Table S1: miRNA measured by custom-made stem-loop based quantitative real-time PCR

miRNA
let-7d*
let-7i
miR-7*
miR-15b*
miR-28-3p
miR-106a
miR-106b*
miR-128a
miR-140-3p
miR-150
miR-181a
miR-199b*
miR-222*
miR-361-3p
miR-423-5p
miR-454
miR-548o
miR-582
miR-590
miR-625
miR-708
miR-766
miR-874
miR-1226
miR-1307
miR-1972
miR-1974
miR-1975
miR-1976
miR-1977
miR-1978
miR-1979

* refers to the star strand of the miRNA duplex that is (partly) complementary to the mature miRNA.

Table S3: Additional information about genetic subtype, immunophenotype and karyotype of ALL cases shown in Figure 1

Position in heatmap	Genetic subtype	Immunophenotype	Karyotype
1	B-other	C-ALL	47-49,XX,add(7)(q3?6),del(9)(p2?2),+mar[cp2]/,XX[10]
2	TEL-AML1	PRE-B-ALL	unknown
3	TEL-AML1	C-ALL	unknown
4	TEL-AML1	C-ALL	unknown
5	TEL-AML1	C-ALL	unknown
6	TEL-AML1	C-ALL	unknown
7	B-other	C-ALL	46,XX,der(1)del(1)(p34)add(1)(q2?2),der(9)t(1;9)(q1?1;q1?2),der(9)t(1;9)(p3?4;q2),add(12)(p11~12)
8	TEL-AML1	C-ALL	unknown
9	Hyperdiploid	C-ALL	55-56,XX,+?X,+4,+5,+6,der(9)t(9;14)(p2?;q1?),+?15,+17,+21,+21,+mar,+mar[29]/46,XX[3]
10	Hyperdiploid	PRE-B-ALL	51-53,XX,+X,?4,+?6,+14,+17,+?18,+21,+21(cp7)/46 ,XX(3)
11	Hyperdiploid	PRE-B ALL	54-56,XX,+i(X)(p10),+4,+?i (6)(p20),add (7)(p1?),-8[5],+9,+10,+14[6],+?17[3],+21,+21,+22[5],+mar[6],inc[9]/50,aberrant[4]/46,XX[16]
12	Hyperdiploid	C-ALL	55,XY,+X,+4,+6,+10,+14,+17,+18,+21,+21[28]
13	Hyperdiploid	C-ALL	54, XX,+X dup(1)(q11q4?),+4,+6,+10,+14,+17,+18,+21[3]/55,idem,+21[21]/46,XX [3]
14	Hyperdiploid	C-ALL	56,XX,+?X,+4,+6,+10,+?12,+14,+?15,+?17,+18,+?19,+21,+?22[cp]
15	B-other	C-ALL	47,XX,+21c
16	Hyperdiploid	PRE-B	50-66,XY,+X,+3,+4[12],+5,+del(6)(q?21)[8],+8[10],+9[7],+10,+del(11)(q1?4)[12],+12[12],+14[11],+?16[7]/50-66,inc[21]
17	Hyperdiploid	C-ALL	57,XY,+X,+Y,t(2;14)(p11;q32),+4,+6,+8,+10,del(12)(p1?),+14,+17,+18,+21,+21[21]/46,XY[4]
18	Hyperdiploid	C-ALL	50-53,XX,+?X,+4,+6,+?11,+?14,+?17,+21,+21,+22[cp9]
19	Hyperdiploid	C-ALL	55,XX,+X,+X,+4,+6,+14,+17,+18,+21,+21/46,XX
20	normal CD34+-cells	N/A	N/A
21	normal CD34+-cells	N/A	N/A
22	normal CD34+-cells	N/A	N/A
23	normal bone marrow	N/A	N/A
24	normal bone marrow	N/A	N/A
25	normal bone marrow	N/A	N/A
26	normal bone marrow	N/A	N/A
27	normal bone marrow	N/A	N/A
28	normal bone marrow	N/A	N/A
29	normal bone marrow	N/A	N/A
30	MLL	PRO-B-ALL	46,XX,der(11)?i(11)(q10)t(4;11)(q21;q23)[13]/46,XX[3]
31	MLL	PRE-B-ALL	46,XX,t(2;11;17;4)(q3?1;q23;q25;q21)[15]
32	MLL	PRE-B-ALL	46,XY,t(11;19)(q23;p13)
33	MLL	PRO-B-ALL	46,XY,der(11)?t(11,19)(q23,p13)[5]/47,XY,+X,idem[7],?46,XY[7]
34	MLL	PRO-B-ALL	46,XY,t(4;11)(q21;q23)
35	MLL	PRO-B-ALL	46,XX,t(11;11;19;19)(p13;q23;p13,p13)
36	MLL	PRO-B-ALL	unknown
37	B-other	PRE-B-ALL	unknown
38	E2A-PBX1	PRE-B-ALL	46,XY,t(1;19)(q23;p13),der(14)t(1;14)(q21;p1?2)[2],der(15)t(1;15)(q21;p1?2),der(22)t(1;22)(q21;p1?2)(+1*der(13)t(1;13)(q21;p1?2),1*der(21)t(1;21)(q21;p1?2)
39	E2A-PBX1	PRE-B-ALL	unknown
40	E2A-PBX1	PRE-B-ALL	unknown
41	E2A-PBX1	C-ALL	unknown
42	E2A-PBX1	PRE-B-ALL	unknown
43	E2A-PBX1	PRE-B-ALL	unknown
44	E2A-PBX1	PRE-B-ALL	unknown
45	E2A-PBX1	PRE-B-ALL	unknown
46	E2A-PBX1	C-ALL	unknown
47	thymocytes	N/A	N/A
48	thymocytes	N/A	N/A
49	thymocytes	N/A	N/A
50	thymocytes	N/A	N/A
51	thymocytes	N/A	N/A
52	thymocytes	N/A	N/A

continuation of Table S3

Position in heatmap	Genetic subtype	Immunophenotype	Karyotype
53	T-ALL	T-ALL	unknown
54	BCR-ABL	PRE-B ALL	46,XY,t(9;22)(q34;q11)[1]/46,XY[19]
55	T-ALL	T-ALL	unknown
56	T-ALL	T-ALL	unknown
57	T-ALL	T-ALL	unknown
58	T-ALL	C-ALL	unknown
59	T-ALL	T-ALL	46,XY
60	T-ALL	T-ALL	unknown
61	T-ALL	T-ALL	unknown
62	T-ALL	T-ALL	46,XY,t(10;14)(q2?4;q11)[2]/46,idem,t(6;7)(p21;q34-35),del(12)(p11)[3]
63	T-ALL	T-ALL	unknown
64	B-other	C-ALL	46,XY
65	TEL-AML1	PRE-B-ALL	unknown
66	B-other	C-ALL	unknown
67	B-other	C-ALL	unknown
68	BCR-ABL	PRE-B-ALL	unknown
69	BCR-ABL	C-ALL	unknown
70	BCR-ABL	PRE-B-ALL	unknown
71	TEL-AML1	C-ALL	unknown
72	TEL-AML1	C-ALL	unknown
73	TEL-AML1	C-ALL	unknown
74	B-other	PRE-B-ALL	unknown
75	TEL-AML1	C-ALL	unknown
76	TEL-AML1	C-ALL	unknown
77	TEL-AML1	C-ALL	unknown
78	TEL-AML1	C-ALL	46,XY
79	MLL	PRO-B-ALL	46,XX,t(4;11;17)(q21;q23;q11)[10]/46,XX[10]
80	MLL	PRO-B-ALL	unknown
81	BCR-ABL	C-ALL	unknown
82	BCR-ABL	C-ALL	unknown
83	normal CD34+-cells	N/A	N/A
84	MLL	PRE-B-ALL	46,XY[18]
85	T-ALL	T-ALL	unknown
86	B-other	C-ALL	unknown
87	B-other	PRE-B-ALL	unknown
88	BCR-ABL	C-ALL	unknown
89	BCR-ABL	C-ALL	47,XY,der(9)del(9)(p13p2?2)t(9;22)(q34;q11),+21c,der(22)t(9;22)[15]/47,idem,add(21)(q22)[7
90	B-other	PRE-B-ALL	unknown
91	B-other	C-ALL	unknown
92	B-other	PRE-B-ALL	47,XX,+21c
93	B-other	C-ALL	unknown
94	Hyperdiploid	C-ALL	55,XX,+X,+4,+6,+10,+14,+18,+21,+21,+22[3]/55,idem,-6,+der(6)t(1:6)(q22;q22)[22]/55,idem,-6,der(6
95	BCR-ABL	C-ALL	58,XY,+X,+5,+6,+8,+8,t(9;22)(q34;q11),+13,+14,+17,+18,+21,+22,+der(22)t(9;22)[24]/46,XY,t(9;22)[1]/46,XY[2
96	BCR-ABL	C-ALL	43-50,XX,+X,i(7)(q10),+10,+21,+21,inc[cp12]
97	Hyperdiploid	C-ALL	55,X,-Y,+X,+3,+6,+10,+?10,+14,+21,+21,+mar2[6],+mar3[5],+ mar4[4], inc[7]
98	Hyperdiploid	C-ALL	49~54,XX,+X,+6,+?12.+14,+?18,+21,+?21,+mar,inc[cp8]/46,XX[4]

Legend to Table S3

The genetic subtype, immunophenotype and karyotype of ALL patients is listed in order of appearance according to the heatmap shown in Figure 1.

Abbreviations: C-ALL, common-ALL; N/A, not applicable

Table S4: Number of discriminative miRNAs at different cut-off values for FDR-corrected p-values per ALL subtype

	P< 10-4	**P< 0.001**	**P< 0.005**	**P< 0.01**	**P< 0.05**
MLL	0	2	8	11	50
TEL-AML1	1	19	43	58	89
BCR-ABL	0	0	0	0	16
E2A-PBX1	0	5	44	53	64
hyperdiploid	4	13	41	48	65
T-ALL	7	21	38	45	79

Table S5: MiRNAs that are expressed at similar level in *E2A-PBX1* and *MLL* -rearranged ALL patients (Figure 1)

miRNA	chromosomal location
454	17q22
1307	10q24.33
1226	3p21.31
1979	4q32.3
484	16p13.11
425-3p	3p21.31
191	3p21.31
425-5p	3p21.31
106a	Xq26.2
15b*	3q26.1
378	5q33.1
422a	15q22.31
15a	13q14.3
141	12p13.31
200c	12p13.31

Table S6: Correlation between expression levels of clustered miRNAs in ALL patients

15a-16 cluster	miR-15a	miR-16
miR-15a	1	0.7*
miR-16	0.7*	1

17-92 cluster	miR-17-3p	miR-17-5p	miR-18a	miR-19a	miR-20a	miR-19b	miR-92
miR-17-3p	1	0.3**	0.4*	0.6*	0.6*	0.6*	0.7*
miR-17-5p	0.3**	1	0.2	0.7*	0.8*	0.8*	0.7*
miR-18a	0.4*	0.2	1	0.4*	0.4*	0.3**	0.4**
miR-19a	0.6*	0.7*	0.4*	1	0.9*	0.9*	0.8*
miR-20a	0.6*	0.8*	0.4*	0.9*	1	0.9*	0.8*
miR-19b	0.6*	0.8*	0.3**	0.9*	0.9*	1	0.9*
miR-92	0.7*	0.7*	0.4**	0.8*	0.8*	0.9*	1

106b-25 cluster	miR-106b	miR-93	miR-25
miR-106b	1	0.8*	0.8*
miR-93	0.8*	1	0.7*
miR-25	0.8*	0.7*	1

106a-363 cluster	miR-106a	miR-18b	miR-20b	miR-19b	miR-92	miR-363
miR-106a	1	0.2	0.4**	0.4**	0.3**	0.3**
miR-18b	0.2	1	0.6*	0.4*	0.3**	0.5*
miR-20b	0.4**	0.6*	1	0.6*	0.5*	0.7*
miR-19b	0.4**	0.4*	0.6*	1	0.9*	0.4**
miR-92	0.3**	0.3**	0.5*	0.9*	1	0.4*
miR-363	0.3**	0.5*	0.7*	0.4**	0.4*	1

222-221 cluster	miR-222	miR-221
miR-222	1.0*	0.8*
miR-221	0.8*	1.0*

371-373 cluster	miR-371	miR-372	miR-373
miR-371	1.0*	0.775	0.7*
miR-372	0.8*	1.0*	0.6*
miR-373	0.7*	0.6*	1.0*

Spearman's correlation coefficient was calculated for the expression levels of miRNAs encoded in the 15a-16, 17-92, 106b-25, 106a-363, 221-222 or 371-373 cluster for all ALL patients. * indicates P < 0.001, ** refers to P < 0.01

Table S7: Target genes for most discriminative miRNAs per subtype of pediatric ALL

top#	miRNA	known target
MLL-1	let-7b	RAS(283), c-MYC(Δ), HMGA2(1), IMP-1(Δ)
MLL-2	let-7c	RAS(283), c-MYC(Δ), HMGA2(1), IMP-1(Δ)
MLL-3	miR-708	unknown
MLL-4	miR-192	ZEB2(7)
MLL-5	miR-196a	HOXB8(67), HOXC8(1), HOXD8(Δ), HMGA2(23), ANXA1 (Δ)
MLL-6	miR-194	unknown
MLL-7	miR-497	unknown
MLL-8	miR-20b	MYLIP(891), RBP1(Δ)
MLL-9	miR-133a	UCP2(Δ), UCP3(Δ)
MLL-10	miR-372	LATS2(4), CD44(56)
TEL-AML1-1	miR-213	unknown
TEL-AML1-2	miR-99a	unknown
TEL-AML1-3	miR-100	unknown
TEL-AML1-4	miR-125b	IRF4(12), PRDM1(124), ERBB2(Δ), ERBB3(Δ), SMO(Δ)
TEL-AML1-5	miR-126*	unknown
TEL-AML1-6	miR-383	unknown
TEL-AML1-7	miR-221	Kit(5), CDKN1B(6), CDKN1C(218)
TEL-AML1-8	miR-126	PLK2(13), HOXA9(Δ)
TEL-AML1-9	miR-629	unknown
TEL-AML1-10	miR-361-5p	unknown
BCR-ABL-1	miR-93	CDKN1A(383), BCL2L11(733), TP53INP1(369), E2F1 (529)
BCR-ABL-2	miR-484	unknown
BCR-ABL-3	miR-331	unknown
BCR-ABL-4	miR-103	unknown
BCR-ABL-5	miR-1226	unknown
BCR-ABL-6	miR-345	unknown
BCR-ABL-7	miR-210	RAD52(Δ)
BCR-ABL-8	miR-301	unknown
BCR-ABL-9	miR-324-5p	SMO(Δ), GLI1(Δ)
BCR-ABL-10	miR-148b	DNMT3B(Δ)
E2A-PBX1-1	miR-126*	unknown
E2A-PBX1-2	miR-126	PLK2(13), HOXA9(Δ)
E2A-PBX1-3	miR-146a	IRAK1(3), TRAF1(Δ)
E2A-PBX1-4	miR-545	unknown
E2A-PBX1-5	miR-24	CDKN2A(Δ), ALK2(Δ), ALK4(Δ), DHFR(Δ)
E2A-PBX1-6	miR-29a	DNMT3A(294), DNMT3B(132), BACE1(750), TTP(Δ)
E2A-PBX1-7	miR-511	unknown
E2A-PBX1-8	miR-365	unknown
E2A-PBX1-9	miR-30d	unknown
E2A-PBX1-10	miR-193a	E2F6(20), Ptk2(Δ), MCL1(32)
hyperdiploid-1	miR-223	NFIA(52), LMO2(61)
hyperdiploid-2	miR-222*	unknown
hyperdiploid-3	miR-98	HMGA2(1)
hyperdiploid-4	miR-511	unknown
hyperdiploid-5	miR-222	c-KIT(5), CDKN1B(6), CDKN1C(218)
hyperdiploid-6	miR-660	unknown
hyperdiploid-7	miR-361-3p	unknown
hyperdiploid-8	miR-374a	unknown
hyperdiploid-9	miR-532-5p	unknown
hyperdiploid-10	miR-501-5p	unknown
T-ALL-1	miR-191	unknown
T-ALL-2	miR-190	unknown
T-ALL-3	miR-151	unknown
T-ALL-4	miR-425-5p	unknown
T-ALL-5	miR-222*	unknown
T-ALL-6	miR-542-5p	unknown
T-ALL-7	miR-708	unknown
T-ALL-8	miR-132	unknown
T-ALL-9	miR-425-3p	unknown
T-ALL-10	miR-342-3p	unknown

The ten most differentially expressed miRNAs are listed for each ALL subtype on the basis of multiple testing (FDR)-corrected p-value (Table 1). This p-value is based on the comparison between expression levels of the indicated subtype and those of the remaining cases without the specified genetic abnormality.

Table lists biologically proven targets (known from literature) for the differentially expressed miRNAs.

* refers to the star strand of the miRNA duplex that is (partly) complementary to the mature miRNA.

( ) Numbers between brackets indicate the rank of the known target genes when predicted by TargetScan release 5.1, April 2009 (http://www.targetscan.org) based on sequence homology.

Δ indicates that proven target gene is not predicted by Target scan.

Table S9: Target genes of miRNAs that are differentially expressed between drug sensitive and resistant precursor B-ALL patients

top#	miRNA	known targets
VCR-1	miR-125b	IRF4(12), PRDM1(124), ERBB2(*), ERBB3(*), SMO(*)
VCR-2	miR-99a	unknown
VCR-3	miR-100	unknown
VCR-4	miR-629	unknown
VCR-5	miR-126*	unknown
VCR-6	miR-126	PLK2(13), HOXA9(*)
VCR-7	miR-9	PRDM1(21)
VCR-8	miR-625	unknown
VCR-9	miR-141	unknown
VCR-10	miR-200c	TCF-8(*)
DNR-1	miR-383	unknown
DNR-2	miR-99a	unknown
DNR-3	miR-125b	IRF4(12), PRDM1(124), ERBB2(*), ERBB3(*), SMO(*)
DNR-4	miR-100	unknown
DNR-5	miR-203	ABL1(459)
DNR-6	let-7c	RAS(283), c-MYC(*), HMGA2(1), IMP-1(*)
DNR-7	miR-126	PLK2(13), HOXA9(*)
DNR-8	miR-126	unknown
DNR-9	miR-335	unknown
DNR-10	miR-199b*	unknown
ASP-1	miR-454	unknown
ASP-2	-	-
ASP-3	-	-
ASP-4	-	-
ASP-5	-	-
ASP-6	-	-
ASP-7	-	-
ASP-8	-	-
ASP-9	-	-
ASP-10	-	-

miRNAs that are differentially expressed between sensitive and resistant cases for vincristine (VCR), daunorubicin (DNR) and L-asparaginase (ASP) are ranked by fold-change in expression level (see also Table 2).

* points to the star strand of the miRNA duplex that is (partly) complementary to the mature miRNA.

Table lists biologically proven targets (known from literature) for the differentially expressed miRNAs.

* refers to the star strand of the miRNA duplex that is (partly) complementary to the mature miRNA.

( ) Numbers between brackets indicate the rank of the known target genes when predicted by TargetScan release 5.1, April 2009 (http://www.targetscan.org) based on sequence homology.

Δ indicates that proven target gene is not predicted by Target scan.