

SUPPLEMENTAL DATA

SUPPLEMENTAL MATERIALS AND METHODS

Cell culture and preparation of the specimens

BL cell lines (BL-CLs) were cultured in RPMI 1640 (Gibco-Invitrogen, Karlsruhe, Germany) supplemented with antibiotics (Gibco-Invitrogen) and 10% fetal bovine serum (FBS) (Gibco-Invitrogen). Cells were treated with Colcemid (0.02 µg/ml) (Gibco-Invitrogen) overnight when they were growing rapidly. BL-CLs and primary material were harvested and fixed with methanol-acetic acid (3:1 v/v) by conventional methods [1].

Multicolor Fluorescence In Situ Hybridization

We performed multicolor fluorescence in situ hybridization (mFISH) using the 24Xcyte color kit for human chromosomes (MetaSystems, Altlussheim, Germany) according to the supplier's recommendations. Briefly, metaphases were hybridized with 24 different chromosome painting probes with specific fluorochrome combinations for all human chromosomes simultaneously. Each paint was labeled with one of the five different fluorochromes (DEAC, FITC, Spectrum Orange, Texas Res, Cy5) or with a unique combination of them. Metaphase chromosomes were counterstained with 4,6-diamino-2-phenylindole (DAPI) (Boehringer/Roche, Mannheim, Germany). After hybridization, gray-scale images of the fluorochromes were acquired using an epifluorescence microscope (Carl Zeiss, Jena, Germany) equipped with a high-resolution cooled CCD camera (Photometrics, München, Germany). A 24-pseudocolor image was built up by overlay of the gray-scale images and analysed by the MetaSystems Isis software package (MetaSystems). Karyotypes were described according to the International System for Human Cytogenetic Nomenclature (ISCN, 2020) [2] and revised using the "CyDAS Online Analysis Site" [3].

Probe selection for metaphase FISH mapping of 1q abnormalities

To determine the exact position of the breakpoints detected by mFISH and possible target genes on 1q, and to uncover cryptic 1q rearrangements, we applied FISH with 37 specific probes covering the whole 1q (supplemental Table S1). Dual-color metaphase FISH was performed on chromosome preparations from all BL patients using two differentially labeled bacterial artificial chromosome (BAC) clones hybridizing to 1q. Biotin-16- or digoxigenin-11-dUTP labeling of DNA by nick translation and FISH was performed according to standard methods as previously described [1, 4]. Briefly a minimum of 10 well-conserved and complete abnormal metaphases were evaluated for each probe. The metaphase chromosomes/nuclei were counterstained with DAPI (Boehringer/Roche). Karyotypes were described according to the ISCN [2]. Cytogenetic position of differentially labeled BAC and P1 artificial chromosomes (PAC) clones on 1q were confirmed by hybridization to normal metaphase spreads obtained from phytohemagglutinin-stimulated peripheral blood lymphocytes of a healthy donor.

For the metaphase FISH analyses, 37 partially overlapping BAC and PAC clones spanning the whole chromosomal band 1q were selected from information archived (on January 2005) by the National Center for Biotechnology Information (NCBI) (<http://www.ncbi.nlm.nih.gov/>) and obtained from the RPCI-1, -3, -4 and -11 libraries (Roswell Park Cancer Institute, Buffalo, NY). Probes selected for this study were summarized in supplemental Table S1 in order to their cytogenetic positions on 1q.

SUPPLEMENTAL TABLES**Supplemental Table S1:** List of the FISH probes used in this study.

Clone	Covered gene region	Mapped to
RP4-666F24	<i>TSHB/TSPAN-2</i>	1p13.1
pUC1.77	Chromosome 1-specific satellite III	1q12
RP11-326G21	<i>PDE4DIP</i>	1q21
RP11-441L11	<i>BCL9</i>	1q21.1
RP11-123P3	<i>BCL9</i>	1q21.1
RP11-533N14	<i>BCL9/ACP6</i>	1q21.1
RP11-433J22	<i>GJA5</i>	1q21.1
RP11-54A4	<i>MCL1</i>	1q21.2
RP11-42A2	Telomeric to <i>MLLT11 (AF1q)</i>	1q21.2
RP11-498A2	Centromeric to <i>MUC1</i>	1q22
RP11-98F1	Telomeric to <i>MUC1</i>	1q22
RP11-110J1	<i>ETV3</i>	1q23.1
RP11-91G5	<i>FCRL4</i>	1q23.1
RP11-130F5	<i>UHMK1</i>	1q23.3
RP11-506O24	<i>PBX1</i>	1q23.3
RP3-395P12	<i>TNFSF4</i>	1q24-q25
RP11-152A16	<i>ABL2</i>	1q24.1-q24.3
RP11-46A10	<i>STX6/XPRI</i>	1q25.2-q31.1
RP11-181K3	<i>LAMC1/LAMC2/NMNAT2</i>	1q31
RP1-53A198	<i>EDEM3</i>	1q31.1
RP11-339I2	<i>TPR</i>	1q31.1
RP11-547I7	<i>FAM5C</i>	1q31.1
RP11-198A7	<i>RGS18</i>	1q31.2
RP11-552K17	<i>KCNT2</i>	1q31.3
RP11-553K8	<i>ATP6V1G3/PTPRC</i>	1q31.3
RP11-31E23	Telomeric to <i>PTPRC</i>	1q31.3
RP11-343H5	<i>LGTN/DYRK3/MAPKAPK2/IL-10</i>	1q32.1
RP11-354K1	NEK2/telomeric to <i>TRAF5</i>	1q32.2
RP11-122M14	<i>NEK2/LPGAT1</i>	1q32.2
RP11-264J19	<i>PPP2R5A</i>	1q32.2-q32.3
RP11-90A5	<i>ATF3/FAM71A</i>	1q32.3
RP11-74E6	<i>SMYD2 (3' extreme)/PTPN14</i>	1q32.3
RP11-66M7	<i>ESRRG</i>	1q41
RP11-135J2	<i>LYPLAL1</i>	1q41
RP11-192M1	<i>LEFTY1/PYCR2/LEFTY2</i>	1q42.1
RP11-91M14	<i>FMN2</i>	1q43
RP11-462C5	<i>OR2M2/OR2M3/OR2M4/OR2M7/OR2T12/OR2T33</i>	1q44

The probes were listed according to their cytogenetic positions on 1q. The clone name, covered gene region and mapped cytogenetic band are given according to information archived on January 2005 by the NCBI.

Supplemental Table S2: List of the qPCR primers used in this study.

Gene	Forward primer	Reverse primer
<i>HMBS</i>	5'-TGAGAGTGATTCGCGTGGGTAC-3'	5'-CCCTGTGGTGGACATAGCAATG-3'
<i>MLLT11 (AF1q)</i>	QuantiTect Primer Assay Hs_MLLT11_1_SG	
<i>ARNT</i>	QuantiTect Primer Assay Hs_ARNT_1_SG	
<i>BCL9</i>	QuantiTect Primer Assay Hs_BCL9_2_SG	
<i>FCRL5 (IRTA2)</i>	QuantiTect Primer Assay Hs_FCRL5_1_SG	
<i>MCL1</i>	QuantiTect Primer Assay Hs_MCL1_1_SG	
<i>PBXIP1</i>	QuantiTect Primer Assay Hs_PBXIP1_1_SG	

Primer for *HMBS* were obtained from Eurofins (Ebersberg, Germany) and QuantiTect Primer Assay from QIAGEN (Hilden, Germany).

Supplemental Table S3: Summary of the significantly dysregulated miRNA regarding their EBV status.

	In EBV+ BL-CLS	In EBV- BL -CLS
Upregulated in BL-CLS with 1q gains and downregulated in BL-CLS without 1q gains	hsa-miR-17	hsa-miR-9
	hsa-miR-17*	hsa-miR-9*
	hsa-miR-18a	hsa-miR-96
	hsa-miR-18b	hsa-miR-148a
	hsa-miR-19b	hsa-miR-181a
	hsa-miR-20a	hsa-miR-181b
	hsa-miR-20a*	hsa-miR-182
	hsa-miR-20b	<u>hsa-miR-183</u>
	hsa-miR-23a	hsa-miR-198
	hsa-miR-27a	hsa-miR-335
	hsa-miR-33a	hsa-miRPlus-B1114
	hsa-miR-92a	hsa-miRPlus-E1117
	hsa-miR-92b	hsa-miRPlus-E1168
	hsa-miR-93	
	hsa-miR-99a	
	hsa-miR-100	
	hsa-miR-106a	
	hsa-miR-125b	
	hsa-miR-181a	
	hsa-miR-181b	
	<u>hsa-miR-183</u>	
	hsa-miR-193a-3p	
	hsa-miRPlus-E1038	
	hsa-miRPlus-F1181	
Downregulated in BL-CLS with 1q gains and upregulated in BL-CLS without 1q gains	hsa-miR-9*	hsa-miR-22
	hsa-miR-124*	hsa-miR-28-5p
	hsa-miR-492	hsa-miR-193b
	hsa-miR-542-5p	
	hsa-miR-583	
	hsa-miR-675	
	hsa-miR-1275	
	hsa-miRPlus-B1114	
	hsa-miRPlus-F1216	
Stronger downregulated in BL-CLS with 1q gains	hsa-miR-138	hsa-miR-155
	hsa-miR-1290	
Stronger downregulated in BL-CLS without 1q gains	hsa-miR-96	hsa-miR-1290
	hsa-miR-182	
	hsa-miR-339-5p	

Five 1q resident miRNAs are highlighted in bold letters. Three miRNAs dysregulated depending on 1q gains but independent of EBV are underlined. BL-CLs: Burkitt lymphoma cell lines. EBV-: EBV-negative BL-CLs. EBV+: EBV-positive BL-CLs. miRNA*: Passenger miRNA strand.

Supplemental Table S4: Summary of the significantly dysregulated miRNA regarding their 1q gain status.

	In BL-CLs with 1q gains	In BL-CLs without 1q gains
Upregulated in EBV+ and downregulated in EBV- BL-CLs	hsa-miR-7	<i>hsa-miR-21</i>
	<i>hsa-miR-21</i>	hsa-miR-105
	hsa-miR-22	<i>hsa-miR-155</i>
	hsa-miR-24	<i>hsa-miR-155*</i>
	hsa-miR-27a	hsa-miR-198
	hsa-miR-99a	<i>hsa-miR-221</i>
	hsa-miR-100	<i>hsa-miR-222</i>
	hsa-miR-125b	hsa-miR-542-5p
	<i>hsa-miR-155</i>	hsa-miR-583
	<i>hsa-miR-155*</i>	hsa-miR-675
	<i>hsa-miR-221</i>	hsa-miR-1275
	<i>hsa-miR-222</i>	hsa-miRPlus-B1114
	hsa-miR-487b	hsa-miRPlus-E1168
	hsa-miR-519d	hsa-miRPlus-F1193
Downregulated in EBV+ and upregulated in EBV- BL-CLs	<i>hsa-miR-9</i>	hsa-miR-15a
	<i>hsa-miR-9*</i>	hsa-miR-28-5p
	hsa-miR-138	hsa-miR-33a
	hsa-miR-335	hsa-miR-339-5p
	hsa-miR-1246	
	hsa-miRPlus-B1114	
Stronger downregulated in EBV+ BL-CLs	hsa-miR-675	hsa-miR-96
	hsa-miR-1290	hsa-miR-125b
		hsa-miR-182
Stronger downregulated in EBV- BL-CLs		hsa-miRPlus-A1027

1q resident miRNAs are highlighted in bold letters. Five miRNAs dysregulated depending on EBV but independent of 1q gains are highlighted in italic bold letters. BL-CLs: Burkitt lymphoma cell lines. EBV-: EBV-negative BL-CLs. EBV+: EBV-positive BL-CLs. miRNA*: Passenger miRNA strand.

Supplemental Table S5: Expression profiles of the in our study significantly dysregulated miRNAs in different cancer entities.

No.	miRNA	Expression in different cancer entities according to the supplemental references ^a	Supplemental references ^b
1	hsa-miRPlus-B1114	gguccacagggagauagg	NRY
2	hsa-miR-9*	-up- and downregulated in AML subtypes and different cancer entities -upregulated in FL -downregulated in BL , ALL	[5-8]
3	hsa-miR-1290	-upregulated in AML, ALL, and different cancer types like colorectal cancer, pancreatic cancer, lung cancer	[9, 10]
4	hsa-miR-96	-upregulated in hepatocellular carcinoma, malignant breast cancer and BL -downregulated in AML and CML	[11-16]
5	hsa-miR-182	-upregulated in AML and BL -downregulated in ALL and osteosarcoma,	[15-20]
6	hsa-miR-181a	-upregulated in AML, MM and ALL -downregulated in prostate cancer	[21-24]
7	hsa-miR-181b	-upregulated in MM -downregulated in BL , B-ALL and CLL	[23, 25-27]
8	hsa-miR-183	-upregulated in BL , MM, AML and classical Hodgkin lymphoma	[15, 16, 20, 23, 28]
9	hsa-miR-125b	-upregulated in MM, T-ALL and AML -downregulated in CLL and oral carcinoma	[23, 29-33]
10	hsa-miR-675	-downregulated in AML	[34]
11	hsa-miR-27a	-upregulated in gastric cancer and MM -downregulated in AML and ALL	[23, 35-37]
12	hsa-miR-99a	-upregulated in T-ALL, leukemia stem cells of AML and AML -downregulated in prostate cancer stem cells and ALL	[29, 30, 38-40]
13	hsa-miR-100	-upregulated MM, AML and SMZL -downregulated in prostate cancer stem cells and ALL	[23, 30, 38, 40, 41]
14	hsa-miRPlus-E1038	gcaugagugguucaguggu	NRY
15	hsa-miR-138	-downregulated in CLL and HCV-positive DLBCL	[42, 43]
16	hsa-miR-33a	-downregulated in lung cancer and triple-negative breast cancer	[44, 45]

17	hsa-miR-339-5p	-downregulated in AML	[46]
18	hsa-miR-542-5p	-upregulated in T-ALL	[47]
19	hsa-miR-583	-downregulated in recurrent prostate cancer	[48]
20	hsa-miR-1275	-upregulated in CML -downregulated in AML and BL	[20, 49, 50]
21	hsa-miR-17	-upregulated in hematologic and solid cancer -downregulated in CLL and oral carcinoma	[23, 32, 33, 51-55]
22	hsa-miR-17*	-upregulated in hematologic and solid cancer -downregulated in prostate cancer and FL	[7, 33, 52, 56]
23	hsa-miR-18a	-upregulated in hematologic and solid cancer	[33, 52, 53, 57]
24	hsa-miR-20a	-upregulated in hematologic and solid cancer -downregulated in oral carcinoma	[7, 8, 23, 32, 33, 52-55]
25	hsa-miR-20a*	-upregulated in hematologic and solid cancer -downregulated in gastric cancer	[33, 52, 58]
26	hsa-miR-19b	-upregulated in hematologic and solid cancer	[20, 23, 33, 52, 53, 55]
27	hsa-miR-92a	-upregulated in hematologic and solid cancer	[20, 23, 33, 52, 53, 55]
28	hsa-miR-106a	-upregulated in BL , hepatocellular carcinoma, breast cancer and MCL	[53, 59, 60]
29	hsa-miR-18b	-upregulated in BL , MCL and breast cancer	[53, 61]
30	hsa-miR-20b	-upregulated in BL , CLL and FL	[7, 53, 62]
31	hsa-miR-93	-upregulated in MCL and breast cancer	[60]
32	hsa-miR-23a	-upregulated in AML and MM -downregulated in CML and BL	[23, 53, 63, 64]
33	hsa-miR-92b	-upregulated in BL , GBC and prostate cancer -downregulated in MCL	[20, 65-67]
34	hsa-miR-193a-3p	-upregulated in renal cell carcinoma and MM -downregulated in NSCLC and AML	[23, 68-70]
35	hsa-miRPlus-F1181	ugaaaugcaaaucuaugcaa	NRY
36	hsa-miR-124*	-upregulated in AML -downregulated in glioma	[54, 71]
37	hsa-miR-492	-upregulated in hepatoblastoma and bladder cancer	[72-74]

		-downregulated in Colorectal cancer	
38	hsa-miRPlus-F1216	ggagagggaaaagaaaaag	NRY
39	hsa-miR-155	-upregulated in gastric cancer, SMZL, oral carcinoma and some B-cell lymphomas (CLL, AML, BL) -downregulated in CML and ALL and BL	[20, 32, 33, 35, 41, 52, 53, 75-83]
40	hsa-miR-9	-up- and downregulated in different AML subtypes and cancer entities -upregulated in FL -downregulated in MM, ALL	[5-7]
41	hsa-miR-335	-upregulated in AML and multiple myeloma -downregulated in MM	[23, 84, 85]
42	hsa-miR-22	-upregulated in CLL and BL -downregulated in T-ALL and AML	[20, 33, 86-88]
43	hsa-miR-198	-upregulated in retinoblastoma -downregulated in pancreatic cancer, NSCLC and MM	[23, 89-91]
44	hsa-miRPlus-E1168	cggcgggagcccgggg	NRY
45	hsa-miR-28-5p	-upregulated in glioblastoma -downregulated in gastric cancer, BL , DLBCL, follicular lymphoma, and CLL	[20, 92-95]
46	hsa-miR-148a	-upregulated in BL , ALL and AML -downregulated in breast cancer	[20, 78, 96, 97]
47	hsa-miRPlus-E1117	aagacgagaagaccuauggagcuu	NRY
48	hsa-miR-193b	-upregulated in SMZL -downregulated in AML, melanoma	[41, 98, 99]
49	hsa-miR-7	-upregulated in breast cancer and renal cell carcinoma -downregulated in T-ALL and gastric cancer stem cells	[100-103]
50	hsa-miR-24	-upregulated in acute leukemia and pancreatic cancer -downregulated in gastric cancer	[78, 104-106]
51	hsa-miR-487b	-upregulated in osteosarcoma -downregulated in colorectal cancer and neuroblastoma	[107-109]
52	hsa-miR-519d	-upregulated in melanoma -downregulated in breast cancer stem cells	[110, 111]
53	hsa-miR-1265	-downregulated in gastric cancer	[112]

54	hsa-miRPlus-E1013	ucccuucguggucgcc	NRY
55	hsa-miRPlus-E1103	ucccuggugguguagu	NRY
56	hsa-miR-1246	-upregulated in T-ALL oral carcinoma and pancreatic cancer	[32, 113, 114]
57	hsa-miR-21	-upregulated in BL , MM, ALL, SMZL, oral carcinoma, CLL and many other cancer entities -downregulated in BL	[20, 23, 32, 33, 41, 52, 53, 78, 80, 81, 115]
58	hsa-miR-155*	-upregulated in glioma, breast cancer and hepatocellular carcinoma -downregulated in mantle cell lymphoma and other non-Hodgkin's lymphomas	[116-119]
59	hsa-miR-221	-upregulated in T-ALL, AML, CLL, cervical cancer, MM and many other cancer entities -downregulated in erythroblastic leukemia and BL	[20, 23, 52, 120-125]
60	hsa-miR-222	-upregulated in CLL and many other cancer entities -downregulated in erythroblastic leukemia and BL	[20, 52, 53, 123-125]
61	hsa-miR-105	-upregulated in esophageal cancer and many different cancer entities -downregulated in gastric cancer and many different cancer entities	[52, 126-128]
62	hsa-miRPlus-F1193	cugggugagagcgggagg	NRY
63	hsa-miR-15a	-downregulated in BL , MCL, CLL, AML and many different cancer entities	[33, 52, 79, 129-132]
64	hsa-miRPlus-A1027	auguuggagcgggcaggugg	NRY

All miRNAs are numbered according to their appearance in Figure 3 (main manuscript). ^a: A report in Burkitt lymphoma is highlighted in bold letters (**BL**) and since miRPlus are not published elsewhere, the appropriate miRNA sequence is indicated here. ^b: Please note that all references are numbered according to their appearance in this table and are summarized in supplemental reference list. NRY: Not reported yet. (T-)ALL: (T cell-). Acute lymphocytic leukemia. AML: Acute myeloid leukemia. CLL: Chronic lymphocytic leukemia. CML: Chronic myeloid leukemia. GBC: Gallbladder cancer. MCL: Mantle cell lymphoma. MM: Multiple myeloma. NSCLC: Non-small cell lung cancer. SMZL: Splenic marginal zone lymphoma.

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