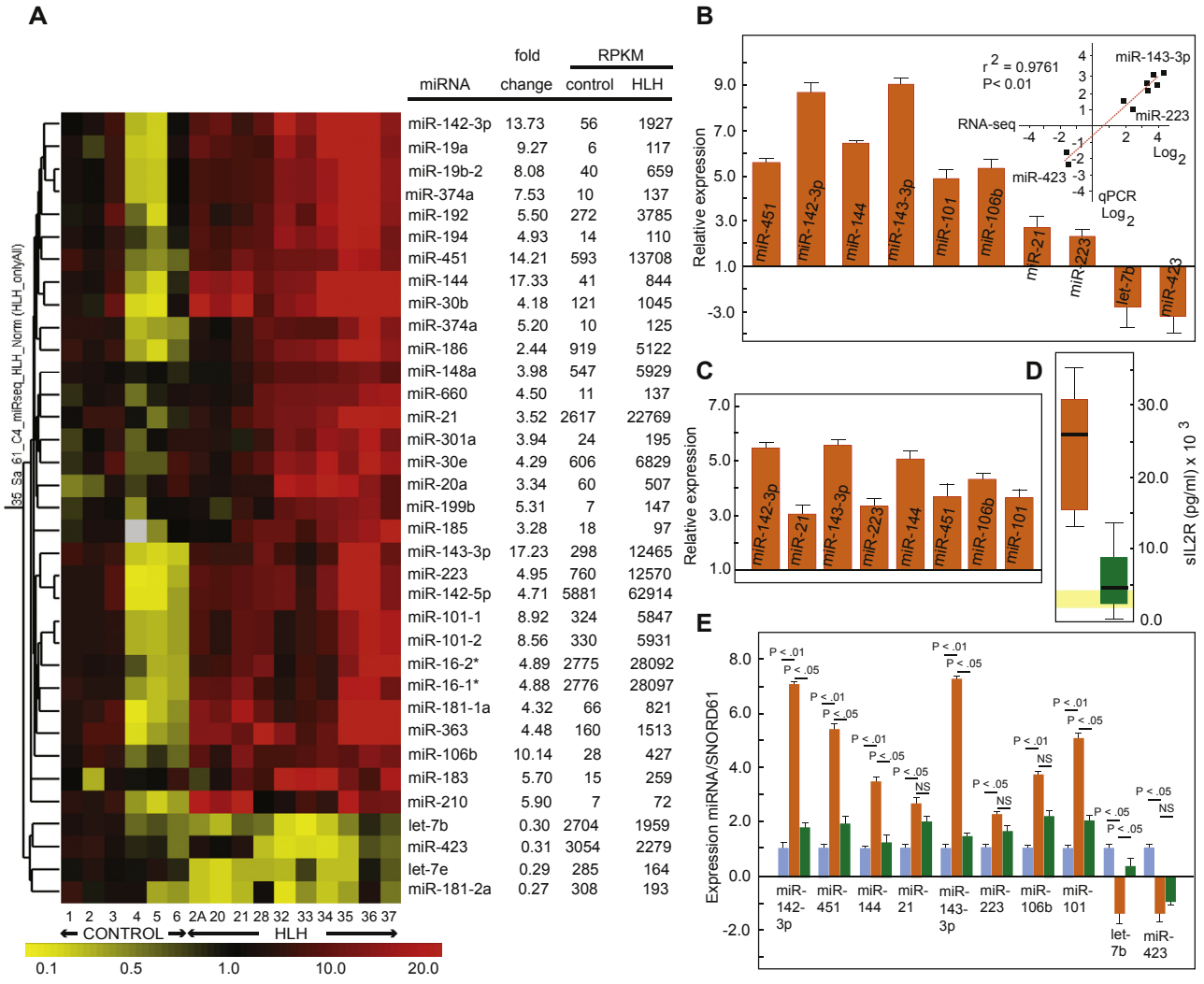


FIG 1. miRNA expression in healthy control subjects and patients with HLH. **A,** Heat map of the differentially expressed miRNAs in which *red* indicates upregulation and *yellow* indicates downregulation. *RPKM*, Reads per kilobase per million. **B,** Quantitative RT-PCR validation of a selected set of differentially expressed miRNAs (8 control subjects and 25 patients with HLH). The *insert* shows the correlation of expression levels between miRNA sequencing and quantitative RT-PCR. **C,** miRNA expression in plasma (6 control subjects and 6 patients with HLH). **D,** Soluble IL-2 receptor *(sIL2R)* plasma levels of patients with active HLH *(red)* and remission *(green)*. The *yellow field* shows the variation of soluble IL-2 receptor levels in control subjects. **E,** Expression of miRNAs in control subjects (*blue*, n = 8), patients with active HLH (*red*, n =10), and patients in remission (*green*, n = 10).

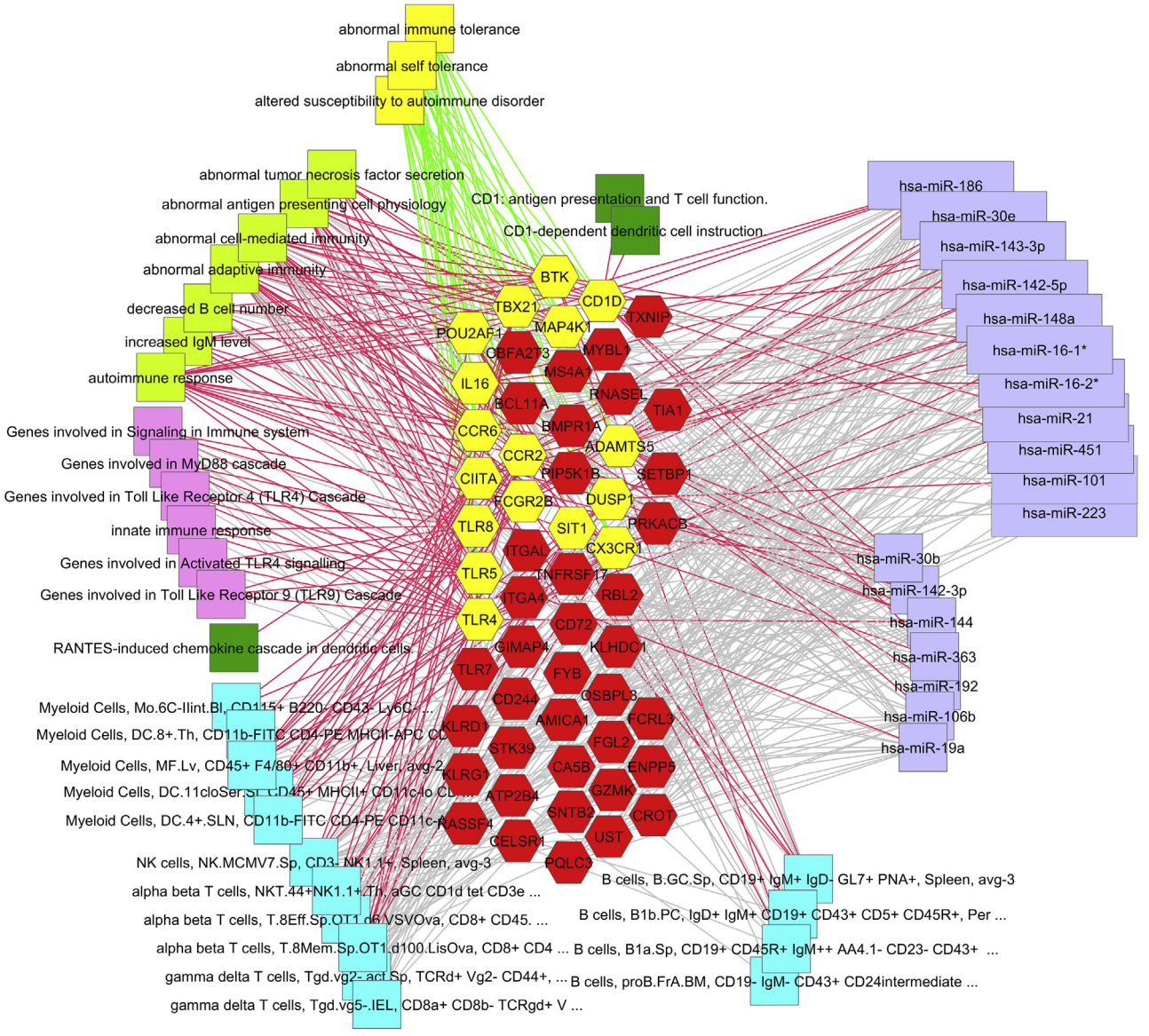


FIG 2. Gene enrichment analysis of the upregulated miRNA targets in patients with HLH. *Violet rectangles* and *squares* on the rightmost indicate miRNAs, and their size reflects the abundance of the individual miRNA (*rectangles,* >5000 reads per kilobase per million; *squares,* <5000 reads per kilobase per million). They are connected through *red* and *gray lines* to their validated target genes (*yellow* and *red hexagons*). Eleven miRNAs *(violet rectangles)* target all genes but Toll-like receptor 5 in the network (see Fig E1). *Yellow squares* (at top) are knockout phenotypes from mouse models with indicated phenotypes and connected with green edges to their corresponding genes *(yellow hexagons)*. The features that are also significant for other genes *(red hexagons)* in the network are connected by *gray lines* that are not concepts related to the tolerance and autoimmune-associated core genes *(yellow hexagons)*.[4] Other phenotypes related to abnormal lymphocyte physiology from mouse models are displayed as *light green squares*. *Dark green squares* are concepts related to immune responses. *Purple squares* on the leftmost indicate pathways. *Squares (turquoise)* at the lowermost of the figure are gene expression signatures from the Immgen Consortium database (https://www.immgen.org).

patients and control subjects (false discovery rate, *P* value cutoff = .05). The relative patterning and distribution of the differentially expressed miRNAs are shown in the heat map (Fig 1, *A*). Upregulated miRNAs, such as miR-16, miR19a, miR19b, miR-21, miR-223, and miR-181a, have previously been found to be dysregulated in patients with various immune/inflammatory disorders.[2] The 6 most upregulated miRNAs in patients with HLH (miR-143, miR-142-3p, miR-451, miR-144, miR-101, and miR-106b) have not yet been associated with immune/inflammatory conditions.

The 6 highly abundant miRNAs with the greatest fold change in expression were chosen for further studies. miR-21 and miR-223 were included because they were found to be associated with immune/inflammatory responses.[2] miR-423 and let-7e were included to represent miRNAs with decreased expression in patients with HLH. Results of the validation study were consistent

with the miRNA sequencing findings (Fig 1, *B*), signifying that these miRNAs were consistently regulated across multiple patients with HLH. The 6 highly abundant miRNAs in PBMCs were also detectable in plasma of control subjects and patients (Fig 1, *C*). We were unsuccessful to detect any of the downregulated miRNAs in plasma obtained from patients.

To test whether dysregulated miRNA expression reflects active HLH, we examined their levels in patients with active disease and remission after HLH-specific therapy (etoposide, dexamethasone, and methotrexate).[1] Soluble IL-2 receptor was used to measure the extent of immune activation,[1] and its levels correlated consistently with disease activity (Fig 1, *D*). Patients who responded to the HLH-specific therapy also exhibited normalization in expression levels of miRNAs (Fig 1, *E*). These changes were statistically significant, confirming that miRNA expression reflects HLH disease activity.

Our previous study demonstrated that 915 mRNAs were downregulated and 230 were upregulated (>2.5-fold, $P < .05$) in patients with active HLH.[3] Herein, we found that 165 of the downregulated and 98 of the upregulated mRNAs were validated targets of the inversely expressed miRNAs (see Tables E6 and E7 in this article's Online Repository at www.jaconline.org). To address the potential effect of miRNAs on HLH pathology, we used ToppMiR, a Web-based analytic workbench that allows miRNAs and their mRNA targets to be coanalyzed through biologically centered approaches.[4] As shown in the interacting network diagram in Fig 2 (and see Fig E1 in this article's Online Repository at www.jacionline.org), the upregulated miRNAs, as illustrated by violet rectangles, and their downregulated targets, which are shown as yellow or red hexagons, identify specific biological processes, functional features, pathways, and mouse gene knockout phenotypes that are connected by red line edges. Note that antigen-presenting cells, $CD8^+$ T cells, natural killer (NK) cells, γδ T cells, and myeloid cells express many of the miRNA targets shown as red hexagons that are also enriched among the HLH-downregulated genes. Thus it is possible to see in the ToppMiR view the preponderance of HLH is in the upregulated miRNAs and downregulated target genes that negatively alter the control of T and NK cell functions, innate immune responses, Toll-like receptor signaling, myeloid differentiation primary response gene–88 cascade, balance between T_H1 and T_H2 response, abnormal adaptive immunity, and the natural termination of the immune/inflammatory responses. The interactive pathways and implicated genes confirm the central role of T cells, NK cells, B cells, myeloid cells, and dendritic cells in the development of HLH. In patients with HLH, the inherited inability to cope adequately with the triggering agents invading the organism stimulates NK cells, $CD8^+$ T, and $CD4^+$ T cells to produce IFN-γ, which turns on macrophages secreting proinflammatory cytokines.[1] Stimulated $CD4^+$ T cells activate T_H0 cells into T_H1 cells, which requires low levels of intracellular cAMP in $CD4^+$ T and regulatory T cells. miR-142-3p maintains low levels of intracellular cAMP by targeting adenyl cyclase 9 mRNA.[5] Increased miR142-3p suppresses the anti-inflammatory function and ultimately potentiates or prolongs the dysregulated immune/inflammatory response in patients with HLH. HLH has a distinct T_H1/T_H2 cytokine pattern; upregulation of miR-21 in patients with HLH could partially explain the increased T_H2 cytokine levels.[6] High IL-10 levels promote M1 differentiation into M2 macrophages, and M2 macrophages fine tune or resolve inflammatory responses, expressing high levels of miR-143-3p.[7] In parallel, activated macrophages produce miR-101, which targets dual specificity phosphatase 1 (DUSP1 [MKP-1]) a critical negative regulator of proinflammatory cytokine/chemokine production through inactivation of mitogen-activated protein kinases (MAPKs; p38 and c-Jun N-terminal kinase MAPK).[8] Upregulated miR-101 through the MAPK/MKP-1/miR-101 axis contributes to the sustained production of IL-6, IL-1β, IL-10, CCL3, and CXCL2.[8] Upregulated miR-30e directly targets granzyme B and perforin and diminishes NK cell cytotoxicity. miR-30e was proved to be a suppressor of human NK cell cytotoxicity.[9] $CD8^+$ T cells and macrophages continue to receive activation and proliferation signals. Together, these findings support a model whereby dysregulated gene expression induces abnormal lymphocyte physiology and abnormal cell-mediated and adaptive immunity, prolongs the immune activation, fails to terminate the immune/inflammatory response and restore homeostasis, and leads to detrimental systemic immunologic dysregulation, which is central to organ injury in patients with HLH.

The downregulated miRNAs and their validated upregulated targets did not produce significant biological associations with apparent connectivity to the biological context of HLH and thus are not likely to be involved in the disease process. Their association with HLH might be secondary to the disease process and represent byproducts rather than effectors of HLH pathogenesis.

HLH is the newest addition to the classification of immunoregulatory disorders and proved by studies to be linked to dysregulated miRNA expression. Future investigations that focus on strongly dysregulated miRNAs and their spatial and temporal expression and targeted genes/pathways will provide insights into the pathology of the immune/inflammatory condition to translate this concept into understanding HLH.

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ONLINE REPOSITORY

Letter to the Editor

MicroRNA Activation Signature in Patients with Hemophagocytic Lymphohistiocytosis and Reversibility with Disease-Specific Therapy

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METHODS

Patients. Institutional Review Board of the Cincinnati Children's Hospital Medical Center approved the study. Patients were selected irrespective of age, race, or gender. The inclusion criteria for patients were (1) presence of disease-causing mutation in one of the known genes linked to HLH; (2) positive family history of HLH; and (3) at least five of the eight HLH-diagnostic criteria: fever, splenomegaly, cytopenias (affecting at least 2 of 3 lineages in the peripheral blood), hypertriglyceridemia, hemophagocytosis, low or absent NK-cell activity, ferritin > 500 ng/mL and elevated sIL-2 receptor (>2500 pg/mL). Patient disease activity was assessed at the time of acquiring samples. All patients met clinical, genetic and laboratory criteria for the diagnosis of HLH as outlined by the Histiocyte Society. Clinical data for patients who were referred for testing between 2009 and 2012 were retrospectively reviewed. The control group for the miRNA-seq analysis consisted of 6 apparently healthy children. Because of the wide range of age of the patients with HLH a broad age range of controls was included (11.4 +/- 5.2 years). Controls were recruited from the outpatient department of Cincinnati Children's Hospital Medical Center using the following exclusion criteria: recent febrile illness and recent use of anti-inflammatory medications. Ten patients with HLH (from No.1 to No. 10 of Table E1) were included in the miRNA-seq analysis. Whole blood was collected from patients with active HLH before specific HLH-therapy was initiated. PBMCs from patients and controls were isolated by Ficoll-Hypaque gradient centrifugation, re-suspended in Trizol (Invitrogen) and stored at -80^{0}C.

In the validation study, ten patients with HLH from the miRNA-seq analysis (No.1 – 10 in Table E1), and 15 patients (No. 11-25 in Table E1) who were not involved in the original miRNA-seq study were included. The control group for the validation study comprised eight

apparently healthy subjects; three of them (controls 1, 3 and 6 of Figure 1A) were also used in the miRNA-seq analysis. The median age of controls included in the validation study was 12.6 years.

For the plasma-miRNA level analysis, six healthy control subjects (median age 10.5 years) who were deemed to be free of inflammatory disease and six patients from the patients' group (median age 7.1 years) who were included who had sufficient quantities of plasma samples available for miRNA isolation.

For the study of reversibility of the differentially expressed miRNAs, ten patients with HLH who responded to HLH-specific therapy (etoposide, dexamethasone, and methotrexate), and PBMCs were available of the active disease stage as well as remission were included. The eight control subjects were as in the validation study.

Genetic Analysis and Clinical Data. The details for mutational analysis of *PRF1*, *UNC13D*, *RAB27A*, *SH2D1A*, *STXBP2*, *STX11*, *SH2D1A*, and *BIRC1* have been described previously.[E1, E2, E3]

Soluble IL2 Receptor. Soluble IL2 receptor (sIL2R) was determined using the Immulite 1000 platform assay system (Siemens Healthcare Diagnostics, Tarrytown, NY). Soluble sIL2R values were normalized, and an average range was obtained for controls.

Small RNA Sequencing using the Illumina microRNA-seq Platform. Total RNA from ~5×10^6 purified PBMCs from controls (n=6) and patients with HLH (n=10) was used to prepare small RNA libraries using an Illumina TruSeq Small RNA kit (San Diego, CA, USA) following

the manufacturer's instructions, except for library size selection. The amount of RNA was determined using a Nanodrop spectrophotometer (ND-1000, Thermo Scientific Waltham, MA, USA), and quality was checked using a Bioanalyzer (Agilent Technologies, Wilmington, DE, USA). RNA molecules were ligated with adapters at their 5′ and 3′ ends using T4 RNA Ligases 2 and 1. After reverse transcription from the 3′ adapter, and RNaseH treatment the second strand was synthesized from the 5′ adapter. The double-stranded cDNA molecules were amplified by PCR with primers tailed with Illumina flowcell specific sequences. RNA libraries were size-selected using a Pippin Prep System (SageScience, Beverly, MA, USA). After quantitation and size verification, the library pool was diluted and separated into individual molecules by hybridization on an Illumina HiSeq flowcell, bridge amplified with an Illumina cBot cluster generation instrument, and then sequenced on an Illumina HiSeq 2000 for 50 cycles in a single direction.

miRNA-seq Data Analysis. To produce microRNA profiles, we used the MiRExpress software package.[E4] After successively grouping identical reads and trimming the library adaptor sequence off, sequence reads were aligned to the pre-miRNA reference sequences in the latest version of the MirBase (release 20) database.[E5] Finally, the alignments to each pre-miRNA were matched to different miRNA counts to obtain a digital readout for each miRNA. A cutoff of ≥100 reads for an individual miRNA was required for further expression analyzes (See Table E2 and E3). Only miRNAs with greater than 100 reads per million were used. The Reads per Million (RPM) count for a miRNA was obtained by dividing the number of reads of a miRNA species by the total number of reads mapping to all miRNAs and multiplying that by 1,000,000, giving the abundance of a miRNA in a million reads. MiRExpress normalized read counts per

miRNA per million per all mapped miRNA reads were used as an estimate of expression level (Table E4 and E5). Fold change was calculated relative to normal for with Welch t-test Benjamini-Hochberg FDR<0.05. Differential expression between controls and patients was assessed using the normalized miRNAs abundances as in Table E4 and E5. A p-value cutoff of 0.05 was used for significance detection.

Target Gene Prediction. Functionally significant miRNAs and their correspondingly most important mRNAs targets in specific biological contexts were identified for understanding the molecular mechanisms underlying HLH. Validated mRNA targets were identified using the miRWalk v. 2.0 database.[E6] We used ToppMiR, (developed in Dr. Bruce Aronow's laboratory) to identify functionally significant miRNAs and their correspondingly most important validated mRNA targets in specific biological contexts to understand the molecular mechanisms underlying HLH.[E7] ToppMiR analysis ranks miRNAs as well as their putative mRNA targets. Additionally, ToppMiR identifies and ranks the potential importance of the miRNA/mRNA interaction by recognizing significant features of the gene sets. The mRNA or gene ranking (target and non-target genes) is based on previously published ToppGene and ToppNet.[E8] ToppMiR ranks the miRNAs integrating the target predictions (compiled from several different prediction algorithms) and their putative targets' relative importance in the context.

Quantitative RT-PCR (qRT-PCR) for validation study. For the validation study, ten patients with HLH who were included in the miRNA-seq analysis, and 15 patients who were not involved in the miRNA-seq study were selected. Small RNAs were purified using a Qiagen miRNeasy isolation kit (SABioscience/Qiagen Sciences, Valencia, CA, USA) according to the

manufacturer's protocol. RNA (200 ng) enriched for small species were reverse-transcribed into first strand cDNA using an RT2 miRNA First Strand kit (SABiosciences/Qiagen). The cDNA was diluted to 100 µl. Diluted cDNA was mixed with RT2 SYBR Green qPCR Master Mix. The mixture was aliquoted to individual wells of a custom made miRNA PCR Array (SABiosciences/Qiagen), which included the primer pairs for has-let-7b, miR-423, miR-21, miR-143, miR-144, miR-142-3p, miR-451, miR-101-1, miR-106b, and miR-223 human miRNAs in addition to SNORD61, C. elegans miR-39, mRTC, and PPC controls. PCR was run on a 7900 Real-Time PCR System (Applied Biosystems, Foster City, CA). The expression levels were normalized to SNORD61, endogenous control. qRT-PCR data were analyzed using the manufacturer's software (http://www.sabiosciences.com/dataanalysis.php). In general, RT-PCR confirms trends of increased and decreased expression in candidate genes identified by the miRNA-seq analysis. However, the miRNA expression levels and fold-differences determined by qRT-PCR were lower compared with those determined by Illumina miRNA-seq analysis. MiRNA-seq and qRT-PCR methods have different sensitivities, and qRT-PCR appears to be less efficient in terms of differential analysis of miRNA expression than the next generation sequencing technology.

Plasma miRNA analysis. For the plasma miRNA level analysis healthy control subjects (n=6) and patients with HLH (n=6) were selected. Blood was collected in EDTA-treated tubes. Multiples of 200 µl of plasma were spiked with C. elegans miR-39 miRNA Serum/Plasma Spike-In Control (1.1×10^8 copies/200 µl), in order to monitor extraction efficiency and reproducibility. Total RNA, including miRNA, was extracted from serum (200 µl) by using an MiRNeasy Serum/Plasma Kit (SABiosciences/Qiagen) in accordance with the manufacturer's

protocol. Two microliters of each RNA sample was used for cDNA synthesis using the miScript II RT kit (Qiagen). The reverse-transcription reaction mix (20µl) was prepared using HISpec buffer, NUCLEics mix, RT mix and RNase-free water. The assay mixture was incubated for 60 min at 37°C, after that denaturation for 5 min at 95°C was performed. Each cDNA was further diluted to 100 µl with RNase-free water and stored at−20°C until use. A custom made miRNA PCR Array (SABiosciences/Qiagen), which included the primer pairs for has-let-7b, miR-423, miR-21, miR-143, miR-144, miR-142-3p, miR-451, miR-101-1, miR-106b, and miR-223 human miRNAs in addition to SNORD61, C. elegans miR-39, PCR control assays, positive PCR control (PPC) assays, and miRNA reverse transcription control (miRTC) assays. PCR was run on a 7900 Real-Time PCR System (Applied Biosystems, Foster City, CA). The expression levels were normalized to SNORD61, endogenous control. qRT-PCR data were analyzed using the manufacturer's software (http://www.sabiosciences.com/dataanalysis.php) SABiosciences makes use of the ΔΔCt method for the relative quantification of miRNAs. Student's t-test was used to examine any differential expression of miRNAs between the HLH and control groups; values of $P < 0.05$ were considered to indicate statistical significance. The plasma miRNA PCR data sets were calibrated using a C. elegans miR-39 assay, which detected the spike-in control that was added to the serum samples. This calibration intended to resolve differences in recovery that may have occurred during the purification procedure, or differences in amplification efficiency.

Reversibility of the differentially expressed miRNAs in patients with HLH. For the study of reversibility of the differentially expressed miRNAs, ten patients with HLH who responded to HLH-specific therapy, and PBMCs were available of the active disease stage as

well as remission were included. The control group included the eight healthy subjects used in the validation study.

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FIGURE LEGEND

Fig. E1. Biological network-based representation of functional association between prioritized miRNAs and their validated targets. Prioritization was determined on the basis of the magnitude of miRNA expression using ToppMir[E6]. Yellow rectangles represent miRNAs (>5000 RPKM) violet squares are miRNAs (<5000 RPKM) in PBMCs from HLH-patient's. Yellow hexagons are genes that are validated targets of miRNAs (> 5000 RPKM) and connected by red edges. TLR5 (red hexagon) is connected by a red line to miR-19a. Green squares are phenotypes of targeted mice and connected with green or red edges to their corresponding genes. The features that are also significant in the network are connected by gray lines. Dark green squares are concepts related to innate immune responses. Purple squares on the leftmost indicate pathway analysis. Squares (turquoise) at the lowermost of the figure are gene expression signatures from the Immgen Consortium database (https://www.immgen.org).

Table E1: Characteristics of Patients with HLH Used in this Study[1]

No.	patient	age	gender	causative genetic mutation	NK function (LU)[2]	sIL2R[3]	remarks
1.	HLH2A	15y	F	*STXBP2* c.[694A>T]; [p. I232L] / ? *STX11* c.[146G>A]; [p. R49Q] / ?	1.0	19,515	recurrent HLH
2.	HLH20	5y	F	NMI[4] in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A,*	4.2	67,553	confirmed HLH, positive family history
3.	HLH21	9y	F	*STXBP2* c.[194G>A]; [p.R65Q**]** / *STXBP2* c.[194G>A]; [p.R65Q]	3.0	45,942	HLH type 5
4.	HLH28	2m	F	*PRF1*, c.[50delT]; c.[1442A>C] p.[L17fsX50[; p.[Q481P]/ c.[50delT]; c.[1442A>C] p.[L17fsX50[; p.[Q481P]	0.0	46,943	HLH type 2
5.	HLH32	11y	M	*LYST* was not tested for mutations	2.3	23,904	HLH developed with association of Chediak-Higashi syndrome
6.	HLH33	19m	M	*STXBP2* c.[1621G>A]; [p.541GS] / c.[1621G>A]; [p.G541S]	2.1	29,827	HLH type 5
7.	HLH34	3m	F	*PRF1*, c.[50delT]; c.[1442A>C] p.[L17fsX50[; p.[Q481P] / c.[50delT]; c.[1442A>C]; [p. L17fsX50]; [p. Q481P]	0.0	41,030	HLH type 2
8.	HLH35	5m	M	*PRF1*, c.[50delT]; c.[1442A>C] [p. L17fsX50]; [p. Q481P] / c.[50delT]; c.[1442A>C] p.[L17fsX50[; p.[Q481P]	0.0	56,203	HLH type 2
9.	HLH37	13y	F	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	5.4	27,855	confirmed HLH
10.	HLH31	5y	M	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	4.1	49,642	suspected familial HLH, positive family history
11.	HLH31	3y	M	*STXBP2* c.[568C>T]; [p. R190C] / ?	5.3	23,563	confirmed HLH
12.	HLH30	18m	M	*UNC13D* c.[847A>G]; p.[I283V] / *UNC13D* c.[847A>G]; p.[I283V]	7.4	75,882	HLH type 3
13.	HHL41	9m	F	*UNC13D* c.2828A>G, [p.N943S)] / ?; *STXBP2* g.1782G>A) / ?	3.1	42,456	confirmed HLH
14.	HLH42	3y	F	*PRF1* c.[666C>A], p.[H222Q] / ?		67,892	confirmed HLH
15.	HLH45	8m	M	*PRF1* c.[50delT] c.[1442 A>C] [L17fsX50]; [p. Q481P] / c.[50delT]; c.[1442A>C] [p. L17fsX50]; p.[Q481P]	0.0	40,564	HLH type 2
16.	HLH51	12y	M	NMI in *PRF1*, other genes were not tested	1.3	23,553	confirmed HLH

17.	HLH14	7y	F	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	4.1	14,518	confirmed HLH
18.	HLH39	2m	M	*PRF1*, c.[50delT]; c.[1442A>C] [p. L17fsX50[; [p. Q481P] / c.[50delT]; c.[1442A>C] [p.L17fsX50[; [p.Q481P]	0.0	51,463	HLH type 2
19.	HLH38	6y	F	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	11.1	41,008	confirmed HLH
20.	HLH40	11m	M	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	6.9	32,115	confirmed HLH
21.	HLH02	12y	M	*UNC13D* g.[1389(+1) g>a] / ? STXBP2 g.[1782(*12) g>a] / ?	2.1	33,914	confirmed HLH
22.	HLH27	8y	M	NMI in *PRF1, UNC13D, STXBP2, STX11, RAB27A, ITK, SH2D1A*	1.1	59,642	confirmed HLH
23.	P-HLH59	7y	M	PRF1 c.[148G>A];[p.V50M] / c.[148G>A];[p.V50M]	9.2	69,543	HLH type 2
24.	P-HLH66	15y	M	*STXBP2* c.[511G>T]; [p.V168L] / ?	0.1	19,743	confirmed HLH, relapse, received HCT[5]
25.	P-HLH96	5y	M	NMI in *PRF1, UNC13D, not tested: STXBP2, STX11, RAB27A, ITK, SH2D1A*	0.0	48,543	confirmed HLH, positive family history

1. Patients were selected irrespective of age, race, or gender. The inclusion criteria for patients were (1) presence of inactivating mutation in one of the genes linked to familial form of hemophagocytic lymphohistiocytosis (HLH); (2) positive family history of HLH; and (3) at least five of the eight hemophagocytic lymphohistiocytosis diagnostic criteria: fever, splenomegaly, cytopenias (affecting at least 2 of 3 lineages in the peripheral blood), hypertriglyceridemia, hemophagocytosis, low or absent NK-cell activity, elevated plasma ferritin (> 500 ng/mL) and sIL-2 receptor (>2400-3400 pg/mL). Patient disease activity was assessed at the time of acquiring samples. All patients met clinical, genetic and laboratory criteria for the diagnosis of HLH as outlined by the Histiocyte Society. Clinical data for patients who were referred for testing between 2009 and 2012 were retrospectively reviewed. For microRNA-seq analysis and validation experiments, whole blood was collected from patients with active HLH before specific HLH-therapy was initiated. Six age-matched pediatric controls were recruited using the following exclusion criteria: recent febrile illness and recent use of anti-inflammatory medications.

2. NK function in normal controls: 5-35 (mean 11.2) lytic units (LU).

3. normal sIL2R levels ranged from 2400-3400 pg/ml.

4. NMI: no mutations identified

5. blood sample taken before allogeneic haematopoietic cell transplantation (HCT)

TABLE E2: microRNA Reads in Controls

No.	CONTROL-1 (C1)		CONTROL-2 (C2)		CONTROL-3 (C3)	
	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads
1.	hsa-mir-486, hsa-miR-486-5p	94249	hsa-mir-486, hsa-miR-486-5p	61283	hsa-mir-486, hsa-miR-486-5p	51297
2.	hsa-mir-181a-1, hsa-miR-181a-5p	37270	hsa-mir-181a1, hsa-miR-181a-5p	53111	hsa-mir-191, hsa-miR-191-5p	44630
3.	hsa-mir-181a-2, hsa-miR-181a-5p	37270	hsa-mir-181a2, hsa-miR-181a-5p	53111	hsa-mir-181a-1, hsa-miR-181a-5p	31662
4.	hsa-mir-191, hsa-miR-191-5p	31135	hsa-mir-191, hsa-miR-191-5p	32376	hsa-mir-181a-2, hsa-miR-181a -5p	31662
5.	hsa-mir-92a-1, hsa-miR-92a-3p	14853	hsa-mir-92a-1, hsa-miR-92a-3p	14582	hsa-let-7a-1, hsa-let-7a-5p	18092
6.	hsa-mir-92a-2, hsa-miR-92a-3p	10422	hsa-let-7a-1, hsa-let-7a-5p	11702	hsa-let-7a-2, hsa-let-7a-5p	18044
7.	hsa-let-7a-1, hsa-let-7a-5p	8768	hsa-let-7a-2, hsa-let-7a-5p	11678	hsa-let-7a-3, hsa-let-7a-5p	18029
8.	hsa-let-7a-2, hsa-let-7a-5p	8761	hsa-let-7a-3, hsa-let-7a-5p	11669	hsa-mir-92a-1, hsa-miR-92a-3p	15485
9.	hsa-let-7a-3, hsa-let-7a-5p	8749	hsa-mir-146b, hsa-miR-146b-5p	11340	hsa-mir-92a-2, hsa-miR-92a-3p	10998
10.	hsa-mir-26a-2, hsa-miR-26a-5p	6631	hsa-mir-92a-2, hsa-miR-92a-3p	10581	hsa-mir-26a-2, hsa-miR-26a-5p	8318
11.	hsa-mir-26a-1, hsa-miR-26a-5p	6627	hsa-mir-150, hsa-miR-150-5p	6721	hsa-mir-26a-1, hsa-miR-26a-5p	8314
12.	hsa-mir-146b, hsa-miR-146b-5p	5564	hsa-mir-26a-2, hsa-miR-26a-5p	6051	hsa-mir-146b, hsa-miR-146b-5p	7965
13.	hsa-mir-30d, hsa-miR-30d-5p	4566	hsa-mir-26a-1, hsa-miR-26a-5p	6045	hsa-mir-30d, hsa-miR-30d-5p	7459
14.	hsa-mir-21, hsa-miR-21-5p	3486	hsa-mir-30d, hsa-miR-30d-5p	4394	hsa-mir-150, hsa-miR-150-5p	4601
15.	hsa-mir-150, hsa-miR-150-5p	2796	hsa-let-7g, hsa-let-7g-5p	1835	hsa-let-7f-2, hsa-let-7f-5p	2448
16.	hsa-mir-22, hsa-miR-22-3p	2296	hsa-let-7f-2, hsa-let-7f-5p	1761	hsa-let-7g, hsa-let-7g-5p	2290
17.	hsa-mir-423, hsa-miR-423-3p	2203	hsa-mir-423, hsa-miR-423-5p	1727	hsa-let-7f-1, hsa-let-7f-5p	2289
18.	hsa-let-7f-2, hsa-let-7f-5p	1990	hsa-mir-342, hsa-miR-342-3p	1725	hsa-mir-423, hsa-miR-423-3p	2127
19.	hsa-let-7g, hsa-let-7g-5p	1910	hsa-mir-423, hsa-miR-423-3p	1681	hsa-mir-423, hsa-miR-423-5p	2026
20.	hsa-let-7f-1, hsa-let-7f-5p	1860	hsa-let-7f-1, hsa-let-7f-5p	1646	hsa-mir-21, hsa-miR-21-5p	1977
21.	hsa-mir-125a, hsa-miR-125a-5p	1508	hsa-mir-125a, hsa-miR-125a-5p	1643	hsa-mir-22, hsa-miR-22-3p	1948
22.	hsa-mir-941-1, hsa-miR-941	1424	hsa-mir-22, hsa-miR-22-3p	1330	hsa-mir-125a, hsa-miR-125a-5p	1869
23.	hsa-mir-30e, hsa-miR-30e-5p	1278	hsa-mir-146a, hsa-miR-146a-5p	1322	hsa-mir-146a, hsa-miR-146a-5p	1817
24.	hsa-let-7b, hsa-let-7b-5p	1212	hsa-mir-25, hsa-miR-25-3p	1292	hsa-mir-941-1, hsa-miR-941	1667
25.	hsa-mir-423, hsa-miR-423-5p	1160	hsa-let-7b, hsa-let-7b-5p	1226	hsa-let-7b, hsa-let-7b-5p	1631
26.	hsa-mir-146a, hsa-miR-146a-5p	1152	hsa-mir-181b-2, hsa-miR-181b-5p	1218	hsa-mir-10a, hsa-miR-10a-5p	1448
27.	hsa-mir-25, hsa-miR-25-3p	1058	hsa-mir-181b-1, hsa-miR-181b-5p	1084	hsa-mir-25, hsa-miR-25-3p	1357
28.	hsa-mir-16-1, hsa-miR-16-5p	891	hsa-mir-21, hsa-miR-21-5p	1038	hsa-mir-342, hsa-miR-342-3p	1176
29.	hsa-mir-16-2, hsa-miR-16-5p	884	hsa-mir-28, hsa-miR-28-3p	953	hsa-mir-151a, hsa-miR-151a-3p	1143
30.	hsa-let-7i, hsa-let-7i-5p	867	hsa-mir-142, hsa-miR-142-5p	742	hsa-mir-151a, hsa-miR-151a-5p	848
31.	hsa-mir-181b-2, hsa-miR-181b-5p	790	hsa-mir-941-1, hsa-miR-941	724	hsa-mir-28, hsa-miR-28-3p	835
32.	hsa-mir-142, hsa-miR-142-5p	766	hsa-mir-151a, hsa-miR-151a-3p	698	hsa-mir-103a-2, hsa-miR-103a-3p	825
33.	hsa-mir-28, hsa-miR-28-3p	765	hsa-mir-16-1, hsa-miR-16-5p	645	hsa-mir-103a-1, hsa-miR-103a-3p	821
34.	hsa-mir-182, hsa-miR-182-5p	754	hsa-mir-16-2, hsa-miR-16-5p	644	hsa-mir-186, hsa-miR-186-5p	764
35.	hsa-mir-151a, hsa-miR-151a-3p	753	hsa-mir-197, hsa-miR-197-3p	631	hsa-mir-127, hsa-miR-127-3p	750
36.	hsa-mir-342, hsa-miR-342-3p	714	hsa-mir-186, hsa-miR-186-5p	618	hsa-let-7i, hsa-let-7i-5p	718
37.	hsa-mir-181b-1, hsa-miR-181b-5p	706	hsa-mir-103a-2, hsa-miR-103a-3p	615	hsa-mir-16-1, hsa-miR-16-5p	713
38.	hsa-mir-103a-2, hsa-miR-103a-3p	701	hsa-mir-103a-1, hsa-miR-103a-3p	607	hsa-mir-16-2, hsa-miR-16-5p	711
39.	hsa-mir-103a-1, hsa-miR-103a-3p	691	hsa-mir-10a, hsa-miR-10a-5p	559	hsa-mir-99b, hsa-miR-99b-5p	707
40.	hsa-mir-186, hsa-miR-186-5p	646	hsa-mir-30c-2, hsa-miR-30c-5p	486	hsa-mir-93, hsa-miR-93-5p	679
41.	hsa-mir-10a, hsa-miR-10a-5p	633	hsa-mir-30c-1, hsa-miR-30c-5p	486	hsa-mir-181b-2, hsa-miR-181b-5p	675
42.	hsa-mir-320a, hsa-miR-320a	625	hsa-mir-151a, hsa-miR-151a-5p	453	hsa-let-7d, hsa-let-7d-5p	674
43.	hsa-mir-197, hsa-miR-197-3p	616	hsa-mir-26b, hsa-miR-26b-5p	420	hsa-mir-223, hsa-miR-223-3p	673
44.	hsa-mir-148a, hsa-miR-148a-3p	611	hsa-mir-320a, hsa-miR-320a	418	hsa-mir-197, hsa-miR-197-3p	666
45.	hsa-mir-93, hsa-miR-93-5p	510	hsa-mir-93, hsa-miR-93-5p	413	hsa-mir-142, hsa-miR-142-5p	615
46.	hsa-mir-30c-2, hsa-miR-30c-5p	483	hsa-mir-223, hsa-miR-223-3p	413	hsa-mir-30c-2, hsa-miR-30c-5p	611
47.	hsa-mir-30c-1, hsa-miR-30c-5p	483	hsa-let-7i, hsa-let-7i-5p	412	hsa-mir-181b-1, hsa-miR-181b-5p	609
48.	hsa-mir-26b, hsa-miR-26b-5p	476	hsa-let-7d, hsa-let-7d-5p	380	hsa-mir-30c-1, hsa-miR-30c-5p	608
49.	hsa-mir-223, hsa-miR-223-3p	437	hsa-mir-99b, hsa-miR-99b-5p	372	hsa-mir-30e, hsa-miR-30e-5p	578
50.	hsa-mir-151a, hsa-miR-151a-5p	412	hsa-mir-182, hsa-miR-182-5p	352	hsa-mir-222, hsa-miR-222-3p	488
51.	hsa-mir-451a, hsa-miR-451a	367	hsa-mir-155, hsa-miR-155-5p	350	hsa-mir-26b, hsa-miR-26b-5p	473
52.	hsa-mir-99b, hsa-miR-99b-5p	354	hsa-mir-30e, hsa-miR-30e-5p	309	hsa-mir-320a, hsa-miR-320a	450
53.	hsa-mir-484, hsa-miR-484	341	hsa-mir-222, hsa-miR-222-3p	305	hsa-mir-378a, hsa-miR-378a-3p	446
54.	hsa-mir-378a, hsa-miR-378a-3p	333	hsa-mir-484, hsa-miR-484	293	hsa-mir-221, hsa-miR-221-3p	440
55.	hsa-mir-140, hsa-miR-140-3p	324	hsa-mir-140, hsa-miR-140-3p	282	hsa-mir-409, hsa-miR-409-3p	431
56.	hsa-mir-126, hsa-miR-126-5p	291	hsa-mir-181a-2, hsa-miR-181a-2-3p	252	hsa-mir-148a, hsa-miR-148a-3p	430
57.	hsa-let-7d, hsa-let-7d-5p	276	hsa-mir-221, hsa-miR-221-3p	251	hsa-mir-484, hsa-miR-484	373
58.	hsa-mir-409, hsa-miR-409-3p	273	hsa-mir-148a, hsa-miR-148a-3p	238	hsa-let-7e, hsa-let-7e-5p	356
59.	hsa-mir-127, hsa-miR-127-3p	238	hsa-let-7e, hsa-let-7e-5p	188	hsa-mir-98, hsa-miR-98-5p	330
60.	hsa-mir-155, hsa-miR-155-5p	238	hsa-mir-98, hsa-miR-98-5p	187	hsa-mir-182, hsa-miR-182-5p	318
61.	hsa-mir-27b, hsa-miR-27b-3p	234	hsa-mir-378a, hsa-miR-378a-3p	177	hsa-mir-140, hsa-miR-140-3p	296
62.	hsa-mir-98, hsa-miR-98-5p	221	hsa-mir-92b, hsa-miR-92b-3p	156	hsa-mir-126, hsa-miR-126-5p	239
63.	hsa-mir-221, hsa-miR-221-3p	207	hsa-mir-146b, hsa-miR-146b-3p	155	hsa-mir-155, hsa-miR-155-5p	237
64.	hsa-mir-192, hsa-miR-192-5p	190	hsa-mir-192, hsa-miR-192-5p	149	hsa-mir-500a, hsa-miR-500a-3p	227
65.	hsa-let-7e, hsa-let-7e-5p	189	hsa-mir-451a, hsa-miR-451a	148	hsa-mir-27b, hsa-miR-27b-3p	217
66.	hsa-mir-222, hsa-miR-222-3p	185	hsa-mir-425, hsa-miR-425-5p	133	hsa-mir-425, hsa-miR-425-5p	199
67.	hsa-let-7d, hsa-let-7d-3p	170	hsa-mir-27b, hsa-miR-27b-3p	131	hsa-let-7d, hsa-let-7d-3p	175
68.	hsa-mir-500a, hsa-miR-500a-3p	156	hsa-mir-361, hsa-miR-361-3p	116	hsa-mir-148b, hsa-miR-148b-3p	169
69.	hsa-mir-92b, hsa-miR-92b-3p	149	hsa-let-7d, hsa-let-7d-3p	115	hsa-mir-589, hsa-miR-589-5p	151
70.	hsa-mir-425, hsa-miR-425-5p	142	hsa-mir-126, hsa-miR-126-5p	114	hsa-mir-23a, hsa-miR-23a-3p	147
71.	hsa-mir-148b, hsa-miR-148b-3p	136	hsa-mir-500a, hsa-miR-500a-3p	114	hsa-mir-92b, hsa-miR-92b-3p	143
72.	hsa-mir-15b, hsa-miR-15b-5p	120	hsa-mir-23a, hsa-miR-23a-3p	113	hsa-mir-15b, hsa-miR-15b-5p	127

73.	hsa-mir-589, hsa-miR-589-5p	118	hsa-mir-589, hsa-miR-589-5p	113	hsa-mir-146b, hsa-miR-146b-3p	125
74.	hsa-mir-146b, hsa-miR-146b-3p	111	hsa-mir-15b, hsa-miR-15b-5p	112	hsa-mir-192, hsa-miR-192-5p	125
75.	hsa-mir-21, hsa-miR-21-3p	110	hsa-mir-148b, hsa-miR-148b-3p	111	hsa-mir-501, hsa-miR-501-3p	124
76.	hsa-mir-744, hsa-miR-744-5p	109	hsa-mir-29a, hsa-miR-29a-3p	109	hsa-mir-361, hsa-miR-361-5p	123
77.	hsa-mir-23a, hsa-miR-23a-3p	108	hsa-mir-584, hsa-miR-584-5p	107	hsa-mir-181a-2, hsa-miR-181a-2 3p	123
78.	hsa-mir-181a-2, hsa-miR-181a-2-3p	106	hsa-let-7c, hsa-let-7c	105	hsa-mir-181c, hsa-miR-181c-5p	120
79.	hsa-mir-29a, hsa-miR-29a-3p	106	hsa-mir-342, hsa-miR-342-5p	104	hsa-mir-361, hsa-miR-361-3p	119
80.	hsa-mir-101-2, hsa-miR-101-3p	104	hsa-mir-181c, hsa-miR-181c-5p	104	hsa-mir-744, hsa-miR-744-5p	118
81.	hsa-mir-1307, hsa-miR-1307-3p	104	hsa-mir-361, hsa-miR-361-5p	104	hsa-mir-29a, hsa-miR-29a-3p	117
82.	hsa-mir-143, hsa-miR-143-3p	104	hsa-mir-744, hsa-miR-744-5p	102	hsa-let-7c, hsa-let-7c	115
83.	hsa-mir-181c, hsa-miR-181c-5p	104	hsa-mir-17, hsa-miR-17-5p	101	hsa-mir-432, hsa-miR-432-5p	113
84.	hsa-mir-361, hsa-miR-361-3p	103	hsa-mir-1307, hsa-miR-1307-3p	100	hsa-mir-17, hsa-miR-17-5p	113
85.	hsa-mir-342, hsa-miR-342-5p	102			hsa-mir-1307, hsa-miR-1307-3p	112
86.	hsa-mir-101-1, hsa-miR-101-3p	102			hsa-mir-3615, hsa-miR-3615	111
87.	hsa-mir-106b, hsa-miR-106b-3p	101			hsa-mir-451a, hsa-miR-451a	111
88.	hsa-mir-20a, hsa-miR-20a-5p	101			hsa-mir-23a, hsa-miR-23a-5p	106
89.	hsa-mir-340, hsa-miR-340-5p	100			hsa-mir-23b, hsa-miR-23b-3p	105
90.	hsa-mir-17, hsa-miR-17-5p	100			hsa-mir-664a, hsa-miR-664a-3p	104
91.	hsa-mir-30a, hsa-miR-30a-5p	100			hsa-mir-143, hsa-miR-143-3p	103
92.					hsa-mir-20a, hsa-miR-20a-5p	103
93.					hsa-mir-30e, hsa-miR-30e-3p	102
94.					hsa-mir-766, hsa-miR-766-3p	102

Table E2: microRNA Reads in Controls (continued)

No.	CONTROL-4 (C4)		CONTROL-5 (C5)		CONTROL-6 (C6)	
	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads
1.	hsa-mir-181a-1, hsa-miR-181a-5p	80850	hsa-mir-181a-1, hsa-miR-181a-5p	39102	hsa-mir-486, hsa-miR-486-5p	30774
2.	hsa-mir-181a-2, hsa-miR-181a-5p	80850	hsa-mir-181a-2, hsa-miR-181a-5p	39102	hsa-mir-146b, hsa-miR-146b-5p	8517
3.	hsa-mir-150, hsa-miR-150-5p	54825	hsa-mir-92a-1, hsa-miR-92a-3p	31573	hsa-mir-181a-1, hsa-miR-181a-5p	8271
4.	hsa-mir-92a-1, hsa-miR-92a-3p	40241	hsa-mir-150, hsa-miR-150-5p	29958	hsa-mir-181a2, hsa-miR-181a-5p	8213
5.	hsa-mir-92a-2, hsa-miR-92a-3p	35684	hsa-let-7a-1, hsa-let-7a-5p	29259	hsa-mir-191, hsa-miR-191-5p	6040
6.	hsa-mir-486, hsa-miR-486-5p	33521	hsa-let-7a-3, hsa-let-7a-5p	29239	hsa-mir-26a-2, hsa-miR-26a-5p	4070
7.	hsa-let-7a-1, hsa-let-7a-5p	26657	hsa-let-7a-2, hsa-let-7a-5p	29229	hsa-mir-26a-1, hsa-miR-26a-5p	4078
8.	hsa-let-7a-2, hsa-let-7a-5p	26656	hsa-mir-92a-2, hsa-miR-92a-3p	27997	hsa-mir-21, hsa-miR-21-5p	3677
9.	hsa-let-7a-3, hsa-let-7a-5p	26656	hsa-mir-486, hsa-miR-486-5p	21750	hsa-mir-451a, hsa-miR-451a	2613
10.	hsa-mir-26a-2, hsa-miR-26a-5p	19246	hsa-mir-26a-2, hsa-miR-26a-5p	15598	hsa-let-7a-1, hsa-let-7a-5p	2408
11.	hsa-mir-26a-1, hsa-miR-26a-5p	19246	hsa-mir-26a-1, hsa-miR-26a-5p	15597	hsa-let-7a-2, hsa-let-7a-5p	2469
12.	hsa-mir-191, hsa-miR-191-5p	15360	hsa-mir-191, hsa-miR-191-5p	12396	hsa-let-7a-3, hsa-let-7a-5p	2469
13.	hsa-mir-142, hsa-miR-142-5p	14109	hsa-let-7g, hsa-let-7g-5p	8444	hsa-mir-142, hsa-miR-142-5p	1844
14.	hsa-let-7g, hsa-let-7g-5p	9275	hsa-let-7f-2, hsa-let-7f-5p	7855	hsa-mir-30e, hsa-miR-30e-5p	1762
15.	hsa-let-7f-2, hsa-let-7f-5p	7644	hsa-let-7f-1, hsa-let-7f-5p	7630	hsa-let-7f-2, hsa-let-7f-5p	1695
16.	hsa-mir-22, hsa-miR-22-3p	7478	hsa-mir-142, hsa-miR-142-5p	7044	hsa-let-7f-1, hsa-let-7f-5p	1657
17.	hsa-let-7f-1, hsa-let-7f-5p	7469	hsa-mir-22, hsa-miR-22-3p	6541	hsa-mir-92a-1, hsa-miR-92a-3p	1548
18.	hsa-mir-423, hsa-miR-423-5p	5151	hsa-mir-423, hsa-miR-423-5p	4901	hsa-mir-16-1, hsa-miR-16-5p	1453
19.	hsa-mir-16-2, hsa-miR-16-5p	4940	hsa-let-7b, hsa-let-7b-5p	3998	hsa-mir-16-2, hsa-miR-16-5p	1429
20.	hsa-mir-16-1, hsa-miR-16-5p	4935	hsa-mir-16-2, hsa-miR-16-5p	3952	hsa-mir-30d, hsa-miR-30d-5p	1282
21.	hsa-mir-25, hsa-miR-25-3p	4482	hsa-mir-16-1, hsa-miR-16-5p	3952	hsa-mir-92a-2, hsa-miR-92a-3p	1262
22.	hsa-let-7b, hsa-let-7b-5p	3914	hsa-mir-423, hsa-miR-423-3p	3622	hsa-mir-150, hsa-miR-150-5p	1142
23.	hsa-mir-26b, hsa-miR-26b-5p	3618	hsa-mir-30d, hsa-miR-30d-5p	3517	hsa-let-7g, hsa-let-7g-5p	1003
24.	hsa-mir-30d, hsa-miR-30d-5p	3472	hsa-let-7i, hsa-let-7i-5p	3202	hsa-mir-182, hsa-miR-182-5p	1002
25.	hsa-mir-423, hsa-miR-423-3p	3198	hsa-mir-25, hsa-miR-25-3p	3111	hsa-mir-342, hsa-miR-342-3p	984
26.	hsa-let-7i, hsa-let-7i-5p	2631	hsa-mir-26b, hsa-miR-26b-5p	2816	hsa-mir-22, hsa-miR-22-3p	984
27.	hsa-mir-28, hsa-miR-28-3p	2187	hsa-mir-21, hsa-miR-21-5p	1973	hsa-mir-146a, hsa-miR-146a-5p	981
28.	hsa-mir-21, hsa-miR-21-5p	1929	hsa-mir-103a-2, hsa-miR-103a-3p	1961	hsa-mir-186, hsa-miR-186-5p	877
29.	hsa-mir-103a-2, hsa-miR-103a-3p	1915	hsa-mir-103a-1, hsa-miR-103a-3p	1958	hsa-mir-148a, hsa-miR-148a-3p	862
30.	hsa-mir-103a-1, hsa-miR-103a-3p	1910	hsa-let-7d, hsa-let-7d-5p	1922	hsa-mir-25, hsa-miR-25-3p	839
31.	hsa-mir-181b-2, hsa-miR-181b-5p	1848	hsa-mir-151a, hsa-miR-151a-5p	1753	hsa-mir-223, hsa-miR-223-3p	837
32.	hsa-mir-151a, hsa-miR-151a-5p	1793	hsa-mir-27b, hsa-miR-27b-3p	1563	hsa-mir-192, hsa-miR-192-5p	815
33.	hsa-mir-181b-1, hsa-miR-181b-5p	1788	hsa-mir-378a, hsa-miR-378a-3p	1468	hsa-mir-26b, hsa-miR-26b-5p	747
34.	hsa-mir-27b, hsa-miR-27b-3p	1732	hsa-mir-28, hsa-miR-28-3p	1454	hsa-let-7i, hsa-let-7i-5p	744
35.	hsa-mir-197, hsa-miR-197-3p	1729	hsa-mir-221, hsa-miR-221-3p	1395	hsa-mir-142, hsa-miR-142-3p	739
36.	hsa-mir-29a, hsa-miR-29a-3p	1641	hsa-mir-197, hsa-miR-197-3p	1373	hsa-mir-103a-2, hsa-miR-103a-3p	734
37.	hsa-let-7d, hsa-let-7d-5p	1472	hsa-mir-126, hsa-miR-126-5p	1337	hsa-mir-101-2, hsa-miR-101-3p	623
38.	hsa-mir-221, hsa-miR-221-3p	1429	hsa-mir-151a, hsa-miR-151a-3p	1150	hsa-mir-103a-1, hsa-miR-103a-3p	592
39.	hsa-mir-186, hsa-miR-186-5p	1424	hsa-mir-29a, hsa-miR-29a-3p	1098	hsa-mir-30c-2, hsa-miR-30c-5p	589
40.	hsa-mir-584, hsa-miR-584-5p	1399	hsa-mir-186, hsa-miR-186-5p	1018	hsa-mir-30c-1, hsa-miR-30c-5p	577
41.	hsa-mir-23a, hsa-miR-23a-3p	1219	hsa-mir-320a, hsa-miR-320a	980	hsa-mir-10a, hsa-miR-10a-5p	569
42.	hsa-mir-151a, hsa-miR-151a-3p	1052	hsa-mir-127, hsa-miR-127-3p	930	hsa-mir-101-1, hsa-miR-101-3p	569
43.	hsa-mir-27a, hsa-miR-27a-3p	1038	hsa-mir-181b-2, hsa-miR-181b-5p	896	hsa-mir-126, hsa-miR-126-5p	561
44.	hsa-mir-125a, hsa-miR-125a-5p	1009	hsa-mir-744, hsa-miR-744-5p	886	hsa-mir-98, hsa-miR-98-5p	556
45.	hsa-mir-342, hsa-miR-342-3p	957	hsa-mir-181b-1, hsa-miR-181b-5p	881	hsa-mir-151a, hsa-miR-151a-3p	547
46.	hsa-mir-126, hsa-miR-126-5p	956	hsa-mir-4286, hsa-miR-4286	879	hsa-mir-28, hsa-miR-28-3p	543
47.	hsa-mir-378a, hsa-miR-378a-3p	948	hsa-mir-223, hsa-miR-223-3p	835	hsa-mir-125a, hsa-miR-125a-5p	542
48.	hsa-mir-320a, hsa-miR-320a	940	hsa-mir-23a, hsa-miR-23a-3p	815	hsa-mir-93, hsa-miR-93-5p	511
49.	hsa-mir-4286, hsa-miR-4286	842	hsa-mir-27a, hsa-miR-27a-3p	813	hsa-mir-181b-2, hsa-miR-181b-5p	501
50.	hsa-mir-451a, hsa-miR-451a	835	hsa-mir-93, hsa-miR-93-5p	799	hsa-mir-143, hsa-miR-143-3p	493
51.	hsa-mir-181a-2, hsa-miR-181a-2-3p	819	hsa-mir-10a, hsa-miR-10a-5p	792	hsa-mir-181b-1, hsa-miR-181b-5p	492
52.	hsa-mir-107, hsa-miR-107	768	hsa-mir-107, hsa-miR-107	770	hsa-mir-140, hsa-miR-140-3p	488
53.	hsa-mir-140, hsa-miR-140-3p	759	hsa-mir-941-1, hsa-miR-941	669	hsa-mir-144, hsa-miR-144-5p	487
54.	hsa-mir-93, hsa-miR-93-5p	707	hsa-let-7d, hsa-let-7d-3p	650	hsa-mir-151a, hsa-miR-151a-5p	483
55.	hsa-let-7d, hsa-let-7d-3p	669	hsa-mir-222, hsa-miR-222-3p	631	hsa-mir-27b, hsa-miR-27b-3p	881
56.	hsa-mir-99b, hsa-miR-99b-5p	664	hsa-mir-148a, hsa-miR-148a-3p	574	hsa-mir-941-1, hsa-miR-941	478

57.	hsa-mir-30c-2, hsa-miR-30c-5p	654	hsa-mir-143, hsa-miR-143-3p	565	hsa-mir-181c, hsa-miR-181c-5p	472
58.	hsa-mir-30c-1, hsa-miR-30c-5p	653	hsa-mir-140, hsa-miR-140-3p	548	hsa-mir-29a, hsa-miR-29a-3p	467
59.	hsa-mir-223, hsa-miR-223-3p	652	hsa-mir-409, hsa-miR-409-3p	546	hsa-mir-423, hsa-miR-423-3p	461
60.	hsa-mir-92b, hsa-miR-92b-3p	643	hsa-mir-125a, hsa-miR-125a-5p	531	hsa-let-7b, hsa-let-7b-5p	449
61.	hsa-mir-146b, hsa-miR-146b-3p	620	hsa-mir-451a, hsa-miR-451a	528	hsa-mir-20a, hsa-miR-20a-5p	445
62.	hsa-mir-744, hsa-miR-744-5p	610	hsa-mir-15a, hsa-miR-15a-5p	513	hsa-mir-19b-2, hsa-miR-19b-3p	444
63.	hsa-mir-222, hsa-miR-222-3p	606	hsa-mir-30c-2, hsa-miR-30c-5p	512	hsa-mir-19b-1, hsa-miR-19b-3p	438
64.	hsa-mir-15a, hsa-miR-15a-5p	595	hsa-mir-30c-1, hsa-miR-30c-5p	512	hsa-mir-21, hsa-miR-21-3p	436
65.	hsa-mir-146b, hsa-miR-146b-5p	569	hsa-mir-584, hsa-miR-584-5p	471	hsa-mir-30b, hsa-miR-30b-5p	431
66.	hsa-mir-361, hsa-miR-361-3p	569	hsa-mir-98, hsa-miR-98-5p	452	hsa-mir-144, hsa-miR-144-3p	430
67.	hsa-mir-155, hsa-miR-155-5p	549	hsa-mir-342, hsa-miR-342-3p	442	hsa-mir-155, hsa-miR-155-5p	427
68.	hsa-mir-10a, hsa-miR-10a-5p	541	hsa-mir-199a-2, hsa-miR-199a-3p	436	hsa-mir-425, hsa-miR-425-5p	422
69.	hsa-mir-148a, hsa-miR-148a-3p	530	hsa-mir-199a-1, hsa-miR-199a-3p	436	hsa-mir-99b, hsa-miR-99b-5p	417
70.	hsa-mir-23b, hsa-miR-23b-3p	503	hsa-mir-199b, hsa-miR-199b-3p	436	hsa-mir-340, hsa-miR-340-5p	402
71.	hsa-mir-106b, hsa-miR-106b-3p	487	hsa-mir-15b, hsa-miR-15b-5p	436	hsa-mir-378a, hsa-miR-378a-3p	382
72.	hsa-mir-941-1, hsa-miR-941	464	hsa-mir-92b, hsa-miR-92b-3p	424	hsa-let-7d, hsa-let-7d-5p	379
73.	hsa-mir-15b, hsa-miR-15b-5p	439	hsa-mir-484, hsa-miR-484	421	hsa-mir-423, hsa-miR-423-5p	378
74.	hsa-mir-199a-2, hsa-miR-199a-3p	433	hsa-let-7c, hsa-let-7c	399	hsa-mir-221, hsa-miR-221-3p	369
75.	hsa-mir-199a-1, hsa-miR-199a-3p	433	hsa-let-7e, hsa-let-7e-5p	382	hsa-mir-183, hsa-miR-183-5p	364
76.	hsa-mir-199b, hsa-miR-199b-3p	433	hsa-mir-106b, hsa-miR-106b-3p	380	hsa-mir-27a, hsa-miR-27a-3p	361
77.	hsa-mir-101-2, hsa-miR-101-3p	431	hsa-mir-23b, hsa-miR-23b-3p	363	hsa-mir-363, hsa-miR-363-3p	359
78.	hsa-mir-484, hsa-miR-484	430	hsa-mir-101-2, hsa-miR-101-3p	349	hsa-mir-484, hsa-miR-484	359
79.	hsa-mir-101-1, hsa-miR-101-3p	429	hsa-mir-146a, hsa-miR-146a-5p	345	hsa-mir-17, hsa-miR-17-5p	355
80.	hsa-mir-5701-1, hsa-miR-5701	416	hsa-mir-101-1, hsa-miR-101-3p	344	hsa-mir-15a, hsa-miR-15a-5p	346
81.	hsa-mir-5701-2, hsa-miR-5701	416	hsa-mir-146b, hsa-miR-146b-3p	332	hsa-mir-15b, hsa-miR-15b-5p	346
82.	hsa-mir-192, hsa-miR-192-5p	375	hsa-mir-126, hsa-miR-126-3p	315	hsa-mir-222, hsa-miR-222-3p	336
83.	hsa-let-7c, hsa-let-7c	362	hsa-mir-30e, hsa-miR-30e-5p	310	hsa-mir-1307, hsa-miR-1307-5p	334
84.	hsa-mir-146a, hsa-miR-146a-5p	360	hsa-mir-654, hsa-miR-654-3p	308	hsa-mir-320a, hsa-miR-320a	332
85.	hsa-mir-1260b, hsa-miR-1260b	342	hsa-mir-652, hsa-miR-652-3p	301	hsa-mir-301a, hsa-miR-301a-3p	330
86.	hsa-mir-342, hsa-miR-342-5p	341	hsa-mir-128-1, hsa-miR-128	290	hsa-mir-30e, hsa-miR-30e-3p	328
87.	hsa-mir-363, hsa-miR-363-3p	335	hsa-mir-155, hsa-miR-155-5p	287	hsa-mir-148b, hsa-miR-148b-3p	324
88.	hsa-mir-128-1, hsa-miR-128	329	hsa-mir-361, hsa-miR-361-3p	285	hsa-mir-361, hsa-miR-361-3p	322
89.	hsa-mir-143, hsa-miR-143-3p	308	hsa-mir-5701-1, hsa-miR-5701	269	hsa-mir-106b, hsa-miR-106b-3p	313
90.	hsa-mir-98, hsa-miR-98-5p	305	hsa-mir-5701-2, hsa-miR-5701	269	hsa-mir-23a, hsa-miR-23a-3p	305
91.	hsa-mir-30e, hsa-miR-30e-5p	297	hsa-mir-128-2, hsa-miR-128	261	hsa-mir-197, hsa-miR-197-3p	299
92.	hsa-mir-3607, hsa-miR-3607-3p	296	hsa-mir-342, hsa-miR-342-5p	254	hsa-mir-141, hsa-miR-141-3p	275
93.	hsa-mir-128-2, hsa-miR-128	296	hsa-mir-146b, hsa-miR-146b-5p	251	hsa-mir-454, hsa-miR-454-3p	256
94.	hsa-mir-28, hsa-miR-28-5p	292	hsa-mir-1260b, hsa-miR-1260b	243	hsa-mir-107, hsa-miR-107	256
95.	hsa-let-7e, hsa-let-7e-5p	285	hsa-mir-192, hsa-miR-192-5p	240	hsa-mir-500a, hsa-miR-500a-3p	254
96.	hsa-mir-652, hsa-miR-652-3p	271	hsa-mir-181a-2, hsa-miR-181a-2-3p	239	hsa-mir-146b, hsa-miR-146b-3p	215
97.	hsa-mir-425, hsa-miR-425-5p	266	hsa-mir-99b, hsa-miR-99b-5p	237	hsa-mir-181a-1, hsa-miR-181a-3p	214
98.	hsa-mir-150, hsa-miR-150-3p	248	hsa-mir-425, hsa-miR-425-5p	220	hsa-mir-769, hsa-miR-769-5p	211
99.	hsa-mir-126, hsa-miR-126-3p	244	hsa-mir-363, hsa-miR-363-3p	219	hsa-mir-29c, hsa-miR-29c-3p	177
100.	hsa-mir-30b, hsa-miR-30b-5p	227	hsa-mir-148b, hsa-miR-148b-3p	217	hsa-mir-19a, hsa-miR-19a-3p	170
101.	hsa-mir-148b, hsa-miR-148b-3p	226	hsa-mir-3607, hsa-miR-3607-3p	217	hsa-mir-126, hsa-miR-126-3p	167
102.	hsa-mir-30e, hsa-miR-30e-3p	193	hsa-mir-23a, hsa-miR-23a-5p	200	hsa-mir-28, hsa-miR-28-5p	157
103.	hsa-mir-130a, hsa-miR-130a-3p	175	hsa-mir-410, hsa-miR-410	198	hsa-mir-874, hsa-miR-874	157
104.	hsa-mir-671, hsa-miR-671-3p	151	hsa-mir-1307, hsa-miR-1307-3p	198	hsa-mir-29b-2, hsa-miR-29b-3p	157
105.	hsa-mir-589, hsa-miR-589-5p	150	hsa-mir-28, hsa-miR-28-5p	194	hsa-mir-30a, hsa-miR-30a-5p	156
106.	hsa-mir-151b, hsa-miR-151b	146	hsa-mir-150, hsa-miR-150-3p	189	hsa-mir-29b-1, hsa-miR-29b-3p	156
107.	hsa-mir-1307, hsa-miR-1307-3p	142	hsa-mir-30b, hsa-miR-30b-5p	184	hsa-mir-374a, hsa-miR-374a-3p	147
108.	hsa-mir-182, hsa-miR-182-5p	135	hsa-mir-151b, hsa-miR-151b	176	hsa-mir-199a-2, hsa-miR-199a-3p	138
109.	hsa-mir-181a-1, hsa-miR-181a 3p	131	hsa-mir-30e, hsa-miR-30e-3p	174	hsa-mir-199a-1, hsa-miR-199a-3p	137
110.	hsa-mir-361, hsa-miR-361-5p	123	hsa-mir-589, hsa-miR-589-5p	170	hsa-mir-199b, hsa-miR-199b-3p	137
111.	hsa-mir-766, hsa-miR-766-3p	121	hsa-mir-130a, hsa-miR-130a-3p	165	hsa-mir-532, hsa-miR-532-5p	133
112.	hsa-mir-181c, hsa-miR-181c-5p	120	hsa-mir-181c, hsa-miR-181c-5p	152	hsa-mir-130a, hsa-miR-130a-3p	131
113.	hsa-mir-574, hsa-miR-574-3p	110	hsa-mir-671, hsa-miR-671-3p	134	hsa-mir-24-2, hsa-miR-24-3p	129
114.	hsa-mir-21, hsa-miR-21-3p	108	hsa-mir-21, hsa-miR-21-3p	125	hsa-mir-24-1, hsa-miR-24-3p	129
115.	hsa-mir-31, hsa-miR-31-5p	106	hsa-mir-431, hsa-miR-431-5p	115	hsa-mir-660, hsa-miR-660-5p	127
116.	hsa-mir-339, hsa-miR-339-3p	104	hsa-mir-3615, hsa-miR-3615	111	hsa-mir-374a, hsa-miR-374a-5p	122
117.	hsa-mir-1275, hsa-miR-1275	103	hsa-mir-574, hsa-miR-574-3p	111	hsa-mir-501, hsa-miR-501-3p	121
118.	hsa-let-7i, hsa-let-7i-3p	101	hsa-mir-31, hsa-miR-31-5p	110	hsa-mir-185, hsa-miR-185-5p	119
119.			hsa-mir-769, hsa-miR-769-5p	109	hsa-mir-20b, hsa-miR-20b-5p	118
120.			hsa-mir-532, hsa-miR-532-5p	103	hsa-mir-106b, hsa-miR-106b-5p	117
121.					hsa-mir-92b, hsa-miR-92b-3p	114
122.					hsa-mir-361, hsa-miR-361-5p	113

123.		hsa-mir-148b, hsa-miR-148b-5p	111
124.		hsa-mir-362, hsa-miR-362-5p	107
125.		hsa-mir-194-2, hsa-miR-194-5p	107
126.		hsa-mir-7-1, hsa-miR-7-5p	106
127.		hsa-mir-7-3, hsa-miR-7-5p	105
128.		hsa-mir-7-2, hsa-miR-7-5p	103

TABLE E3: microRNA Reads in Patients with HLH

No.	HLH-2A		HLH-20		HLH-21		HLH-28	
	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads
1.	hsa-mir-486, hsa-miR-486-5p	223798	hsa-mir-486, hsa-miR-486-5p	49196	hsa-mir-486, hsa-miR-486-5p	343775	hsa-mir-486, hsa-miR-486-5p	123179
2.	hsa-mir-181a-2, hsa-miR-181a-5p	76988	hsa-mir-181a-1, hsa-miR-181a-5p	47133	hsa-mir-181a-1, hsa-miR-181a-5p	96995	hsa-mir-181a-1, hsa-miR-181a-5p	73173
3.	hsa-mir-181a-1, hsa-miR-181a-5p	76987	hsa-mir-181a-2, hsa-miR-181a-5p	47133	hsa-mir-181a-2, hsa-miR-181a-5p	96995	hsa-mir-181a-2, hsa-miR-181a-5p	73173
4.	hsa-mir-92a-1, hsa-miR-92a-3p	49116	hsa-mir-191, hsa-miR-191-5p	29592	hsa-mir-92a-1, hsa-miR-92a-3p	66385	hsa-mir-92a-1, hsa-miR-92a-3p	33175
5.	hsa-mir-92a-2, hsa-miR-92a-3p	44287	hsa-let-7a-1, hsa-let-7a-5p	28591	hsa-mir-92a-2, hsa-miR-92a-3p	60258	hsa-mir-92a-2, hsa-miR-92a-3p	29832
6.	hsa-mir-150, hsa-miR-150-5p	19069	hsa-let-7a-3, hsa-let-7a-5p	28585	hsa-let-7a-1, hsa-let-7a-5p	38368	hsa-mir-150, hsa-miR-150-5p	17578
7.	hsa-let-7a-1, hsa-let-7a-5p	16604	hsa-let-7a-2, hsa-let-7a-5p	28579	hsa-let-7a-3, hsa-let-7a-5p	38364	hsa-mir-142, hsa-miR-142-5p	12152
8.	hsa-let-7a-3, hsa-let-7a-5p	16601	hsa-mir-92a-1, hsa-miR-92a-3p	25188	hsa-let-7a-2, hsa-let-7a-5p	38358	hsa-let-7a-2, hsa-let-7a-5p	8046
9.	hsa-let-7a-2, hsa-let-7a-5p	16600	hsa-mir-92a-2, hsa-miR-92a-3p	22523	hsa-mir-150, hsa-miR-150-5p	32534	hsa-let-7a-3, hsa-let-7a-5p	8045
10.	hsa-mir-142, hsa-miR-142-5p	13844	hsa-mir-143, hsa-miR-143-3p	14426	hsa-mir-16-1, hsa-miR-16-5p	16541	hsa-let-7a-1, hsa-let-7a-5p	8045
11.	hsa-mir-16-2, hsa-miR-16-5p	11026	hsa-mir-26a-2, hsa-miR-26a-5p	9758	hsa-mir-16-2, hsa-miR-16-5p	16538	hsa-mir-451a, hsa-miR-451a	5504
12.	hsa-mir-16-1, hsa-miR-16-5p	11025	hsa-mir-26a-1, hsa-miR-26a-5p	9758	hsa-let-7f-2, hsa-let-7f-5p	14848	hsa-mir-22, hsa-miR-22-3p	5362
13.	hsa-mir-22, hsa-miR-22-3p	8276	hsa-mir-423, hsa-miR-423-3p	9617	hsa-let-7f-1, hsa-let-7f-5p	14689	hsa-mir-16-2, hsa-miR-16-5p	5315
14.	hsa-let-7f-2, hsa-let-7f-5p	7385	hsa-mir-22, hsa-miR-22-3p	8850	hsa-mir-26a-2, hsa-miR-26a-5p	14654	hsa-mir-16-1, hsa-miR-16-5p	5315
15.	hsa-let-7f-1, hsa-let-7f-5p	7329	hsa-mir-25, hsa-miR-25-3p	8367	hsa-mir-26a-1, hsa-miR-26a-5p	14653	hsa-mir-26a-2, hsa-miR-26a-5p	3927
16.	hsa-mir-451a, hsa-miR-451a	7225	hsa-mir-16-2, hsa-miR-16-5p	7791	hsa-mir-191, hsa-miR-191-5p	13227	hsa-mir-26a-1, hsa-miR-26a-5p	3927
17.	hsa-mir-26a-2, hsa-miR-26a-5p	6737	hsa-mir-16-1, hsa-miR-16-5p	7791	hsa-mir-142, hsa-miR-142-5p	12567	hsa-mir-25, hsa-miR-25-3p	3920
18.	hsa-mir-26a-1, hsa-miR-26a-5p	6737	hsa-mir-4286, hsa-miR-4286	5800	hsa-mir-22, hsa-miR-22-3p	12337	hsa-mir-191, hsa-miR-191-5p	3723
19.	hsa-mir-25, hsa-miR-25-3p	5839	hsa-mir-423, hsa-miR-423-5p	4919	hsa-let-7g, hsa-let-7g-5p	12171	hsa-mir-21, hsa-miR-21-5p	3723
20.	hsa-mir-191, hsa-miR-191-5p	5001	hsa-mir-197, hsa-miR-197-3p	4687	hsa-mir-25, hsa-miR-25-3p	11789	hsa-let-7i, hsa-let-7i-5p	3194
21.	hsa-let-7g, hsa-let-7g-5p	4753	hsa-let-7b, hsa-let-7b-5p	4668	hsa-mir-103a-2, hsa-miR-103a-3p	10092	hsa-let-7g, hsa-let-7g-5p	2981
22.	hsa-mir-21, hsa-miR-21-5p	4657	hsa-mir-150, hsa-miR-150-5p	4552	hsa-mir-103a-1, hsa-miR-103a-3p	10090	hsa-mir-423, hsa-miR-423-5p	2962
23.	hsa-mir-423, hsa-miR-423-5p	4278	hsa-let-7i, hsa-let-7i-5p	4490	hsa-mir-451a, hsa-miR-451a	8700	hsa-mir-103a-2, hsa-miR-103a-3p	2903
24.	hsa-let-7i, hsa-let-7i-5p	4049	hsa-mir-223, hsa-miR-223-3p	4176	hsa-let-7i, hsa-let-7i-5p	8013	hsa-mir-103a-1, hsa-miR-103a-3p	2903
25.	hsa-mir-103a-2, hsa-miR-103a-3p	3861	hsa-let-7f-2, hsa-let-7f-5p	3893	hsa-mir-107, hsa-miR-107	7823	hsa-let-7f-2, hsa-let-7f-5p	2838
26.	hsa-mir-103a-1, hsa-miR-103a-3p	3860	hsa-let-7f-1, hsa-let-7f-5p	3841	hsa-mir-423, hsa-miR-423-5p	5490	hsa-let-7f-1, hsa-let-7f-5p	2818
27.	hsa-mir-107, hsa-miR-107	2803	hsa-let-7g, hsa-let-7g-5p	3639	hsa-mir-423, hsa-miR-423-3p	5483	hsa-mir-181b-2, hsa-miR-181b-5p	2472
28.	hsa-mir-423, hsa-miR-423-3p	2741	hsa-mir-221, hsa-miR-221-3p	3606	hsa-mir-30d, hsa-miR-30d-5p	5185	hsa-mir-181b-1, hsa-miR-181b-5p	2465
29.	hsa-mir-181b-2, hsa-miR-181b-5p	2686	hsa-mir-27a, hsa-miR-27a-3p	3298	hsa-mir-26b, hsa-miR-26b-5p	4673	hsa-mir-423, hsa-miR-423-3p	2315
30.	hsa-mir-181b-1, hsa-miR-181b-5p	2672	hsa-mir-23a, hsa-miR-23a-3p	3082	hsa-mir-93, hsa-miR-93-5p	3387	hsa-mir-107, hsa-miR-107	2203
31.	hsa-mir-30d, hsa-miR-30d-5p	2240	hsa-mir-103a-2, hsa-miR-103a-3p	2958	hsa-mir-15a, hsa-miR-15a-5p	3063	hsa-mir-143, hsa-miR-143-3p	1848
32.	hsa-mir-15a, hsa-miR-15a-5p	2075	hsa-mir-103a-1, hsa-miR-103a-3p	2951	hsa-mir-378a, hsa-miR-378a-3p	3008	hsa-mir-30d, hsa-miR-30d-5p	1715
33.	hsa-mir-143, hsa-miR-143-3p	1989	hsa-mir-21, hsa-miR-21-5p	2919	hsa-let-7d, hsa-let-7d-5p	2936	hsa-mir-21, hsa-miR-21-3p	1524
34.	hsa-mir-223, hsa-miR-223-3p	1976	hsa-mir-451a, hsa-miR-451a	2786	hsa-mir-106b, hsa-miR-106b-3p	2733	hsa-mir-320a, hsa-miR-320a	1441
35.	hsa-mir-27a, hsa-miR-27a-3p	1958	hsa-mir-92b, hsa-miR-92b-3p	2549	hsa-mir-27b, hsa-miR-27b-3p	2555	hsa-mir-92b, hsa-miR-92b-3p	1388
36.	hsa-mir-320a, hsa-miR-320a	1937	hsa-mir-30d, hsa-miR-30d-5p	2496	hsa-mir-21, hsa-miR-21-5p	2504	hsa-mir-223, hsa-miR-223-3p	1373

37.	hsa-mir-92b, hsa-miR-92b-3p	1650	hsa-mir-142, hsa-miR-142-5p	2455	hsa-mir-181b-2, hsa-miR-181b-5p	2491	hsa-mir-27a, hsa-miR-27a-3p	1371
38.	hsa-mir-106b, hsa-miR-106b-3p	1581	hsa-let-7d, hsa-let-7d-5p	2372	hsa-mir-181b-1, hsa-miR-181b-5p	2445	hsa-mir-106b, hsa-miR-106b-3p	1238
39.	hsa-mir-93, hsa-miR-93-5p	1510	hsa-mir-15b, hsa-miR-15b-5p	2332	hsa-mir-151a, hsa-miR-151a-5p	2386	hsa-mir-93, hsa-miR-93-5p	1062
40.	hsa-mir-26b, hsa-miR-26b-5p	1502	hsa-mir-148a, hsa-miR-148a-3p	2310	hsa-let-7b, hsa-let-7b-5p	2157	hsa-mir-4286, hsa-miR-4286	1037
41.	hsa-let-7b, hsa-let-7b-5p	1479	hsa-mir-93, hsa-miR-93-5p	2132	hsa-mir-186, hsa-miR-186-5p	2090	hsa-mir-27b, hsa-miR-27b-3p	1024
42.	hsa-mir-21, hsa-miR-21-3p	1437	hsa-mir-941-1, hsa-miR-941	2116	hsa-mir-28, hsa-miR-28-3p	1946	hsa-mir-15a, hsa-miR-15a-5p	992
43.	hsa-mir-27b, hsa-miR-27b-3p	1417	hsa-mir-106b, hsa-miR-106b-3p	1842	hsa-mir-221, hsa-miR-221-3p	1757	hsa-mir-186, hsa-miR-186-5p	980
44.	hsa-mir-192, hsa-miR-192-5p	1233	hsa-mir-140, hsa-miR-140-3p	1712	hsa-mir-223, hsa-miR-223-3p	1682	hsa-mir-101-2, hsa-miR-101-3p	929
45.	hsa-mir-101-2, hsa-miR-101-3p	1219	hsa-mir-26b, hsa-miR-26b-5p	1667	hsa-mir-320a, hsa-miR-320a	1644	hsa-mir-101-1, hsa-miR-101-3p	925
46.	hsa-mir-101-1, hsa-miR-101-3p	1215	hsa-mir-378a, hsa-miR-378a-3p	1623	hsa-mir-92b, hsa-miR-92b-3p	1614	hsa-let-7b, hsa-let-7b-5p	905
47.	hsa-let-7d, hsa-let-7d-5p	1199	hsa-mir-28, hsa-miR-28-3p	1557	hsa-mir-363, hsa-miR-363-3p	1599	hsa-mir-221, hsa-miR-221-3p	819
48.	hsa-mir-4286, hsa-miR-4286	1124	hsa-mir-107, hsa-miR-107	1555	hsa-mir-15b, hsa-miR-15b-5p	1426	hsa-mir-363, hsa-miR-363-3p	775
49.	hsa-mir-186, hsa-miR-186-5p	1019	hsa-mir-27b, hsa-miR-27b-3p	1530	hsa-mir-27a, hsa-miR-27a-3p	1407	hsa-mir-23a, hsa-miR-23a-3p	769
50.	hsa-mir-197, hsa-miR-197-3p	1001	hsa-let-7d, hsa-let-7d-3p	1450	hsa-mir-140, hsa-miR-140-3p	1377	hsa-mir-29a, hsa-miR-29a-3p	747
51.	hsa-mir-144, hsa-miR-144-3p	981	hsa-mir-186, hsa-miR-186-5p	1428	hsa-mir-101-2, hsa-miR-101-3p	1336	hsa-mir-197, hsa-miR-197-3p	725
52.	hsa-mir-378a, hsa-miR-378a-3p	969	hsa-mir-222, hsa-miR-222-3p	1337	hsa-mir-101-1, hsa-miR-101-3p	1327	hsa-mir-28, hsa-miR-28-3p	720
53.	hsa-mir-363, hsa-miR-363-3p	965	hsa-mir-424, hsa-miR-424-3p	1257	hsa-mir-29a, hsa-miR-29a-3p	1269	hsa-mir-192, hsa-miR-192-5p	713
54.	hsa-mir-30e, hsa-miR-30e-5p	942	hsa-mir-320a, hsa-miR-320a	1123	hsa-mir-143, hsa-miR-143-3p	1256	hsa-mir-30e, hsa-miR-30e-5p	710
55.	hsa-mir-1260b, hsa-miR-1260b	898	hsa-mir-30c-2, hsa-miR-30c-5p	1023	hsa-mir-192, hsa-miR-192-5p	1240	hsa-mir-148a, hsa-miR-148a-3p	709
56.	hsa-mir-148a, hsa-miR-148a-3p	890	hsa-mir-30c-1, hsa-miR-30c-5p	1023	hsa-mir-30e, hsa-miR-30e-5p	1237	hsa-mir-144, hsa-miR-144-3p	699
57.	hsa-mir-221, hsa-miR-221-3p	777	hsa-mir-425, hsa-miR-425-5p	964	hsa-mir-652, hsa-miR-652-3p	1128	hsa-mir-26b, hsa-miR-26b-5p	667
58.	hsa-mir-144, hsa-miR-144-5p	776	hsa-mir-425, hsa-miR-425-5p	964	hsa-mir-652, hsa-miR-652-3p	1128	hsa-mir-26b, hsa-miR-26b-5p	667
59.	hsa-mir-151a, hsa-miR-151a-5p	760	hsa-mir-21, hsa-miR-21-3p	948	hsa-mir-4286, hsa-miR-4286	1120	hsa-let-7d, hsa-let-7d-5p	645
60.	hsa-mir-28, hsa-miR-28-3p	714	hsa-mir-23b, hsa-miR-23b-3p	918	hsa-mir-148a, hsa-miR-148a-3p	1110	hsa-mir-151a, hsa-miR-151a-5p	537
61.	hsa-mir-29a, hsa-miR-29a-3p	702	hsa-mir-181b-2, hsa-miR-181b-5p	764	hsa-mir-151a, hsa-miR-151a-3p	1083	hsa-mir-146b, hsa-miR-146b-3p	505
62.	hsa-mir-652, hsa-miR-652-3p	689	hsa-mir-181b-1, hsa-miR-181b-5p	749	hsa-mir-126, hsa-miR-126-5p	1040	hsa-mir-652, hsa-miR-652-3p	505
63.	hsa-mir-15b, hsa-miR-15b-5p	661	hsa-mir-15a, hsa-miR-15a-5p	683	hsa-mir-941-1, hsa-miR-941	1039	hsa-mir-140, hsa-miR-140-3p	489
64.	hsa-mir-486, hsa-miR-486-3p	650	hsa-mir-3615, hsa-miR-3615	666	hsa-mir-23a, hsa-miR-23a-3p	972	hsa-mir-484, hsa-miR-484	484
65.	hsa-let-7d, hsa-let-7d-3p	584	hsa-mir-128-1, hsa-miR-128	636	hsa-mir-484, hsa-miR-484	966	hsa-mir-342, hsa-miR-342-3p	480
66.	hsa-mir-126, hsa-miR-126-5p	578	hsa-mir-128-2, hsa-miR-128	611	hsa-let-7d, hsa-let-7d-3p	956	hsa-let-7d, hsa-let-7d-3p	448
67.	hsa-mir-140, hsa-miR-140-3p	577	hsa-mir-652, hsa-miR-652-3p	574	hsa-mir-30c-2, hsa-miR-30c-5p	863	hsa-mir-23b, hsa-miR-23b-3p	432
68.	hsa-mir-484, hsa-miR-484	531	hsa-mir-29a, hsa-miR-29a-3p	571	hsa-mir-30c-1, hsa-miR-30c-5p	863	hsa-mir-1260b, hsa-miR-1260b	412
69.	hsa-mir-155, hsa-miR-155-5p	527	hsa-mir-345, hsa-miR-345-5p	549	hsa-mir-128-1, hsa-miR-128	859	hsa-mir-15b, hsa-miR-15b-5p	387
70.	hsa-mir-424, hsa-miR-424-3p	521	hsa-mir-484, hsa-miR-484	495	hsa-mir-128-2, hsa-miR-128	834	hsa-mir-424, hsa-miR-424-3p	377
71.	hsa-mir-23b, hsa-miR-23b-3p	477	hsa-mir-148b, hsa-miR-148b-3p	464	hsa-mir-144, hsa-miR-144-5p	795	hsa-mir-361, hsa-miR-361-3p	352
72.	hsa-mir-128-1, hsa-miR-128	431	hsa-mir-30e, hsa-miR-30e-5p	393	hsa-mir-361, hsa-miR-361-3p	790	hsa-mir-146b, hsa-miR-146b-5p	350
73.	hsa-mir-146b, hsa-miR-146b-3p	430	hsa-mir-146b, hsa-miR-146b-5p	387	hsa-mir-155, hsa-miR-155-5p	692	hsa-mir-941-1, hsa-miR-941	328
74.	hsa-mir-16-2, hsa-miR-16-2-3p	425	hsa-mir-181c, hsa-miR-181c-5p	369	hsa-mir-127, hsa-miR-127-3p	690	hsa-mir-125a, hsa-miR-125a-5p	325
75.	hsa-mir-128-2, hsa-miR-128	422	hsa-mir-146b, hsa-miR-146b-3p	367	hsa-mir-424, hsa-miR-424-3p	671	hsa-mir-144, hsa-miR-144-5p	324

76.	hsa-mir-146b, hsa-miR-146b-5p	416	hsa-mir-589, hsa-miR-589-5p	334	hsa-mir-486, hsa-miR-486-3p	669	hsa-mir-128-1, hsa-miR-128	321
77.	hsa-mir-342, hsa-miR-342-3p	416	hsa-mir-199a-2, hsa-miR-199a-3p	329	hsa-mir-144, hsa-miR-144-3p	650	hsa-mir-486, hsa-miR-486-3p	316
78.	hsa-mir-151a, hsa-miR-151a-3p	412	hsa-mir-199a-1, hsa-miR-199a-3p	328	hsa-mir-342, hsa-miR-342-3p	636	hsa-mir-128-2, hsa-miR-128	316
79.	hsa-mir-941-1, hsa-miR-941	405	hsa-mir-199b, hsa-miR-199b-3p	328	hsa-mir-98, hsa-miR-98-5p	623	hsa-mir-142, hsa-miR-142-3p	310
80.	hsa-mir-30c-2, hsa-miR-30c-5p	403	hsa-mir-99b, hsa-miR-99b-5p	322	hsa-mir-146b, hsa-miR-146b-5p	601	hsa-mir-126, hsa-miR-126-5p	284
81.	hsa-mir-30c-1, hsa-miR-30c-5p	403	hsa-mir-30e, hsa-miR-30e-3p	306	hsa-mir-584, hsa-miR-584-5p	580	hsa-mir-155, hsa-miR-155-5p	275
82.	hsa-mir-125a, hsa-miR-125a-5p	337	hsa-mir-182, hsa-miR-182-5p	304	hsa-mir-146b, hsa-miR-146b-3p	537	hsa-mir-181c, hsa-miR-181c-5p	246
83.	hsa-mir-130a, hsa-miR-130a-3p	335	hsa-mir-574, hsa-miR-574-3p	285	hsa-mir-222, hsa-miR-222-3p	537	hsa-mir-16-2, hsa-miR-16-2-3p	241
84.	hsa-mir-425, hsa-miR-425-5p	325	hsa-mir-363, hsa-miR-363-3p	284	hsa-mir-182, hsa-miR-182-5p	536	hsa-mir-151a, hsa-miR-151a-3p	241
85.	hsa-mir-361, hsa-miR-361-3p	322	hsa-mir-155, hsa-miR-155-5p	263	hsa-mir-744, hsa-miR-744-5p	504	hsa-mir-425, hsa-miR-425-5p	235
86.	hsa-mir-320b-2, hsa-miR-320b	305	hsa-mir-744, hsa-miR-744-5p	255	hsa-mir-130a, hsa-miR-130a-3p	487	hsa-mir-320b-2, hsa-miR-320b	217
87.	hsa-mir-320b-1, hsa-miR-320b	303	hsa-mir-24-2, hsa-miR-24-3p	253	hsa-mir-1260b, hsa-miR-1260b	475	hsa-mir-320b-1, hsa-miR-320b	217
88.	hsa-let-7c, hsa-let-7c	280	hsa-mir-24-1, hsa-miR-24-3p	253	hsa-mir-23b, hsa-miR-23b-3p	454	hsa-mir-150, hsa-miR-150-3p	215
89.	hsa-mir-148b, hsa-miR-148b-3p	274	hsa-mir-1307, hsa-miR-1307-3p	250	hsa-mir-5701-1, hsa-miR-5701	451	hsa-mir-30c-2, hsa-miR-30c-5p	209
90.	hsa-mir-127, hsa-miR-127-3p	246	hsa-mir-192, hsa-miR-192-5p	237	hsa-mir-5701-2, hsa-miR-5701	451	hsa-mir-30c-1, hsa-miR-30c-5p	209
91.	hsa-mir-142, hsa-miR-142-3p	236	hsa-mir-769, hsa-miR-769-5p	219	hsa-let-7c, hsa-let-7c	435	hsa-mir-148b, hsa-miR-148b-3p	208
92.	hsa-mir-181c, hsa-miR-181c-5p	231	hsa-mir-151a, hsa-miR-151a-5p	217	hsa-mir-181a-1, hsa-miR-181a-3p	432	hsa-mir-181a-1, hsa-miR-181a-3p	204
93.	hsa-mir-98, hsa-miR-98-5p	225	hsa-mir-145, hsa-miR-145-5p	194	hsa-mir-3607, hsa-miR-3607-3p	420	hsa-mir-342, hsa-miR-342-5p	186
94.	hsa-mir-181a-1, hsa-miR-181a-3p	215	hsa-mir-130b, hsa-miR-130b-3p	185	hsa-mir-151b, hsa-miR-151b	419	hsa-mir-222, hsa-miR-222-3p	175
95.	hsa-mir-30b, hsa-miR-30b-5p	215	hsa-mir-361, hsa-miR-361-5p	175	hsa-mir-16-2, hsa-miR-16-2-3p	405	hsa-mir-130a, hsa-miR-130a-3p	173
96.	hsa-mir-182, hsa-miR-182-5p	206	hsa-mir-361, hsa-miR-361-3p	175	hsa-mir-148b, hsa-miR-148b-3p	399	hsa-mir-1307, hsa-miR-1307-3p	170
97.	hsa-mir-106b, hsa-miR-106b-5p	202	hsa-let-7i, hsa-let-7i-3p	175	hsa-mir-146a, hsa-miR-146a-5p	362	hsa-mir-127, hsa-miR-127-3p	161
98.	hsa-mir-1268b, hsa-miR-1268b	198	hsa-mir-130b, hsa-miR-130b-5p	168	hsa-mir-30b, hsa-miR-30b-5p	352	hsa-mir-4485, hsa-miR-4485	150
99.	hsa-mir-342, hsa-miR-342-5p	196	hsa-mir-671, hsa-miR-671-3p	160	hsa-mir-106b, hsa-miR-106b-5p	330	hsa-mir-3615, hsa-miR-3615	145
100.	hsa-mir-1268a, hsa-miR-1268a	191	hsa-mir-181a-1, hsa-miR-181a-3p	159	hsa-mir-199a-2, hsa-miR-199a-3p	322	hsa-mir-10a, hsa-miR-10a-5p	143
101.	hsa-mir-1307, hsa-miR-1307-3p	187	hsa-mir-101-2, hsa-miR-101-3p	147	hsa-mir-199a-1, hsa-miR-199a-3p	322	hsa-mir-1307, hsa-miR-1307-5p	140
102.	hsa-mir-3615, hsa-miR-3615	183	hsa-mir-101-1, hsa-miR-101-3p	146	hsa-mir-199b, hsa-miR-199b-3p	322	hsa-mir-182, hsa-miR-182-5p	138
103.	hsa-mir-584, hsa-miR-584-5p	177	hsa-mir-30b, hsa-miR-30b-5p	146	hsa-mir-1307, hsa-miR-1307-3p	322	hsa-mir-5701-1, hsa-miR-5701	129
104.	hsa-mir-99b, hsa-miR-99b-5p	173	hsa-mir-342, hsa-miR-342-3p	142	hsa-mir-409, hsa-miR-409-3p	321	hsa-mir-5701-2, hsa-miR-5701	129
105.	hsa-mir-126, hsa-miR-126-3p	167	hsa-mir-500a, hsa-miR-500a-3p	139	hsa-mir-21, hsa-miR-21-3p	308	hsa-mir-30b, hsa-miR-30b-5p	128
106.	hsa-mir-222, hsa-miR-222-3p	161	hsa-let-7c, hsa-let-7c	138	hsa-mir-532, hsa-miR-532-5p	303	hsa-mir-106b, hsa-miR-106b-5p	128
107.	hsa-mir-150, hsa-miR-150-3p	159	hsa-mir-505, hsa-miR-505-3p	138	hsa-mir-126, hsa-miR-126-3p	279	hsa-mir-1268b, hsa-miR-1268b	127
108.	hsa-mir-744, hsa-miR-744-5p	158	hsa-mir-193a, hsa-miR-193a-5p	136	hsa-mir-150, hsa-miR-150-3p	278	hsa-mir-19b-1, hsa-miR-19b-3p	127
109.	hsa-mir-378c, hsa-miR-378c	157	hsa-mir-16-2, hsa-miR-16-2-3p	133	hsa-mir-342, hsa-miR-342-5p	277	hsa-mir-19b-2, hsa-miR-19b-3p	127
110.	hsa-mir-532, hsa-miR-532-5p	153	hsa-mir-5701-1, hsa-miR-5701	131	hsa-mir-125a, hsa-miR-125a-5p	273	hsa-mir-146a, hsa-miR-146a-5p	122
111.	hsa-mir-589, hsa-miR-589-5p	151	hsa-mir-5701-2, hsa-miR-5701	131	hsa-mir-30e, hsa-miR-30e-3p	268	hsa-let-7c, hsa-let-7c	119
112.	hsa-mir-19b-1, hsa-miR-19b-3p	150	hsa-mir-98, hsa-miR-98-5p	128	hsa-mir-589, hsa-miR-589-5p	260	hsa-mir-1268a, hsa-miR-1268a	119
113.	hsa-mir-19b-2, hsa-miR-19b-3p	150	hsa-mir-1249, hsa-miR-1249	125	hsa-mir-340, hsa-miR-340-5p	246	hsa-mir-532, hsa-miR-532-5p	117
114.	hsa-mir-130b, hsa-miR-130b-3p	142	hsa-mir-378c, hsa-miR-378c	124	hsa-mir-99b, hsa-miR-99b-5p	246	hsa-let-7i, hsa-let-7i-3p	112

115.	hsa-mir-10a, hsa-miR-10a-5p	139	hsa-mir-486, hsa-miR-486-3p	122	hsa-let-7i, hsa-let-7i-3p	237	hsa-mir-345, hsa-miR-345-5p	109
116.	hsa-mir-210, hsa-miR-210	131	hsa-mir-320b-2, hsa-miR-320b	120	hsa-mir-17, hsa-miR-17-5p	237	hsa-mir-584, hsa-miR-584-5p	108
117.	hsa-mir-28, hsa-miR-28-5p	126	hsa-mir-320b-1, hsa-miR-320b	120	hsa-mir-28, hsa-miR-28-5p	236	hsa-mir-589, hsa-miR-589-5p	107
118.	hsa-mir-5701-1, hsa-miR-5701	124	hsa-mir-106b, hsa-miR-106b-5p	118	hsa-mir-501, hsa-miR-501-3p	231	hsa-mir-378c, hsa-miR-378c	103
119.	hsa-mir-5701-2, hsa-miR-5701	124	hsa-mir-3614, hsa-miR-3614-5p	117	hsa-mir-3615, hsa-miR-3615	217		
120.	hsa-mir-4732, hsa-miR-4732-3p	122	hsa-mir-17, hsa-miR-17-5p	116	hsa-mir-20a, hsa-miR-20a-5p	213		
121.	hsa-mir-151b, hsa-miR-151b	118	hsa-mir-1268b, hsa-miR-1268b	114	hsa-mir-181c, hsa-miR-181c-5p	199		
122.	hsa-mir-32, hsa-miR-32-5p	116	hsa-mir-151a, hsa-miR-151a-3p	114	hsa-mir-1285-1, hsa-miR-1285-3p	196		
123.	hsa-mir-1307, hsa-miR-1307-5p	113	hsa-mir-1268a, hsa-miR-1268a	113	hsa-mir-4732, hsa-miR-4732-3p	195		
124.	hsa-mir-1285-2, hsa-miR-1285-3p	111	hsa-mir-501, hsa-miR-501-3p	109	hsa-mir-654, hsa-miR-654-3p	194		
125.	hsa-mir-1285-1, hsa-miR-1285-3p	111	hsa-mir-532, hsa-miR-532-5p	109	hsa-mir-1285-2, hsa-miR-1285-3p	193		
126.	hsa-mir-199a-2, hsa-miR-199a-3p	107	hsa-mir-375, hsa-miR-375	107	hsa-mir-345, hsa-miR-345-5p	192		
127.	hsa-mir-199a-1, hsa-miR-199a-3p	107	hsa-mir-10a, hsa-miR-10a-5p	106	hsa-mir-15b, hsa-miR-15b-3p	191		
128.	hsa-mir-199b, hsa-miR-199b-3p	107	hsa-let-7e, hsa-let-7e-5p	103	hsa-mir-17, hsa-miR-17-3p	190		
129.	hsa-mir-345, hsa-miR-345-5p	106	hsa-mir-331, hsa-miR-331-3p	101	hsa-mir-1275, hsa-miR-1275	182		
130.	hsa-mir-146a, hsa-miR-146a-5p	104			hsa-mir-378c, hsa-miR-378c	180		
131.	hsa-mir-30a, hsa-miR-30a-5p	102			hsa-mir-210, hsa-miR-210	179		
132.	hsa-mir-17, hsa-miR-17-3p	101			hsa-mir-320b-2, hsa-miR-320b	177		
133.					hsa-mir-320b-1, hsa-miR-320b	177		
134.					hsa-mir-1307, hsa-miR-1307-5p	176		
135.					hsa-mir-769, hsa-miR-769-5p	169		
136.					hsa-mir-142, hsa-miR-142-3p	161		
137.					hsa-mir-339, hsa-miR-339-3p	159		
138.					hsa-mir-10a, hsa-miR-10a-5p	154		
139.					hsa-mir-193a, hsa-miR-193a-5p	149		
140.					hsa-mir-19b-1, hsa-miR-19b-3p	148		
141.					hsa-mir-19b-2, hsa-miR-19b-3p	148		
142.					hsa-mir-30a, hsa-miR-30a-5p	144		
143.					hsa-mir-130b, hsa-miR-130b-3p	143		
144.					hsa-mir-185, hsa-miR-185-5p	137		
145.					hsa-mir-1268b, hsa-miR-1268b	134		
146.					hsa-mir-500a, hsa-miR-500a-3p	133		
147.					hsa-mir-1268a, hsa-miR-1268a	133		
148.					hsa-mir-410, hsa-miR-410	129		
149.					hsa-mir-331, hsa-miR-331-3p	125		
150.					hsa-mir-629, hsa-miR-629-5p	112		
151.					hsa-mir-361, hsa-miR-361-5p	112		
152.					hsa-mir-130b, hsa-miR-130b-5p	111		

TABLE E3: microRNA Reads in Patients with HLH (continued A)

No.	HLH-32-lim		HLH-33		HLH-34		HLH-35	
	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads	miRNA species	No. of reads
1.	hsa-mir-486, hsa-miR-486-5p	307749	hsa-mir-146b, hsa-miR-146b-5p	89485	hsa-mir-142, hsa-miR-142-5p	237175	hsa-mir-181a-1, hsa-miR-181a-5p	140231
2.	hsa-mir-146b, hsa-miR-146b-5p	85817	hsa-mir-486, hsa-miR-486-5p	72679	hsa-mir-181a-1, hsa-miR-181a-5p	206459	hsa-mir-181a-2, hsa-miR-181a-5p	140231
3.	hsa-mir-181a-1, hsa-miR-181a-5p	82713	hsa-mir-191, hsa-miR-191-5p	49080	hsa-mir-181a-2, hsa-miR-181a-5p	206459	hsa-mir-16-1, hsa-miR-16-5p	97119
4.	hsa-mir-181a2, hsa-miR-181a-5p	82713	hsa-mir-181a-1, hsa-miR-181a-5p	37302	hsa-mir-26a-2, hsa-miR-26a-5p	169806	hsa-mir-16-2, hsa-miR-16-5p	97112
5.	hsa-mir-191, hsa-miR-191-5p	60640	hsa-mir-181a-2, hsa-miR-181a-5p	37302	hsa-mir-26a-1, hsa-miR-26a-5p	169801	hsa-mir-486, hsa-miR-486-5p	92977
6.	hsa-mir-26a-2, hsa-miR-26a-5p	40790	hsa-mir-26a-2, hsa-miR-26a-5p	30721	hsa-mir-16-1, hsa-miR-16-5p	113580	hsa-mir-26a-2, hsa-miR-26a-5p	92288
7.	hsa-mir-26a-1, hsa-miR-26a-5p	40785	hsa-mir-26a-1, hsa-miR-26a-5p	30715	hsa-mir-16-2, hsa-miR-16-5p	113570	hsa-mir-26a-1, hsa-miR-26a-5p	92284
8.	hsa-mir-21, hsa-miR-21-5p	38677	hsa-mir-21, hsa-miR-21-5p	19598	hsa-let-7f-2, hsa-let-7f-5p	93950	hsa-mir-191, hsa-miR-191-5p	78326
9.	hsa-mir-451a, hsa-miR-451a	26213	hsa-let-7a-1, hsa-let-7a-5p	15393	hsa-let-7f-1, hsa-let-7f-5p	92058	hsa-let-7f-2, hsa-let-7f-5p	69779
10.	hsa-let-7a-1, hsa-let-7a-5p	24708	hsa-let-7a-2, hsa-let-7a-5p	15371	hsa-mir-22, hsa-miR-22-3p	89722	hsa-let-7f-1, hsa-let-7f-5p	68217
11.	hsa-let-7a-2, hsa-let-7a-5p	24699	hsa-let-7a-3, hsa-let-7a-5p	15365	hsa-mir-21, hsa-miR-21-5p	86741	hsa-let-7a-1, hsa-let-7a-5p	66538
12.	hsa-let-7a-3, hsa-let-7a-5p	24689	hsa-mir-142, hsa-miR-142-5p	13838	hsa-let-7a-1, hsa-let-7a-5p	84255	hsa-let-7a-3, hsa-let-7a-5p	66523
13.	hsa-mir-142, hsa-miR-142-5p	19404	hsa-mir-30e, hsa-miR-30e-5p	10785	hsa-let-7a-2, hsa-let-7a-5p	84219	hsa-let-7a-2, hsa-let-7a-5p	66510
14.	hsa-mir-30e, hsa-miR-30e-5p	17622	hsa-let-7f-2, hsa-let-7f-5p	9132	hsa-let-7a-3, hsa-let-7a-5p	84215	hsa-mir-22, hsa-miR-22-3p	63428
15.	hsa-let-7f-2, hsa-let-7f-5p	16595	hsa-let-7g, hsa-let-7g-5p	9047	hsa-let-7g, hsa-let-7g-5p	59563	hsa-mir-142, hsa-miR-142-5p	55401
16.	hsa-let-7f-1, hsa-let-7f-5p	16057	hsa-let-7f-1, hsa-let-7f-5p	8780	hsa-mir-486, hsa-miR-486-5p	58887	hsa-mir-143, hsa-miR-143-3p	50594
17.	hsa-mir-92a-1, hsa-miR-92a-3p	15488	hsa-mir-92a-1, hsa-miR-92a-3p	8524	hsa-mir-92a-1, hsa-miR-92a-3p	55985	hsa-mir-92a-1, hsa-miR-92a-3p	49335
18.	hsa-mir-16-1, hsa-miR-16-5p	14053	hsa-mir-30d, hsa-miR-30d-5p	7955	hsa-mir-150, hsa-miR-150-5p	55207	hsa-mir-223, hsa-miR-223-3p	47148
19.	hsa-mir-16-2, hsa-miR-16-5p	14029	hsa-mir-342, hsa-miR-342-3p	7891	hsa-mir-191, hsa-miR-191-5p	53231	hsa-mir-92a-2, hsa-miR-92a-3p	43952
20.	hsa-mir-30d, hsa-miR-30d-5p	11824	hsa-mir-150, hsa-miR-150-5p	6788	hsa-mir-92a-2, hsa-miR-92a-3p	50238	hsa-mir-21, hsa-miR-21-5p	39021
21.	hsa-mir-92a-2, hsa-miR-92a-3p	11622	hsa-mir-92a-2, hsa-miR-92a-3p	6547	hsa-mir-26b, hsa-miR-26b-5p	39981	hsa-mir-451a, hsa-miR-451a	28839
22.	hsa-mir-150, hsa-miR-150-5p	11421	hsa-mir-182, hsa-miR-182-5p	5751	hsa-mir-451a, hsa-miR-451a	39540	hsa-mir-26b, hsa-miR-26b-5p	26942
23.	hsa-let-7g, hsa-let-7g-5p	10030	hsa-mir-451a, hsa-miR-451a	4833	hsa-mir-126, hsa-miR-126-5p	36031	hsa-let-7g, hsa-let-7g-5p	23072
24.	hsa-mir-182, hsa-miR-182-5p	10022	hsa-mir-16-1, hsa-miR-16-5p	4747	hsa-mir-223, hsa-miR-223-3p	34825	hsa-mir-25, hsa-miR-25-3p	22263
25.	hsa-mir-342, hsa-miR-342-3p	9984	hsa-mir-16-2, hsa-miR-16-5p	4737	hsa-mir-143, hsa-miR-143-3p	31142	hsa-mir-148a, hsa-miR-148a-3p	17431
26.	hsa-mir-22, hsa-miR-22-3p	8395	hsa-mir-186, hsa-miR-186-5p	4687	hsa-mir-27b, hsa-miR-27b-3p	30903	hsa-let-7i, hsa-let-7i-5p	16478
27.	hsa-mir-146a, hsa-miR-146a-5p	8251	hsa-mir-22, hsa-miR-22-3p	4568	hsa-mir-30d, hsa-miR-30d-5p	30188	hsa-mir-30d, hsa-miR-30d-5p	14503
28.	hsa-mir-186, hsa-miR-186-5p	6477	hsa-mir-148a, hsa-miR-148a-3p	4468	hsa-mir-27a, hsa-miR-27a-3p	20621	hsa-mir-27b, hsa-miR-27b-3p	13872
29.	hsa-mir-148a, hsa-miR-148a-3p	6262	hsa-mir-10a, hsa-miR-10a-5p	3281	hsa-mir-25, hsa-miR-25-3p	19780	hsa-mir-103a-2, hsa-miR-103a-3p	13818
30.	hsa-mir-25, hsa-miR-25-3p	5329	hsa-mir-192, hsa-miR-192-5p	3229	hsa-mir-15a, hsa-miR-15a-5p	19412	hsa-mir-103a-1, hsa-miR-103a-3p	13786
31.	hsa-mir-223, hsa-miR-223-3p	4337	hsa-mir-146a, hsa-miR-146a-5p	2672	hsa-let-7i, hsa-let-7i-5p	19115	hsa-mir-126, hsa-miR-126-5p	11522
32.	hsa-mir-192, hsa-miR-192-5p	4151	hsa-mir-25, hsa-miR-25-3p	2641	hsa-mir-103a-2, hsa-miR-103a-3p	17271	hsa-mir-150, hsa-miR-150-5p	10955
33.	hsa-mir-26b, hsa-miR-26b-5p	3472	hsa-mir-26b, hsa-miR-26b-5p	2415	hsa-mir-103a-1, hsa-miR-103a-3p	17262	hsa-mir-27a, hsa-miR-27a-3p	10275
34.	hsa-let-7i, hsa-let-7i-5p	3045	hsa-mir-223, hsa-miR-223-3p	2215	hsa-mir-148a, hsa-miR-148a-3p	16286	hsa-mir-186, hsa-miR-186-5p	9278
35.	hsa-mir-142, hsa-miR-142-3p	2829	hsa-mir-143, hsa-miR-143-3p	1871	hsa-mir-186, hsa-miR-186-5p	15947	hsa-mir-15a, hsa-miR-15a-5p	8362

36.	hsa-mir-103a-2, hsa-miR-103a-3p	2744	hsa-mir-101-2, hsa-miR-101-3p	1715	hsa-mir-146b, hsa-miR-146b-5p	14745	hsa-mir-378a, hsa-miR-378a-3p	7665
37.	hsa-mir-101-2, hsa-miR-101-3p	2734	hsa-mir-142, hsa-miR-142-3p	1698	hsa-mir-101-2, hsa-miR-101-3p	13816	hsa-mir-182, hsa-miR-182-5p	7598
38.	hsa-mir-103a-1, hsa-miR-103a-3p	2721	hsa-let-7i, hsa-let-7i-5p	1681	hsa-mir-101-1, hsa-miR-101-3p	13712	hsa-mir-30c-2, hsa-miR-30c-5p	6893
39.	hsa-mir-30c-2, hsa-miR-30c-5p	2639	hsa-mir-126, hsa-miR-126-5p	1606	hsa-mir-151a, hsa-miR-151a-5p	11632	hsa-mir-30c-1, hsa-miR-30c-5p	6892
40.	hsa-mir-30c-1, hsa-miR-30c-5p	2637	hsa-mir-101-1, hsa-miR-101-3p	1550	hsa-mir-30e, hsa-miR-30e-5p	11534	hsa-mir-93, hsa-miR-93-5p	6771
41.	hsa-mir-10a, hsa-miR-10a-5p	2499	hsa-mir-30c-2, hsa-miR-30c-5p	1528	hsa-mir-29a, hsa-miR-29a-3p	11497	hsa-mir-28, hsa-miR-28-3p	5778
42.	hsa-mir-101-1, hsa-miR-101-3p	2494	hsa-mir-30c-1, hsa-miR-30c-5p	1527	hsa-mir-192, hsa-miR-192-5p	10110	hsa-mir-30e, hsa-miR-30e-5p	5649
43.	hsa-mir-126, hsa-miR-126-5p	2341	hsa-mir-103a-2, hsa-miR-103a-3p	1324	hsa-mir-151a, hsa-miR-151a-3p	9606	hsa-mir-423, hsa-miR-423-3p	5308
44.	hsa-mir-98, hsa-miR-98-5p	1916	hsa-mir-103a-1, hsa-miR-103a-3p	1312	hsa-mir-28, hsa-miR-28-3p	9494	hsa-let-7d, hsa-let-7d-5p	4694
45.	hsa-mir-151a, hsa-miR-151a-3p	1817	hsa-mir-151a, hsa-miR-151a-3p	1274	hsa-mir-107, hsa-miR-107	8443	hsa-mir-23a, hsa-miR-23a-3p	4680
46.	hsa-mir-28, hsa-miR-28-3p	1803	hsa-mir-98, hsa-miR-98-5p	1231	hsa-mir-378a, hsa-miR-378a-3p	7624	hsa-mir-151a, hsa-miR-151a-5p	4581
47.	hsa-mir-125a, hsa-miR-125a-5p	1721	hsa-mir-125a, hsa-miR-125a-5p	1207	hsa-mir-23a, hsa-miR-23a-3p	7529	hsa-mir-101-2, hsa-miR-101-3p	4437
48.	hsa-mir-93, hsa-miR-93-5p	1716	hsa-mir-28, hsa-miR-28-3p	1125	hsa-mir-93, hsa-miR-93-5p	6942	hsa-mir-101-1, hsa-miR-101-3p	4381
49.	hsa-mir-181b-2, hsa-miR-181b-5p	1610	hsa-mir-29a, hsa-miR-29a-3p	897	hsa-mir-98, hsa-miR-98-5p	6402	hsa-mir-107, hsa-miR-107	4376
50.	hsa-mir-143, hsa-miR-143-3p	1483	hsa-mir-27b, hsa-miR-27b-3p	827	hsa-mir-221, hsa-miR-221-3p	6272	hsa-let-7b, hsa-let-7b-5p	4323
51.	hsa-mir-181b-1, hsa-miR-181b-5p	1472	hsa-mir-140, hsa-miR-140-3p	737	hsa-mir-363, hsa-miR-363-3p	6120	hsa-mir-140, hsa-miR-140-3p	4318
52.	hsa-mir-140, hsa-miR-140-3p	1188	hsa-mir-151a, hsa-miR-151a-5p	737	hsa-mir-423, hsa-miR-423-3p	5087	hsa-mir-98, hsa-miR-98-5p	4175
53.	hsa-mir-144, hsa-miR-144-5p	1137	hsa-mir-93, hsa-miR-93-5p	674	hsa-let-7b, hsa-let-7b-5p	5071	hsa-mir-15b, hsa-miR-15b-5p	4103
54.	hsa-mir-151a, hsa-miR-151a-5p	1103	hsa-mir-99b, hsa-miR-99b-5p	584	hsa-mir-30b, hsa-miR-30b-5p	4916	hsa-mir-181b-2, hsa-miR-181b-5p	3987
55.	hsa-mir-27b, hsa-miR-27b-3p	1101	hsa-mir-181b-2, hsa-miR-181b-5p	584	hsa-mir-126, hsa-miR-126-3p	4857	hsa-mir-181b-1, hsa-miR-181b-5p	3913
56.	hsa-mir-941-1, hsa-miR-941	1028	hsa-mir-30b, hsa-miR-30b-5p	559	hsa-mir-146a, hsa-miR-146a-5p	4641	hsa-mir-192, hsa-miR-192-5p	3908
57.	hsa-mir-181c, hsa-miR-181c-5p	922	hsa-mir-181b-1, hsa-miR-181b-5p	550	hsa-mir-30c-2, hsa-miR-30c-5p	4490	hsa-mir-151a, hsa-miR-151a-3p	3868
58.	hsa-mir-29a, hsa-miR-29a-3p	877	hsa-let-7b, hsa-let-7b-5p	506	hsa-mir-30c-1, hsa-miR-30c-5p	4490	hsa-mir-199a-2, hsa-miR-199a-3p	3797
59.	hsa-mir-423, hsa-miR-423-3p	871	hsa-mir-423, hsa-miR-423-3p	494	hsa-let-7d, hsa-let-7d-5p	4407	hsa-mir-199a-1, hsa-miR-199a-3p	3796
60.	hsa-let-7b, hsa-let-7b-5p	840	hsa-mir-21, hsa-miR-21-3p	441	hsa-mir-181b-2, hsa-miR-181b-5p	4272	hsa-mir-199b, hsa-miR-199b-3p	3796
61.	hsa-mir-20a, hsa-miR-20a-5p	785	hsa-mir-425, hsa-miR-425-5p	433	hsa-mir-181b-1, hsa-miR-181b-5p	4208	hsa-mir-423, hsa-miR-423-5p	3720
62.	hsa-mir-19b-2, hsa-miR-19b-3p	754	hsa-mir-19b-2, hsa-miR-19b-3p	415	hsa-mir-423, hsa-miR-423-5p	4194	hsa-mir-221, hsa-miR-221-3p	3262
63.	hsa-mir-19b-1, hsa-miR-19b-3p	748	hsa-mir-19b-1, hsa-miR-19b-3p	412	hsa-mir-140, hsa-miR-140-3p	4138	hsa-mir-181a-1, hsa-miR-181a-3p	3209
64.	hsa-mir-21, hsa-miR-21-3p	746	hsa-mir-20a, hsa-miR-20a-5p	404	hsa-mir-15b, hsa-miR-15b-5p	3949	hsa-mir-30e, hsa-miR-30e-3p	3200
65.	hsa-mir-30b, hsa-miR-30b-5p	691	hsa-mir-183, hsa-miR-183-5p	381	hsa-mir-584, hsa-miR-584-5p	3905	hsa-mir-425, hsa-miR-425-5p	3193
66.	hsa-mir-144, hsa-miR-144-3p	685	hsa-mir-423, hsa-miR-423-5p	379	hsa-mir-21, hsa-miR-21-3p	3890	hsa-mir-10a, hsa-miR-10a-5p	2900
67.	hsa-mir-155, hsa-miR-155-5p	637	hsa-mir-941-1, hsa-miR-941	348	hsa-mir-340, hsa-miR-340-5p	3788	hsa-mir-29a, hsa-miR-29a-3p	2688
68.	hsa-mir-425, hsa-miR-425-5p	622	hsa-mir-181c, hsa-miR-181c-5p	322	hsa-mir-181a-1, hsa-miR-181a-3p	3709	hsa-mir-340, hsa-miR-340-5p	2611
69.	hsa-mir-99b, hsa-miR-99b-5p	607	hsa-mir-221, hsa-miR-221-3p	320	hsa-mir-199a-2, hsa-miR-199a-3p	3595	hsa-mir-4286, hsa-miR-4286	2567
70.	hsa-mir-340, hsa-miR-340-5p	572	hsa-let-7d, hsa-let-7d-5p	311	hsa-mir-199a-1, hsa-miR-199a-3p	3594	hsa-mir-941-1, hsa-miR-941	2547
71.	hsa-mir-378a, hsa-miR-378a-3p	562	hsa-mir-27a, hsa-miR-27a-3p	311	hsa-mir-199b, hsa-miR-199b-3p	3594	hsa-mir-30b, hsa-miR-30b-5p	2530
72.	hsa-let-7d, hsa-let-7d-5p	559	hsa-mir-340, hsa-miR-340-5p	303	hsa-mir-342, hsa-miR-342-3p	3373	hsa-mir-197, hsa-miR-197-3p	2327
73.	hsa-mir-423, hsa-miR-423-5p	538	hsa-mir-378a, hsa-miR-378a-3p	302	hsa-mir-142, hsa-miR-142-3p	3266	hsa-mir-126, hsa-miR-126-3p	2291

74.	hsa-mir-221, hsa-miR-221-3p	529	hsa-mir-155, hsa-miR-155-5p	281	hsa-mir-23b, hsa-miR-23b-3p	3173	hsa-mir-363, hsa-miR-363-3p	2289
75.	hsa-mir-183, hsa-miR-183-5p	504	hsa-mir-363, hsa-miR-363-3p	274	hsa-mir-361, hsa-miR-361-3p	2975	hsa-mir-106b, hsa-miR-106b-3p	2098
76.	hsa-mir-27a, hsa-miR-27a-3p	481	hsa-mir-148b, hsa-miR-148b-3p	263	hsa-mir-181c, hsa-miR-181c-5p	2914	hsa-mir-584, hsa-miR-584-5p	2056
77.	hsa-mir-363, hsa-miR-363-3p	479	hsa-mir-144, hsa-miR-144-5p	250	hsa-mir-30e, hsa-miR-30e-3p	2913	hsa-mir-222, hsa-miR-222-3p	1922
78.	hsa-mir-484, hsa-miR-484	469	hsa-mir-484, hsa-miR-484	247	hsa-mir-222, hsa-miR-222-3p	2859	hsa-mir-128-1, hsa-miR-128	1895
79.	hsa-mir-17, hsa-miR-17-5p	465	hsa-mir-222, hsa-miR-222-3p	234	hsa-mir-99b, hsa-miR-99b-5p	2776	hsa-mir-144, hsa-miR-144-5p	1772
80.	hsa-mir-15a, hsa-miR-15a-5p	446	hsa-mir-1307, hsa-miR-1307-5p	232	hsa-mir-10a, hsa-miR-10a-5p	2738	hsa-mir-128-2, hsa-miR-128	1737
81.	hsa-mir-15b, hsa-miR-15b-5p	446	hsa-mir-361, hsa-miR-361-3p	227	hsa-mir-28, hsa-miR-28-5p	2679	hsa-mir-21, hsa-miR-21-3p	1495
82.	hsa-mir-222, hsa-miR-222-3p	416	hsa-mir-30e, hsa-miR-30e-3p	226	hsa-mir-106b, hsa-miR-106b-3p	2395	hsa-mir-146a, hsa-miR-146a-5p	1492
83.	hsa-mir-1307, hsa-miR-1307-5p	394	hsa-mir-146b, hsa-miR-146b-3p	225	hsa-mir-128-1, hsa-miR-128	2268	hsa-mir-484, hsa-miR-484	1282
84.	hsa-mir-320a, hsa-miR-320a	382	hsa-mir-141, hsa-miR-141-3p	210	hsa-mir-425, hsa-miR-425-5p	2222	hsa-mir-345, hsa-miR-345-5p	1255
85.	hsa-mir-301a, hsa-miR-301a-3p	380	hsa-mir-29c, hsa-miR-29c-3p	203	hsa-mir-125a, hsa-miR-125a-5p	2217	hsa-mir-146b, hsa-miR-146b-5p	1227
86.	hsa-mir-30e, hsa-miR-30e-3p	368	hsa-mir-23a, hsa-miR-23a-3p	202	hsa-mir-128-2, hsa-miR-128	2159	hsa-mir-199b, hsa-miR-199b-5p	1171
87.	hsa-mir-148b, hsa-miR-148b-3p	344	hsa-mir-17, hsa-miR-17-5p	198	hsa-mir-144, hsa-miR-144-3p	2054	hsa-mir-142, hsa-miR-142-3p	1160
88.	hsa-mir-361, hsa-miR-361-3p	342	hsa-mir-500a, hsa-miR-500a-3p	195	hsa-mir-19b-2, hsa-miR-19b-3p	1987	hsa-mir-181c, hsa-miR-181c-5p	1130
89.	hsa-mir-106b, hsa-miR-106b-3p	313	hsa-mir-769, hsa-miR-769-5p	190	hsa-mir-19b-1, hsa-miR-19b-3p	1984	hsa-mir-17, hsa-miR-17-5p	1085
90.	hsa-mir-23a, hsa-miR-23a-3p	305	hsa-mir-30a, hsa-miR-30a-5p	188	hsa-mir-24-2, hsa-miR-24-3p	1911	hsa-mir-28, hsa-miR-28-5p	1075
91.	hsa-mir-197, hsa-miR-197-3p	299	hsa-mir-144, hsa-miR-144-3p	188	hsa-mir-24-1, hsa-miR-24-3p	1911	hsa-mir-99b, hsa-miR-99b-5p	1071
92.	hsa-mir-141, hsa-miR-141-3p	275	hsa-mir-301a, hsa-miR-301a-3p	183	hsa-mir-941-1, hsa-miR-941	1847	hsa-let-7d, hsa-let-7d-3p	1066
93.	hsa-mir-454, hsa-miR-454-3p	256	hsa-mir-15b, hsa-miR-15b-5p	180	hsa-mir-16-2, hsa-miR-16-2-3p	1833	hsa-mir-23b, hsa-miR-23b-3p	1050
94.	hsa-mir-107, hsa-miR-107	256	hsa-mir-320a, hsa-miR-320a	179	hsa-mir-4286, hsa-miR-4286	1828	hsa-mir-532, hsa-miR-532-5p	1034
95.	hsa-mir-500a, hsa-miR-500a-3p	254	hsa-mir-29b-2, hsa-miR-29b-3p	174	hsa-mir-182, hsa-miR-182-5p	1381	hsa-mir-130a, hsa-miR-130a-3p	1033
96.	hsa-mir-146b, hsa-miR-146b-3p	215	hsa-mir-29b-1, hsa-miR-29b-3p	174	hsa-mir-144, hsa-miR-144-5p	1368	hsa-mir-16-2, hsa-miR-16-2-3p	1005
97.	hsa-mir-181a-1, hsa-miR-181a-3p	214	hsa-mir-107, hsa-miR-107	167	hsa-mir-106b, hsa-miR-106b-5p	1290	hsa-mir-106b, hsa-miR-106b-5p	1001
98.	hsa-mir-769, hsa-miR-769-5p	211	hsa-mir-28, hsa-miR-28-5p	163	hsa-mir-155, hsa-miR-155-5p	1278	hsa-mir-19b-2, hsa-miR-19b-3p	994
99.	hsa-mir-29c, hsa-miR-29c-3p	177	hsa-mir-197, hsa-miR-197-3p	160	hsa-mir-20a, hsa-miR-20a-5p	1241	hsa-mir-19b-1, hsa-miR-19b-3p	993
100.	hsa-mir-19a, hsa-miR-19a-3p	170	hsa-mir-106b, hsa-miR-106b-3p	155	hsa-mir-148b, hsa-miR-148b-3p	1235	hsa-mir-744, hsa-miR-744-5p	955
101.	hsa-mir-126, hsa-miR-126-3p	167	hsa-mir-126, hsa-miR-126-3p	151	hsa-mir-17, hsa-miR-17-5p	1183	hsa-mir-769, hsa-miR-769-5p	955
102.	hsa-mir-28, hsa-miR-28-5p	157	hsa-mir-15a, hsa-miR-15a-5p	148	hsa-mir-130a, hsa-miR-130a-3p	1155	hsa-mir-320a, hsa-miR-320a	953
103.	hsa-mir-874, hsa-miR-874	157	hsa-mir-221, hsa-miR-221-5p	148	hsa-mir-654, hsa-miR-654-3p	1101	hsa-mir-24-2, hsa-miR-24-3p	877
104.	hsa-mir-29b-2, hsa-miR-29b-3p	157	hsa-mir-454, hsa-miR-454-3p	145	hsa-mir-146b, hsa-miR-146b-3p	991	hsa-mir-24-1, hsa-miR-24-3p	877
105.	hsa-mir-30a, hsa-miR-30a-5p	156	hsa-mir-181a-1, hsa-miR-181a-3p	143	hsa-mir-32, hsa-miR-32-5p	933	hsa-mir-342, hsa-miR-342-3p	876
106.	hsa-mir-29b-1, hsa-miR-29b-3p	156	hsa-mir-874, hsa-miR-874	142	hsa-mir-197, hsa-miR-197-3p	930	hsa-mir-127, hsa-miR-127-3p	865
107.	hsa-mir-374a, hsa-miR-374a-3p	147	hsa-mir-7-1, hsa-miR-7-5p	136	hsa-mir-92b, hsa-miR-92b-3p	921	hsa-mir-92b, hsa-miR-92b-3p	827
108.	hsa-mir-199a-2, hsa-miR-199a-3p	138	hsa-mir-7-3, hsa-miR-7-5p	133	hsa-mir-484, hsa-miR-484	915	hsa-mir-361, hsa-miR-361-3p	816
109.	hsa-mir-199a-1, hsa-miR-199a-3p	137	hsa-mir-7-2, hsa-miR-7-5p	133	hsa-mir-769, hsa-miR-769-5p	906	hsa-mir-20a, hsa-miR-20a-5p	770
110.	hsa-mir-199b, hsa-miR-199b-3p	137	hsa-let-7e, hsa-let-7e-5p	132	hsa-mir-532, hsa-miR-532-5p	904	hsa-mir-654, hsa-miR-654-3p	745
111.	hsa-mir-532, hsa-miR-532-5p	133	hsa-mir-199a-2, hsa-miR-199a-3p	130	hsa-mir-29c, hsa-miR-29c-3p	889	hsa-mir-148b, hsa-miR-148b-3p	729

112.	hsa-mir-130a, hsa-miR-130a-3p	131	hsa-mir-31, hsa-miR-31-5p	130	hsa-mir-127, hsa-miR-127-3p	881	hsa-mir-500a, miR-500a-3p	671
113.	hsa-mir-24-2, hsa-miR-24-3p	129	hsa-mir-19a, hsa-miR-19a-3p	129	hsa-mir-151b, hsa-miR-151b	861	hsa-mir-652, hsa-miR-652-3p	661
114.	hsa-mir-24-1, hsa-miR-24-3p	129	hsa-mir-199a-1, hsa-miR-199a-3p	128	hsa-mir-320a, hsa-miR-320a	842	hsa-mir-155, hsa-miR-155-5p	651
115.	hsa-mir-660, hsa-miR-660-5p	127	hsa-mir-199b, hsa-miR-199b-3p	128	hsa-mir-410, hsa-miR-410	839	hsa-mir-450b, hsa-miR-450b-5p	649
116.	hsa-mir-374a, hsa-miR-374a-5p	125	hsa-mir-130a, hsa-miR-130a-3p	127	hsa-mir-345, hsa-miR-345-5p	808	hsa-mir-27a, hsa-miR-27a-5p	628
117.	hsa-mir-501, hsa-miR-501-3p	124	hsa-mir-374a, hsa-miR-374a-3p	124	hsa-mir-744, hsa-miR-744-5p	745	hsa-mir-1260b, hsa-miR-1260b	622
118.	hsa-mir-185, hsa-miR-185-5p	120	hsa-mir-194-2, hsa-miR-194-5p	123	hsa-let-7c, hsa-let-7c	728	hsa-mir-144, hsa-miR-144-3p	597
119.	hsa-mir-20b, hsa-miR-20b-5p	118	hsa-mir-92b, hsa-miR-92b-3p	123	hsa-mir-411, hsa-miR-411-5p	724	hsa-mir-454, hsa-miR-454-3p	583
120.	hsa-mir-106b, hsa-miR-106b-5p	117	hsa-mir-361, hsa-miR-361-5p	122	hsa-mir-181a-2, hsa-miR-181a-2-3p	722	hsa-mir-15b, hsa-miR-15b-3p	583
121.	hsa-mir-92b, hsa-miR-92b-3p	114	hsa-mir-660, hsa-miR-660-5p	122	hsa-mir-141, hsa-miR-141-3p	699	hsa-mir-183, hsa-miR-183-5p	498
122.	hsa-mir-361, hsa-miR-361-5p	113	hsa-mir-24-2, hsa-miR-24-3p	120	hsa-let-7d, hsa-let-7d-3p	661	hsa-mir-410, hsa-miR-410	483
123.	hsa-mir-148b, hsa-miR-148b-5p	113	hsa-mir-24-1, hsa-miR-24-3p	120	hsa-mir-652, hsa-miR-652-3p	653	hsa-mir-130b, hsa-miR-130b-3p	455
124.	hsa-mir-362, hsa-miR-362-5p	112	hsa-mir-362, hsa-miR-362-5p	118	hsa-mir-30a, hsa-miR-30a-5p	614	hsa-let-7c, hsa-let-7c	446
125.	hsa-mir-194-2, hsa-miR-194-5p	109	hsa-mir-148b, hsa-miR-148b-5p	117	hsa-mir-378c, hsa-miR-378c	580	hsa-mir-125a, hsa-miR-125a-5p	429
126.	hsa-mir-7-1, hsa-miR-7-5p	106	hsa-mir-374a, hsa-miR-374a-5p	115	hsa-mir-301a, hsa-miR-301a-3p	519	hsa-mir-409, hsa-miR-409-3p	428
127.	hsa-mir-7-3, hsa-miR-7-5p	103	hsa-mir-501, hsa-miR-501-3p	114	hsa-mir-424, hsa-miR-424-3p	501	hsa-mir-424, hsa-miR-424-3p	424
128.	hsa-mir-7-2, hsa-miR-7-5p	103	hsa-mir-100, hsa-miR-100-5p	105	hsa-mir-589, hsa-miR-589-5p	494	hsa-let-7e, hsa-let-7e-5p	417
129.	hsa-let-7e, hsa-let-7e-5p	102	hsa-mir-664a, hsa-miR-664a-3p	104	hsa-mir-15b, hsa-miR-15b-3p	482	hsa-mir-26b, hsa-miR-26b-3p	408
130.	hsa-mir-181a-2, hsa-miR-181a-2-3p	102	hsa-mir-194-1, hsa-miR-194-5p	103	hsa-mir-454, hsa-miR-454-3p	473	hsa-mir-130b, hsa-miR-130b-5p	400
131.			hsa-mir-223, hsa-miR-223-5p	102	hsa-mir-500a, hsa-miR-500a-3p	470	hsa-mir-421, hsa-miR-421	396
132.			hsa-mir-532, hsa-miR-532-5p	101	hsa-mir-409, hsa-miR-409-3p	469	hsa-mir-301a, hsa-miR-301a-3p	394
133.			hsa-mir-20b, hsa-miR-20b-5p	101	hsa-mir-873, hsa-miR-873-5p	461	hsa-mir-1307, hsa-miR-1307-5p	393
134.					hsa-let-7e, hsa-let-7e-5p	453	hsa-mir-582, hsa-miR-582-5p	388
135.					hsa-mir-339, hsa-miR-339-5p	452	hsa-mir-424, hsa-miR-424-5p	386
136.					hsa-mir-150, hsa-miR-150-3p	439	hsa-mir-361, hsa-miR-361-5p	382
137.					hsa-mir-361, hsa-miR-361-5p	432	hsa-mir-148a, hsa-miR-148a-5p	375
138.					hsa-mir-660, hsa-miR-660-5p	430	hsa-mir-660, hsa-miR-660-5p	373
139.					hsa-mir-339, hsa-miR-339-3p	422	hsa-mir-589, hsa-miR-589-5p	368
140.					hsa-mir-132, hsa-miR-132-3p	418	hsa-mir-151b, hsa-miR-151b	364
141.					hsa-mir-374a, hsa-miR-374a-5p	418	hsa-mir-181a-2, hsa-miR-181a-2-3p	360
142.					hsa-mir-3607, hsa-miR-3607-3p	413	hsa-mir-29c, hsa-miR-29c-3p	348
143.					hsa-mir-378d-2, hsa-miR-378d	385	hsa-mir-339, hsa-miR-339-5p	343
144.					hsa-mir-378d-1, hsa-miR-378d	380	hsa-mir-378c, hsa-miR-378c	336
145.					hsa-mir-424, hsa-miR-424-5p	379	hsa-mir-5701-1, hsa-miR-5701	331
146.					hsa-mir-450b, hsa-miR-450b-5p	377	hsa-mir-5701-2, hsa-miR-5701	331
147.					hsa-mir-130b, hsa-miR-130b-3p	375	hsa-mir-338, hsa-miR-338-3p	321
148.					hsa-mir-5701-1, hsa-miR-5701	363	hsa-mir-582, hsa-miR-582-3p	320
149.					hsa-mir-5701-2, hsa-	353	hsa-mir-1307, hsa-miR-	309

			miR-5701		1307-3p
150.			hsa-mir-27a, hsa-miR-27a-5p	340	hsa-mir-374b, hsa-miR-374b-5p	299
151.			hsa-mir-17, hsa-miR-17-3p	337	hsa-mir-501, hsa-miR-501-3p	292
152.			hsa-mir-374b, hsa-miR-374b-5p	336	hsa-mir-339, hsa-miR-339-3p	289
153.			hsa-mir-335, hsa-miR-335-3p	321	hsa-mir-3607, hsa-miR-3607-3p	285
154.			hsa-mir-374a, hsa-miR-374a-3p	304	hsa-mir-450a-1, hsa-miR-450a-5p	285
155.			hsa-let-7i, hsa-let-7i-3p	300	hsa-mir-450a-2, hsa-miR-450a-5p	285
156.			hsa-mir-501, hsa-miR-501-3p	286	hsa-mir-145, hsa-miR-145-5p	258
157.			hsa-mir-1260b, hsa-miR-1260b	284	hsa-mir-1285-1, hsa-miR-1285-3p	256
158.			hsa-mir-1307, hsa-miR-1307-5p	278	hsa-mir-574, hsa-miR-574-3p	250
159.			hsa-mir-130b, hsa-miR-130b-5p	273	hsa-mir-1285-2, hsa-miR-1285-3p	247
160.			hsa-mir-194-2, hsa-miR-194-5p	259	hsa-mir-486, hsa-miR-486-3p	240
161.			hsa-mir-335, hsa-miR-335-5p	259	hsa-mir-411, hsa-miR-411-5p	240
162.			hsa-mir-194-1, hsa-miR-194-5p	249	hsa-mir-3615, hsa-miR-3615	232
163.			hsa-mir-30d, hsa-miR-30d-3p	239	hsa-mir-17, hsa-miR-17-3p	231
164.			hsa-mir-342, hsa-miR-342-5p	238	hsa-mir-671, hsa-miR-671-3p	230
165.			hsa-mir-26b, hsa-miR-26b-3p	235	hsa-mir-223, hsa-miR-223-5p	230
166.			hsa-mir-338, hsa-miR-338-3p	233	hsa-mir-185, hsa-miR-185-5p	226
167.			hsa-mir-381, hsa-miR-381-3p	231	hsa-mir-146b, hsa-miR-146b-3p	224
168.			hsa-mir-889, hsa-miR-889	229	hsa-mir-32, hsa-miR-32-5p	208
169.			hsa-mir-421, hsa-miR-421	228	hsa-mir-331, hsa-miR-331-3p	207
170.			hsa-mir-1307, hsa-miR-1307-3p	224	hsa-mir-374a, hsa-miR-374a-5p	204
171.			hsa-mir-185, hsa-miR-185-5p	222	hsa-mir-335, hsa-miR-335-3p	201
172.			hsa-mir-29b-2, hsa-miR-29b-3p	219	hsa-mir-548k, hsa-miR-548k	197
173.			hsa-mir-29b-1, hsa-miR-29b-3p	218	hsa-mir-194-2, hsa-miR-194-5p	174
174.			hsa-mir-3615, hsa-miR-3615	216	hsa-mir-873, hsa-miR-873-5p	173
175.			hsa-mir-450a-1, hsa-miR-450a-5p	214	hsa-mir-145, hsa-miR-145-3p	168
176.			hsa-mir-450a-2, hsa-miR-450a-5p	214	hsa-let-7i, hsa-let-7i-3p	166
177.			hsa-mir-19a, hsa-miR-19a-3p	205	hsa-mir-378d-2, hsa-miR-378d	166
178.			hsa-mir-132, hsa-miR-132-5p	204	hsa-mir-194-1, hsa-miR-194-5p	165
179.			hsa-mir-148a, hsa-miR-148a-5p	192	hsa-mir-378d-1, hsa-miR-378d	163
180.			hsa-mir-331, hsa-miR-331-3p	179	hsa-mir-425, hsa-miR-425-3p	151
181.			hsa-mir-431, hsa-miR-431-5p	178	hsa-mir-374a, hsa-miR-374a-3p	148
182.			hsa-mir-7-1, hsa-miR-7-1-3p	176	hsa-mir-23a, hsa-miR-23a-5p	147
183.			hsa-mir-20b, hsa-miR-20b-5p	169	hsa-mir-548e, hsa-miR-548e	147
184.			hsa-mir-574, hsa-miR-574-3p	167	hsa-mir-340, hsa-miR-340-3p	144
185.			hsa-mir-140, hsa-miR-140-5p	156	hsa-mir-100, hsa-miR-100-5p	140
186.			hsa-mir-199b, hsa-miR-199b-5p	151	hsa-mir-4454, hsa-miR-4454	138
187.			hsa-mir-548k, hsa-miR-	149	hsa-mir-338, hsa-miR-	135

			548k		338-5p
188.			hsa-mir-766, hsa-miR-766-3p	148	hsa-mir-431, hsa-miR-431-5p	131
189.			hsa-mir-1285-1, hsa-miR-1285-3p	146	hsa-mir-335, hsa-miR-335-5p	131
190.			hsa-mir-1285-2, hsa-miR-1285-3p	145	hsa-mir-181c, hsa-miR-181c-3p	129
191.			hsa-mir-301b, hsa-miR-301b	137	hsa-mir-191, hsa-miR-191-3p	125
192.			hsa-mir-671, hsa-miR-671-3p	130	hsa-mir-576, hsa-miR-576-5p	123
193.			hsa-mir-148b, hsa-miR-148b-5p	129	hsa-mir-140, hsa-miR-140-5p	122
194.			hsa-mir-18a, hsa-miR-18a-5p	127	hsa-mir-19a, hsa-miR-19a-3p	118
195.			hsa-mir-576, hsa-miR-576-5p	127	hsa-mir-502, hsa-miR-502-3p	114
196.			hsa-mir-582, hsa-miR-582-3p	127	hsa-mir-505, hsa-miR-505-3p	113
197.			hsa-mir-425, hsa-miR-425-3p	120	hsa-mir-22, hsa-miR-22-5p	110
198.			hsa-mir-199a-2, hsa-miR-199a-5p	118	hsa-mir-532, hsa-miR-532-3p	108
199.			hsa-mir-199a-1, hsa-miR-199a-5p	118	hsa-mir-210, hsa-miR-210	103
200.			hsa-mir-136, hsa-miR-136-3p	114	hsa-mir-221, hsa-miR-221-5p	103
201.			hsa-mir-181c, hsa-miR-181c-3p	114	hsa-mir-628, hsa-miR-628-5p	102
202.			hsa-mir-1275, hsa-miR-1275	110	hsa-mir-6503, hsa-miR-6503-3p	102
203.			hsa-mir-223, hsa-miR-223-5p	108	hsa-mir-30d, hsa-miR-30d-3p	100
204.			hsa-mir-22, hsa-miR-22-5p	104	hsa-mir-548o-2, hsa-miR-548o-3p	100

TABLE E4: Normalized miRNA Expression Levels of Controls

miRNA	Control-1	Control-2	Control-3	Control-4	Control-5	Control-5
	Normalized	Normalized	Normalized	Normalized	Normalized	Normalized
hsa-miR-142-3p	1.011334	1.2525696	2.7550132	0.38770706	0.2017686	0.9886662
hsa-miR-19a	1.2351274	0.76487255	2.315864	0.23158643	0.19850263	1.2505666
hsa-miR-19b	1.1493344	0.9854914	2.254464	0.26523104	0.22734086	1.0145087
hsa-miR-19b	1.1493344	0.9854914	2.254464	0.26523104	0.22734086	1.0145087
hsa-miR-374a	0.9271523	1.1483079	4.7682114	0.5960265	0.17029329	1.0728477
hsa-miR-192	1.3544074	1.0735853	2.0514758	0.80722684	0.50616145	0.92641467
hsa-miR-194	2.6257153	1.4092141	2.3631437	0.525143	0.45012262	0.5907859
hsa-miR-451	1.4529384	1.1378943	2.796254	0.38629022	0.15884134	0.8621058
hsa-miR-144	1.5048196	0.8875083	5.6609883	0.16123068	0.09213182	1.1124916
hsa-miR-30b	1.7282072	1.7349821	1.568329	0.28549677	0.39153844	0.43167114
hsa-miR-374a	2.4739504	1.3927577	2.361498	0.33735684	0.14458151	0.60724235
hsa-miR-186	1.406916	1.2456993	1.0294989	0.91587853	0.9705011	0.86163723
hsa-miR-148a	0.83875716	1.12507	1.422722	0.5649742	0.87493	1.3053752
hsa-miR-660	1.0526316	2.3466923	2.5263157	0.9473684	0.54135334	0.85263157
hsa-miR-21	0.77384704	0.9802961	2.126174	0.62461376	1.0197039	1.8879222
hsa-miR-301a	0.8233585	1.1766413	3.9901216	0.6650203	0.6514484	3.078094
hsa-miR-30e	0.49227494	0.63638544	1.43373	0.7682472	1.2317529	2.8596697
hsa-miR-20a	0.7967479	1.0807787	1.0623306	0.43631437	0.9756098	1.0243902
hsa-miR-199b-5p	0.8641975	1.2232416	1.2345679	----------	0.47619048	1.0
hsa-miR-142-5p	2.868493	1.7737164	2.4415433	0.22628343	0.16075969	0.2102423
hsa-miR-101	1.6787156	1.6671917	4.187006	0.07630525	0.11068455	0.33280832
hsa-mir-101-2	1.6073093	1.6119623	4.0275965	0.09509603	0.10548467	0.39269066
hsa-miR-16	1.6228437	1.6079552	1.8123944	0.31734154	0.3003059	0.39204487
hsa-miR-16	1.6186885	1.605463	1.8099135	0.31734163	0.30068386	0.39453685
hsa-miR-181a	1.6551045	1.2987916	1.3518792	0.7012084	0.3248842	0.3411284
hsa-miR-363	1.9519953	1.5804666	1.6198646	0.4195333	0.25471663	0.34611496
hsa-miR-106b	1.5547704	1.9839855	4.1460543	0.07067137	0.2423019	0.44522968
hsa-miR-143	1.5002435	3.408527	3.7018993	0.124208465	0.38201934	0.49975643
hsa-miR-185	1.1666666	2.5688071	2.074074	0.5833333	0.83333325	0.61249995
hsa-miR-183	1.0181818	0.3152627	1.2727273	0.95454544	0.9818182	2.4054544
hsa-miR-210	1.696498	1.5758754	2.403372	0.4241245	0.18176763	0.38171205
hsa-let-7b	1.3022792	1.64753	1.4110798	0.6118783	0.6977209	0.54440194
hsa-miR-423-5p	1.7268265	2.0349283	1.1267451	0.8684418	0.87325495	0.5249874
hsa-let-7e	0.95637584	1.5876486	1.0436242	0.9463088	1.535954	0.8562081
hsa-miR-181a-2	2.5199647	0.91078466	1.0892155	1.1630605	0.35208297	0.39876363

Table E5: Normalized miRNA Expression Levels of Patients with HLH

miRNA	HLH-2A	HLH-20	HLH-21	HLH-28	HLH-32-lim
	Normalized	Normalized	Normalized	Normalized	Normalized
hsa-miR-142-3p	3.8312838	5.4054055	2.5265913	5.1630344	29.607676
hsa-miR-19a	5.893475	4.1685553	3.1958926	2.6400852	12.196883
hsa-miR-19b	3.0867407	2.8070285	2.9440644	3.481157	9.172572
hsa-miR-19b	3.0867407	2.8070285	2.9440644	3.481157	9.106265
hsa-miR-374a	3.699474	1.5894039	2.2649007	4.649007	9.801324
hsa-miR-192	4.146168	2.57518	4.030717	4.528055	11.662352
hsa-miR-194	3.6669471	3.238382	6.774346	5.0413733	6.3892403
hsa-miR-451	11.704809	9.577214	13.62456	5.8006177	8.409643
hsa-miR-144	25.88586	11.608608	25.635681	4.1597514	8.95726
hsa-miR-30b	1.523962	0.97449565	2.4118767	5.358203	4.255805
hsa-miR-374a	1.3610604	1.2369752	2.5301766	4.2506967	7.3093987
hsa-miR-186	0.9373421	0.9682427	1.8584334	3.1459987	4.6307693
hsa-miR-148a	1.3113426	1.1220356	1.5809783	5.3454156	7.070881
hsa-miR-660	2.0580761	1.3684211	3.4105263	5.4	7.578946
hsa-miR-21	1.7393818	1.4935368	0.90406525	2.4793196	7.86203
hsa-miR-301a	2.0048888	1.0766995	2.850087	4.503138	10.3236475
hsa-miR-30e	1.453677	1.1768188	1.8452852	1.742355	17.876043
hsa-miR-20a	1.1303616	0.8093948	2.4243903	1.2520325	5.109304
hsa-miR-199b-5p	1.0344827	0.9876543	3.3333335	5.3333335	5.6790123
hsa-miR-142-5p	2.6205046	2.4706166	2.2994912	6.2529254	2.8133962
hsa-miR-101	4.4265146	3.6196082	4.6734037	5.606676	6.0652895
hsa-miR-101	4.232448	3.4644783	4.484058	5.413761	6.3956738
hsa-miR-16	3.3723567	1.7460352	4.8896217	4.5339427	1.5561559
hsa-miR-16	3.3668242	1.743329	4.882929	4.52662	1.5570241
hsa-miR-181a	2.5290554	2.5774148	4.912249	7.8118415	1.2381698
hsa-miR-363	5.2351246	4.51581	8.385422	2.7269669	1.5965573
hsa-miR-106b	8.860728	6.0306244	13.992933	5.3851595	2.21437
hsa-miR-143	9.020105	9.001459	5.5060887	75.23964	9.113491
hsa-miR-185	4.4051723	1.8148147	7.9916673	3.033333	2.9166665
hsa-miR-183	0.7702194	1.2090908	4.696364	2.577273	24.245453
hsa-miR-210	17.242855	11.875486	22.77549	1.0178989	1.2723736
hsa-let-7b	0.45816004	0.30111465	0.6459158	0.57464653	0.168358
hsa-miR-423-5p	1.3352534	0.9929839	1.656426	0.2561577	0.12705635
hsa-let-7e	0.23744503	0.15100673	0.3080537	0.314094	0.2751678
hsa-miR-181a-2*	0.22630982	0.14461336	0.29630357	1.052239	0.0923064

Table E5: Normalized miRNA Expression Levels Of Patients With HLH (continued)

miRNA	HLH-33	HLH-34	HLH-35	HLH-36	HLH-37
	Normalized	Normalized	Normalized	Normalized	Normalized
hsa-miR-142-3p	9.464237	36.99652	114.884415	29.346123	9.75215
hsa-miR-19a	6.5669017	19.684847	50.310143	19.684847	8.783743
hsa-miR-19b	8.011432	12.499011	33.64547	21.958918	10.592665
hsa-miR-19b	7.9705553	12.399552	33.634033	21.925766	10.582007
hsa-miR-374a*	4.4089627	14.602648	46.037907	26.092712	9.451279
hsa-miR-192	8.162068	11.244289	34.719536	18.25741	6.805317
hsa-miR-194	5.907859	7.023789	16.297544	14.397673	7.342625
hsa-miR-451	9.407512	34.20887	36.61386	34.400707	24.194504
hsa-miR-144*	11.761004	30.553213	62.954105	31.672873	30.6108
hsa-miR-30b	3.9774005	3.9455657	9.167399	18.713362	9.286802
hsa-miR-374a	8.630328	10.289383	27.51203	29.125143	11.060486
hsa-miR-186	4.249901	4.799471	6.4814687	7.87784	4.4196544
hsa-miR-148a	6.5615563	7.432496	7.8082995	12.886792	13.300209
hsa-miR-660	7.883922	10.026316	21.34301	27.894737	18.930452
hsa-miR-21	5.329297	11.63689	10.2384205	17.39872	7.547394
hsa-miR-301a	9.077332	18.050549	8.714057	22.76903	12.031438
hsa-miR-30e	13.960563	21.906235	16.60635	9.558753	4.514385
hsa-miR-20a	6.2328763	7.4458003	9.099149	10.376695	4.6951222
hsa-miR-199b-5p	2.7397256	7.0370364	10.217113	12.407407	69.702385
hsa-miR-142-5p	1.3836184	2.9587626	41.899868	24.10996	5.430639
hsa-miR-101	2.1166868	7.3194346	95.23585	26.828148	8.265495
hsa-miR-101	2.2620747	7.6468396	91.33848	25.761702	7.9778767
hsa-miR-16	2.4334216	3.456509	11.113917	18.654491	15.381489
hsa-miR-16	2.4317732	3.457056	11.095844	18.627216	15.358758
hsa-miR-181a*	2.8738902	2.027819	8.848427	23.430468	19.547874
hsa-miR-363	3.2542565	2.0932963	16.38651	17.830168	6.4306583
hsa-miR-106b	2.7010021	4.134276	40.550747	39.811543	22.738514
hsa-miR-143	3.2563434	5.417681	82.97023	75.845085	118.81899
hsa-miR-185	4.135274	5.784722	4.693486	9.138888	7.0624995
hsa-miR-183	18.18213	24.054543	6.5830717	3.0863636	15.279546
hsa-miR-210	3.006636	2.1206226	17.111227	6.220493	7.0207763
hsa-let-7b	0.07168365	0.2096157	0.5121645	0.84362006	0.69349647
hsa-miR-423-5p	0.17359054	0.13526973	0.24241394	0.70300037	0.6012787
hsa-let-7e	0.7757194	0.24161075	0.2603564	0.9278524	0.6746765
hsa-miR-181a-2*	0.42960405	0.21230471	0.38673195	1.4184415	0.53405845

Table E6: Validated Downregulated mRNA Targets of the Upregulated miRNAs Expressed in Patients with HLH

No.	GENE NAME	ACCESSION NO.	DESCRIPTION
1.	*ABAT*	AF237813	4-aminobutyrate aminotransferase
2.	*ABCC5*	BE550362	ATP-binding cassette, sub-family C (CFTR/MRP), member 5
3.	*ACACB*	AI057637	acetyl-Coenzyme A carboxylase beta
4.	*ACADSB*	BE897866	acyl-Coenzyme A dehydrogenase, short/branched chain
5.	*ADAMTS5*	NM_007038	ADAM metallopeptidase with thrombospondin type 1 motif, 5 (aggrecanase-2)
6.	*ADARB1*	NM_015833	adenosine deaminase, RNA-specific, B1 (RED1 homolog rat)
7.	*ADRB2*	NM_000024	adrenergic, beta-2-, receptor, surface
8.	*ADRBK2*	AI651212	adrenergic, beta, receptor kinase 2
9.	*AKAP7*	AL137063	A kinase (PRKA) anchor protein 7
10.	*AKR7A2*	AI144075	aldo-keto reductase family 7, member A2 (aflatoxin aldehyde reductase)
11.	*ALDH3A2*	NM_000382	aldehyde dehydrogenase 3 family, member A2
12.	*ANXA6*	NM_001155	annexin A6
13.	*ARRB1*	BE207758	arrestin, beta 1
14.	*ATP10D*	AI478147	ATPase, Class V, type 10D
15.	*ATP2B4*	AW517686	ATPase, Ca++ transporting, plasma membrane 4
16.	*BACE1*	BF939127	Beta-site APP-cleaving enzyme 1
17.	*BBS10*	NM_024685	Bardet-Biedl syndrome 10
18.	*BCAS4*	AA207074	breast carcinoma amplified sequence 4
19.	*BCL11A*	AF080216	B-cell CLL/lymphoma 11A (zinc finger protein)
20.	*BMPR1A*	NM_004329	bone morphogenetic protein receptor, type IA
21.	*BOC*	W72626	Boc homolog (mouse)
22.	*BTN3A1*	U90552	butyrophilin, subfamily 3, member A1
23.	*C15orf40*	AW193603	chromosome 15 open reading frame 40
24.	*C20orf197*	NM_173644	chromosome 20 open reading frame 197
25.	*C2orf43*	AK021672	chromosome 2 open reading frame 43
26.	*C9orf64*	AW983691	chromosome 9 open reading frame 64
27.	*CA5B*	AW003516	carbonic anhydrase VB, mitochondrial
28.	*CACNA2D3*	NM_018398	calcium channel, voltage-dependent, alpha 2/delta 3 subunit
29.	*CCNG2*	BF061444	cyclin G2
30.	*CCR2*	NM_000647	chemokine (C-C motif) receptor 2
31.	*CD1D*	NM_001766	CD1D molecule
32.	*CELSR1*	AL031588	cadherin, EGF LAG seven-pass G-type receptor 1 (flamingo homolog)
33.	*CHRM3*	AI718964	cholinergic receptor, muscarinic 3
34.	*CIITA*	NM_000246	class II, major histocompatibility complex, transactivator
35.	*CNTNAP2*	AU144598	contactin associated protein-like 2
36.	*COL4A3*	AI694562	collagen, type IV, alpha 3 (Goodpasture antigen)
37.	*COMMD8*	NM_017845	COMM domain containing 8
38.	*CROT*	AW517412	Carnitine O-octanoyltransferase
39.	*CSRP2BP*	AF252257	CSRP2 binding protein
40.	*CTR9*	BF197009	Ctr9, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae)
41.	*CYB5B*	BE501733	cytochrome b5 type B (outer mitochondrial membrane)
42.	*CYBASC3*	AA683481	cytochrome b, ascorbate dependent 3
43.	*DIP2C*	N31807	DIP2 disco-interacting protein 2 homolog C (Drosophila)
44.	*DLG3*	T62872	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)
45.	*DUSP1*	AA530892	dual specificity phosphatase 1
46.	*E2F5*	U15642	E2F transcription factor 5, p130-binding
47.	*EHBP1*	AB020710	EH domain binding protein 1
48.	*ELP4*	NM_019040	elongation protein 4 homolog (S. cerevisiae)
49.	*ENPP5*	AA609053	ectonucleotide pyrophosphatase/phosphodiesterase 5 (putative function)
50.	*EVI5*	AF008915	ecotropic viral integration site 5
51.	*FCRL3*	AY043466	Fc receptor-like 3
52.	*FGL2*	AW135176	fibrinogen-like 2
53.	*GALK2*	AI923944	galactokinase 2
54.	*GIMAP4*	NM_018326	GTPase, IMAP family member 4
55.	*GLCE*	W87398	UDP-glucuronic acid epimerase
56.	*GZMK*	NM_002104	granzyme K (granzyme 3; tryptase II)

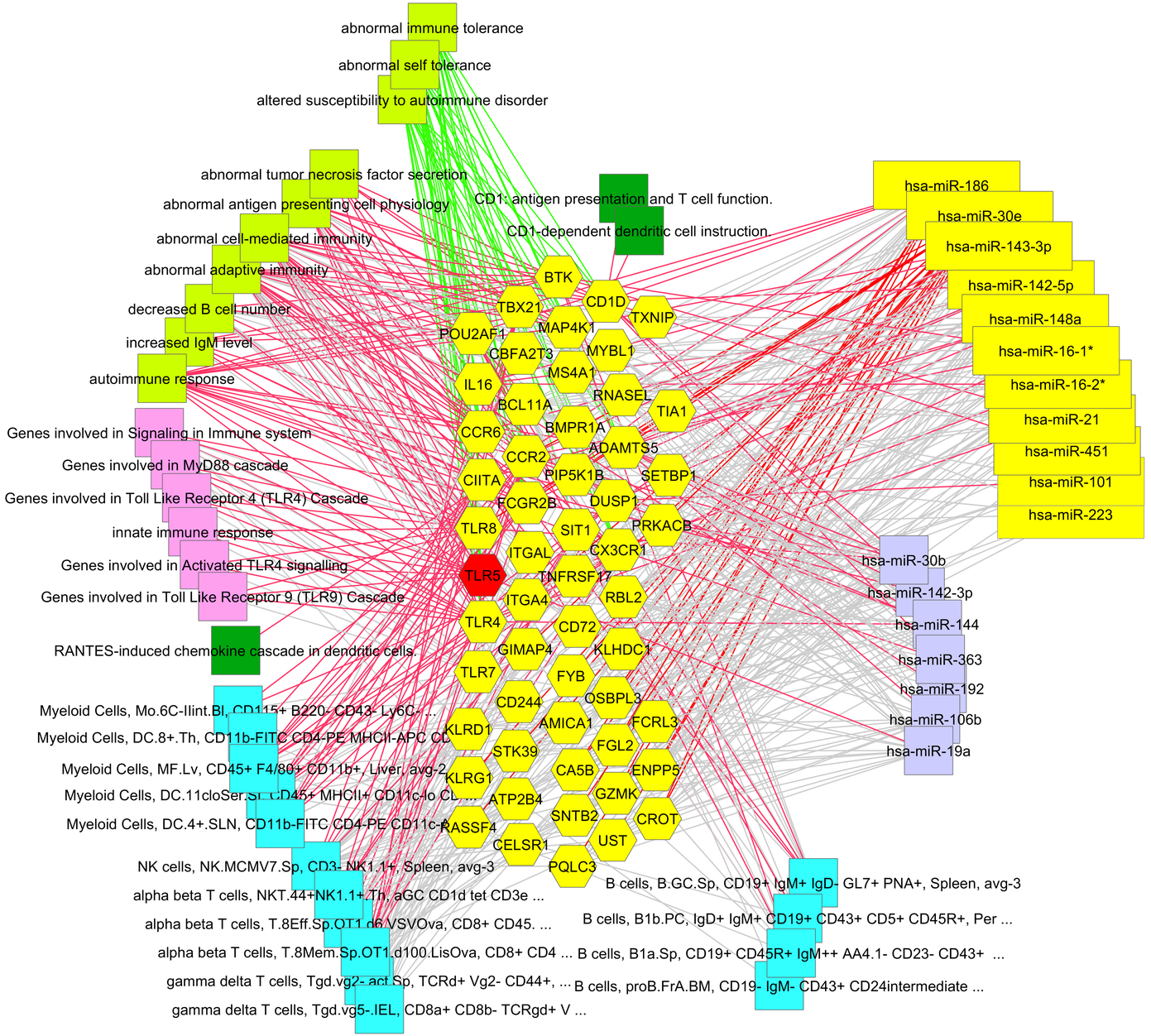
57.	*HDAC9*	NM_014707	histone deacetylase 9
58.	*HP*	AA070330	haptoglobin
59.	*HSD17B4*	NM_000414	hydroxysteroid (17-beta) dehydrogenase 4
60.	*HSDL2*	BC004331	hydroxysteroid dehydrogenase like 2
61.	*HSPA1L*	D85730	heat shock 70kDa protein 1-like
62.	*IDH1*	NM_005896	isocitrate dehydrogenase 1 (NADP+), soluble
63.	*IFNGR2*	N51405	interferon gamma receptor 2 (interferon gamma transducer 1)
64.	*IL16*	M90391	interleukin 16 (lymphocyte chemoattractant factor)
65.	*ITGAL*	BC008777	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated)
66.	*ITPA*	AF219116	inosine triphosphatase (nucleoside triphosphate pyrophosphatase)
67.	*KCNH8*	NM_144633	potassium voltage-gated channel, subfamily H (eag-related), member 8
68.	*KIF5A*	AA810707	kinesin family member 5A
69.	*KLHDC1*	NM_172193	kelch domain containing 1
70.	*KLHL23*	W72315	Kelch-like 23 (Drosophila)
71.	*KLRC4*	U96845	killer cell lectin-like receptor subfamily C, member 4
72.	*KLRD1*	NM_007334	killer cell lectin-like receptor subfamily D, member 1
73.	*KLRF1*	NM_016523	killer cell lectin-like receptor subfamily F, member 1
74.	*KLRG1*	AF081675	killer cell lectin-like receptor subfamily G, member 1
75.	*LARGE*	AB011181	like-glycosyltransferase
76.	*LDLRAP1*	AA169780	low density lipoprotein receptor adaptor protein 1
77.	*LIMA1*	NM_016357	LIM domain and actin binding 1
78.	*LRBA*	AI659561	LPS-responsive vesicle trafficking, beach and anchor containing
79.	*LRRK2*	AK026776	leucine-rich repeat kinase 2
80.	*MAP4K1*	AA744529	mitogen-activated protein kinase kinase kinase kinase 1
81.	*MBD5*	AI911379	methyl-CpG binding domain protein 5
82.	*MEF2C*	AL536517	MADS box transcription enhancer factor 2, polypeptide C
83.	*METTL6*	AK027185	methyltransferase like 6
84.	*MIB1*	BE048628	mindbomb homolog 1 (Drosophila)
85.	*MOXD1*	AY007239	monooxygenase, DBH-like 1
86.	*MRPS14*	AA013164	mitochondrial ribosomal protein S14
87.	*MTRF1*	NM_004294	mitochondrial translational release factor 1
88.	*MYBL1*	AW592266	v-myb myeloblastosis viral oncogene homolog (avian)-like 1
89.	*NAGA*	NM_000262	N-acetylgalactosaminidase, alpha-
90.	*NCAM1*	AA126505	neural cell adhesion molecule 1
91.	*NUP43*	NM_024647	nucleoporin 43kDa
92.	*OSBPL3*	AY008372	oxysterol binding protein-like 3
93.	*PAXIP1*	AA873827	PAX interacting (with transcription-activation domain) protein 1
94.	*PDGFD*	NM_025208	platelet derived growth factor D
95.	*PDZD4*	BC002606	PDZ domain containing 4
96.	*PIGN*	NM_012327	phosphatidylinositol glycan anchor biosynthesis, class N
97.	*PON2*	NM_000305	paraoxonase 2
98.	*POU2AF1*	NM_006235	POU domain, class 2, associating factor 1
99.	*PQLC3*	AL516202	PQ loop repeat containing 3
100.	*PRKACB*	AA130247	protein kinase, cAMP-dependent, catalytic, beta
101.	*PROCR*	AK021431	protein C receptor, endothelial (EPCR)
102.	*PTPDC1*	BE046919	protein tyrosine phosphatase domain containing 1
103.	*PTPN18*	AW575379	protein tyrosine phosphatase, non-receptor type 18 (brain-derived)
104.	*PTPRO*	NM_002848	protein tyrosine phosphatase, receptor type, O
105.	*QRSL1*	NM_018292	glutaminyl-tRNA synthase (glutamine-hydrolyzing)-like 1
106.	*RAB40B*	NM_006822	RAB40B, member RAS oncogene family
107.	*RABL2B*	NM_007081	RAB, member of RAS oncogene family-like 2B
108.	*RASSF4*	N49935	Ras association (RalGDS/AF-6) domain family 4
109.	*RBL2*	BF110947	retinoblastoma-like 2 (p130)
110.	*RECK*	NM_021111	reversion-inducing-cysteine-rich protein with kazal motifs
111.	*RGS18*	AF076642	regulator of G-protein signalling 18
112.	*RIMS3*	NM_014747	regulating synaptic membrane exocytosis 3
113.	*RNASEL*	AI669749	ribonuclease L (2',5'-oligoisoadenylate synthetase-dependent)
114.	*RNF170*	NM_030954	ring finger protein 170
115.	*RNF43*	AK000271	ring finger protein 43
116.	*S100Z*	AF437876	S100 calcium binding protein, zeta
117.	*SCD5*	AL571375	stearoyl-CoA desaturase 5
118.	*SCN3A*	AF225986	sodium channel, voltage-gated, type III, alpha

119.	*SEC61A2*	AW237290	Sec61 alpha 2 subunit (S. cerevisiae)
120.	*SETD4*	NM_017438	SET domain containing 4
121.	*SGCB*	AI678717	sarcoglycan, beta (43kDa dystrophin-associated glycoprotein)
122.	*SIN3B*	AB014600	SIN3 homolog B, transcription regulator (yeast)
123.	*SLC22A5*	NM_003060	solute carrier family 22 (organic cation transporter), member 5
124.	*SMC6*	AW069285	structural maintenance of chromosomes 6
125.	*SMYD4*	AI971520	SET and MYND domain containing 4
126.	*SNTB2*	AI695684	syntrophin, beta 2 (dystrophin-associated protein A1, 59kDa)
127.	*STEAP4*	AA650281	STEAP family member 4
128.	*STK38*	AF034187	serine/threonine kinase 38
129.	*STRBP*	AK025613	spermatid perinuclear RNA binding protein
130.	*STX7*	N32035	syntaxin 7
131.	*TBRG1*	AW291696	transforming growth factor beta regulator 1
132.	*TCL1A*	X82240	T-cell leukemia/lymphoma 1A
133.	*TEP1*	BF197089	telomerase-associated protein 1
134.	*TIA1*	AL046419	TIA1 cytotoxic granule-associated RNA binding protein
135.	*TK2*	BE895437	thymidine kinase 2, mitochondrial
136.	*TLR10*	AF296673	toll-like receptor 10
137.	*TLR4*	T79640	Toll-like receptor 4
138.	*TLR5*	AF051151	Toll-like receptor 5
139.	*TLR7*	NM_016562	Toll-like receptor 7
140.	*TLR8*	AW872374	Toll-like receptor 8
141.	*TMEM14A*	NM_014051	transmembrane protein 14A
142.	*TMOD2*	AW207699	tropomodulin 2 (neuronal)
143.	*TMTC2*	AI862551	transmembrane and tetratricopeptide repeat containing 2
144.	*TMTC2*	AI765006	transmembrane and tetratricopeptide repeat containing 2
145.	*TNFAIP8L2*	AF271774	tumor necrosis factor, alpha-induced protein 8-like 2
146.	*TNFRSF17*	NM_001192	tumor necrosis factor receptor superfamily, member 17
147.	*TPD52*	BE974098	tumor protein D52
148.	*TRIM14*	NM_014788	tripartite motif-containing 14
149.	*TRPC1*	NM_003304	transient receptor potential cation channel, subfamily C, member 1
150.	*TXNIP*	AA812232	thioredoxin interacting protein
151.	*USP28*	AB040948	ubiquitin specific peptidase 28
152.	*USP34*	AL050376	ubiquitin specific peptidase 34
153.	*USP45*	AW195800	ubiquitin specific peptidase 45
154.	*USP54*	AI076941	ubiquitin specific peptidase 54
155.	*UST*	NM_005715	uronyl-2-sulfotransferase
156.	*VPREB3*	NM_013378	pre-B lymphocyte gene 3
157.	*VPS41*	AW963328	vacuolar protein sorting 41 (yeast)
158.	*ZC3H14*	BF970253	zinc finger CCCH-type containing 14
159.	*ZFP28*	AA831323	zinc finger protein 28 homolog (mouse)
160.	*ZNF365*	NM_014951	zinc finger protein 365
161.	*ZNF418*	AI971569	zinc finger protein 418
162.	*ZNF451*	BE326219	zinc finger protein 451
163.	*ZNF512*	NM_032434	zinc finger protein 512
164.	*ZNF594*	AA872562	zinc finger protein 594
165.	*ZNF83*	M27877	zinc finger protein 83

Table E7: Validated Upregulated mRNA Targets of the Downregulated miRNAs

No.	GENE NAME	ACCESSION NO.	DESCRIPTION
1.	*ADIPOR1*	NM_015999	adiponectin receptor 1
2.	*ANPEP*	NM_001150	alanyl (membrane) aminopeptidase (aminopeptidase N)
3.	*ATF3*	NM_001674	activating transcription factor 3
4.	*AXUD1*	AI091372	AXIN1 up-regulated 1
5.	*AZIN1*	NM_015878	antizyme inhibitor 1
6.	*B3GNT5*	BE672260	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5
7.	*BACH1*	AF026199	BTB and CNC homology 1, basic leucine zipper transcription factor 1
8.	*BCAT1*	AI652662	branched chain aminotransferase 1, cytosolic
9.	*BRE*	AW080339	brain and reproductive organ-expressed (TNFRSF1A modulator)
10.	*CCL22*	NM_002990	chemokine (C-C motif) ligand 22
11.	*CCL7*	NM_006273	chemokine (C-C motif) ligand 7
12.	*CD164*	AF263279	CD164 molecule, sialomucin
13.	*CD44*	U94903	CD44 molecule (Indian blood group)
14.	*CDC42*	R37664	cell division cycle 42 (GTP binding protein, 25kDa)
15.	*CDCP1*	NM_022842	CUB domain containing protein 1
16.	*CLN8*	AF123759	ceroid-lipofuscinosis, neuronal 8 (epilepsy, progressive)
17.	*CPD*	NM_001304	carboxypeptidase D
18.	*CPEB2*	AI948598	cytoplasmic polyadenylation element binding protein 2
19.	*DLC1*	AA524250	deleted in liver cancer 1
20.	*DLX2*	NM_004405	distal-less homeobox 2
21.	*DOCK4*	AW452588	dedicator of cytokinesis 4
22.	*DUSP16*	AB052156	dual specificity phosphatase 16
23.	*DUSP4*	NM_001394	dual specificity phosphatase 4
24.	*ERAF*	NM_016633	erythroid associated factor
25.	*FLJ36031*	BE466274	hypothetical protein FLJ36031
26.	*FNDC3B*	AW058617	fibronectin type III domain containing 3B
27.	*FREQ*	AA045247	frequenin homolog (Drosophila)
28.	*FURIN*	NM_002569	furin (paired basic amino acid cleaving enzyme)
29.	*G0S2*	NM_015714	G0/G1switch 2
30.	*GAB2*	AI792896	GRB2-associated binding protein 2
31.	*GLUL*	NM_002065	glutamate-ammonia ligase (glutamine synthetase)
32.	*GRB10*	U66065	growth factor receptor-bound protein 10
33.	*GYPA*	U00178	glycophorin A (MNS blood group)
34.	*ICAM1*	NM_000201	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor
35.	*IRAK2*	AI246590	interleukin-1 receptor-associated kinase 2
36.	*JMJD3*	AA521267	jumonji domain containing 3
37.	*JOSD1*	NM_014876	Josephin domain containing 1
38.	*KIF1B*	AK023184	kinesin family member 1B
39.	*LIMK2*	AF085978	LIM domain kinase 2
40.	*LMNA*	M13452	lamin A/C
41.	*MAP3K8*	NM_005204	mitogen-activated protein kinase kinase kinase 8
42.	*MEF2D*	AL530331	MADS box transcription enhancer factor 2, polypeptide D
43.	*MMP19*	U38321	matrix metallopeptidase 19
44.	*MN1*	NM_002430	meningioma (disrupted in balanced translocation) 1
45.	*MPP1*	NM_002436	membrane protein, palmitoylated 1, 55kDa
46.	*MYO10*	BC041694	Myosin X
47.	*NFKB1*	M55643	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
48.	*NFKB2*	NM_002502	nuclear factor of kappa light polypeptide gene enhancer in B-cells 2
49.	*NFKBIA*	AI078167	nuclear factor of kappa light polypeptide gene enhancer in B-cells
50.	*OLR1*	AF035776	oxidised low density lipoprotein (lectin-like) receptor 1
51.	*ORM1*	NM_000607	orosomucoid 1
52.	*PDE4B*	L20966	phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4)
53.	*PDE4D*	AF012074	phosphodiesterase 4D, cAMP-specific (phosphodiesterase E3)
54.	*PHLDA1*	NM_007350	pleckstrin homology-like domain, family A, member 1
55.	*PLEK2*	NM_016445	pleckstrin 2
56.	*PURB*	AA495775	purine-rich element binding protein B
57.	*RAB13*	NM_002870	RAB13, member RAS oncogene family

58.	*RAB8B*	NM_016530	RAB8B, member RAS oncogene family
59.	*RALA*	NM_005402	v-ral simian leukemia viral oncogene homolog A (ras related)
60.	*RBM38*	AL109955	RNA binding motif protein 38
61.	*RBMS1*	BC029493	RNA binding motif, single stranded interacting protein 1
62.	*RGR*	AI867408	Ral-GDS related protein Rgr
63.	*RGS16*	U94829	regulator of G-protein signalling 16
64.	*RIOK3*	AW006290	RIO kinase 3 (yeast)
65.	*RNF12*	BE966018	ring finger protein 12
66.	*RRAGD*	AF272036	Ras-related GTP binding D
67.	*RUNX1*	D43967	runt-related transcription factor 1 (acute myeloid leukemia 1)
68.	*RYBP*	NM_012234	RING1 and YY1 binding protein
69.	*SCD*	AA678241	stearoyl-CoA desaturase (delta-9-desaturase)
70.	*SEMA3F*	U38276	sema domain, immunoglobulin domain (Ig)
71.	*SIRPA*	BG745857	signal-regulatory protein alpha
72.	*SLC25A37*	BG251467	solute carrier family 25, member 37
73.	*SLC2A3*	NM_006931	solute carrier family 2 (facilitated glucose transporter), member 3
74.	*SLC45A4*	AL832732	solute carrier family 45, member 4
75.	*SLC6A6*	NM_003043	solute carrier family 6 (neurotransmitter transporter, taurine)
76.	*SLC7A11*	NM_014331	solute carrier family 7, (cationic amino acid transporter, y+ system)
77.	*SLC7A5*	AB018009	solute carrier family 7 (cationic amino acid transporter, y+ system)
78.	*SMAD7*	NM_005904	SMAD, mothers against DPP homolog 7 (Drosophila)
79.	*SOCS1*	AB005043	suppressor of cytokine signaling 1
80.	*SOCS3*	AI244908	suppressor of cytokine signaling 3
81.	*SOCS3*	BG035761	suppressor of cytokine signaling 3
82.	*SOD2*	X15132	superoxide dismutase 2, mitochondrial
83.	*SPAG9*	AB011088	sperm associated antigen 9
84.	*SQSTM1*	NM_003900	sequestosome 1
85.	*STCH*	NM_006948	stress 70 protein chaperone, microsome-associated, 60kDa
86.	*SURF4*	AL518882	surfeit 4
87.	*TBC1D22B*	AK021840	TBC1 domain family, member 22B
88.	*TFDP1*	AW007021	transcription factor Dp-1
89.	*TFPI*	AF021834	tissue factor pathway inhibitor (lipoprotein-associated coagulation)
90.	*TIPARP*	AL556438	TCDD-inducible poly(ADP-ribose) polymerase
91.	*TMEM88*	AL544576	transmembrane protein 88
92.	*TNF*	NM_000594	tumor necrosis factor (TNF superfamily, member 2)
93.	*TNFAIP3*	NM_006290	tumor necrosis factor, alpha-induced protein 3
94.	*TP53INP2*	AL109824	tumor protein p53 inducible nuclear protein 2
95.	*TPM3*	AY004867	tropomyosin 3
96.	*UNC84B*	BG231709	Unc-84 homolog B (C. elegans)
97.	*WDR26*	BG177759	WD repeat domain 26
98.	*YTHDF3*	AK093081	YTH domain family, member 3


abnormal immune tolerance
abnormal self tolerance
altered susceptibility to autoimmune disorder
abnormal tumor necrosis factor secretion
abnormal antigen presenting cell physiology
abnormal cell-mediated immunity
abnormal adaptive immunity
decreased B cell number
increased IgM level
autoimmune response
Genes involved in Signaling in Immune system
Genes involved in MyD88 cascade
Genes involved in Toll Like Receptor 4 (TLR4) Cascade
innate immune response
Genes involved in Activated TLR4 signalling
Genes involved in Toll Like Receptor 9 (TLR9) Cascade
RANTES-induced chemokine cascade in dendritic cells.
CD1: antigen presentation and T cell function.
CD1-dependent dendritic cell instruction.
BTK
TBX21
CD1D
TXNIP
MAP4K1
POU2AF1
MYBL1
CBFA2T3
MS4A1
IL16
RNASEL
BCL11A
TIA1
BMPR1A
CCR6
ADAMTS5
CCR2
PIP5K1B
SETBP1
CIITA
DUSP1
FCGR2B
PRKACB
SIT1
TLR8
CX3CR1
ITGAL
TLR5
TNFRSF17
RBL2
ITGA4
CD72
TLR4
KLHDC1
GIMAP4
FYB
TLR7
OSBPL3
CD244
AMICA1
FCRL3
KLRD1
FGL2
STK39
ENPP5
CA5B
KLRG1
GZMK
ATP2B4
CROT
SNTB2
RASSF4
UST
CELSR1
PQLC3
hsa-miR-186
hsa-miR-30e
hsa-miR-143-3p
hsa-miR-142-5p
hsa-miR-148a
hsa-miR-16-1*
hsa-miR-16-2*
hsa-miR-21
hsa-miR-451
hsa-miR-101
hsa-miR-223
hsa-miR-30b
hsa-miR-142-3p
hsa-miR-144
hsa-miR-363
hsa-miR-192
hsa-miR-106b
hsa-miR-19a
Myeloid Cells, Mo.6C-IIint.BI, CD115+ B220- CD43- Ly6C- ...
Myeloid Cells, DC.8+.Th, CD11b-FITC CD4-PE MHCII-APC CD ...
Myeloid Cells, MF.Lv, CD45+ F4/80+ CD11b+, Liver, avg-2
Myeloid Cells, DC.11cloSer.Sp, CD45+ MHCII+ CD11c-lo CL ...
Myeloid Cells, DC.4+.SLN, CD11b-FITC CD4-PE CD11c-A ...
NK cells, NK.MCMV7.Sp, CD3- NK1.1+, Spleen, avg-3
alpha beta T cells, NKT.44+NK1.1+.Th, aGC CD1d tet CD3e ...
alpha beta T cells, T.8Eff.Sp.OT1.d6.VSVOva, CD8+ CD45. ...
alpha beta T cells, T.8Mem.Sp.OT1.d100.LisOva, CD8+ CD4 ...
gamma delta T cells, Tgd.vg2- act.Sp, TCRd+ Vg2- CD44+, ...
gamma delta T cells, Tgd.vg5-.IEL, CD8a+ CD8b- TCRgd+ V ...
B cells, B.GC.Sp, CD19+ IgM+ IgD- GL7+ PNA+, Spleen, avg-3
B cells, B1b.PC, IgD+ IgM+ CD19+ CD43+ CD5+ CD45R+, Per ...
B cells, B1a.Sp, CD19+ CD45R+ IgM++ AA4.1- CD23- CD43+ ...
B cells, proB.FrA.BM, CD19- IgM- CD43+ CD24intermediate ...