The MYC/miR-150/MYB/ZDHHC11 network in B-cell lymphoma

Liu, Yichen

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Chapter 2

The role of the MYC/miR-150/MYB/ZDHHC11 network in Hodgkin lymphoma and diffuse large B-cell lymphoma

Yichen Liu[1#], Lotteke J.Y.M Ziel-Swier[1#], Annika Seitz[1], Debora de Jong[1], Jasper Koerts[1], Bea Rutgers[1], Rianne Veenstra[1], Fazlyn R. Abdul Razak[2], Agnieszka Dzikiewicz-Krawczyk[3], Anke van den Berg[1], Joost Kluiver[1,*]

[1]Department of Pathology and Medical Biology, University Medical Center Groningen, University of Groningen, Groningen, the Netherlands

[2]Neogenix Laboratoire SDB BHD, Kelana Jaya, Petaling Jaya, Selangor, Malaysia

[3]Institute of Human Genetics, Polish Academy of Sciences, Poznan, Poland

[#]Authors share the first authorship, *Corresponding author

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Abstract

We previously described involvement of the MYC/miR-150/MYB/ZDHHC11 network in the growth of Burkitt lymphoma (BL) cells. Here we studied the relevance of this network in the two other B-cell lymphomas: Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL). Expression levels of the network components were assessed at the RNA and protein level. The effect of modulating levels of the network components on cell growth was determined through GFP competition assay. AGO2-RNA immunoprecipitation was performed to validate targeting by miR-150. Expression levels of MYC, MYB and ZDHHC11 were increased, while miR-150 levels were decreased similar to the pattern observed in BL. Knockdown of MYC, MYB and ZDHHC11, decreased growth of HL and DLBCL cells. In contrast, overexpression of miR-150 did not induce clear phenotypes in HL and limited effects in DLBCL. This could not be explained by differences in overexpression levels. Furthermore, we showed that in HL ZDHHC11 and MYB are efficiently targeted by miR-150. To conclude, MYC, MYB and ZDHHC11 are critical for growth of HL and DLBCL cells consistent with the role observed in BL cells, while low endogenous miR-150 levels appeared to be less critical for growth of HL and DLBCL cells, despite effective targeting of ZDHHC11 and MYB.

Keywords

miR-150, ZDHHC11, B-cell lymphoma

1. Introduction

Burkitt lymphoma (BL) is a highly aggressive germinal center (GC) B-cell derived lymphoma subtype occurring most commonly in children. The hallmark of BL is the translocation of the MYC gene locus to one of the immunoglobulin gene loci, which results in high expression of the oncogenic transcription factor MYC[1]. MYC regulates the expression of many protein-coding and non-coding genes[2-6]. One of the non-coding targets is the MYC-repressed microRNA-150 (miR-150), an important tumor suppressor in lymphoma[6-8]. Two validated targets of miR-150 in B-cells are the transcription factor MYB[9,10] and ZDHHC11[11]. The ZDHHC11 gene encodes a protein that belongs to the zinc finger DHHC domain-containing (zDHHC) enzyme (S-palmitoyltransferase) family of 24 members. ZDHHC proteins affect the stability, localization and function of other proteins through palmitoylation[12]. Besides a protein-coding transcript, two other transcripts have been identified from the ZDHHC11 locus in BL: a linear long non-coding (lnc) and a circular non-coding (circ) RNA transcript. All three transcripts contain up to 18 binding sites for miR-150 and were shown to bind miR-150. In BL, MYC, MYB and ZDHHC11 show increased levels and miR-150 decreased levels compared to normal germinal center (GC) B-cells. Knockdown of MYB, MYC and all ZDHHC11 transcripts strongly inhibited cell growth in BL, while overexpression of miR-150 inhibited BL growth by targeting of MYB and ZDHHC11[11]. Here we studied the relevance of the MYC/miR-150/MYB/ZDHHC11 network in two other GC B-cell derived lymphomas, i.e. Hodgkin lymphoma (HL) and diffuse large B-cell lymphoma (DLBCL)

2. Materials and Methods

2.1 Culture of cell lines and sorting of GC B-cells

Cell lines used throughout the manuscript are listed in Supplemental Table S1, including their origin and culture conditions. Cell lines were either cultured in RPMI 1640 (Gibco, Waltham, MA, USA; Lonza BioWhittaker, Walkersville, MD, USA in case of ST486), McCoys5A (Lonza BioWhittaker) or DMEM (Lonza BioWhittaker), supplemented with 10-20% fetal bovine serum (Cambrex Biosciences, Walkersville, USA). All media were supplemented with 100 units/mL of penicillin, 100 µg/mL of streptomycin and 2 mM glutamine (Cambrex Biosciences). The origin of the cell lines was confirmed with STR DNA analyses on a regular basis and mycoplasma tests were performed to exclude contamination. The cultures were maintained at 37°C in a humidified air atmosphere supplemented with

5% CO2. GC B-cells (defined as CD20+IgD−CD38+) were sorted from routinely removed tonsil specimens as described previously[13]. Written permission for the use of the tonsil tissues to isolate GC B-cells was obtained from the parents of the children. The study protocol was consistent with international ethical guidelines (the Declaration of Helsinki and the International Conference on Harmonization Guidelines for Good Clinical Practice).

2.2 DNA constructs and viral transfection

Lentiviral shRNAs constructs targeting all ZDHHC11 transcripts, MYC and MYB were described and tested previously[11]. Non-targeting control shRNA constructs were consistently used as negative controls. Lentiviral vectors for miR-150 overexpression and empty vector controls were described previously[14]. Lentiviral transfections were performed as previously described[15,16], aiming for an infection percentage of 10-50% to follow the effect on cell growth over time. To validate miRNA overexpression levels, we infected cells aiming at an infection percentage of >70%. In case of low GFP percentages, infected cells were puromycin selected for 1-2 weeks. Cells were harvested and stored at -20°C until further processing.

2.3 GFP competition assay

The percentages of GFP positive cells were measured on the BD Accuri™ C6 Plus Cell Analyzer (BD Biosciences, Franklin Lakes, NJ) at day 4 post-transfection and monitored tri-weekly for three weeks. Data were analyzed using FlowJo software (version 10, Tree-star, Ashland, OR, USA). To determine the effect on cell growth, the percentage of GFP positive cells at day 4, 6 or 8 (depending on the time reaching the maximal GFP percent-age which varied per construct and cell line) was set to 100% and the fold difference relative to this starting point was calculated for each time point. To determine significant differences in the GFP assays, we used mixed model analysis as described previously [11].

2.4 RNA isolation and RT-qPCR

Total RNA was isolated using the miRNeasy mini or micro kit (Qiagen, German-town, MD) in combination with Phase Lock Gel Heavy tubes (5 Prime, Hilden, Germany). Primers used for quantification of the transcript levels are shown in Supplementary Table S2. For quantification of the circular ZDHHC11 transcript an input of 10 ng of cDNA was used and for the other transcripts we used

an input of 1 ng in a final volume of 10 µl. Synthesis of cDNA and amplification were performed as described previously[11]. Expression levels were normalized to U6 and expressed as 2-delta Ct. For quantification of miRNA overexpression, multiplex miRNA-specific cDNA synthesis and RT-qPCR was performed using the TaqMan MicroRNA Reverse Transcription Kit and TaqMan MicroRNA Assays (both Applied Biosystems) according to the manufacturer's protocol. The MicroRNA Assay IDs were as follows: 000473 (miR-150-5p), 000391 (miR-16-5p), 002308 (miR-17-5p) and 001006 (RUN48). MiRNA levels were normalized to RNU48 and ex-pressed as 2-delta Ct.

2.5 AGO2 RNA immunoprecipitation

Immunoprecipitation of AGO2-containing RISC complexes was performed as described previously[17] with some small modifications. EZView protein G beads (Merck Life Science NV, Amsterdam, the Netherlands) were pre-blocked using 5% BSA and 2 µg/µl salmon sperm sonicated ssDNA (Merck Life Science NV). Lysates from 30-40 million L428 and SUPHD1 cells were incubated with anti-AGO2 antibody (clone 2E12-1C9, Abnova, Taiwan) coated beads overnight at 4°C while gently rocking. As a negative control, cells were also incubated with anti-IgG antibody (Millipore BV, the Netherlands) coated beads. Total RNA of the total fractions (TF) and immunoprecipitated (IP) fractions was isolated as described above and used for analysis by microarray using an Agilent SurePrint G3 Human GE 8x60K microarray (Agilent ID 72363) as described previously[11]. The microarray data were deposited in the Gene Expression Omnibus (GSE188310). Genes were identified as specific targets of miR-150 when the IP/TF ratio in the HL cells transfected with the miR-150 overexpression vector was ≥ two fold higher than the IP/TF ratio in the HL cells transfected with the empty overexpression vector. For comparison to the miR-150-specific targets previously identified in BL[11], we focused on genes for which probes were present on both microarrays.

2.6 Western blot

Whole cell protein lysates were prepared using cell lysis buffer (Cell Signaling) supplemented with 1 mM PMSF. The total protein concentration was measured using the Pierce BCA Protein Assay kit (Thermo Fisher Scientific). After denaturing by boiling for 5 min at 100°C in loading buffer, proteins were separated by SDS-PAGE using 10% acrylamide gels. Next, the proteins were transferred to nitrocellulose membranes using the Bio-Rad Wet electroblotting system (Life Science Technologies).

Antibodies were diluted in 5% milk in Tris-buffered saline + Tween-20. The primary, secondary and tertiary antibody solutions used are listed in Supplementary Table 3. For detection of GAPDH, Pierce™ ECL Western Blotting Substrate (Thermo Fisher Scientific, USA) was applied to the blots. SuperSignal West Pico Chemiluminescent Substrate (Thermo Fisher Scientific, USA) was applied to the blots for detection of the other proteins. Protein bands were visualized with a ChemiDoc MP scanner and bands were quantified using the Image Lab 6.0 software (both BioRad, Veenendaal, The Netherlands). Protein levels were normalized to GAPDH or to the total amount of protein loaded on gel.

2.7 Analysis of deposited microarray and RNA-seq data

For cHL, normalized and log2 transformed microarray expression data of probes detecting all three ZDHHC11 transcripts (Affymetrix probe set 232417_x_at)were retrieved from the GEO accession viewer (http://www.ncbi.nlm.nih.gov/geo/; GSE39132 (5 CD77+ GC B-cell samples) and GSE39133 (29 HRS cell samples) for the Steidl cohort; GSE12453 (10 CD77-/+ GC B-cell samples and 12 HRS cell samples) for the Tiacci cohort; GSE12453 (12 HRS cell samples) and GSE83441 (5 CD30+ GC B-cell samples) for the Weniger cohort)[18-20]. For DLBCL, TMM-normalized RNA-seq expression data for ZDHHC11 mRNA was selected from the Scott & Ennishi cohort (n=283, Scott et al., 2014; Ennishi et al., 2017)[21,22]. Assignment into cell-of-origin groups was performed using Lymph2Cx digital gene expression profiling. Normalized and log2 transformed microarray expression data of the Visco cohort (n=489) for all ZDHHC11 transcripts using the Affymetrix probe as describes above was obtained from the NCBI Gene Expression Omnibus (GEO accession number GSE31312) via the R2: Genomics Analysis and Visualization Platform (http://r2.amc.nl) (Visco et al., 2012)[23]. Assignment into cell-of-origin groups was performed using TMA immunohistochemistry.

2.8 Statistical analysis

GraphPad Prism 6 (GraphPad Software Inc., La Jolla, CA, USA) was used to perform the statistical analysis. Data was represented as mean with SD, median or median with interquartile range. Statistical analysis of the differences between median was calculated with the one-sided Mann Whitney test for comparison of two groups, or the Kruskal-Wallis test with Dunn's post-hoc test when more than two groups were compared.

3. Results

3.1 Expression of network components in B-cell lymphoma

In our previous study, we already showed similar expression patterns for the network components in HL and DLBCL as compared to BL, i.e. increased MYB, MYC and ZDHHC11 levels and decreased miR-150 levels compared to GC B-cells[11]. As a next step, we tested the expression levels of the three individual ZDHHC11 transcripts in a set of 30 B-cell lymphoma cell lines and GC B-cells. The levels of each of the three distinct ZDHHC11 transcripts were increased in BL, HL and DLBCL cell lines compared to GC B-cells (Fig. 1), with significant differences for BL and HL in comparison to GC B-cells. The expression patterns were similar to the results observed for the general primer set targeting all three ZDHHC11 transcripts (Fig. S1). For DLBCL we observed the same trend, albeit less pronounced and not significantly different. Expression levels for each of the ZDHHC11 transcripts was consistently low in GC B-cells and increased in the cell lines, albeit at variable levels, especially for circZDHHC11. For completeness, we also determined the mRNA expression levels of MYC, MYB and miR-150 in this extended cell line panel (Fig. S1). The expression patterns of the other network components also showed the same trend in HL and DLBCL as observed for BL in line with our previous results[11].

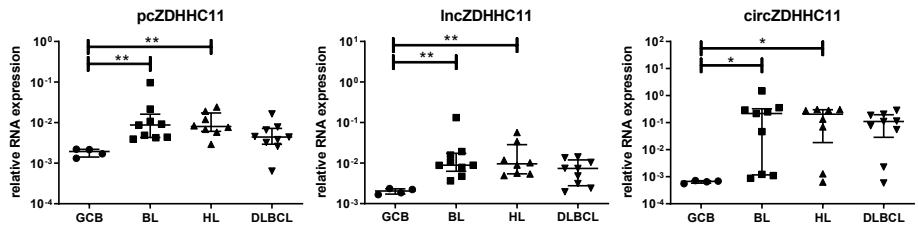

Figure 1. Expression pattern of the three ZDHHC11 transcripts in B-cell lymphoma cell lines and germinal center B-cells (GCB). Relative RNA expression of the protein coding ZDHHC11 (pcZDHHC11), linear non-coding ZDHHC11 (lncZDHHC11) and circular ZDHHC11 (circZDHHC11) in GC B-cells sorted from tonsils (n=4), Burkitt lymphoma (BL, n=9), Hodgkin lymphoma (HL, n=8) and diffuse large B-cell lymphoma (DLBCL, n=9) cell lines was determined by RT-qPCR. The expression was normalized to U6. Kruskal-Wallis test with Dunn's post-hoc tests were used to assess significance; * $p < 0.05$, ** $p < 0.01$, data are represented as median with interquartile range. For better visualization in the figures, expression levels of circZDHHC11 were multiplied with 1000.

Next, we tested presence of MYC and MYB protein in a subset of the HL and DLBCL cell lines also used for functional follow-up experiments (Fig. 2 and Fig. S2). MYC protein levels were higher in KMH2, L428 and L540 HL cell lines as compared to SUPHD1. In DLBCL cell lines, SUDHL4, SUDHL5 and

U2932 had higher levels compared to WSU-DLCL2. MYB protein was detected in two of the cHL cell lines and in all DLBCL, with again lower levels in WSU-DLCL2. The two MYB negative cHL cell lines, i.e. L428 and SUPHD1, harbor a nonsense mutation in MYB that leads to a truncated MYB protein, which cannot be detected with the antibody raised against the C-terminus of MYB that was used in the WB[24]. Despite testing multiple commercially available ZDHHC11 antibodies, we were unable to reliably detect the ZDHHC11 protein. Overall, the observed expression patterns of the three individual ZDHHC11 transcripts and the other network components, i.e. MYC, MYB and miR-150, in HL and DLBCL cell lines are similar to those observed in BL. No obvious correlation could be observed between MYC mRNA and protein levels in either HL or DLBCL cell lines. MYB mRNA and protein levels did show a moderate correlation in both HL and DLBCL, with exception of the two HL cell lines with a truncating mutation in MYB, resulting in loss of the binding site of the MYB-antibody.

To confirm expression of ZDHHC11, i.e. the novel component of the MYC-miR150-MYB network, in primary cHL and DLBCL we analyzed previously published expression profiling studies. The levels of the ZDHHC11 transcripts were moderate to strongly increased in purified primary HRS cells compared to GC B-cells in all three cohorts (Fig. S3). A possible explanation for the observed variation in ZDHHC11 increases may be related to the different approaches used to isolate GC B-cells. ZDHHC11 was also expressed in primary DLBCL cases with significantly higher levels in GCB DLBCL com-pared to ABC DLBCL cases in both cohorts. These data indicate that ZDHHC11 is ex-pressed in primary HRS and DLBCL cells, further underscoring the potential relevance of this network in HL and DLBCL.

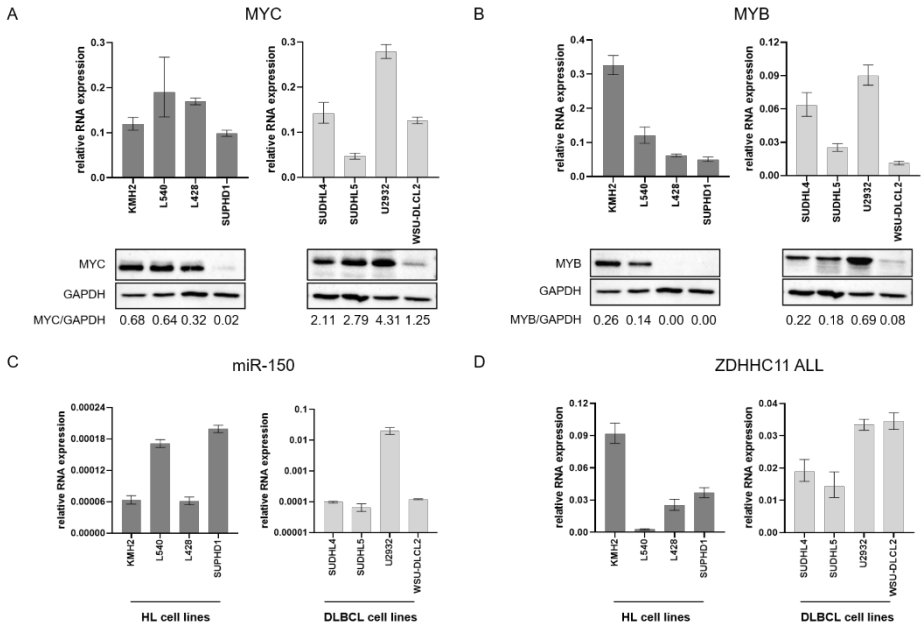

Figure 2. MYC and MYB protein and MYC, MYB, miR-150 and ZDHCC11 transcript levels in HL and DLBCL cell lines. Relative RNA expression (upper panels) of (A) MYC, (B) MYB, (C) miR-150, and (D) ZDHHC11 all transcripts (ZDHHC11 ALL) in 4 HL (KMH2, L540, L428, SUPHD1) and 4 DLBCL (SUDHL4, SUDHL5, U2932, WSU-DLCL2) cell lines. The RNA levels were normalized to U6. Kruskal-Wallis test with Dunn's post-hoc tests were used to assess significant differences; * $p < 0.05$, ** $p < 0.01$, data are represented as median with interquartile range. Western blots (lower panels) showing (A) MYC and (B) MYB protein levels. GAPDH was used as a loading control and for quantification, fold differences relative to the ST486 BL cell line are shown below the blots (see full blot, including ST486 in Figure S2 for uncropped blots).

3.2 Effect of MYC, MYB, ZDHHC11 and miR-150 on growth of HL and DLBCL cell lines

Next, we tested the effect of MYC, MYB or ZDHHC11 knockdown in HL and DLBCL cell lines. The effectiveness of the shRNAs targeting MYC, MYB and ZDHHC11 transcripts has been shown in our previous publication and were confirmed for MYC and MYB in the L540 HL cell line (Fig. S4)[5,11]. Knockdown of MYC revealed a strong negative effect on growth, with a relative decrease in GFP positive cells of more than 40% in most cell lines at day 22 after infection (Fig. 3). Two HL cell lines, KMH2 and L428, and one DLBCL cell line, WSU-DLCL2, showed a milder effect on growth upon MYC knock-down with a decrease in GFP of 20-35%. Knockdown of MYB induced a mild effect in the two HL cell lines with nonsense mutations, SUPHD1 (33%) and L428 (12%), while it had a strong inhibiting effect on

growth of the other HL and all DLBCL cell lines, with a decrease in GFP of more than 40%.

Knockdown of all ZDHHC11 transcripts also inhibited growth of cHL and DLBCL cell lines, albeit at variable levels ranging from mild to strong effects. In HL, both shRNAs showed a strong phenotype in SUPHD1 and L540, with a reduction of 78% and 40% for shRNA 1 and 82% and 70% for shRNA 2. The effects on growth of KMH2 and L428 cells were milder with 40 and 20% for shRNA 1 and 35 and 40% for shRNA 2. In DLBCL cell lines U2932 and WSU-DLCL2, the reduction in GFP was most prominent for shRNA 2 with 40 and 60%, and moderate for shRNA 1 with 10 and 40%. In the two other DLBCL cell lines, SUDHL4 and SUDHL5, only mild effects were observed for shRNA 1 and no effects for shRNA 2. Thus, similar to BL, inhibition of all ZDHCC11 transcripts resulted in a decrease in growth in all HL and two of the four DLBCL cell lines, while knockdown of MYC and MYB decreased cell growth in all cell lines.

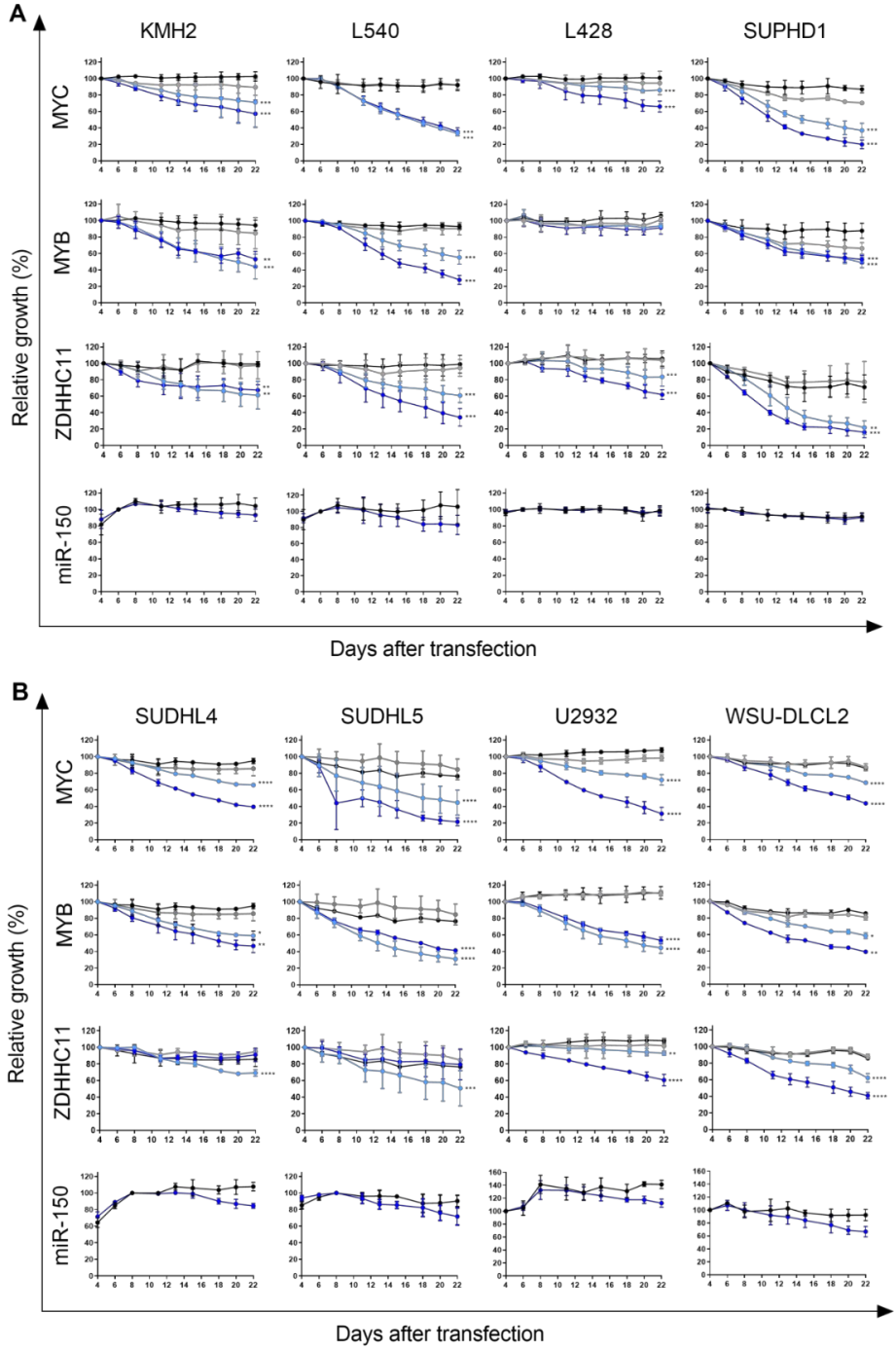
A
KMH2
L540
L428
SUPHD1
MYC
MYB
ZDHHC11
miR-150
Relative growth (%)
Days after transfection
B
SUDHL4
SUDHL5
U2932
WSU-DLCL2
MYC
MYB
ZDHHC11
miR-150
Relative growth (%)
Days after transfection

Figure 3. Effect of MYC, MYB and ZDHHC11 knockdown and miR-150 overexpression on growth of HL and DLBCL cell lines. (A) HL and (B) DLBCL cell lines were infected with lentivirus carrying a shRNA 1 construct targeting MYC, MYB or ZDHHC11 transcripts (two shRNAs per transcript, shRNA 1 in light and shRNA 2 in dark blue) or shRNA control vectors (black and grey). An overexpression vector was used for miR-150 (dark blue), and an empty overexpression vector as a control (black). The effect on cell growth was assessed by following the percentage of GFP+ cells for three weeks post-transfection (n = 3), with the GFP percentage normalized to day four, six or eight after transfection. Mixed model analysis was used to determine significant differences; * $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$.

3.3 MiR-150 targets ZDHHC11 and MYB in HL cells

To explore whether differences in the genes targeted by miR-150 could explain the lack of a phenotype for miR-150 overexpression, we performed AGO2-RNA immunoprecipitation (AGO2-RIP) in two HL cell lines, i.e. L428 and SUPHD1. A good efficiency of the AGO2-RIP was confirmed by showing enrichment of the AGO2 protein by Western blot as well as by enrichment of miR-150, miR-16 and miR-17 by RT-qPCR in the IP fractions (Fig. S6). The numbers of IP enriched probes upon miR-150 overexpression were 225 for L428, 46 for SUPHD1, 65 for ST486 and 27 for DG75. Similar to the results in BL, we also showed a clear enrichment of ZDHHC11 and MYB probes upon miR-150 overexpression in the HL cell lines (Fig. 4A and Table S4). This indicated that upon miR-150 overexpression, ZDHHC11 and MYB transcripts are targeted by miR-150 in HL cells. In a more de-tailed analysis of the AGO2-IP fraction by RT-qPCR, we showed that the three individual transcripts of ZDHHC11 were all enriched in the HL cell lines upon miR-150 overexpression (Fig. 4B). In line with our results in BL, the circZDHHC11 transcript was the most enriched transcript in both cell lines. The fold enrichment of the pcZDHHC11 transcript was with less than 2, lower than the enrichment of the two other ZDHHC11 transcripts, suggesting a less effective interaction with miR-150. Consistent with the findings in BL, we also observed a decrease in MYB protein levels upon miR-150 overexpression in KMH2 and L428 supporting effective targeting by miR-150 (Fig. 4C, D and Fig. S7). Comparison of the other miR-150 target genes identified in the AGO2-RIP experiments in BL and HL revealed no obvious differences between BL and HL that might explain the lack of a phenotype in HL (Fig. S8). In ST486, we identified the previously confirmed miR-150 target EGR2, while this gene was not AGO2-IP enriched in the other cell lines. Thus, our data indicate that although miR-150 can effectively bind to the transcripts of ZDHHC11 and MYB, it does not induce a clear phenotype in HL.

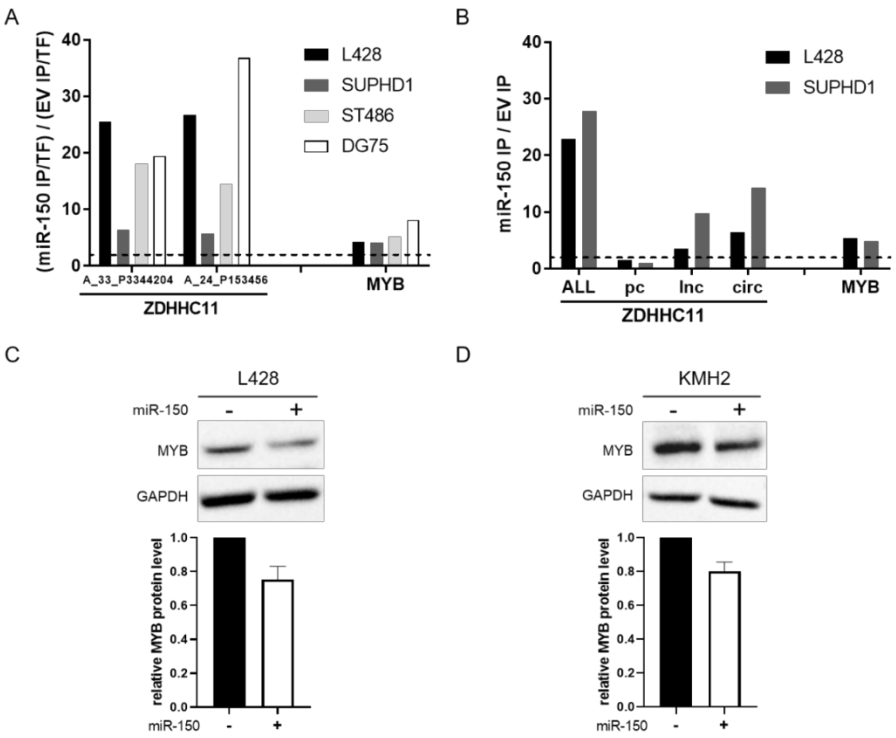

Figure 4. MiR-150 targets ZDHHC11 and MYB in HL cell lines. (A) Microarray analysis showing increased enrichment of ZDHHC11 (2 probes) and MYB tran-scripts in the AGO2 immunoprecipitated (IP) fraction upon miR-150 overexpression in HL (L428 in black, SUPHD1 in dark grey) and BL cell lines (ST486 in light grey, DG75 in white). The dotted line indicates a fold change of 2. (B) RT-qPCR analysis showing increased enrichment of ZDHHC11 transcripts (all three transcripts, ALL; protein-coding transcript, pc; linear non-coding transcript, lnc; circular non-coding transcript, circ) and MYB in the AGO2-IP fraction upon miR-150 overex-pression in L428 (black) and SUPDH1 (dark grey). The increase in IP enrichment was calculated as the ratio IP / total fraction (TF) fraction in miR-150 overexpressing cells over the ratio IP / TF in empty overexpression vector (EV) cells. Western blots showing MYB levels in the HL cell lines (C) L428 and (D) KMH2 infected with EV(miR-150 -) or miR-150 overexpression vector (miR-150 +). The relative expression was normalized to GAPDH (n=2,see also Fig. S7).

4. Discussion

The MYC/miR-150/MYB/ZDHHC11 network was previously established in BL and was shown to have a cell growth regulatory effect[11]. Here we explored the role of the network in HL and DLBCL. The expression of the four components of the network showed the same pattern in cHL and DLBCL as compared to BL. Analysis of the three individual ZDHHC11 products, the protein coding, the long non-coding and the circular ZDHHC11 transcripts, in cHL and DLBCL also showed patterns that were

consistent with those observed in BL. Despite having similar expression patterns of the network components and similar effects upon knockdown of MYC, MYB and ZDHHC11 on cell growth, miR-150 overexpression induced no or limited effects on growth of four cHL and four DLBCL cell lines.
Next, we explored why miR-150 overexpression did not affect growth of cHL and DLBCL cell lines. A first potential explanation might be that the achieved miR-150 levels are insufficient to induce a phenotype. Comparison of miR-150 overexpression efficiencies of HL and DLBCL with BL cell lines showed that the combined endogenous and ectopic levels were in the same range in all three lymphoma subtypes and thus an unlikely ex-planation for the lack of phenotype upon overexpression of miR-150 in cHL and DLBCL.

As a second possible explanation we determined whether miR-150 targets MYB and ZDHHC11 in cHL because these cell lines showed the weakest effect on cell growth upon miR-150 overexpression. Probes for both MYB and ZDHHC11 were among the most enriched targets, with IP enrichment levels similar to those observed in BL[11]. Effective targeting of MYB by miR-150 was also confirmed at the protein level. Together, these data show that miR-150 efficiently targets both MYB and ZDHHC11 transcripts in cHL and that the lack of inducing a phenotype could not be explained by lack of targeting these two transcripts.

A third possible explanation is that in BL the effect of miR-150 on cell growth is caused by a combined regulation of multiple target genes including MYB and ZDHHC11, but also other genes. This could imply that in cHL the efficiency of miR-150 for targeting MYB and ZDHHC11 is insufficient to cause a clear effect on cell growth. It has indeed been shown that the miR-150 target gene repertoire can highly differ between different hematopoietic malignancies, e.g. MYB, FLT3, CBL and EGR2 in MLL-rearranged AML cells[25,26], and DKC1 and AKT2 in NK/T-cell lymphoma[8]. EGR2 is enriched in the IP fraction upon miR-150 OE in ST486, while it is not expressed in DG75 and not enriched in the IP fractions of the two HL cell lines that do not show a phenotype (L428 and SUPHD1) upon miR-150 overexpression. None of the other reported miR-150 target genes were ex-pressed (FLT3) or IP enriched (CBL, DKC1 and AKT2). Analysis of other genes specifically enriched in the AGO2-IP of BL or cHL revealed no obvious candidates that might explain the lack of a phenotype in cHL. As our AGO2-IP analysis was focused on protein coding genes, it is possible that next to targeting MYB and ZDHHC11 transcripts, specific ncRNAs (e.g. lncRNAs or circRNAs) are targeted by miR-150 in only BL or HL. So, it re-mains unclear

why miR-150 overexpression does not show a clear phenotype in cHL.

We were unable to define the miR-150 target genes in DLBCL cell lines, as the lentiviral infection efficiencies were insufficient to allow isolation of sufficient infected cells for the AGO2-IP procedure. We expect that the efficiencies for targeting of miR-150 to MYB and ZDHHC11 in DLBCL will also be good in DLBCL but this needs to be established. So, we cannot rule out that in DLBCL the limited phenotype upon miR-150 overexpression is related to poor efficiency to target MYB and ZDHHC11. A second limitation of our study is that we used a subset of the cell lines for studying the effect of miR-150 overexpression on growth. So, we cannot exclude the possibility that miR-150 may inhibit growth in other HL or DLBCL cell lines. Lastly, as the efficiencies of the shRNAs against MYC, MYB and ZDHHC11 were not re-tested in all cell lines we cannot rule out that differences in the ex-tend of the phenotype are caused by differences in shRNA efficiencies between cell lines.

5. Conclusion

In conclusion, although MYC, MYB and ZDHHC11 all have important roles on growth of cHL and DLBCL, the network as defined in BL with a critical role of miR-150 is not broadly applicable to other GC B-cell derived lymphoma subtypes. Based on our data, induction of miR-150 might present an attractive therapeutic approach for BL, but not for other GC B-cell derived lymphomas. The lymphoma specific role of ZDHHC11 remains to be elucidated and studying the individual ZDHHC11 products might provide further mechanistic insights in different B-cell lymphoma subtypes.

Supplementary figures and tables

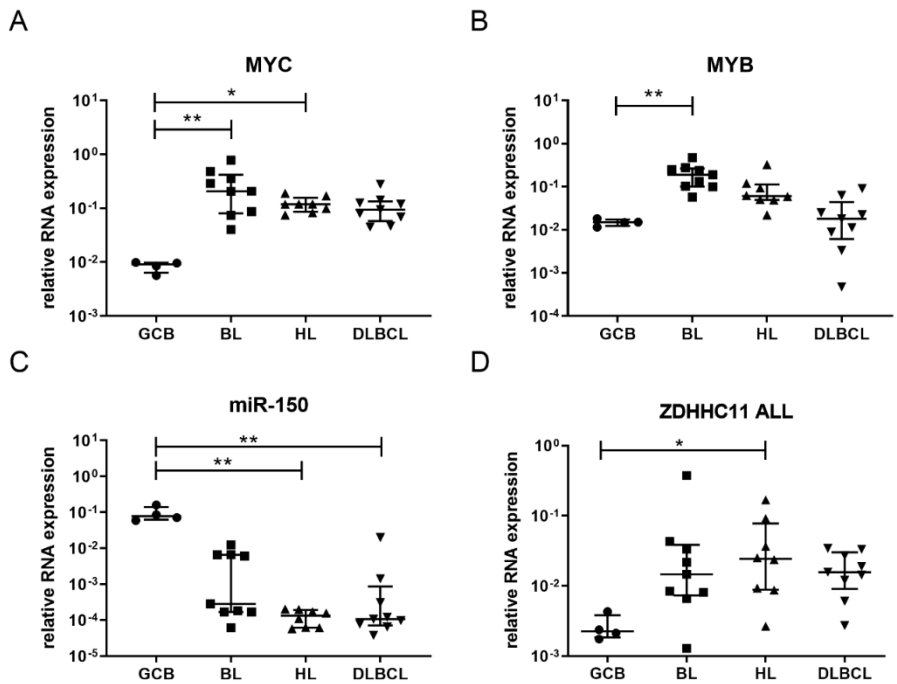

Figure S1. Expression of MYC, MYB, miR-150 and all ZDHHC11 transcripts in B-cell lymphoma cell lines. Relative MYC, MYB, miR-150 and all three ZDHHC11 transcripts (ZDHHC11 ALL) levels in GC B-cells sorted from tonsils (n=4), Burkitt lymphoma (BL, n=9), Hodgkin lymphoma (HL, n=8) and diffuse large B-cell lymphoma (DLBCL, n=9) cell lines were determined by qRT-PCR. Expression levels were normalized to *U6*. Kruskal-Wallis combined with Dunn's post-hoc tests were used to assess significant differences; * $p < 0.05$, ** $p < 0.01$, data are represented as median with interquartile range.

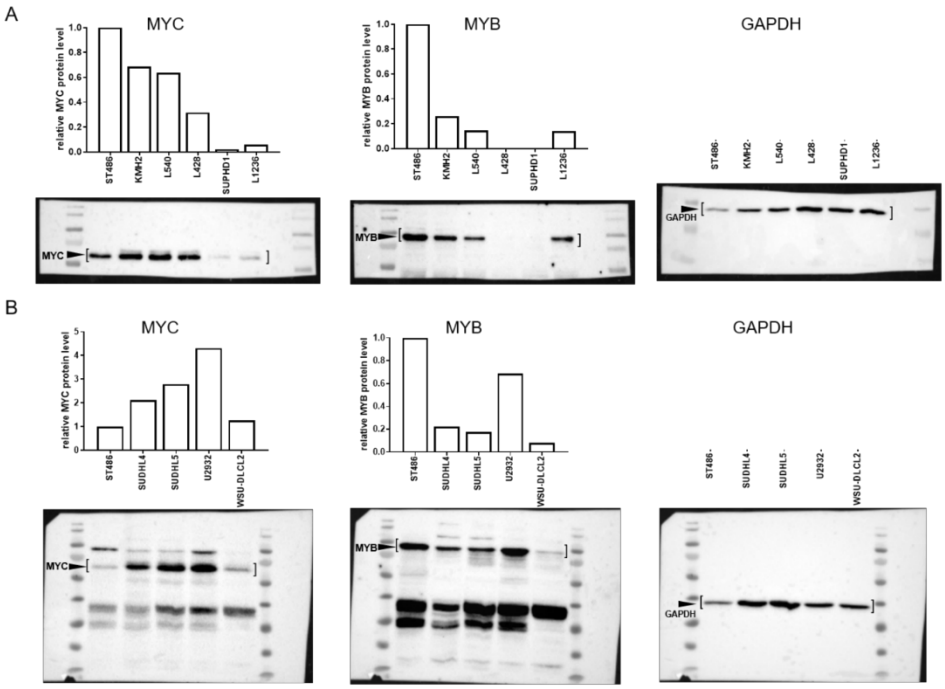

Figure S2. Original immunoblots for MYC, MYB and GAPDH in HL and DLBCL cell lines. (A) The HL blot was cut into two pieces, with the upper part being incubated with the C-terminal anti-MYB antibody (anti-c-Myb [ANA236B], shown in the middle) and the lower part being incubated with the anti-GAPDH antibody (shown on the right). After imaging, the antibodies were stripped from the blot. Next, the upper part was incubated with the anti-MYC antibody (shown on the left). (B) The DLBCL blot was subsequently incubated with anti-MYB antibody (middle blot), anti-MYC antibody (left blot) and anti-GAPDH antibody (the right blot). Efficiency of stripping was checked after each stripping procedure. For HL and DLBCL 20 µg of total protein was loaded per lane, while protein loading for the BL cell line ST486 was 3-fold lower to prevent over exposure. The MYB and MYC levels were normalized to GAPDH levels to correct for loading. The relative protein levels of calibrator sample ST486 were set to 1 for each blot and all other protein levels were expressed relative to the calibrator sample. Arrowheads indicate the position of the specific protein bands.

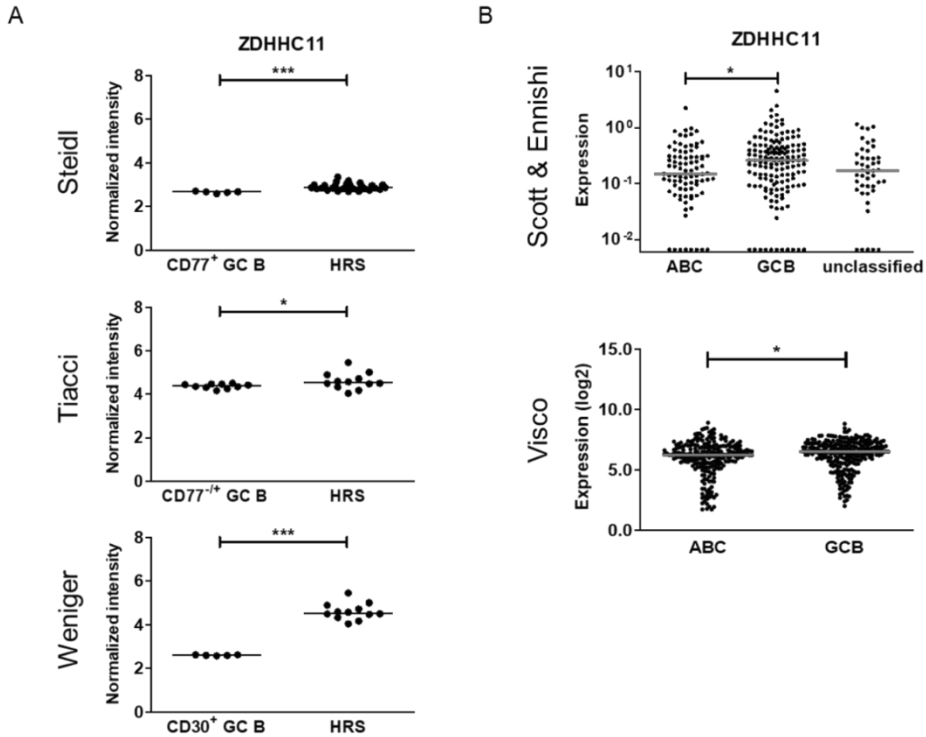

Figure S3. Expression of ZDHHC11 in primary cases of cHL and DLBCL. (A) Expression levels of all ZDHHC11 transcripts in GC B-cells and microdissected HRS cells based on microarray data from indicated studies. (B) Expression of ZDHHC11 in primary ABC, GCB and unclassified DLBCL cases based on RNA sequencing (Scott & Ennishi cohort). Expression of ZDHHC11 in primary ABC and GCB cases based on microarray analysis (Visco cohort). A Kruskal-Wallis with Dunn's post-hoc test was used for the Scott & Ennishi cohort, while the one-sided Mann Whitney test was used for the other cohorts; * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, horizontal lines indicate median values.

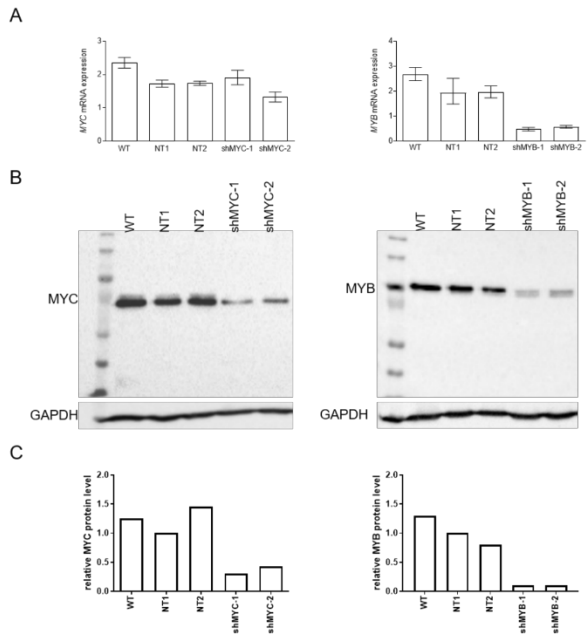

Figure S4. Knockdown efficiency tests of shRNAs targeting MYC and MYB. Knockdown efficiencies of MYC and MYB were determined at (A) RNA level as assessed by RT-qPCR; expression levels were normalized to U6, and at (B) protein level by Western blot in the L540 HL cell line; protein levels were normalized to GAPDH. (C) Quantification results of the relative MYC and MYB protein levels indicating a clear downregulation and good efficiency of the shRNA constructs.

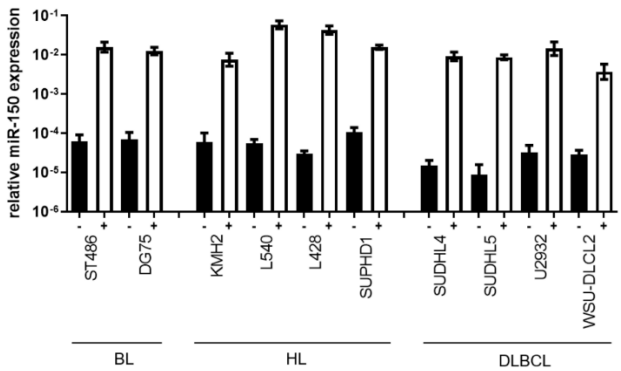

Figure S5. Efficiency of miR-150 overexpression in BL, HL and DLBCL cell lines. The relative miR-150 levels are shown in multiple cell lines upon transfection with control vector (-) or miR-150 overexpression vector (+). MiR-150 levels were normalized to RNU48.

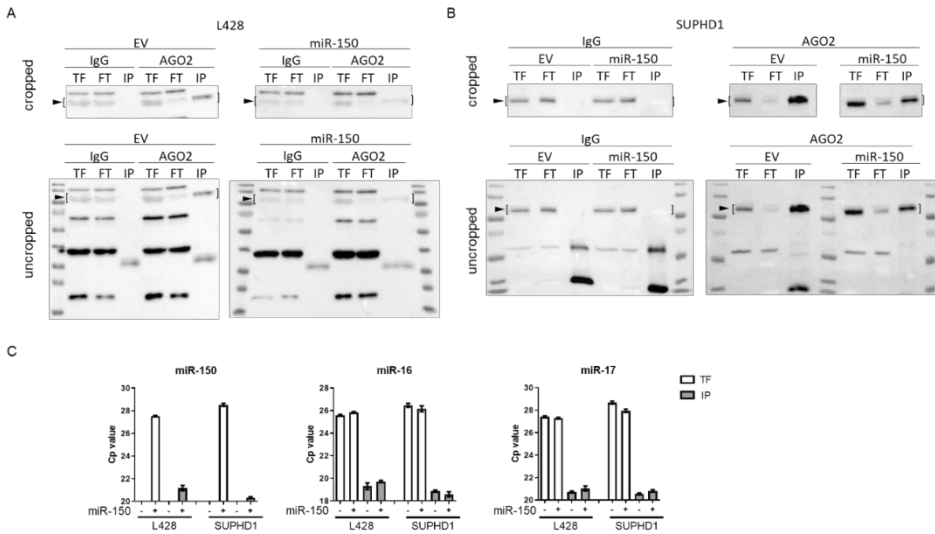

Figure S6. Efficiency of the AGO2 RNA Immuno Precipitation assessed by Western blot and qRT-PCR. The cropped (upper) and uncropped (lower) blots of (A) L428 and (B) SUPHD1 samples. L428 and SUPHD1 HL cell lines were transfected with the miR-150 overexpression vector (miR-150) or empty overexpression vector (EV) and cells were harvested for AGO2-IP. Blots containing total (TF), flow through (FT) and immune-precipitation (IP) fractions of the anti-IgG (control) and anti-AGO2 IPs were incubated with anti-AGO2 antibody to visualize AGO2 enrichment in the IP fraction. Arrowheads on the blots indicate the position of the AGO2 protein bands. (C) Cp values of the indicated miRNAs are shown for the TF (white) and IP fractions (grey) of the HL cell lines L428 and SUPHD1 infected with an empty overexpression vector (-) or the miR-150 overexpression vector (+). In case of miR-150, no expression was observed in cells infected with the empty overexpression vector.

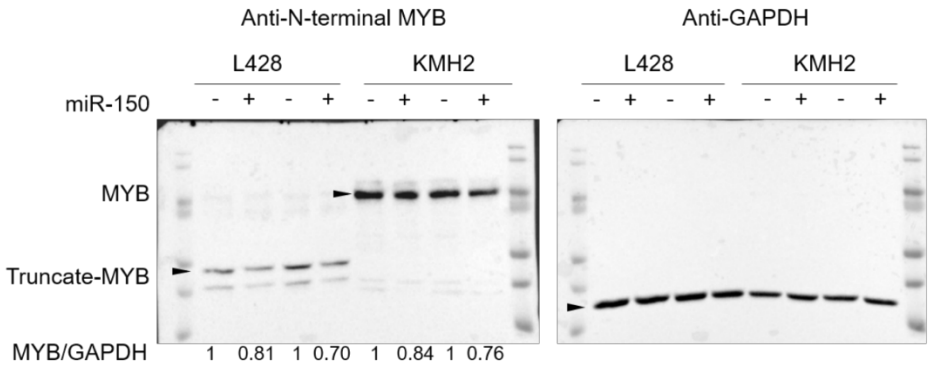

Figure S7. Original immunoblots showing MYB levels in BL and HL cell lines upon overexpression of miR-150. L428 and KMH2 cells were transfected with empty overexpression vector (-) or miR-150 overexpression vector (+) are indicated above the blot. Samples from 2 independent experiments were analyzed. The blot was incubated with the anti-N-terminal-MYB antibody (clone EP769Y, left blot). In the MYB mutated cell line L428, a truncated MYB protein can be detected. In KMH2, full-length MYB protein was detected. After generating the images, the blot was stripped and re-incubated with the anti-GAPDH antibody (right blot). Arrowheads on the blots indicate the position of specific protein bands. Expression of MYB protein was normalized to GAPDH and relative quantification (fold change) of the blots are indicated below the blot.

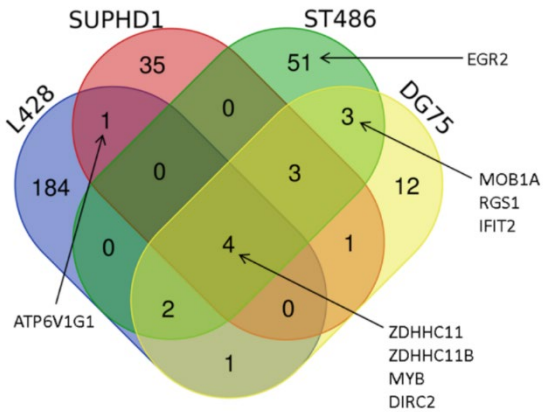

Figure S8. Overlap of miR-150 targets identified in HL and BL cell lines. Venn diagram showing the overlap of miR-150 targets identified in the AGO2-IP of the HL cell lines L428 and SUPHD1 and the BL cell lines ST486 and DG75. Only genes for which the probes were present on both arrays have been used to generate the image.

Table S1. Cell lines and culturing media

	Type	EBV	Origin	Culturing media	FBS
HEK 293T	human embryonic kidney cell	-	ATCC	DMEM	10%
DG75	BL	-	DSMZ	RPMI-1640	10%
CA46	BL	-	DSMZ	RPMI-1640	10%
ST486	BL	-	ATCC	RPMI-1640	20%
BL41	BL	-	DSMZ	RPMI-1640	10%
BL65	BL	+	[1]	RPMI-1640	20%
Namalwa	BL	+	DSMZ	RPMI-1640	10%
Jijoye	BL	+	DSMZ	RPMI-1640	10%
Raji	BL	+	DSMZ	RPMI-1640	10%
Ramos	BL	-	ATCC	RPMI-1640	10%
L428	HL, nodular sclerosis	-	DSMZ	RPMI-1640	10%
L1236	HL, mixed cellularity	-	DSMZ	RPMI-1640	10%
KMH2	HL, mixed cellularity	-	DSMZ	RPMI-1640	10%
DEV	HL, nodular lymphocyte-predominant	-	[2]	RPMI-1640	20%
L540	HL, nodular sclerosis	-	DSMZ	RPMI-1640	20%
L591	HL, nodular sclerosis	+	DSMZ	RPMI-1640	10%
SUPHD1	Hl, nodular sclerosis	-	DSMZ	McCoy 5A	20%
HDLM2	HL, nodular sclerosis	-	DSMZ	RPMI-1640	10%
U2932	DLBCL, ABC	-	DSMZ	RPMI-1640	10%
Ocily3	DLBCL, ABC	-	DSMZ	RPMI-1640	20%
SUDHL16	DLBCL, GCB	-	DSMZ	RPMI-1640	20%
SUDHL10	DLBCL, GCB	-	DSMZ	RPMI-1640	20%
SUDHL6	DLBCL, GCB	-	DSMZ	RPMI-1640	10%
SUDHL5	DLBCL, GCB	-	DSMZ	RPMI-1640	10%
SUDHL4	DLBCL, GCB	-	DSMZ	RPMI-1640	10%
SUDHL2	DLBCL, ABC	-	DSMZ	RPMI-1640	20%
WSU-DLCL2	DLBCL, GCB	-	DSMZ	RPMI-1640	10%

1. Lenoir GM, Vuillaume M, Bonnardel C. The use of lymphomatous and lymphoblastoid cell lines in the study of Burkitt's lymphoma. IARC Sci Publ. 1985;(60):309-18. PMID: 3934070.
2. Atayar C, Kok K, Kluiver J, Bosga A, van den Berg E, van der Vlies P, Blokzijl T, Harms G, Davelaar I, Sikkema-Raddatz B, Martin-Subero JI, Siebert R, Poppema S, van den Berg A. BCL6 alternative breakpoint region break and homozygous deletion of 17q24 in the nodular lymphocyte predominance type of Hodgkin's lymphoma-derived cell line DEV. Hum Pathol. 2006 Jun;37(6):675-83. doi: 10.1016/j.humpath.2006.01.018. PMID: 16733207.

Table S2. Sequences of the qRT-PCR primers

Name	Sequence (5'-3')
MYC-F	GCTCATTTCTGAAGAGGACTTGTTG
MYC-R	TTACGCACAACACTTCCGTAGCT
MYB-F	CCAACTGTTCACGCAGACCT
MYB-R	CTTCTGATGCTGGTGCCATT
ZDHHC11_ALL-F	CACTTGGGCTGCAACAAGAA
ZDHHC11_ALL-R	GGTGGGGTTTCAGGGTAGAAG
pcZDHHC11-F	TGTCGAGCACTCCCCAGA
pcZDHHC11-R	GCAACGGAAAACGGCTCTC
lncZDHHC11-F	AGCACTTCCTGAAAGCCAGC
lncZDHHC11-R	GAAGAACGCAACAGGCATCG
circZDHHC11-F	GGCATCCTCTGTATTTTAATGAACTCT
circZDHHC11-R	GTTGCAGCCAGAAGCCAAG
U6-F	TGGAACGATACAGAGAAGATTAGCA
U6-R	AAAATATGGAACGCTTCACGAATT

F = forward primer, R = reverse primer, S = sense sequence, AS = antisense sequence.

Table S3. Antibodies used for western blot analysis.

Name	Dilution	Catalog number, company
rabbit monoclonal anti-c-MYC [Y69]	1:1000	ab32072, Abcam, Cambridge, UK
rat monoclonal anti-c-Myb [ANA236B] (C-terminal)	1:500	ab169111, Abcam, Cambridge, UK
rabbit monoclonal anti-c-Myb (phospho S11) [EP769Y] (N-terminal)	1:500	ab45150, Abcam, Cambridge, UK
mouse monoclonal anti-GAPDH antibody	1:50000	NB600-502, Novus Biologicals, UK
mouse monoclonal anti-AGO2 antibody (clone 2E12-1C9)	1:400	H00027161-M01, Abnova, Taiwan
goat anti-Rabbit Immunoglobulins/HRP	1:1000	P0448, Dako, USA
goat anti-mouse Immunoglobulins/HRP	1:1000	P0447, Dako, USA
rabbit anti-goat immunoglobulins/HRP	1:1000	P0449, Dako, USA

Table S4. MiR-150 target genes identified by AGO2-RIP-Chip in L428 and SUPHD1-miR-150 cells.

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_24_P153456	ZDHHC11	26.7	1.0	26.7	5.7	1.0	5.7
A_33_P3344204	ZDHHC11	25.5	1.0	25.5	6.4	1.0	6.4
A_33_P3345643	ZDHHC11B	22.5	1.0	22.5	6.2	1.0	6.2
A_23_P31073	MYB	4.2	1.0	4.2	4.5	1.1	4.1
A_23_P20882	ATP6V1G1	2.2	1.0	2.2	2.5	1.0	2.5
A_23_P80778	DIRC2	4.7	2.3	2.0	10.5	4.9	2.1
A_23_P115467	S100A5	6.0	1.0	6.0	1.0	#N/A	#N/A
A_21_P0001246	LOC101927851	8.8	1.5	5.8	1.0	2.5	0.4
A_21_P0007561	XLOC_009764	14.1	2.7	5.2	#N/A	#N/A	#N/A
A_21_P0000463	SNORD105B	15.5	3.2	4.9	1.0	1.2	0.8
A_21_P0000260	SNORD58A	9.9	2.0	4.9	1.0	1.3	0.8
A_33_P3243405	GPR182	16.0	3.4	4.8	#N/A	#N/A	#N/A
A_33_P3419945	Lnc-PTPN9-1	9.1	2.1	4.3	1.7	2.3	0.7
A_21_P0000361	SNORA79	7.7	1.8	4.2	#N/A	#N/A	#N/A
A_23_P136870	MAGEA6	4.2	1.0	4.2	#N/A	#N/A	#N/A
A_33_P3249529	PCNX	8.6	2.0	4.2	1.0	1.0	1.0
A_21_P0000354	SCARNA8	8.8	2.1	4.2	5.0	9.2	0.5
A_21_P0011028	LOC102724910	11.0	2.7	4.1	1.7	2.6	0.6
A_33_P7314857	LOC100506085	4.0	1.0	4.0	#N/A	#N/A	#N/A
A_33_P3278220	RABEPK	10.3	2.6	4.0	1.2	2.2	0.6
A_33_P3367396	FAM177B	4.0	1.0	4.0	#N/A	#N/A	#N/A
A_21_P0008515	XLOC_010856	15.3	4.0	3.9	1.0	1.0	1.0
A_22_P00025249	lnc-CEACAM18-2	3.8	1.0	3.8	1.0	1.0	1.0
A_21_P0000494	SNORA16B	29.6	7.8	3.8	1.5	5.2	0.3
A_19_P00315716	SNORA71A	10.1	2.6	3.8	1.3	2.1	0.6
A_22_P00006901	SCARNA10	5.4	1.4	3.8	1.2	1.8	0.7
A_22_P00014382	lnc-SEZ6L2-1	6.3	1.7	3.8	1.1	1.9	0.5
A_22_P00025115	LINC02332	4.0	1.1	3.7	1.0	1.0	1.0
A_33_P3417459	SCARNA9L	3.7	1.0	3.7	#N/A	#N/A	#N/A
A_21_P0014782	LOC105376108	3.7	1.0	3.7	1.0	1.0	1.0
A_22_P00022141	lnc-TLCD2-2	3.7	1.0	3.6	1.0	#N/A	#N/A
A_22_P00001561	lncRNA	4.4	1.2	3.6	1.9	2.2	0.8

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0000356	SCARNA11	19.0	5.2	3.6	6.3	10.8	0.6
A_33_P3267612	MIR143HG	4.5	1.2	3.6	1.0	1.0	1.0
A_21_P0004252	lnc-SNX18-1	10.0	2.8	3.6	#N/A	#N/A	#N/A
A_33_P3288871	SLC38A1	3.6	1.0	3.6	#N/A	#N/A	#N/A
A_33_P3366493	TPD52L2 pseudogene	4.0	1.1	3.6	#N/A	#N/A	#N/A
A_21_P0005184	lnc-WDR27-1	3.6	1.0	3.6	1.0	1.0	1.0
A_22_P00020980	lnc-C7orf45-1	3.6	1.0	3.6	1.0	#N/A	#N/A
A_22_P00018036	lnc-ZNF236-1	4.1	1.2	3.5	1.0	1.0	1.0
A_33_P3236416	GPR179	10.3	2.9	3.5	1.0	1.0	1.0
A_21_P0008478	lnc-SERPINA12-1	3.8	1.1	3.5	#N/A	#N/A	#N/A
A_21_P0000222	SNORD46	6.0	1.7	3.5	#N/A	#N/A	#N/A
A_21_P0000563	SNORA80B	15.2	4.4	3.5	3.5	7.0	0.5
A_33_P3331426	XLOC_l2_008130	9.7	2.8	3.5	1.3	2.0	0.7
A_21_P0010155	LOC284825	6.8	2.0	3.4	1.8	3.0	0.6
A_21_P0011549	XLOC_l2_005871	3.4	1.0	3.4	1.0	1.1	0.9
A_33_P3215557	ADAMTS7	3.4	1.0	3.4	1.0	1.0	1.0
A_33_P3219459	TMEM240	3.4	1.0	3.4	1.0	#N/A	#N/A
A_21_P0000310	SNORA12	18.7	5.5	3.4	3.5	6.7	0.5
A_33_P3291776	NANS	3.4	1.0	3.4	1.9	1.0	1.9
A_21_P0007229	lncRNA	9.2	2.7	3.4	1.0	1.0	1.0
A_21_P0000386	SNORD89	5.6	1.7	3.4	#N/A	#N/A	#N/A
A_33_P3346680	CDC37P2	3.4	1.0	3.4	1.0	1.0	1.0
A_22_P00010319	lnc-MUC5B-1	3.3	1.0	3.3	#N/A	#N/A	#N/A
A_23_P140967	MEFV	3.3	1.0	3.3	1.0	#N/A	#N/A
A_21_P0000351	SCARNA22	10.2	3.0	3.3	1.8	3.4	0.5
A_21_P0000359	SNORA71D	5.7	1.7	3.3	1.0	1.2	0.8
A_21_P0000317	SNORA22	23.4	7.1	3.3	3.7	11.0	0.3
A_21_P0000350	SCARNA20	5.2	1.6	3.3	1.5	1.8	0.9
A_21_P0000262	SNORA27	18.6	5.7	3.3	8.1	22.9	0.4
A_22_P00012687	LOC100507156	3.3	1.0	3.3	1.0	1.0	1.0
A_33_P3628409	PKI55	3.3	1.0	3.3	1.0	#N/A	#N/A
A_23_P129413	DPEP3	3.3	1.0	3.3	1.0	1.0	1.0
A_21_P0006193	lnc-STX17-1	3.2	1.0	3.2	#N/A	#N/A	#N/A

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0007890	lncRNA	3.3	1.0	3.2	1.0	1.0	1.0
A_33_P3299140	GTF3C5	3.2	1.0	3.2	#N/A	#N/A	#N/A
A_23_P44956	RPL35A	4.6	1.4	3.2	1.9	1.2	1.6
A_21_P0000353	SCARNA23	13.2	4.1	3.2	1.6	#N/A	#N/A
A_21_P0000477	SNORA11B	17.2	5.4	3.2	4.2	7.3	0.6
A_24_P504621	HIGD1AP11	3.2	1.0	3.2	#N/A	#N/A	#N/A
A_33_P3265866	PYY3	3.5	1.1	3.2	#N/A	#N/A	#N/A
A_24_P233078	PYY2	4.0	1.3	3.1	1.0	1.0	1.0
A_33_P3337627	TRPC6	5.9	1.9	3.1	1.5	2.4	0.6
A_22_P00011743	lnc-PER2-1	3.1	1.0	3.1	1.0	1.0	1.0
A_33_P3231923	LOC101927285	6.9	2.2	3.1	1.4	1.8	0.8
A_21_P0000322	SNORA34	39.2	12.6	3.1	8.8	23.6	0.4
A_21_P0000478	SNORA11C	15.2	4.9	3.1	6.2	6.7	0.9
A_24_P21770	YPEL4	3.4	1.1	3.1	1.0	1.0	1.0
A_22_P00011643	lnc-PDCD11-2	3.1	1.0	3.1	1.0	1.0	1.0
A_23_P27133	KRT15	3.1	1.0	3.1	1.0	1.0	1.0
A_23_P49674	ARHGEF15	6.1	2.0	3.1	1.0	1.6	0.6
A_23_P50815	TTYH1	3.1	1.0	3.1	1.0	1.0	1.0
A_22_P00001847	THOC7-AS1	7.3	2.4	3.1	1.4	1.9	0.7
A_23_P416314	HRASLS5	5.0	1.6	3.1	1.3	1.7	0.7
A_21_P0013455	ZNF767P	8.6	2.8	3.1	1.0	#N/A	#N/A
A_33_P3271196	AMOTL1	3.3	1.1	3.1	1.0	1.0	1.0
A_19_P00315967	MLYCD	3.2	1.0	3.1	#N/A	#N/A	#N/A
A_33_P3302428	TNRC6C	5.2	1.7	3.0	1.2	1.8	0.7
A_21_P0000867	ZBTB20-AS1	4.5	1.5	3.0	1.2	1.8	0.7
A_33_P3415491	WDR90	3.0	1.0	3.0	1.0	1.0	1.0
A_33_P3363082	SCARNA5	7.3	2.4	3.0	4.2	7.5	0.6
A_33_P3849275	FHL1	3.0	1.0	3.0	1.0	1.0	1.0
A_22_P00018950	TMEM231	3.0	1.0	3.0	1.0	1.0	1.0
A_22_P00007673	lnc-HIATL1-1	3.4	1.1	3.0	1.0	1.0	1.0
A_33_P3327140	lncRNA	8.0	2.7	3.0	1.5	1.9	0.8
A_33_P3214803	PRDM13	3.0	1.0	3.0	1.0	1.0	1.0
A_33_P3709317	SNORA28	15.1	5.1	3.0	26.7	35.0	0.8

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0011923	WDPCP	3.0	1.0	3.0	1.0	1.0	1.0
A_19_P00802433	LINC01564	11.0	3.7	3.0	1.0	1.0	1.0
A_21_P0005807	lnc-GFRA2-1	8.9	3.0	3.0	1.0	#N/A	#N/A
A_19_P00808834	LINC01478	3.0	1.0	3.0	#N/A	#N/A	#N/A
A_21_P0011822	lnc-ZAP70-2	3.2	1.1	2.9	#N/A	#N/A	#N/A
A_23_P50146	SIGLEC15	3.4	1.1	2.9	1.0	1.0	1.0
A_33_P3334180	PLCH2	3.3	1.1	2.9	1.0	1.0	1.0
A_19_P00801735	SEPT7-AS1	3.1	1.1	2.9	1.0	1.0	1.0
A_24_P152468	LOC100128364	3.0	1.0	2.9	1.0	1.0	1.0
A_22_P00006567	lnc-FLYWCH2-1	3.0	1.0	2.9	#N/A	#N/A	#N/A
A_21_P0000340	SNORA60	4.2	1.4	2.9	1.1	2.2	0.5
A_23_P396981	CCDC66	4.0	1.4	2.9	1.0	#N/A	#N/A
A_33_P3351606	MIR124-2HG	2.9	1.0	2.9	1.0	1.0	1.0
A_33_P3271975	LOC100132368	2.9	1.0	2.9	1.0	#N/A	#N/A
A_23_P68910	SSTR3	3.6	1.2	2.9	1.0	1.0	1.0
A_24_P924862	RAPH1	3.6	1.3	2.9	1.5	1.4	1.1
A_21_P0000237	SNORA10	6.2	2.2	2.9	2.1	3.5	0.6
A_21_P0009268	lnc-MAP2K6-2	11.5	4.0	2.9	1.0	1.0	1.0
A_22_P00017446	lnc-VPS4A-1	3.9	1.4	2.9	1.0	1.0	1.0
A_33_P3236340	LOC100133131	4.2	1.5	2.9	1.6	2.3	0.7
A_22_P00003471	lnc-CCDC69-1	2.9	1.0	2.9	#N/A	#N/A	#N/A
A_21_P0000336	SNORA54	31.2	11.0	2.8	22.8	30.0	0.8
A_33_P3311046	OR2M7	2.8	1.0	2.8	#N/A	#N/A	#N/A
A_22_P00009316	LOC100507205	3.3	1.2	2.8	1.0	1.4	0.7
A_21_P0000324	SNORA36A	7.7	2.7	2.8	#N/A	#N/A	#N/A
A_33_P3403643	LOC101059906	2.9	1.0	2.8	1.0	1.0	1.0
A_33_P3322192	RP11-74K11.1	2.8	1.0	2.8	1.0	1.0	1.0
A_33_P3882624	POT1	3.1	1.1	2.8	1.0	1.0	1.0
A_24_P47681	CAND1	4.1	1.5	2.8	1.0	1.3	0.8
A_21_P0012967	CTC-338M12.9	3.6	1.3	2.8	1.0	1.0	1.0
A_22_P00016235	SNORD57	7.5	2.7	2.8	1.0	1.0	1.0
A_21_P0000212	SNORA68	5.9	2.1	2.8	1.8	4.0	0.4
A_21_P0007854	lnc-HNF1A-1	12.3	4.4	2.8	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0003889	FLJ36777	3.0	1.1	2.8	#N/A	#N/A	#N/A
A_23_P42288	VWA7	3.1	1.1	2.8	1.0	1.0	1.0
A_33_P3391375	LANCL3	6.4	2.3	2.8	1.6	2.0	0.8
A_19_P00321789	RP3-523C21.2	2.8	1.0	2.8	1.0	1.0	1.0
A_22_P00005191	lnc-DKK3-1	2.9	1.0	2.7	1.0	1.0	1.0
A_32_P207243	LOC100134253	26.1	9.5	2.7	3.7	9.6	0.4
A_21_P0000493	SCARNA14	8.8	3.2	2.7	4.2	6.7	0.6
A_33_P3335576	LOC100287006	2.7	1.0	2.7	1.0	#N/A	#N/A
A_33_P3274245	ENDOV	3.5	1.3	2.7	1.0	#N/A	#N/A
A_33_P3368109	EIF4BP3	2.7	1.0	2.7	1.0	1.0	1.0
A_21_P0000308	SNORA9	8.3	3.1	2.7	4.3	9.5	0.5
A_23_P119448	PPP6R1	10.7	3.9	2.7	1.0	1.0	1.0
A_19_P00805812	lnc-UQCRFS1-9	11.1	4.1	2.7	#N/A	#N/A	#N/A
A_33_P3386686	LOC100132874	2.7	1.0	2.7	1.0	1.0	1.0
A_21_P0009285	lnc-C1QTNF1-1	2.7	1.0	2.7	1.0	#N/A	#N/A
A_33_P3312504	PSD4	2.7	1.0	2.7	1.0	1.0	1.0
A_21_P0011573	AC004448.5	2.7	1.0	2.7	1.0	1.0	1.0
A_23_P115573	SHISA4	2.7	1.0	2.7	1.0	1.0	1.0
A_22_P00003107	lnc-MFAP4-3	2.7	1.0	2.7	1.0	1.0	1.0
A_33_P3356577	SIRPB1	2.7	1.0	2.7	1.0	1.0	1.0
A_33_P3629247	ANKMY1	3.2	1.2	2.7	1.0	1.2	0.9
A_22_P00002486	lnc-C16orf13-3	3.0	1.1	2.7	1.0	1.0	1.0
A_24_P307289	TMEM95	3.5	1.3	2.7	1.0	1.0	1.0
A_21_P0000325	SNORA37	15.7	5.9	2.7	5.0	9.3	0.5
A_21_P0000369	SNORA16A	19.5	7.3	2.7	1.4	3.8	0.4
A_22_P00007888	LINC00092	3.1	1.2	2.7	1.0	1.0	1.0
A_24_P292470	UCP3	2.7	1.0	2.7	1.0	1.0	1.0
A_22_P00011325	lnc-OST4-2	2.7	1.0	2.7	1.0	1.0	1.0
A_33_P3452003	LOC143286	3.6	1.4	2.7	1.8	1.9	0.9
A_33_P3255434	MEG3	3.1	1.2	2.6	#N/A	#N/A	#N/A
A_22_P00008937	C12orf80	2.6	1.0	2.6	1.0	1.0	1.0
A_21_P0004128	lnc-EMB-3	2.6	1.0	2.6	1.0	#N/A	#N/A
A_33_P3241250	LOC100132217	2.8	1.1	2.6	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_23_P15357	LGALS3BP	2.7	1.0	2.6	1.0	1.0	1.0
A_33_P3376478	CYP17A1	2.7	1.0	2.6	#N/A	#N/A	#N/A
A_24_P51683	CDK5R2	2.6	1.0	2.6	1.0	1.0	1.0
A_24_P106542	RSPO3	3.6	1.4	2.6	1.0	1.1	0.9
A_21_P0006079	LINC01506	2.9	1.1	2.6	1.0	#N/A	#N/A
A_22_P00002950	lnc-C5orf47-2	2.6	1.0	2.6	1.0	1.0	1.0
A_33_P3228739	LRRC3C	2.6	1.0	2.6	1.0	1.0	1.0
A_23_P17307	MRGBP	2.6	1.0	2.6	2.3	2.2	1.1
A_33_P3213419	LOC100129447	2.6	1.0	2.6	1.0	1.0	1.0
A_22_P00010493	lnc-NBAS-1	4.3	1.7	2.6	1.0	1.0	1.0
A_22_P00012128	lnc-POLR1E-2	2.6	1.0	2.6	1.0	1.0	1.0
A_23_P67896	SCN3A	3.0	1.2	2.6	#N/A	#N/A	#N/A
A_22_P00001270	lnc-ANKRD53-1	2.9	1.1	2.6	1.0	1.0	1.0
A_33_P3310976	lnc-CDH4-1	2.6	1.0	2.6	1.0	1.0	1.0
A_21_P0013089	XLOC_l2_013056	2.6	1.0	2.6	1.0	1.0	1.0
A_22_P00004142	lnc-CLDN6-2	3.5	1.4	2.6	1.0	1.0	1.0
A_21_P0000295	SNORA67	11.8	4.6	2.6	1.8	3.3	0.5
A_33_P3287379	COG8	3.3	1.3	2.6	1.0	1.0	1.0
A_21_P0011562	XLOC_l2_005933	3.2	1.3	2.6	1.0	1.0	1.0
A_21_P0012148	XLOC_l2_008632	2.5	1.0	2.5	1.0	1.3	0.8
A_19_P00315764	LOC644277	2.7	1.1	2.5	1.0	1.0	1.0
A_32_P52330	LOC113230	2.8	1.1	2.5	1.0	1.0	1.0
A_21_P0000331	SNORA44	17.7	7.0	2.5	#N/A	#N/A	#N/A
A_33_P3410821	LOC100134360	3.8	1.5	2.5	1.0	1.0	1.0
A_21_P0010382	lnc-LARGE1-11	2.5	1.0	2.5	#N/A	#N/A	#N/A
A_33_P3383696	SPEG	6.9	2.7	2.5	13.8	12.4	1.1
A_19_P00315843	SCARNA16	5.7	2.2	2.5	4.1	6.4	0.6
A_21_P0000347	SNORA76C	3.0	1.2	2.5	1.0	1.0	1.0
A_21_P0003242	lnc-EPHA6-1	2.7	1.1	2.5	1.0	1.0	1.0
A_22_P00019886	HNF4A-AS1	2.5	1.0	2.5	1.0	1.0	1.0
A_21_P0009382	LINC01563	2.5	1.0	2.5	1.0	1.0	1.0
A_21_P0000126	TGFBR3L	2.8	1.1	2.5	1.0	1.0	1.0
A_33_P3247624	REP15	11.6	4.6	2.5	#N/A	#N/A	#N/A

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0000300	SNORA48	7.4	2.9	2.5	1.0	1.6	0.6
A_24_P255384	RPL31P43	2.5	1.0	2.5	1.0	1.2	0.8
A_21_P0008580	LOC101929151	2.5	1.0	2.5	1.0	1.0	1.0
A_22_P00023919	lnc-MEGF10-1	2.9	1.2	2.5	1.0	1.0	1.0
A_21_P0007948	lnc-AL359392.1-2	2.9	1.2	2.5	1.2	2.2	0.5
A_21_P0000225	SNORD83B	7.7	3.1	2.5	1.0	1.0	1.0
A_23_P352535	PPP1R16B	2.5	1.0	2.5	1.0	1.0	1.0
A_22_P00006862	TCEB3-AS1	3.0	1.2	2.5	1.0	1.0	1.0
A_21_P0001708	lnc-HMCN1-2	11.4	4.6	2.5	1.0	1.0	1.0
A_23_P75790	MYRF	2.6	1.0	2.5	1.0	1.0	1.0
A_21_P0008072	lnc-AL445989.1-2	2.7	1.1	2.5	1.0	1.0	1.0
A_22_P00016483	LOC148413	2.5	1.0	2.5	1.0	2.0	0.5
A_32_P207124	CT47A11	2.8	1.1	2.5	1.0	1.0	1.0
A_33_P3258324	LOC102724279	2.7	1.1	2.5	1.0	1.0	1.0
A_33_P3358233	NES	3.0	1.2	2.5	1.0	1.0	1.0
A_33_P3306207	KLRG2	2.8	1.1	2.5	1.0	1.0	1.0
A_33_P3279124	FAM21C	2.5	1.0	2.5	1.0	1.0	1.0
A_19_P00317653	LINC00969	2.5	1.0	2.5	1.0	1.0	1.0
A_22_P00000643	lnc-ACSM5-1	2.5	1.0	2.5	#N/A	#N/A	#N/A
A_22_P00000427	BOLA3-AS1	2.9	1.2	2.5	1.0	1.0	1.0
A_19_P00325604	LINC-ROR	2.5	1.0	2.5	#N/A	#N/A	#N/A
A_33_P3350673	HOPX	3.2	1.3	2.5	#N/A	#N/A	#N/A
A_23_P48455	AMN	2.5	1.0	2.5	1.0	1.0	1.0
A_21_P0006850	lnc-LYZL1-2	2.5	1.0	2.5	1.0	#N/A	#N/A
A_23_P67952	MYCNOS	2.5	1.0	2.5	1.0	1.0	1.0
A_22_P00023006	lnc-CHRNA6-1	2.5	1.0	2.5	1.0	1.0	1.0
A_33_P3311717	TGIF1	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3258316	XLOC_l2_013837	2.4	1.0	2.4	1.0	1.0	1.0
A_22_P00003321	lnc-CARHSP1-1	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3287310	TMEM273	2.4	1.0	2.4	1.0	1.0	1.0
A_22_P00017056	lnc-TUBB-7	2.4	1.0	2.4	#N/A	#N/A	#N/A
A_22_P00016785	LINC00967	2.9	1.2	2.4	1.0	1.0	1.0
A_22_P00013897	lnc-RPS21-2	3.1	1.3	2.4	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0009788	lnc-ZNF793-1	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3380751	ST8SIA1	2.4	1.0	2.4	1.4	2.2	0.6
A_23_P47282	ST14	2.4	1.0	2.4	1.0	#N/A	#N/A
A_21_P0002612	lnc-GPR39-2	2.4	1.0	2.4	1.0	#N/A	#N/A
A_22_P00005332	lnc-DOLPP1-1	2.4	1.0	2.4	1.0	1.0	1.0
A_21_P0000307	SNORA2B	9.3	3.8	2.4	4.3	8.6	0.5
A_33_P3239759	PPAN-P2RY11	3.9	1.6	2.4	1.0	1.0	1.0
A_21_P0013085	XLOC_l2_013031	3.3	1.4	2.4	1.1	1.6	0.7
A_22_P00014771	lnc-SLC36A4-1	3.1	1.3	2.4	1.0	1.0	1.0
A_21_P0002398	lnc-KIDINS220-6	3.2	1.3	2.4	1.0	1.0	1.0
A_21_P0012616	XLOC_l2_010854	2.6	1.1	2.4	1.0	1.0	1.0
A_23_P254212	RPA4	7.0	2.9	2.4	1.0	1.0	1.0
A_33_P3239102	GOLGA6L10	4.4	1.8	2.4	1.2	1.7	0.7
A_33_P3350202	MOCS3	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3323019	LOC729856	2.6	1.1	2.4	1.0	1.0	1.0
A_33_P3344991	TBC1D3L	2.7	1.1	2.4	1.0	1.0	1.0
A_22_P00012807	lnc-RAP1GDS1-3	2.4	1.0	2.4	1.0	#N/A	#N/A
A_23_P373031	CACNA1C	2.4	1.0	2.4	1.0	1.0	1.0
A_22_P00014270	MFI2-AS1	3.6	1.5	2.4	1.0	1.0	1.0
A_33_P3329462	DLEU1-AS1	3.1	1.3	2.4	1.0	#N/A	#N/A
A_33_P3284715	SCARNA7	4.4	1.9	2.4	1.0	1.0	1.0
A_21_P0004750	lnc-SUPT3H-1	9.5	4.0	2.4	1.0	1.0	1.0
A_23_P89155	CDK3	3.9	1.6	2.4	1.0	1.7	0.6
A_33_P3285868	CYGB	2.4	1.0	2.4	1.0	1.0	1.0
A_22_P00011520	lnc-PAXIP1-1	2.9	1.2	2.4	1.0	1.0	1.0
A_33_P3247403	TOR3A	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3221960	IL18RAP	3.0	1.3	2.4	1.0	2.0	0.5
A_33_P3293913	BICC1	8.2	3.5	2.4	#N/A	#N/A	#N/A
A_22_P00024468	lnc-CTNNA2-1	3.2	1.3	2.4	1.0	1.0	1.0
A_33_P3335371	MAML3	2.4	1.0	2.4	1.0	1.0	1.0
A_24_P368943	EVX1	2.4	1.0	2.4	1.0	1.0	1.0
A_21_P0000299	SNORA19	24.9	10.5	2.4	11.3	17.7	0.6
A_21_P0003216	LOC101927440	4.1	1.7	2.4	1.0	#N/A	#N/A

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0000236	SNORA64	8.8	3.7	2.4	2.8	3.8	0.7
A_33_P3308153	MTM1	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3267482	KIAA1804	3.2	1.4	2.4	1.0	1.0	1.0
A_24_P280497	FBRSL1	2.4	1.0	2.4	1.0	1.0	1.0
A_33_P3343981	AATK	3.1	1.3	2.3	1.0	1.0	1.0
A_33_P3401284	RMRP	4.1	1.8	2.3	1.0	1.0	1.0
A_21_P0000479	SNORA11D	14.7	6.3	2.3	4.5	7.2	0.6
A_33_P3381292	lnc-FGF3-3	2.3	1.0	2.3	1.0	1.0	1.0
A_24_P18802	VPS18	7.4	3.1	2.3	1.0	1.0	1.0
A_21_P0004883	lnc-UBR2-1	2.3	1.0	2.3	1.0	1.0	1.0
A_21_P0000218	SNORD35A	3.5	1.5	2.3	#N/A	#N/A	#N/A
A_21_P0000309	SNORA11	5.2	2.2	2.3	2.9	4.6	0.6
A_22_P00006278	lnc-FAM76A-1	3.0	1.3	2.3	1.0	1.0	1.0
A_33_P3406828	MAFIP	2.4	1.0	2.3	1.0	1.0	1.0
A_23_P157465	UBXN8	2.6	1.1	2.3	2.0	1.3	1.5
A_33_P3275722	LY6G6D	2.4	1.0	2.3	1.0	1.0	1.0
A_22_P00014899	lnc-SLC9A1-1	2.3	1.0	2.3	1.0	1.0	1.0
A_21_P0011595	XLOC_l2_006101	5.7	2.4	2.3	1.0	#N/A	#N/A
A_33_P3318946	HAPLN2	2.9	1.3	2.3	1.0	1.0	1.0
A_21_P0000258	SNORD26	7.3	3.1	2.3	1.0	1.0	1.0
A_22_P00020414	lnc-TTC7B-2	2.7	1.2	2.3	1.0	#N/A	#N/A
A_33_P3287113	UVSSA	2.3	1.0	2.3	1.0	1.0	1.0
A_22_P00000419	TM4SF19-AS1	2.3	1.0	2.3	1.0	1.0	1.0
A_33_P3365666	DTX2	2.5	1.1	2.3	1.0	1.0	1.0
A_33_P3278826	LTK	3.4	1.5	2.3	1.0	1.0	1.0
A_21_P0000593	SNORA70D	2.9	1.3	2.3	#N/A	#N/A	#N/A
A_22_P00017762	CCNT2-AS1	9.7	4.2	2.3	1.0	1.0	1.0
A_22_P00016775	TRIM52-AS1	2.6	1.1	2.3	1.0	1.0	1.0
A_21_P0014853	GS1-24F4.2	2.3	1.0	2.3	1.0	1.0	1.0
A_21_P0000348	SNORA80A	4.7	2.0	2.3	1.0	1.0	1.0
A_33_P3239143	ZNF497	2.3	1.0	2.3	1.0	1.0	1.0
A_22_P00024619	lnc-RP11-503N18.3.1-3	2.4	1.0	2.3	1.0	1.0	1.0
A_33_P3234540	ABCA17P	2.3	1.0	2.3	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_22_P00012570	lnc-PTP4A2-1	2.3	1.0	2.3	1.0	1.0	1.0
A_22_P00006290	RAD51-AS1	2.9	1.3	2.3	1.0	1.0	1.0
A_33_P3305105	VWA5A	2.4	1.0	2.3	1.0	#N/A	#N/A
A_19_P00808072	lnc-RTL1-2	2.4	1.0	2.3	1.0	1.0	1.0
A_33_P3474250	TRIM44	2.3	1.0	2.3	1.0	1.7	0.6
A_21_P0013166	FOXL3	2.3	1.0	2.3	1.0	1.0	1.0
A_33_P3359354	C1orf86	2.5	1.1	2.3	1.0	1.0	1.0
A_33_P3396459	POLR2H	2.3	1.0	2.3	1.0	1.0	1.0
A_22_P00001924	lnc-BAI3-3	2.4	1.1	2.3	1.0	1.0	1.0
A_24_P229871	LINC00469	2.3	1.0	2.3	2.8	4.1	0.7
A_21_P0000303	SNORA75	3.1	1.4	2.3	#N/A	#N/A	#N/A
A_21_P0000341	SNORA61	5.3	2.3	2.3	1.0	1.4	0.7
A_21_P0000474	SNORA38B	9.8	4.3	2.3	#N/A	#N/A	#N/A
A_33_P3798739	LOC286382	2.3	1.0	2.3	1.0	1.0	1.0
A_21_P0000342	SNORA5B	7.2	3.2	2.3	3.0	2.1	1.5
A_33_P3412556	PPIAP28	2.3	1.0	2.3	1.0	#N/A	#N/A
A_21_P0007321	lnc-SOX6-1	9.4	4.2	2.3	1.0	1.0	1.0
A_33_P3303519	CLEC12B	3.0	1.3	2.3	1.1	2.3	0.5
A_22_P00014685	lnc-SLC25A21-1	2.6	1.1	2.3	1.0	1.0	1.0
A_33_P3338360	SCARNA13	5.2	2.3	2.3	3.1	2.9	1.0
A_23_P325726	ACOT11	2.8	1.2	2.3	1.0	#N/A	#N/A
A_22_P00007594	lnc-HDDC3-1	2.3	1.0	2.3	1.0	1.0	1.0
A_33_P3393537	PTAFR	2.4	1.0	2.3	1.0	1.0	1.0
A_19_P00315581	LINC01122	4.2	1.9	2.3	1.2	1.5	0.8
A_21_P0004987	lnc-GMDS-4	2.3	1.0	2.3	1.0	1.0	1.0
A_33_P3297468	SLC34A3	2.2	1.0	2.2	1.0	1.0	1.0
A_21_P0009377	lnc-NLGN2-1	2.2	1.0	2.2	1.0	1.0	1.0
A_21_P0002976	lnc-GPR27-2	2.8	1.2	2.2	1.0	1.0	1.0
A_22_P00010068	LOC101927204	2.2	1.0	2.2	1.0	1.0	1.0
A_33_P3338152	HIF3A	2.2	1.0	2.2	1.0	1.0	1.0
A_22_P00015927	lnc-TCL1B-2	10.0	4.5	2.2	1.0	1.0	1.0
A_22_P00023975	PAQR9-AS1	3.2	1.4	2.2	1.0	1.0	1.0
A_33_P3229288	ACE	2.2	1.0	2.2	1.0	1.1	0.9

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_22_P00003762	lnc-CDIPT-2	2.2	1.0	2.2	1.0	1.0	1.0
A_33_P3335682	PPP1R14A	2.2	1.0	2.2	1.0	1.0	1.0
A_23_P164341	VAMP2	2.5	1.1	2.2	1.0	1.0	1.0
A_22_P00011225	lnc-OPRL1-1	2.4	1.1	2.2	1.0	1.0	1.0
A_22_P00011704	lnc-PDZD7-1	2.4	1.1	2.2	1.0	1.0	1.0
A_22_P00015195	LOC100996842	2.3	1.0	2.2	1.0	1.0	1.0
A_33_P3308456	PRAC2	2.5	1.1	2.2	1.0	1.0	1.0
A_19_P00319372	LINC00969	2.7	1.2	2.2	1.0	1.0	1.0
A_33_P3306327	CELF5	3.8	1.7	2.2	1.2	1.8	0.7
A_23_P111311	AKAP12	2.9	1.3	2.2	#N/A	#N/A	#N/A
A_33_P3309365	SLC25A3P1	2.5	1.1	2.2	1.0	1.0	1.0
A_22_P00019757	VDAC1P8	2.6	1.2	2.2	1.0	1.1	0.9
A_33_P3280950	A2M-AS1	2.2	1.0	2.2	1.0	1.0	1.0
A_23_P163711	FAM57B	3.0	1.4	2.2	1.0	1.0	1.0
A_33_P3359683	IL16	2.5	1.2	2.2	1.0	1.0	1.0
A_21_P0013931	THC2673826	2.2	1.0	2.2	#N/A	#N/A	#N/A
A_33_P3227217	SNORA81	27.0	12.3	2.2	27.6	44.4	0.6
A_33_P3374365	LOC100129702	2.2	1.0	2.2	1.0	1.0	1.0
A_33_P3365932	WASH1	2.2	1.0	2.2	1.0	1.0	1.0
A_23_P131060	CYP4F8	2.2	1.0	2.2	1.0	1.0	1.0
A_33_P7618758	LINC01541	6.8	3.1	2.2	2.2	1.9	1.2
A_21_P0000592	SNORA70G	3.3	1.5	2.2	1.4	1.6	0.8
A_21_P0005689	LOC101929622	2.4	1.1	2.2	1.0	1.1	0.9
A_33_P3225298	XKR9	2.2	1.0	2.2	1.0	1.0	1.0
A_22_P00003110	lnc-C9orf103-1	2.2	1.0	2.2	1.0	1.0	1.0
A_22_P00018112	LOC102724231	2.2	1.0	2.2	1.0	1.0	1.0
A_21_P0006395	lnc-PTGES2-1	2.2	1.0	2.2	1.0	1.0	1.0
A_24_P932736	HMBOX1	11.5	5.3	2.2	1.0	1.0	1.0
A_33_P3383226	GP9	2.2	1.0	2.2	#N/A	#N/A	#N/A
A_23_P424734	EXOC3L1	2.4	1.1	2.1	#N/A	#N/A	#N/A
A_19_P00321388	LINC00511	2.2	1.0	2.1	1.0	1.0	1.0
A_33_P3312754	LOC102467146	2.1	1.0	2.1	1.0	1.0	1.0
A_33_P3303176	MRGPRG	3.1	1.4	2.1	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_21_P0000220	SNORD33	4.9	2.3	2.1	1.4	2.4	0.6
A_21_P0000397	SCARNA18	2.6	1.2	2.1	2.5	2.7	0.9
A_24_P359191	SLC6A6	2.1	1.0	2.1	1.0	1.0	1.0
A_23_P313031	LOC101930506	2.4	1.1	2.1	1.0	1.0	1.0
A_21_P0012294	GGTLC4P	2.1	1.0	2.1	1.0	1.0	1.0
A_21_P0000394	SNORD110	6.9	3.3	2.1	1.2	#N/A	#N/A
A_22_P00003569	SNHG18	2.4	1.1	2.1	1.0	1.0	1.0
A_23_P155463	LRRC2	9.8	4.6	2.1	1.0	#N/A	#N/A
A_22_P00004304	lnc-CNTLN-2	2.2	1.0	2.1	1.0	1.0	1.0
A_33_P3354771	MEF2BNB	2.3	1.1	2.1	1.0	1.0	1.0
A_23_P219197	RGS3	2.1	1.0	2.1	3.0	3.3	0.9
A_33_P3359308	KLHL29	2.6	1.3	2.1	1.0	1.0	1.0
A_21_P0000257	SNORD27	10.2	4.8	2.1	1.0	1.0	1.0
A_24_P88079	MUC6	2.1	1.0	2.1	1.0	1.0	1.0
A_21_P0010415	lnc-APOL1-1	2.7	1.3	2.1	1.0	1.0	1.0
A_33_P3399468	LOC100133182	2.1	1.0	2.1	1.0	1.0	1.0
A_22_P00002236	KCNMA1-AS1	8.7	4.1	2.1	#N/A	#N/A	#N/A
A_33_P3248272	UBXN8	2.7	1.3	2.1	1.7	1.3	1.3
A_33_P3411080	FSCN2	2.1	1.0	2.1	1.0	1.0	1.0
A_22_P00013961	lnc-RTL1-2	2.3	1.1	2.1	1.0	1.0	1.0
A_21_P0012105	CRYGEP	2.6	1.2	2.1	1.0	1.0	1.0
A_33_P3400429	UBE3A	2.2	1.1	2.1	1.8	1.4	1.3
A_22_P00007112	lnc-GLUD1-3	2.1	1.0	2.1	1.0	1.0	1.0
A_32_P98732	GCM1	2.1	1.0	2.1	#N/A	#N/A	#N/A
A_22_P00002900	CTBP1-AS2	2.1	1.0	2.1	1.0	1.0	1.0
A_24_P396327	TYW3	2.5	1.2	2.1	1.2	1.7	0.7
A_32_P145153	RPL31	2.1	1.0	2.1	1.2	1.0	1.2
A_33_P3300635	PFKFB2	2.1	1.0	2.1	1.0	1.0	1.0
A_22_P00005789	lnc-EPB41-2	2.1	1.0	2.1	1.0	1.0	1.0
A_33_P3306192	KBTBD13	2.1	1.0	2.1	1.0	1.0	1.0
A_22_P00015513	LOC101929294	2.1	1.0	2.1	1.3	1.2	1.1
A_21_P0000591	SNORA70F	2.7	1.3	2.1	#N/A	#N/A	#N/A
A_21_P0014334	LOC101928557	2.4	1.1	2.1	1.0	1.0	1.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_22_P00003512	lnc-CCL1-1	2.6	1.3	2.0	1.0	1.0	1.0
A_24_P131589	CD86	8.0	3.9	2.0	1.0	1.0	1.0
A_33_P3301689	ZNF326	2.0	1.0	2.0	1.0	1.0	1.0
A_21_P0007619	LINC02385	2.0	1.0	2.0	1.0	1.0	1.0
A_33_P3292130	XLOC_l2_013383	2.0	1.0	2.0	1.0	1.0	1.0
A_21_P0000363	SNORA25	7.1	3.5	2.0	16.0	19.7	0.8
A_22_P00024993	LOC102724231	2.0	1.0	2.0	1.0	1.0	1.0
A_22_P00009473	PSMG3-AS1	2.0	1.0	2.0	1.0	1.0	1.0
A_21_P0009324	lnc-CCR7-1	2.5	1.2	2.0	1.0	1.0	1.0
A_23_P107801	C19orf44	2.2	1.1	2.0	1.0	1.0	1.0
A_22_P00013941	lnc-RRP8-1	2.3	1.1	2.0	1.0	1.0	1.0
A_23_P389987	TLX2	4.7	2.3	2.0	1.0	1.0	1.0
A_21_P0002061	LOC101927577	2.9	1.4	2.0	1.0	1.0	1.0
A_21_P0000270	SNORA63	4.6	2.3	2.0	1.7	2.8	0.6
A_24_P120934	GADD45G	3.0	1.5	2.0	1.0	1.0	1.0
A_21_P0001923	LINC01911	9.3	4.6	2.0	1.0	1.0	1.0
A_21_P0000301	SNORA5A	7.3	3.6	2.0	1.9	1.8	1.1
A_33_P3241741	SNORA23	3.7	1.8	2.0	3.8	4.0	1.0
A_33_P3393091	DA197111	2.0	1.0	2.0	#N/A	#N/A	#N/A
A_22_P00009574	LOC100506113	2.3	1.2	2.0	1.0	1.0	1.0
A_22_P00000222	LOC100506585	2.0	1.0	2.0	1.0	1.0	1.0
A_33_P3367171	SLC22A8	2.1	1.0	2.0	1.0	1.0	1.0
A_33_P3410849	C8orf58	2.0	1.0	2.0	1.0	1.0	1.0
A_33_P3219811	PTGDS	2.2	1.1	2.0	1.0	1.0	1.0
A_22_P00017815	LINC00638	2.5	1.2	2.0	1.0	1.0	1.0
A_24_P206344	ZNF746	2.0	1.0	2.0	1.0	1.0	1.0
A_21_P0000251	SNORA65	6.2	3.1	2.0	4.2	4.6	0.9
A_21_P0009735	LOC102723811	3.3	1.6	2.0	#N/A	#N/A	#N/A
A_23_P94009	LSM8	2.2	1.1	2.0	3.2	2.1	1.5
A_21_P0007070	lnc-RPP30-2	9.4	4.7	2.0	1.0	1.0	1.0
A_23_P53467	IKBIP	1.1	1.0	1.1	4.0	1.0	4.0
A_24_P370670	ZMYM6NB	1.9	3.2	0.6	3.2	1.0	3.2
A_22_P00016998	DSCR9	4.0	7.4	0.5	6.1	2.1	3.0

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_23_P25121	FKBP11	6.3	10.3	0.6	8.2	2.8	2.9
A_33_P3267296	FKBP11	5.8	10.0	0.6	6.9	2.4	2.9
A_24_P52697	H19	24.1	37.0	0.7	3.0	1.0	2.9
A_23_P41664	LRRC70	#N/A	#N/A	#N/A	2.9	1.0	2.8
A_24_P931443	GPR68	1.0	1.0	1.0	3.4	1.2	2.8
A_24_P166613	EPDR1	1.0	1.3	0.8	2.8	1.0	2.8
A_33_P3352827	SLAMF1	#N/A	#N/A	#N/A	3.9	1.4	2.7
A_23_P28318	NDUFAF7	1.5	1.0	1.5	2.6	1.0	2.6
A_23_P86283	LAPTM5	1.0	1.3	0.8	2.6	1.0	2.6
A_24_P343271	RMND1	1.2	1.0	1.2	2.5	1.0	2.5
A_24_P393565	ZNF396	#N/A	#N/A	#N/A	2.5	1.0	2.5
A_33_P3412160	CLCC1	1.0	1.0	1.0	2.6	1.0	2.5
A_23_P17287	IAH1	1.0	1.0	1.0	3.8	1.5	2.5
A_19_P00319413	lnc-NRG1-2	1.3	3.0	0.4	4.7	1.9	2.5
A_23_P136504	SLC25A21	1.0	1.0	1.0	5.2	2.1	2.5
A_23_P114232	PRDX4	3.1	1.8	1.7	8.9	3.6	2.5
A_23_P77415	OSGIN1	1.9	1.3	1.5	3.4	1.4	2.4
A_24_P810290	PPAPDC1A	1.0	1.7	0.6	2.4	1.0	2.4
A_33_P3262789	REEP6	1.0	1.0	1.0	2.5	1.0	2.4
A_33_P3330811	C8orf59	1.0	1.0	1.0	2.5	1.1	2.4
A_23_P68472	DPM1	1.0	1.0	1.0	3.8	1.6	2.4
A_21_P0011758	XLOC_l2_007097	2.0	4.7	0.4	2.8	1.2	2.4
A_23_P98350	BIRC3	1.1	2.3	0.5	2.3	1.0	2.3
A_21_P0006091	XLOC_007776	1.2	1.5	0.8	2.3	1.0	2.3
A_24_P317762	LY6E	1.0	1.2	0.8	2.3	1.0	2.3
A_21_P0002904	LINC01326	1.1	2.4	0.5	2.3	1.0	2.3
A_21_P0007787	LINC00944	1.8	2.0	0.9	3.6	1.6	2.3
A_33_P3295523	RAC3	1.5	1.3	1.1	2.3	1.0	2.3
A_32_P14762	OOEP	1.1	1.6	0.7	3.6	1.6	2.3
A_23_P53856	N4BP2L2	2.2	1.2	1.9	3.1	1.4	2.3
A_21_P0007481	LINC00944	2.5	2.4	1.1	3.8	1.7	2.2
A_24_P389916	LRRC32	4.7	6.2	0.7	3.4	1.5	2.2
A_23_P98252	ARL2	3.7	6.4	0.6	14.6	6.6	2.2

Probe name	Gene symbol	L428			SUPHD1		
		miR-150 IP/TF	EV IP/TF	miR150/ EV	miR-150 IP/TF	EV IP/TF	miR150/ EV
A_22_P00005132	LINC00944	1.6	2.1	0.8	3.5	1.6	2.2
A_23_P385217	ARL8B	1.0	1.0	1.0	2.7	1.2	2.2
A_33_P3255229	SETD7	1.0	1.0	1.0	2.2	1.0	2.2
A_23_P251499	PCOLCE	1.0	1.0	1.0	2.2	1.0	2.2
A_24_P16913	ABCC4	1.0	1.3	0.8	7.9	3.7	2.2
A_21_P0010896	LINC00864	1.0	1.0	1.0	4.2	2.0	2.1
A_21_P0012475	XLOC_l2_010489	3.5	7.9	0.4	3.2	1.5	2.1
A_23_P380318	EGR4	1.5	1.3	1.2	2.7	1.3	2.1
A_23_P107693	ZNF586	#N/A	#N/A	#N/A	2.4	1.2	2.1
A_21_P0007789	LINC00944	#N/A	#N/A	#N/A	3.9	1.9	2.1
A_23_P396867	HM13	1.0	1.0	1.0	2.1	1.0	2.1
A_22_P00018617	LOC101927027	1.0	1.3	0.8	2.4	1.2	2.0
A_23_P162355	HOXC5	3.6	5.2	0.7	3.6	1.8	2.0
A_33_P3294449	DCAF6	#N/A	#N/A	#N/A	2.6	1.3	2.0
A_23_P131653	PIGF	1.1	1.0	1.1	3.8	1.9	2.0
A_22_P00016858	lnc-TRPT1-1	1.7	2.1	0.8	2.5	1.2	2.0
A_33_P3370832	FAM117B	1.0	1.0	1.0	2.1	1.1	2.0

#N/A means “No value available”

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