Genomic profiling of adult acute lymphoblastic leukemia by single nucleotide polymorphism oligonucleotide microarray and comparison to pediatric acute lymphoblastic leukemia

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Online Supplementary Data

Design and Methods

Sample information of high-density single nucleotide polymorphism-array analysis

High quality genomic DNA (gDNA) was isolated from adult ALL cells and subjected to GeneChip Human mapping processing protocols of either XbaI 50 K (N= 34; B-1, -2, -6, -10, -11, -12, -13, -16, -17, -19, -28, -31, -33, -36, -37, -41, -43, -45, -48, -49, -50, -51, -52, -53, -54, -55, -56, -57, -58, -59, -60, -61, T-2, -13), Hind 50 K (N=6; B-3, -15, -18, -22, -29, -44) or NspI 250K arrays (N=35; B-4, -14, -5, -7, -8, -9, -20, -21, -23, -24, -25, -26, -27, -30, -32, -34, -35, -38, -39, -40, -42, -46, -47, T-1 ,-3 ,-4 ,-5 ,-6 ,-7 ,-8 ,-9 ,-10 ,-11 ,-12 ,-14) (Affymetrix, Santa Clara, CA, USA) as described previously.[1,2]

Quantitative real-time polymerase chain reaction

Real-time reverse transcriptase polymerase chain reaction (RT-PCR) was performed by using ThermoScript RT-PCR Systems (Invitrogen) according to the manufacturer's protocol. Gene-dosage of target regions in samples at diagnosis and the expression level of FOXO3 in cell line samples were determined by quantitative real-time PCR (iCycler, Bio-Rad, Hercules, CA, USA) using SYBR Green. A region on chromosome 2p21 was used as a control to determine the relative gene-dosage because it is a region that rarely has copy number changes in malignancy.[3] β-actin was used as a control to determine the relative amount. The delta threshold cycle value (ΔCt) was calculated from the given Ct value by the formula ΔCt = (Ct sample - Ct control). The fold change was calculated as $2^{-\Delta Ct}$. The primers are listed in *Online Supplementary Table S15*.

Validation of copy-number neutral loss-of-heterozygosity and genomic copy number change

For confirmation of genomic copy number changes, quantitative real-time PCR was performed on the gDNA from the hybridized ALL samples and either DNA from matched normal gDNA from case # B-14 or normal control gDNA. The detection of CNN-LOH was validated by PCR of genomic DNA and subsequent direct sequencing of SNP in a region of CNN-LOH in an ALL sample *versus* the corresponding matched normal sample (*Online Supplementary Figure S2A-E*).

Determination of single nucleotide polymorphism sequences in copy-number neutral loss-of-heterozygosity region

To validate CNN-LOH, two independent SNP sequences (rs10481545 and rs10810528) at chromosome 9p in B-ALL case #B-14 were determined. The genomic region of each SNP site was amplified by genomic PCR using specific primers, and PCR products were purified and sequenced. The primers are listed in *Online Supplementary Table S15*.

Methylation analysis of the FOXO3 gene

Genomic DNA was isolated and modified by sodium bisulfate using the EZ DNA Methylation Kit (Zymo Research, Orange, CA. USA). The CpG island (-614 to -122) of the *FOXO3* gene was amplified from the bisulfate-modified genomic DNA with specific primers which are listed in *Online Supplementary Table S15*. For the PCR amplification, a total volume of 10 μL was used, containing modified genomic DNA, 0.5 μM of each primer, 5.0 μL of FailSafe PCR PreMix E (Epicentre Biotechnologies, Madison, WI) and 1.0 U platinum Taq (Invitrogen). PCR products were subcloned into pCR 2.1 vector (Invitrogen) and sequenced.

Determination of PAX5 fusion sequences

To validate a PAX5 fusion product, primers for *PAX5* and *ETV6* covering the corresponding break point in B-ALL case # B-20 were used as previously specified.[3] The primers are listed in *Online Supplementary Table S15*. The fused region was amplified by PCR from cDNA, and PCR products were purified and directly sequenced.

Statistical analysis

For specific copy number changes, either Wilcoxon's rank-sum test or the Mann-Whitney U-test was used to assess differences between adult and pediatric ALL subgroups. Differences in the occurrence of

genetic abnormalities between different subgroups of adult and pediatric ALL samples were analyzed using Pearsons's χ^2 test.

Results

Validation of the single nucleotide polymorphism-array analysis

Typical results of SNP-array analysis are displayed in *Online Supplementary Figure S2*. Case #B-14 (B-ALL) had 9p CNN-LOH (9p-terminal to 9p13.2, 37.5 Mb) with two homozygously deleted regions, 9p23 (containing the *PTPRD* gene) and 9p21.3 (containing the *CDKN2A* and *CDKN2B* genes) (*Online Supplementary Figure S2A*); case #B-26 (B-ALL) had amplification of 2p16.1-p15 (3.5 Mb) containing the *REL* and *BCL11A* genes (*Online Supplementary Figure SD[i]*); and case #T-7 (T-ALL) had amplification of 19q12-q13.2 (9.6 Mb) containing the *AKT2* gene (*Online Supplementary Figure S2E[i]*).

We validated these SNP-array results using several techniques. To verify 9p CNN-LOH in case #B-14, we first determined loss of heterozygosity (LOH) by nucleotide sequencing of two SNP sites (rs10481545 and rs10810528). As shown in *Online Supplementary Figure S2B*, these two SNP sites showed homozygosity in the sample taken at diagnosis as opposed to heterozygosity of the SNP in the matched gDNA sample obtained at the time of remission, showing that ALL case #B-14 had LOH in that region. To exclude the possibility of a heterozygous deletion, gene-dosage of the region was measured by quantitative genomic real-time PCR (QG RT-PCR). The level of gene-dosage of the region in ALL case #B-14 was comparable to that of the normal matched control sample, indicating that the 9p region of case #B-14 represented CNN-LOH with a copy number of n = 2 throughout (*Online Supplementary Figure S2C[i]*).

Next, we validated copy number changes. QG RT-PCR revealed that levels of gene-dosage of the *PTPRD* and the *CDKN2A* genes were significantly decreased in case #B-14 compared to in the normal matched control sample (*Online Supplementary Figure SC [ii] and [iii]*, respectively), consistent with the SNP array data (*Online Supplementary Figure S1A[i,ii]*). Similar results were obtained using specific primers for *CDKN2A* and *CDKN2B* (*Online Supplementary Figure S7*). Levels of gene-dosage of *REL*, *BCL11A* (case #B-26), and *AKT2* (case #T-7) genes were approximately 5-, 11-, and 8-fold higher, respectively, in the ALL samples than in the normal controls (*Online Supplementary Figures S2D[ii],[iii] and 1E[ii]*) comparable to the SNP array data (*Online Supplementary Figures S2D[i] and 2E[i]*). Taken together, these results demonstrated that SNP-array analysis accurately reflected the genomic abnormalities.

Amplifications and homozygous deletions in adult acute lymphoblastic leukemia samples

As shown in *Online Supplementary Figures S2D* and *2E*, a few samples had chromosomal amplifications (copy number change ≥ 5). As described above, case #B-26 (B-ALL) had amplification of 2p16.1-p15 (3.5 Mb, containing the *REL* and *BCL11A* genes) and #T-7 (T-ALL) had an amplification of 19q12-q13.2 (9.6 Mb, containing the *AKT2* gene). Homozygous deletions of genomic regions of adult ALL are listed in *Online Supplementary Table S3*. Ten cases (15%) had homozygous deletion of 9p21.3 including *CDKN2A/B*. Homozygous deletions at 1q23.2-q23.3, 9p23, 10p11.21, 10q24.1, 13q14.2, 13q14.11 and 18p11.21 were identified as unique alterations, each occurring in only one sample. These deleted regions contain several genes whose loss may contribute to leukemogenesis.

Chromosomal regions of copy-number neutral loss-of-heterozygosity in adult acute lymphoblastic leukemia samples

Unlike karyotypic or comparative genomic hybridization studies, SNP-array analysis can detect CNN-LOH. Disease-related CNN-LOH usually represents chromosomal recombination often involving the telomeres. As shown in *Online Supplementary Table S7*, whole or partial chromosome CNN-LOH were observed in 17 samples (26%); three of these cases (18%) had 9p CNN-LOH. Seventeen regions of CNN-LOH were detected, each involving only one sample (*Online Supplementary Table S7*). Of note, case #B-26 had three CNN-LOH regions, and case #T-1 had two CNN-LOH regions.

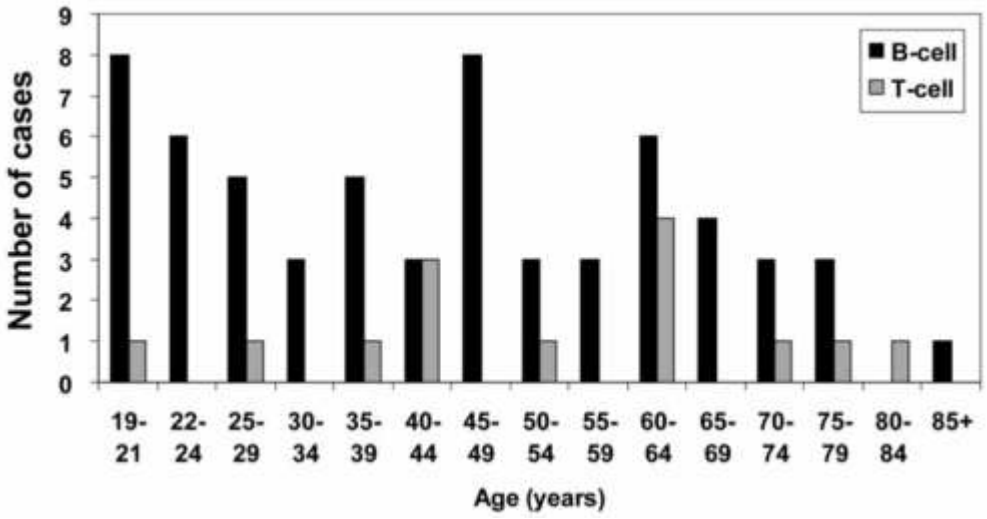
Discussion

Apart from the analysis of our adult ALL sample set, we also compared the results from this analysis with a previously published data set of 399 pediatric ALL to discover possible differences in the types and frequencies of genomic lesions detected with SNP arrays between these two age groups. Due to the hybridization of the samples to two different types of SNP arrays with different technical specifications, we had to find a smallest common denominator threshold for the lesions detected in order to make the data comparable. Since the median inter-marker distance of interrogated SNP on the smaller 50K arrays is approximately 47kb and we require at least three consecutive SNP to be involved in a lesion, we set the size threshold of genomic lesions to be 141kb. This meant that all lesions detected with the 250K arrays that were smaller than 141kb were eliminated from all analyses comparing the adult and pediatric data set.

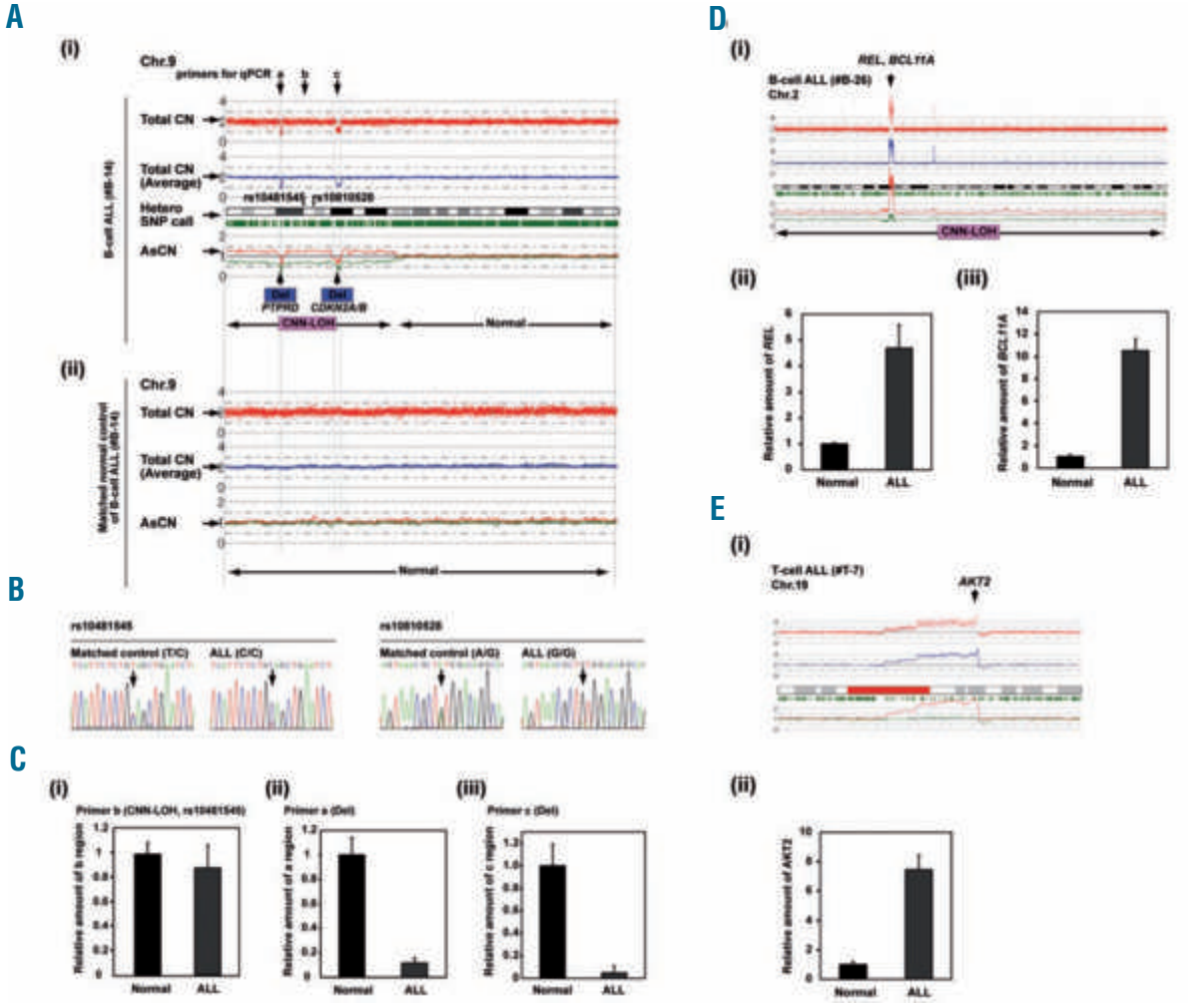
References

1. O'Neil J, Look AT. Mechanisms of transcription factor deregulation in lymphoid cell transformation. Oncogene. 2007;26(47):6838-49.
2. Nannya Y, Sanada M, Nakazaki K, Hosoya N, Wang L, Hangaishi A, et al. A robust algorithm for copy number detection using high-density oligonucleotide single nucleotide polymorphism genotyping arrays. Cancer Res. 2005;65(14):6071-9.
3. Kawamata N, Ogawa S, Zimmermann M, Kato M, Sanada M, Hemminki K, et al. Molecular allelokaryotyping of pediatric acute lymphoblastic leukemias by high-resolution single nucleotide polymorphism oligonucleotide genomic microarray. Blood. 2008;111(2):776-84.

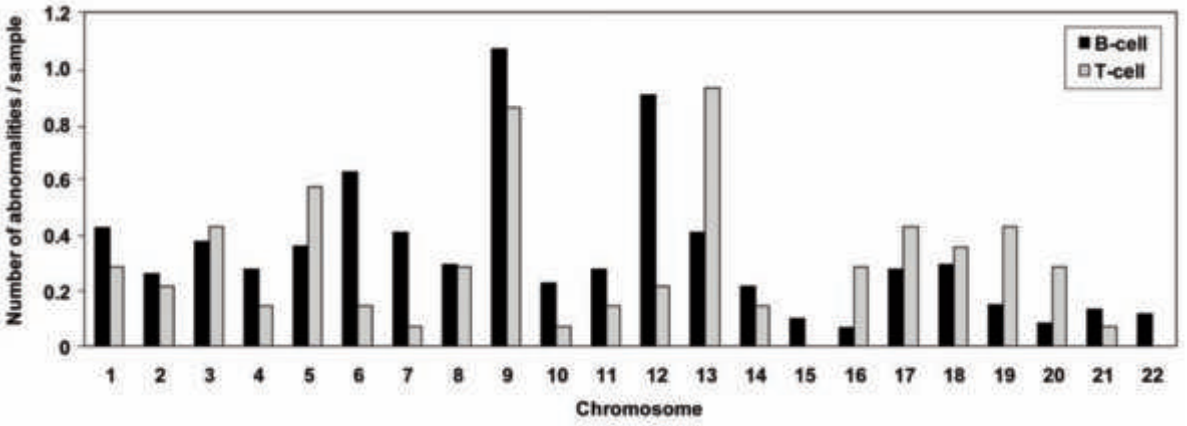
Online Supplementary Tables 1-15. (SEE ATTACHED PDF)



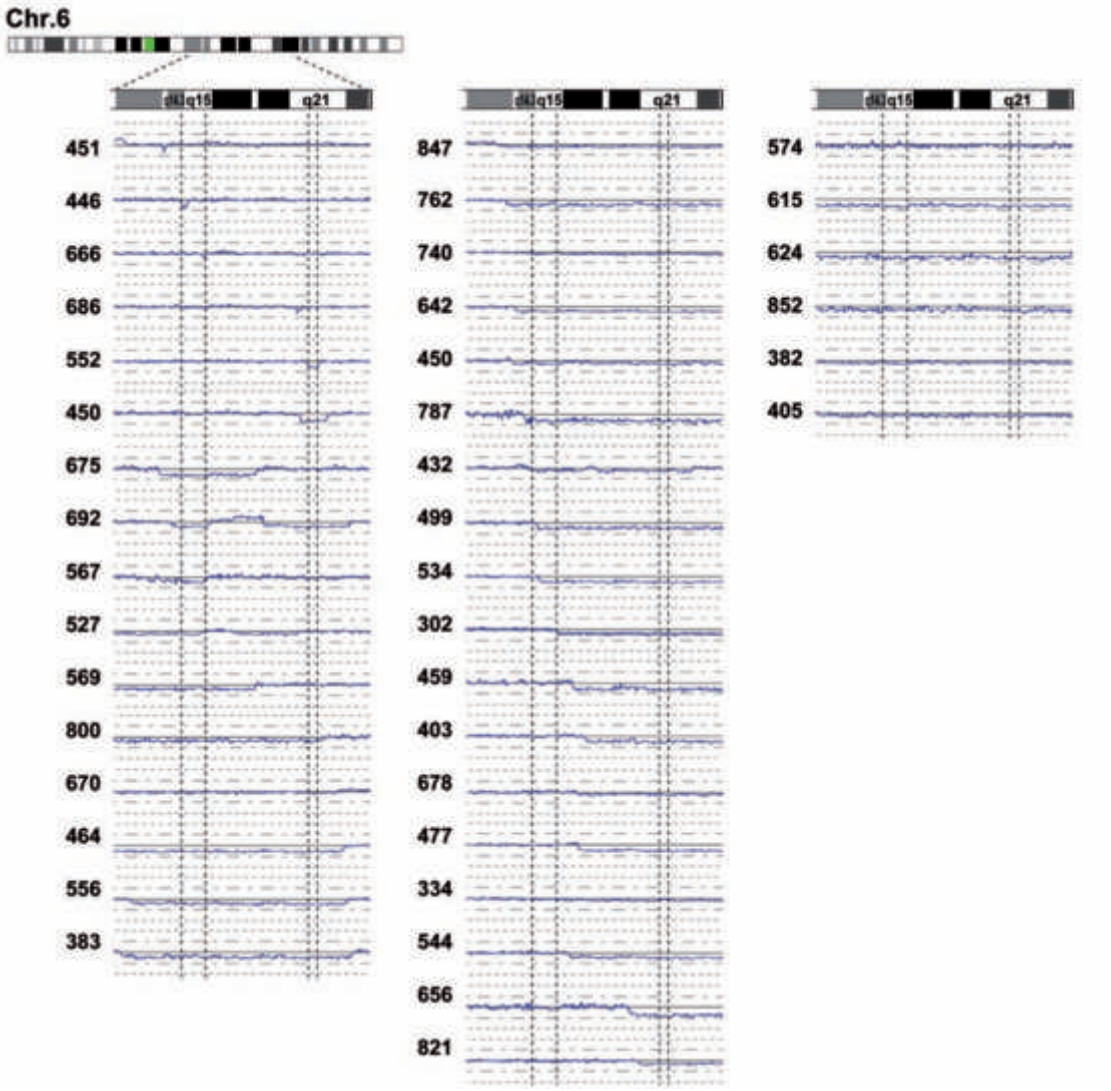
Online Supplementary Figure S1. Distribution of adult ALL samples for SNP-array sorted by age. The number of adult ALL samples: displayed by age. Black = B-cell type ALL; gray = T-cell type ALL.



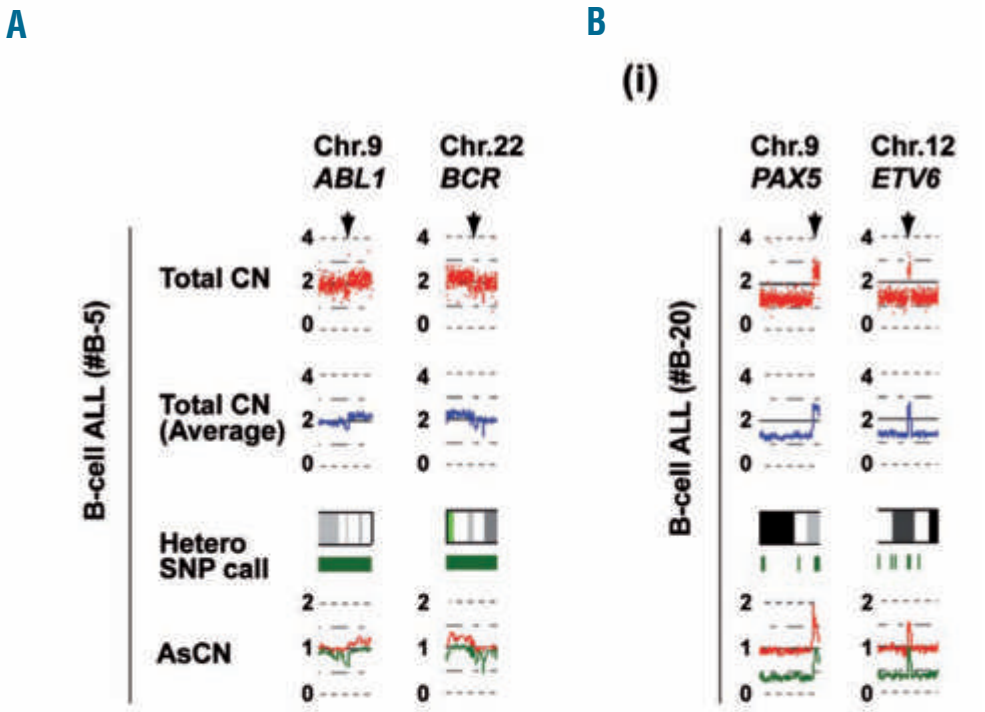
Online Supplementary Figure S2. Validation of SNP-array results. (A) SNP-array results from chromosome 9 of B-ALL case #B-14. Red dots are SNP sites as probes and indicate total copy number (CN). The blue line is an average copy number and shows gene dosage. Level 2 indicates normal copy number (2N). Green bars are heterozygous (hetero) SNP calls. Red and green lines show allele-specific copy number (AsCN). If the green line is lower than baseline, the region is deleted; if the red line is higher than baseline, the region is duplicated or amplified. The chromosome has two homozygous deletions (Del) and CNN-LOH which is represented by one allele being deleted and the other allele duplicated. (i) B-ALL case #B-14; (ii), matched control sample. Del = deletion, CNN-LOH = copy number neutral loss of heterozygosity. (B) Nucleotide sequencing of SNP sites. SNP sequences at rs10481545 (chr9:14,386,583-14,387,083) and rs10810528 (chr9:16,038,594-16,039,094) were determined in the CNN-LOH region of case #B-14 and the matched normal control sample from the same patient's bone marrow during remission. The matched control sample had a heterozygous SNP (rs10481545; T/C, rs10810528; A/G); while the ALL sample had a homozygous SNP (rs10481545; C/C, rs10810528; G/G). (C) Relative gene-dosage of the deleted and the CNN-LOH regions in the B-ALL case #B-14. The gene-dosage of deleted (site "a" for *PTPRD* exon B4 [ii] and "c" for *CDKN2A/B* [iii]) and CNN-LOH ([i] site "b" for rs10481545) were measured by quantitative genomic real-time PCR. Levels of gene-dosage were determined as a ratio between target gene and the reference genomic DNA, 2p21. The levels of ALL genomic DNA in the deleted regions were lower than levels in normal genomic DNA; whereas in the CNN-LOH region, DNA levels were comparable to those of normal genomic DNA. (D) (i) SNP-array result of chromosome 2 of B-ALL case #B-26. Relative gene-dosage in the *REL* (ii) and *BCL11A* (iii) gene regions was amplified in this case compared to normal DNA. (E) (i) SNP-array result of chromosome 19 of T-ALL case #T-7. (ii) Relative gene-dosage of the *AKT2* gene region which was amplified in this case compared to normal DNA.



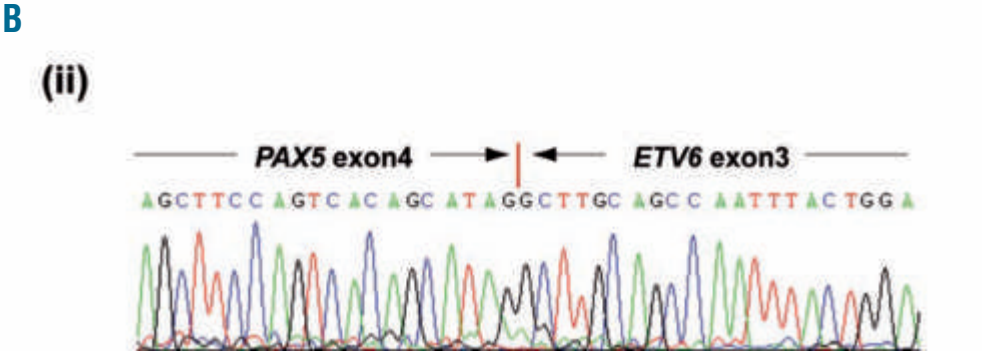
Online Supplementary Figure S3. Distribution of abnormalities in adult ALL samples sorted by chromosome. Numbers of abnormalities per sample are displayed by chromosome. The most common abnormalities were found on chromosome 9. Black = B-cell type ALL; gray = T-cell type ALL.

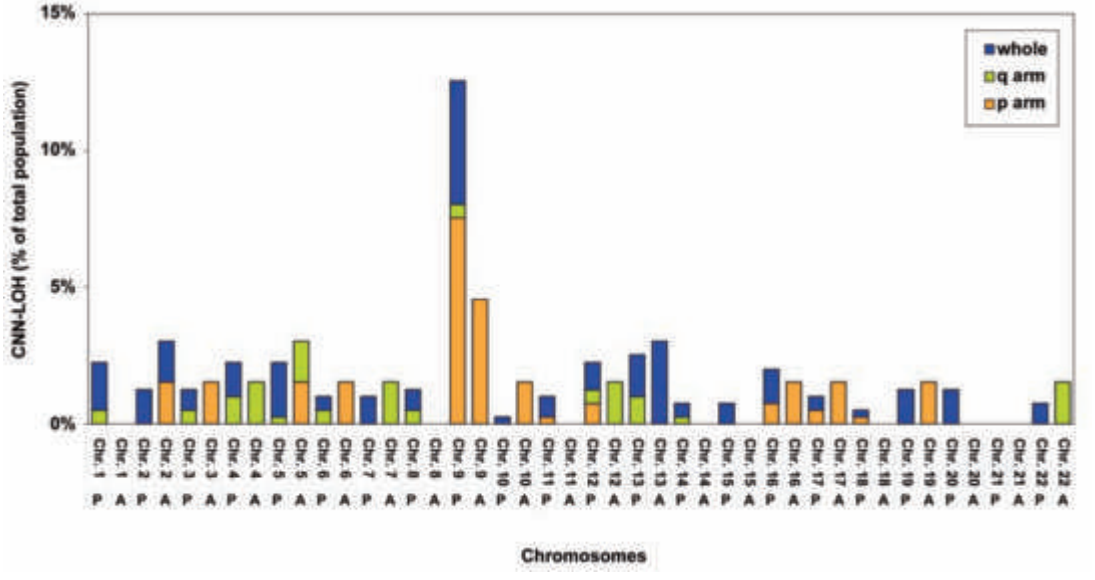


Online Supplementary Figure S4. Deletions on chromosome 6q in a collection of pediatric ALL samples. The anonymous sample number of pediatric ALL (Ref. 7) is shown on the left. Blue line = average copy number / shows gene dosage; dotted line = the region of chromosome 6q15 and 6q21 which was commonly deleted in adult ALL in Figure 2A.

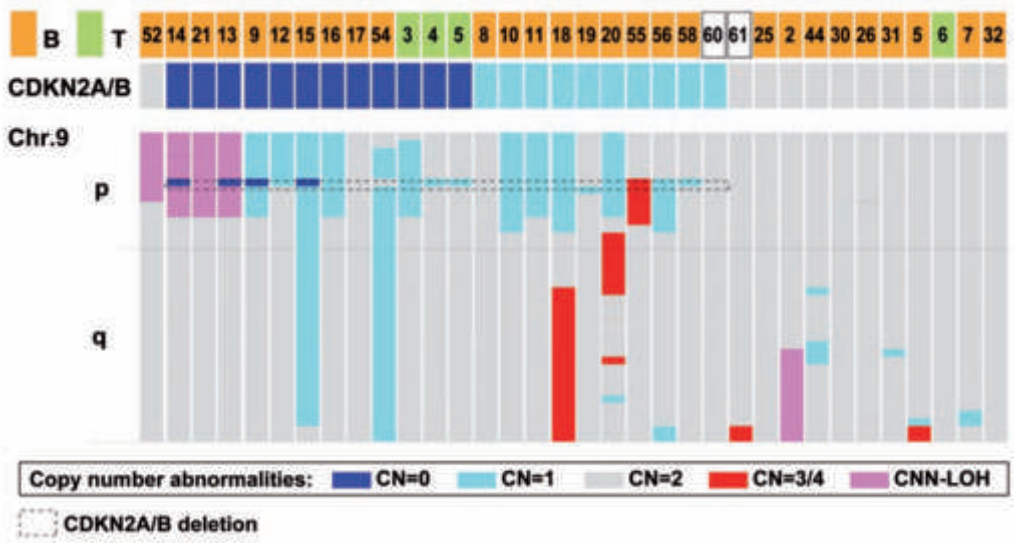


Online Supplementary Figure S5. Identification of an unbalanced translocation in adult ALL by SNP-array analysis. (A) Adult ALL case #B-5 had a duplication of a region of the *ABL* gene and the *BCR* gene. The karyotype of the case was t(1;10)(p11;q23),t(4;13)(q31;q34),i(8)(q10),+i(8)(q10), t(9;22)(q34;q11), +der(22)t(9;22)(q34;q11) (*Online Supplementary Table S2*). (B) (i) Adult ALL case #B-20 had a duplication of the amino end of the *PAX5* gene and the carboxyl end of the *ETV6* gene. The karyotype of the case was +8, der(9)r(9)ins(9;12), der(12)t(9;12)(?;q15) (*Online Supplementary Table S2*). (ii) The nucleotide sequence shows a fusion of the *PAX5* and *ETV6* gene in adult ALL case # B-20. Total CN = total copy number; Hetero SNP call = heterozygous SNP calls; AsCN = allele-specific copy number.

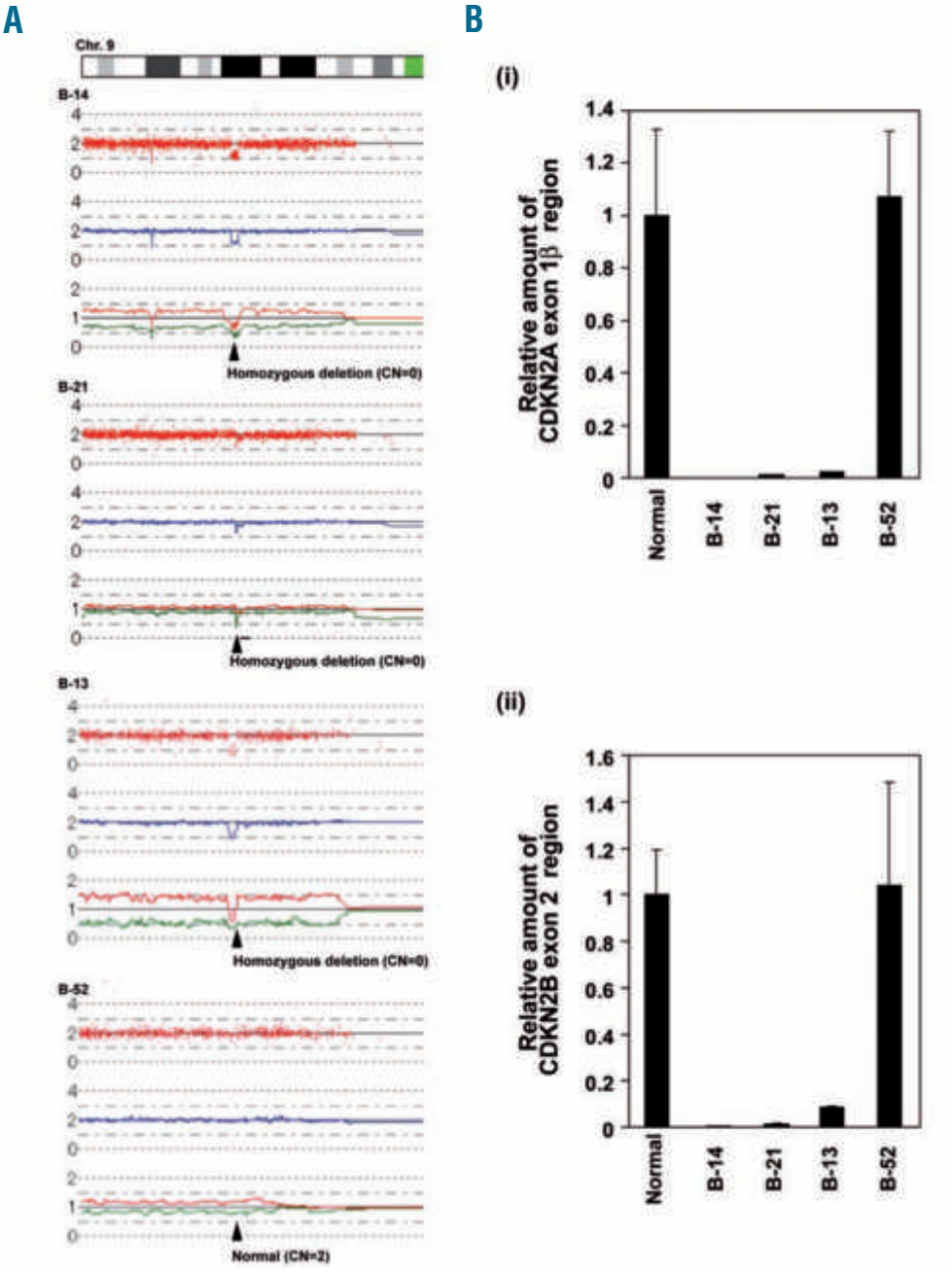




Online Supplementary Figure S6. Comparison of frequency of CNN-LOH between adult and childhood ALL. The number of CNN-LOH on each chromosome for the adult and childhood ALL samples is expressed as a percent of the entire adult and pediatric ALL population, respectively. The most frequent common CNN-LOH was chromosome 9p which includes whole chromosome CNN-LOH, in both pediatric (12%) and adult (5%) samples (P=0.07). Whole = whole chromosome; P = pediatric ALL samples; A = adult ALL samples.



Online Supplementary Figure S7. Summary of abnormalities on chromosome 9 in adult ALL. Thirty-four cases of 75 adult ALL showed abnormalities on chromosome 9. Orange, B-cell type ALL; light green, T-cell type ALL; white, null-ALL, (cases #B-60, -61). Copy number of the *CDKN2A/B* region is presented below the sample number. Gray = normal copy number; red = duplication; blue = heterozygous deletion; dark blue = homozygous deletion; pink = CNN-LOH; p = short arm; q = long arm; CN = copy number; 0 = 0 N (homozygous deletion); 1 = 1 N (heterozygous deletion); 2 = 2 N (normal); ¾ = 3 or 4 N (duplication); CNN-LOH = copy number neutral loss of heterozygosity. The dotted line indicates the region containing focal *CDKN2A/B* deletions. The order of groups is arranged based on status of *CDKN2A/B* deletions.



Online Supplementary Figure S8. Validation of SNP-array results using specific primers for *CDKN2A* and B. (A) SNP-array results from chromosome 9 of ALL cases #B-13, -14, -21 and -52. The balck arrow shows the status of copy number of the *CDKN2A/B* region; Case #B-13, -14, -21 showed homozygous deletions, case #B-52 showed a normal copy number of two in this region. (B) Relative gene-dosages of *CDKN2A/B* regions in ALL case #B-13, -14, -21 and -52. The gene-dosage of the deleted region (*CDKN2A* exon 1 beta [i] and *CDKN2B* exon 2 [ii]) were measured by quantitative genomic real-time PCR. Levels of gene-dosage were determined as a ratio between target gene and a reference region of genomic DNA on chromosome 2p21 known to exhibit a copy number state of N =2.

Online Supplementary Table S1. Clinical features of the 75 adult ALL cases and the 399 pediatric ALL cases.

		Adult		Pediatric	
	Cases	N.	%	N.	%
Sex					
	Male	45	60	230	57
	Female	30	40	169	43
Immunophenotype					
	B-cell	58	77	339	85
	T-cell	14	19	49	12
	Null or mix	3	4	0	0
	Unknown	0	0	11	3
WBC					
	Below 100×10^9/L	41	55	362	91
	Over 100×10^9/L	10	13	37	9
	Unknown	23	31	0	0
BCR/ABL					
	Yes	14	19	6	2
	No	59	79	379	95
	Unknown	2	3	14	3
MLL/AF4					
	Yes	4	5	0	0
	No	61	92	0	0
	Unknown	10	15	399	100

The information for the 399 pediatric samples are from Kawamata *et al*.[3]

Age of patients at diagnosis: 19-86 years; WBC indicates white blood cell count ($\times 10^9$/L) in peripheral blood at diagnosis; *BCR-ABL* and *MLL-AF4* fusions were examined by karyotyping, RT-PCR and/or FISH analysis.

Online Supplementary Table S2. Karyotype of adult ALL samples.

Case #	Karyotype	Ethnic group	Abnormalities in SNP-array
B-1	46,XY,t(9;22)(q34;q11) [18], 46,XY [2]	A	+
B-2	-	A	+
B-3	46,XY,t(9;22)(q34;q11) [2], 46,XY [18]	A	-
B-4	45,XX,-7,t(9;22)(q34;q11) [17], 46,XX [3]	C	+
B-5	48,XX,t(1;10)(p11;q23),t(4;13)(q31;q34),i(8)(q10),+i(8)(q10),t(9;22)(q34;q11),+der(22)t(9;22)(q34;q11) [11], 46,XX [8]	C	+
B-6	45,XX,del(3)(p11),-7,t(9;22)(q34;q11) [17], 46,XX [17]	A	+
B-7	46,XX,der(6)t(6;9)(q25;p13),der(9)t(6;9)(q25;p13)t(9;22)(q34;q11),der(22)t(9;22)(q34;q11) [13], 47,XX,der(6)t(6;9)(q25;p13),der(9)t(6;9)(q25;p13)t(9;22)(q34;q11),der(22)t(9;22)(q34;q11),+der(22)t(9;22)(q34;q11) [2]	C	+
B-8	46,XY,t(9;22)(q34;q11) [9], 46,XY [6]	C	+
B-9	46,XX,der(9;12)(q10;q10)t(9;22)(q34;q11),der(22)t(9;22)(q34;q11) [2], 46,XX [22]	C	+
B-10	46,XY	A	+
B-11	46,XX,i(8)(q10),der(9)t(8;9)(q11;p22)t(9;22)(q34;q11),i(17)(q10),der(22)t(9;22) [3], 46,XX,t(3;11)(p25;q13),i(8)(q10),der(9)t(8;9)(q11;p22)t(9;22)(q34;q11), i(17)(q10),der(22)t(9;22) (cell:7) [1], 46,XX-8,der(9)t(8;9)(q11;p22)t(9;22)(q34;q11),+der(9)t(8;9)t(9;22),i(17)(q10),der(22)t(9;22) (cell:5) [3], 46,XX [13]	A	+
B-12	46XY [20]	A	+
B-13	46,XY [19], 47,XY,+mar [1]	A	+
B-14	45,X,-Y,t(2;14;8)(p11;q32;q11) [9], 46,XY [12]	C	+
B-15	-	A	+
B-16	45,XY,9p-,q+,-11,14p+,22q+ [8] ,46XY [2]	A	+
B-17	46,XX,add(4)(q31),add(6)(q15),del(6)(q11),dic(9;22)(p22;p11),add(16)(p13),-17,+2mar,inc [1], 46,XX,add(4)(q31),add(6)(q15),del(6)(q11),dic(9;22)(p22;p11),add(16)(p13)[1], 46XY[18]	A	+
B-18	46,XY,i(9)(q10) [5], 46XY[11]	A	+

B-19	46,XX [5]	A	+
B-20	47,XY,+8,der(9)r(9)ins(9;12),der(12)t(9;12)(?;q15) [10]	C	+
B-21	46,XY,t(4;11)(q21;q23) [19], 46,XY [1]	C	+
B-22	46,XX,t(4;11)(q21;q23) [2],	A	+
	46,XX,t(4;11)(q21;q23),add(7)(p22) [1], 45,XX,-15 [1]		
B-23	46,XX,t(4;11)(q21;q23) [17], 46,XX [3]	C	+
B-24	46,XX,t(4;11)(q21;q23) [9], 46,XX [3]	C	-
B-25	48,XY,+5,+10,t(11;14)(24;q32) [5], 46,XY [18]	C	+
B-26	46,XX [10]	C	+
B-27	46,XY [17]	C	+
B-28	46,XX	A	+
B-29	t(4;18)(q32;q21)[9], 46,XY[11]	A	+
B-30	46,XX [20]	C	+
B-31	46,XY [20]	A	+
B-32	46,Y,t(X;16)(q25;p13) [5], 46,XY [13]	C	+
B-33	46,XY	A	+
B-34	45,X,-Y [30]	C	+
B-35	48,XY,+X,+14 [4], 46,XY [3]	C	+
B-36	46,XY	A	+
B-37	-	A	+
B-38	46,XY [18]	C	+
B-39	46,XY [22]	C	+
B-40	46,XY [20]	C	+
B-41	46,XX	A	+
B-42	-	A	+
B-43	-	A	+
B-44	46,XX,der(6)t(1;6)(q21;q21),add(9)(q22) [4], 46XX[7]	A	+
B-45	-	A	+
B-46	46,XX [20]	C	+
B-47	46,XY [20]	C	+
B-48	46,XX	A	+
B-49	46,XX	A	+
B-50	46,XY	A	-
B-51	46,XY [20]	A	-
B-52	46,XY [20/20]	A	+
B-53	46,XX [19/20]	A	-

B-54	41,XY,1p-,3p-,-6,-6,7p+,-9,10p+,11q+,12p+,-13,15p+,-17,20p+,-22,+mar [17/20]、46XY[3/20]	A	+
B-55	46, XY, del(9)(p21)	A	+
B-56	47,XX,der(9)del(9)(p22)t(9;22)(q34;q11),der(22)t(9;22) ,+der(22)t(9;22) (cell:3) [7/20],46,XX,der(9)del(9)(p22)t(9;22)(q34;q11),der(22)t(9;22) [3/20] , 46,idem,-5 [1/20], 47,idem,t(1;2)(p36;p21) [1/20] , 47,idem,t(4;7)(q35;q11),t(8;14)(q24;q22) [1/20] , 47,idem,add(10)(q22),add(14)(q22) [1/20] ,46,XX [6/20]	A	+
B-57	46,XY [10/10]	A	-
B-58	46,XX,t(9;22)(q34;q11)[3/6]	A	+
B-59 (Null-1)	46,XX	A	+
B-60 (Null-2)	ND	A	+
B-61(mix)	47, XY, 4p+, t(9; 22)(q34; q11), +21p+	A	+
T-1	46,XY,der(18)t(17;18)(q11;p11) [9], 46,XY [6]	C	+
T-2	-	A	+
T-3	46,XY [6]	C	+
T-4	46,XY,del(6)(q15),t(7;10)(q34;q24),del(9)(p21) [5], 46,XY [20]	C	+
T-5	47,XY,del(9)(p21p22),+del(17)(p11) [12], 46,XY [6]	C	+
T-6	46,XY,t(3;20),t(6;8),del(14)(q?22) [3], 46,XY [1]	C	+
T-7	45,XY,-4,del(5)(q13q33),der(5)t(4;5)(q11;p13),der(6)t(6;10)(q15;p13),der(10)t(6;10)(q?;p13),der(10)t(10;11)(p13;q14),der(11)t(6;11)(q?;q14),der(16)t(10;16)(?;p13),der(17)t(9;17)(?;p11),dup(19) [7], 46,XY [14]	C	+
T-8	48,XX,+13,+13 [12], 46,XX [8]	C	+
T-9	46,XY,t(2;3)(p12;p25),del(13)(q14q21),inv(14)(p11q31),t(14;22)(q31;q11) [7]	C	+
T-10	46,XY [25]	C	+
T-11	46,XX [6]	C	+
T-12	46,XX [4]	C	+
T-13	46,XY	A	+
T-14	46,XY [25]	C	+

Karyotype of 75 adult ALL samples are listed. Note, N.A., karyotype is not available; A, Asian (Japanese); C, Caucasian (German); +, abnormalities detected; -, abnormalities not

detected.

Online Supplementary Table S3. Chromosomal regions with homozygous deletions in adult ALL samples.

Case #	Chromosome	Physical localization		Size (Mb)	Gene(s) in the region	9p CNN-LOH
		Proximal	Distal			
B-9	9	20,675,097	22,203,270	1.53	*CDKN2, CDKN2B*	-
B-13	1	157,283,331	157,465,549	0.18	*SLAMF6, CD84, SLAMF1, CD48*	+
	9	21,362,123	22,185,820	0.82	*CDKN2A, CDKN2B*	
B-14	9	9,821,068	9,979,624	0.16	*PTPRD*	+
	9	21,161,267	22,203,270	1.04	*CDKN2A, CDKN2B*	
B-15	9	20,801,421	24,224,540	3.42	*CDKN2A, CDKN2B*	-
B-16	9	21,971,583	22,731,961	0.76	*CDKN2A, CDKN2B*	-
B-17	9	21,362,123	22,448,191	1.09	*CDKN2A, CDKN2B*	-
B-21	9	21,775,261	22,043,895	0.27	*CDKN2A, CDKN2B*	+
B-54	9	21362123	24709895	3.35	*CDKN2A, CDKN2B*	-
B-25	10	36,742,576	36,963,391	0.22	*no gene*	-
B-35	10	98,441,682	98,547,438	0.11	*PIK3AP1*	-
	13	43,750,858	43,903,713	0.15	*C13orf21*	
T-3	9	21,859,079	21,978,896	0.12	*CDKN2A, CDKN2B*	-
	9	24,504,390	24,505,111	0.001	*no gene*	
T-4	9	21,854,535	22,021,005	0.17	*CDKN2A, CDKN2B*	-
	18	12,769,947	12,853,142	0.08	*PTPN2*	
T-5	9	21,854,535	21,995,330	0.14	*CDKN2A, CDKN2B*	-
T-6	13	47,708,790	47,783,811	0.08	*ITM2B, RB1*	-

Homozygous deleted regions in adult ALL samples are displayed. Of note, eight B-ALL and three T-ALL samples had homozygous deletions of the *CDKN2A* and *CDKN2B* genes. Three of 11 samples (27%) with homozygous deletions of the *CDKN2A* and *CDKN2B* genes had 9p CNN-LOH.

Online Supplementary Table S4. Chromosomal regions with heterozygous deletions in adult ALL samples.

Case #	Chromosome	Physical localization		Size (kb)
		Proximal	Distal	
B-1	2	207,815,051	207,835,859	20.808
B-1	8	60,241,236	60,586,442	345.206
B-1	20	10,375,960	10,399,891	23.931
B-2	8	60,212,394	60,315,650	103.256
B-4	6	135,416,061	135,491,008	74.947
B-4	7	141,322	158,605,053	158463.731
B-4	13	63,132,563	63,271,229	138.666
B-5	7	49,921,199	50,228,460	307.261
B-5	8	180,568	36,086,137	35905.569
B-5	9	28,696,215	29,173,429	477.214
B-5	9	129,725,026	130,700,428	975.402
B-5	13	107,712,675	108,056,227	343.552
B-5	15	23,588,168	23,614,127	25.959
B-5	19	51,484,755	53,451,790	1967.035
B-5	21	34,213,413	34,481,781	268.368
B-5	22	21,043,189	21,860,252	817.063
B-5	22	21,888,534	22,566,087	677.553
B-6	3	135,814	89,708,135	89572.321
B-6	7	11,143,952	54,332,606	43188.654
B-6	7	54,869,406	62,940,814	8071.408
B-6	7	66,800,898	88,353,793	21552.895
B-6	7	89,094,056	152,213,592	63119.536
B-6	19	51,886,094	63,437,743	11551.649
B-7	3	170,773,726	170,848,641	74.915
B-7	9	124,615,546	130,577,960	5962.414
B-7	13	47,895,694	48,070,777	175.083
B-7	22	21,970,272	23,470,307	1500.035
B-8	1	71,863,321	72,199,546	336.225
B-8	1	91,883,441	91,958,069	74.628
B-8	1	195,646,518	195,769,906	123.388
B-8	1	229,202,044	229,387,526	185.482

B-8	2	159,898,170	159,960,416	62.246
B-8	3	113,538,401	113,673,530	135.129
B-8	4	109,414,395	109,797,599	383.204
B-8	6	28,358,892	28,424,457	65.565
B-8	7	50,012,062	50,101,537	89.475
B-8	7	50,198,172	50,228,460	30.288
B-8	9	21,899,000	21,995,330	96.330
B-8	9	37,045,109	37,106,493	61.384
B-8	10	7,355,095	7,452,885	97.790
B-8	13	47,895,694	48,072,129	176.435
B-8	15	23,604,165	23,625,311	21.146
B-8	19	16,931,679	17,043,939	112.260
B-9	1	77,465,104	77,487,725	22.621
B-9	2	168,001,355	168,005,991	4.636
B-9	4	99,864,266	99,930,528	66.262
B-9	4	182,659,373	182,659,523	0.150
B-9	5	88,161,609	89,251,989	1090.380
B-9	5	124,159,516	124,597,462	437.946
B-9	6	26,220,872	26,335,083	114.211
B-9	8	60,184,925	60,404,370	219.445
B-9	8	71,360,722	71,468,721	107.999
B-9	9	30,910	20,668,602	20637.692
B-9	9	22,231,296	38,737,064	16505.768
B-9	9	77,634,986	77,869,156	234.170
B-9	9	118,898,901	118,984,706	85.805
B-9	12	50,446	36,215,633	36165.187
B-9	12	45,782,194	46,844,331	1062.137
B-9	13	79,815,528	80,256,687	441.159
B-9	19	19,716,893	21,547,316	1830.423
B-10	1	222,694,353	244,505,070	21810.717
B-10	2	207,864,043	208,124,438	260.395
B-10	6	112,276,043	155,347,544	43071.501
B-10	9	239,391	42,930,351	42690.960
B-10	13	47,908,486	78,819,049	30910.563
B-10	17	68,436,446	68,676,913	240.467
B-11	1	227,843,862	227,850,515	6.653

B-11	3	60,073,349	60,604,879	531.530
B-11	8	104,014,618	104,922,843	908.225
B-11	9	239,391	38,705,865	38466.474
B-11	11	61,241,557	65,214,745	3973.188
B-11	17	451,209	18,772,157	18320.948
B-12	8	180,568	5,568,296	5387.728
B-12	9	239,391	11,611,204	11371.813
B-12	9	11,980,405	22,923,651	10943.246
B-13	7	108,057,359	158,554,645	50497.286
B-14	1	102,370,195	102,561,809	191.614
B-14	2	224,000,431	224,177,568	177.137
B-14	5	103,733,405	103,785,495	52.090
B-15	9	305,185	20,801,210	20496.025
B-15	9	24,245,420	130,083,358	105837.938
B-15	20	33,372,659	62,376,958	29004.299
B-16	2	8,564,879	8,765,284	200.405
B-16	3	46,977,895	47,303,748	325.853
B-16	3	60,073,349	60,099,620	26.271
B-16	3	113,538,483	113,659,820	121.337
B-16	7	37,719,741	38,028,579	308.838
B-16	9	239,391	21,948,524	21709.133
B-16	9	22,785,727	36,988,416	14202.689
B-16	11	55,248,049	134,082,843	78834.794
B-16*	12	90,671,883	91,035,857*	363.974
B-16	13	106,138,282	106,515,980	377.698
B-16	19	14,603,924	14,801,001	197.077
B-17	6	108,940,080	109,998,869	1058.789
B-17	9	20,115,458	21,204,877	1089.419
B-17	9	22,448,980	24,209,684	1760.704
B-17	9	32,872,662	33,916,496	1043.834
B-17	12	7,272,323	10,756,021	3483.698
B-17	12	11,674,778	12,214,885	540.107
B-17	12	47,543,869	49,380,405	1836.536
B-17	16	3,165,870	4,858,366	1692.496
B-17	17	24,399,965	27,138,320	2738.355
B-18	3	14,547,600	14,547,647	0.047

B-18	9	305,185	42,602,035	42296.850
B-19	4	115,764,934	116,947,077	1182.143
B-19	7	1,307,029	61,522,282	60215.253
B-19	9	21,362,123	27,316,904	5954.781
B-19	11	118,899,695	122,795,061	3895.366
B-19	14	62,410,549	62,863,736	453.187
B-19	18	51,803,567	52,002,040	198.473
B-20	9	30,910	36,989,024	36958.114
B-20	9	38,429,042	38,761,831	332.789
B-20	9	84,969,107	87,137,689	2168.582
B-20	9	116,272,876	119,488,620	3215.744
B-20	12	50,446	11,862,890	11812.444
B-20	12	12,321,303	17,155,604	4834.301
B-20	12	18,108,642	19,428,275	1319.633
B-20	12	19,865,082	23,348,440	3483.358
B-20	12	26,187,859	27,252,626	1064.767
B-20	12	27,938,350	29,096,612	1158.262
B-20	12	32,577,224	33,886,076	1308.852
B-20	12	62,102,441	62,226,007	123.566
B-20	12	74,157,020	74,211,419	54.399
B-20	12	82,027,233	82,091,386	64.153
B-20	12	84,519,381	84,615,646	96.265
B-20	12	87,184,335	89,769,388	2585.053
B-20	12	101,809,017	102,037,277	228.260
B-20	12	128,001,947	128,169,376	167.429
B-21	7	141,322	57,730,637	57589.315
B-21	7	61,547,528	158,605,053	97057.525
B-21	9	22,044,356	22,841,021	796.665
B-21	9	106,062,097	106,175,966	113.869
B-21	10	67,747,770	67,755,493	7.723
B-21	10	67,776,810	67,777,502	0.692
B-21	11	99,017,466	99,017,836	0.370
B-22	7	250,149	57,423,201	57173.052
B-23	6	92,286,311	92,398,633	112.322
B-25	1	66,512,785	66,541,283	28.498
B-25	1	72,724,625	72,782,125	57.500

B-25	1	155,416,772	155,713,348	296.576
B-25	2	136,726,957	136,864,961	138.004
B-25	2	242,636,531	242,712,341	75.810
B-25	3	11,524,596	11,681,197	156.601
B-25	3	60,041,884	60,393,761	351.877
B-25	3	66,566,151	66,616,274	50.123
B-25	4	86,859,192	86,879,164	19.972
B-25	5	142,616,649	142,708,224	91.575
B-25	5	150,137,617	150,297,043	159.426
B-25	5	157,485,991	158,451,346	965.355
B-25	6	156,698,540	156,967,182	268.642
B-25	7	47,324,508	47,445,704	121.196
B-25	7	49,987,339	50,101,537	114.198
B-25	7	50,198,172	50,228,460	30.288
B-25	9	36,905,243	37,265,174	359.931
B-25	11	2,992,900	3,024,682	31.782
B-25	11	33,138,854	33,332,671	193.817
B-25	11	36,582,372	36,595,940	13.568
B-25*	12	90,784,636	91,053,257*	268.621
B-25	12	107,444,583	110,980,362	3535.779
B-25	13	43,727,300	43,903,713	176.413
B-25	13	66,711,848	66,896,963	185.115
B-25	14	64,612,382	64,632,059	19.677
B-25	18	51,409,607	51,895,543	485.936
B-25	19	19,716,893	19,831,113	114.220
B-26	6	20,236,536	21,015,860	779.324
B-26	6	84,007,856	94,822,978	10815.122
B-26	6	102,071,607	120,194,720	18123.113
B-26	6	120,260,146	120,714,956	454.810
B-26	6	120,846,098	125,616,395	4770.297
B-26	6	127,030,775	145,513,203	18482.428
B-26	6	152,485,274	157,222,155	4736.881
B-26	13	57,945,845	58,080,227	134.382
B-26	15	18,427,103	100,192,115	81765.012
B-26	17	18,901	18,857,962	18839.061
B-26	18	59,157,272	76,115,554	16958.282

B-27	12	11,703,867	11,806,014	102.147
B-28	3	113,613,279	113,659,820	46.541
B-28	4	15,668,755	15,669,100	0.345
B-28	4	109,373,737	109,423,970	50.233
B-28	17	451,209	19,615,696	19164.487
B-28	20	10,375,960	10,399,891	23.931
B-29	2	24,312,037	24,796,536	484.499
B-29	3	165,852,108	165,861,395	9.287
B-29	4	62,026,967	62,629,702	602.735
B-29	8	114,148,247	114,629,553	481.306
B-29	10	284,953	135,211,857	134926.904
B-29	11	38,307,265	38,912,117	604.852
B-29	12	98,097,757	132,294,671	34196.914
B-29	13	18,425,192	70,742,696	52317.504
B-29	17	450,509	20,683,212	20232.703
B-29	19	6,189,414	24,194,887	18005.473
B-30	3	60,064,354	60,976,902	912.548
B-30	3	113,525,909	113,595,833	69.924
B-30	3	113,646,191	113,673,070	26.879
B-30	9	29,307,860	29,638,921	331.061
B-30	9	37,131,508	37,382,087	250.579
B-30	11	57,758,417	57,813,314	54.897
B-30	13	47,895,694	48,063,054	167.360
B-31	4	70,511,010	191,091,333	120580.323
B-31	9	70,403,235	73,112,263	2709.028
B-31	9	97,459,759	98,425,723	965.964
B-31	17	451,209	18,772,157	18320.948
B-32	3	69,584,543	69,654,266	69.723
B-32	5	158,386,361	158,451,346	64.985
B-32	9	24,504,390	24,505,111	0.721
B-32	11	76,733,974	76,871,480	137.506
B-33	1	72,525,150	72,769,476	244.326
B-33*	12	90,972,766	91,035,857*	63.091
B-33	15	55,118,321	55,253,067	134.746
B-34	18	67,590,053	67,592,593	2.540
B-35	1	59,083,267	59,184,074	100.807

B-35	3	113,528,954	113,673,530	144.576
B-35	10	97,458,579	98,407,920	949.341
B-35	10	98,609,853	99,302,528	692.675
B-35	11	36,582,372	36,595,940	13.568
B-35*	12	90,784,636	91,053,257*	268.621
B-35	13	19,257,699	19,307,931	50.232
B-35	13	43,727,300	43,742,835	15.535
B-35	13	68,428,545	114,092,980	45664.435
B-35	14	19,336,854	19,502,884	166.030
B-35	14	105,716,891	106,176,088	459.197
B-36	6	161,781,319	162,010,871	229.552
B-38*	12	90,784,636	91,053,257*	268.621
B-38	15	91,947,628	91,959,244	11.616
B-39	14	86,533,539	86,656,689	123.150
B-40	5	113,355,383	113,360,599	5.216
B-40	8	15,995,420	16,065,839	70.419
B-41	4	26,115,291	26,115,900	0.609
B-41	5	128,593,792	129,475,223	881.431
B-41	5	150,312,614	150,568,806	256.192
B-41	7	125,812,696	125,813,467	0.771
B-41	14	70,728,006	70,845,546	117.540
B-42	1	2,221,742	7,114,855	4893.113
B-42	2	38,684,566	46,583,071	7898.505
B-42	2	128,290,273	129,170,097	879.824
B-42	6	86,489,649	90,950,621	4460.972
B-43	3	82,032,992	85,222,091	3189.099
B-43	6	67,405,141	67,646,218	241.077
B-43	13	101,333,357	101,333,631	0.274
B-44	6	93,065,830	170,822,590	77756.760
B-44	9	69,575,157	71,306,413	1731.256
B-44	9	93,306,655	103,683,632	10376.977
B-45	8	116,079,356	117,997,280	1917.924
B-45	18	59,627,434	59,742,040	114.606
B-46	16	3,934,697	4,300,315	365.618
B-47	18	1,725,368	1,815,170	89.802
B-48	14	55,687,409	55,893,871	206.462

B-49	19	51,019,549	51,019,773	0.224
B-52	14	50,126,350	51,949,076	1822.726
B-52	18	36,326,162	36,588,882	262.720
B-54	1	45,027,620	142,417,280	97389.660
B-54	3	135,814	90,045,737	89909.923
B-54	4	55,808,411	67,039,329	11230.918
B-54	4	70,675,661	73,779,321	3103.660
B-54	4	75,936,632	191,091,333	115154.701
B-54	5	141,856,833	157,661,635	15804.802
B-54	6	54,077,891	64,444,019	10366.128
B-54	6	82,794,175	108,657,232	25863.057
B-54	6	111,387,447	124,382,232	12994.785
B-54	6	138,044,330	170,770,193	32725.863
B-54	7	33,766,223	43,472,173	9705.950
B-54	7	47,225,158	54,491,738	7266.580
B-54	9	7,184,521	21,204,877	14020.356
B-54	9	24,710,232	138,166,210	113455.978
B-54	10	259,695	2,255,199	1995.504
B-54	11	98,207,847	102,241,629	4033.782
B-54	11	105,450,587	115,354,106	9903.519
B-54	13	18,042,610	114,051,465	96008.855
B-54	17	451,209	6,915,690	6464.481
B-54	17	11,063,899	16,776,778	5712.879
B-54	17	31,462,117	31,503,652	41.535
B-56	9	21,133,020	42,930,351	21797.331
B-56	9	130,736,916	138,166,210	7429.294
B-56	20	10,375,960	10,407,613	31.653
B-58	7	49,598,672	50,089,428	490.756
B-58	9	19,520,883	19,933,585	412.702
B-58	9	21,133,020	22,685,667	1552.647
B-58*	12	90,662,387	91,035,857*	373.470
B-58	15	55,118,321	55,191,405	73.084
B-59	13	106,870,516	106,883,619	13.103
B-60	1	190,962,106	191,660,170	698.064
B-60	2	88,274,497	88,993,415	718.918
B-60	4	133,300,542	133,513,765	213.223

B-60	5	142,962,374	143,278,239	315.865
B-60	9	8,117,420	8,179,112	61.692
B-60	9	21,948,524	21,971,583	23.059
B-60	9	36,927,603	36,988,416	60.813
B-60	12	67,491,554	67,695,739	204.185
B-60*	12	90,972,766	91,035,857*	63.091
B-61	8	124,781,880	125,014,361	232.481
B-61	9	11,980,405	12,140,471	160.066
B-61	10	8,313,669	9,370,093	1056.424
B-61	13	43,583,946	43,743,243	159.297
B-61	17	64,445,396	64,624,957	179.561
T-1	1	102,370,195	102,561,809	191.614
T-1	18	210,071	1,055,350	845.279
T-2	13	49,630,676	50,272,626	641.950
T-2	17	26,677,010	28,109,086	1432.076
T-3	3	85,603,747	85,659,887	56.140
T-3	4	161,925,165	163,109,094	1183.929
T-3	5	53,208,596	72,217,160	19008.564
T-3	5	165,703,458	165,711,472	8.014
T-3	8	111,886,767	112,158,168	271.401
T-3	8	112,409,593	112,491,933	82.340
T-3	9	3,177,859	21,854,552	18676.693
T-3	9	21,988,733	24,467,128	2478.395
T-3	9	24,518,103	37,947,229	13429.126
T-3	10	22,723,357	22,941,760	218.403
T-3	13	88,805,179	89,315,863	510.684
T-3	16	45,065,445	88,690,776	43625.331
T-4	6	87,408,292	113,933,187	26524.895
T-4	9	20,687,467	21,836,327	1148.860
T-4	9	22,043,687	24,332,423	2288.736
T-5	2	129,220,262	144,446,011	15225.749
T-5	2	145,361,978	146,121,302	759.324
T-5	9	19,566,362	21,836,327	2269.965
T-5	9	22,013,795	22,571,260	557.465
T-5	17	18,901	21,491,135	21472.234
T-5	18	513,832	804,730	290.898

T-6	1	26,936,965	27,319,391	382.426
T-6	2	180,729,136	182,606,925	1877.789
T-6	3	35,670,516	36,676,438	1005.922
T-6	3	142,912,781	143,336,624	423.843
T-6	3	192,529,472	193,865,691	1336.219
T-6	5	6,326,004	6,692,763	366.759
T-6	5	160,951,790	161,332,954	381.164
T-6	9	21,438,448	21,504,364	65.916
T-6	12	11,739,760	11,904,839	165.079
T-6	12	121,412,843	121,587,474	174.631
T-6	13	39,516,616	47,686,991	8170.375
T-6	13	47,809,265	51,499,724	3690.459
T-6	14	60,848,668	90,748,299	29899.631
T-6	20	34,934,264	36,233,880	1299.616
T-6	20	48,737,169	49,760,837	1023.668
T-7	5	49,596,616	120,374,182	70777.566
T-7	5	120,619,324	180,629,495	60010.171
T-7	6	71,989,993	72,962,342	972.349
T-7	11	83,266,085	83,271,705	5.620
T-7	11	87,787,086	87,791,549	4.463
T-7	16	31,010	3,500,902	3469.892
T-7	16	56,137,979	59,246,299	3108.320
T-7	17	7,797,163	8,039,908	242.745
T-7	18	72,436,933	76,115,554	3678.621
T-7	19	45,625,821	48,954,385	3328.564
T-8	13	49,039,346	51,891,413	2852.067
T-8	16	66,144,782	66,901,470	756.688
T-9	18	7,730,473	7,750,682	20.209
T-10	1	212,248,859	212,250,274	1.415
T-10	13	86,998,038	87,040,058	42.020
T-14	3	1,795,234	1,957,593	162.359

*: Next SNP is located on chr.12, 91,067,704 in B-16, -33, -58, -60.

**: Next SNP is located on chr.12, 91,067,786 in B-25, -35, -38.

Samples with either * or ** have a breakpoint including the *BTG1* gene, which is located on chr12:91,061,034-91,063,751, between the distal SNP position of the deletion and the next SNP position.

Online Supplementary Table S5. Chromosomal regions with duplications in adult ALL samples.

Case #	Chromosome	Physical localization		Size (Mb)
		Proximal	Distal	
B-2	22	17,376,298	21,479,136	4.103
B-4	11	37,686,392	37,842,579	0.156
B-5	8	39,579,937	146,263,538	106.684
B-5	9	130,737,915	138,303,776	7.566
B-5	22	21,043,189	21,860,252	0.817
B-7	4	79,105,930	79,347,118	0.241
B-9	11	73,090,662	73,289,168	0.199
B-10	1	145,940,029	222,350,209	76.410
B-10	6	155,411,268	159,732,853	4.322
B-10	6	166,350,307	168,114,434	1.764
B-10	6	170,538,106	170,538,754	0.001
B-10	17	35,542,587	59,512,051	23.969
B-11	8	104,954,123	143,902,698	38.949
B-11	17	19,211,040	78,181,864	58.971
B-12	5	260,504	8,439,088	8.179
B-12	8	72,632,955	143,902,698	71.270
B-13	1	142,930,664	156,376,000	13.445
B-13	1	159,817,168	207,743,233	47.926
B-13	2	6,197,627	66,870,455	60.673
B-13	4	70,949,406	90,168,373	19.219
B-13	12	39,535,217	67,695,739	28.161
B-13	14	70,281,911	106,312,036	36.030
B-15	1	142,397,633	244,850,724	102.453
B-15	13	27,870,164	27,871,703	0.002
B-15	13	97,290,935	97,536,766	0.246
B-15	22	15,271,316	24,267,224	8.996
B-18	9	68,229,855	137,012,035	68.782
B-19	7	61,873,591	158,554,645	96.681
B-19	22	15,263,131	48,983,486	33.720
B-20	8	180,568	146,263,538	146.083
B-20	9	37,003,845	38,398,920	1.395

B-20	9	42,937,560	73,633,747	30.696
B-20	9	73,897,065	75,672,529	1.775
B-20	9	80,967,779	81,360,161	0.392
B-20	9	99,536,920	102,358,221	2.821
B-20	12	11,892,519	12,239,176	0.347
B-20	12	17,166,271	18,046,715	0.880
B-20	12	19,489,402	19,835,818	0.346
B-20	12	23,376,393	26,158,915	2.783
B-20	12	27,282,464	27,934,654	0.652
B-20	12	29,101,388	29,639,626	0.538
B-20	12	30,453,672	30,472,248	0.019
B-20	12	30,836,646	32,565,912	1.729
B-20	12	33,914,038	36,144,018	2.230
B-20	12	36,963,675	37,424,739	0.461
B-20	12	39,609,747	39,866,444	0.257
B-20	12	40,102,269	43,107,259	3.005
B-20	12	64,620,042	71,645,433	7.025
B-20	12	74,219,915	76,934,523	2.715
B-20	12	78,280,312	79,003,423	0.723
B-20	12	89,898,474	90,011,617	0.113
B-20	12	102,125,488	104,828,077	2.703
B-20	12	104,856,274	104,888,198	0.032
B-20	12	105,027,304	125,446,051	20.419
B-20	12	125,532,812	125,755,075	0.222
B-20	12	126,920,657	127,172,564	0.252
B-22	7	61,534,066	158,624,663	97.091
B-23	1	38,748,243	38,804,841	0.057
B-23	3	1,829,320	1,900,851	0.072
B-25	4	152,075,949	152,427,171	0.351
B-25	5	81,949	141,535,648	141.454
B-25	5	142,784,880	150,135,905	7.351
B-25	5	150,331,183	157,460,757	7.130
B-25	5	158,476,547	180,629,495	22.153
B-25	10	148,946	36,714,060	36.565
B-25	10	36,974,657	135,311,386	98.337
B-26	3	189,039,683	189,208,815	0.169

B-26	5	27,340,648	27,575,247	0.235
B-26	6	119,769	20,217,821	20.098
B-26	6	21,026,230	32,320,242	11.294
B-26	6	32,321,030	33,459,229	1.138
B-26	6	33,473,618	84,005,449	50.532
B-26	6	94,823,810	102,023,284	7.199
B-26	6	120,213,981	120,227,364	0.013
B-26	6	120,736,258	120,836,788	0.101
B-26	6	125,630,589	126,918,273	1.288
B-26	6	145,522,349	152,476,914	6.955
B-26	6	157,235,840	170,792,391	13.557
B-26	9	29,389,206	30,261,809	0.873
B-26	11	201,447	58,173,418	57.972
B-26	11	101,832,951	102,080,964	0.248
B-26	12	50,446	132,387,995	132.338
B-26	16	10,771,851	10,920,235	0.148
B-26	17	19,109,505	78,599,918	59.490
B-26	18	3,585,765	3,646,607	0.061
B-26	18	5,981,270	8,406,950	2.426
B-26	18	8,954,794	12,918,541	3.964
B-26	18	17,794,465	18,308,835	0.514
B-26	18	25,199,079	31,326,956	6.128
B-26	18	36,454,751	37,405,315	0.951
B-26	18	40,768,446	41,912,886	1.144
B-26	18	44,764,374	45,785,476	1.021
B-26	18	48,460,051	51,959,733	3.500
B-26	18	56,255,932	59,129,566	2.874
B-26	20	17,408	12,242,875	12.225
B-28	21	36,119,347	46,924,583	10.805
B-29	8	114,860,437	146,052,174	31.192
B-29	12	39,022,206	39,111,754	0.090
B-30	1	143,879,621	245,326,460	101.447
B-31	5	260,504	81,651,106	81.391
B-31	5	81,653,831	91,374,861	9.721
B-31	6	150,610	170,770,193	170.620
B-31	8	90,610,612	143,902,698	53.292

B-31	10	259,695	135,228,726	134.969
B-31	17	19,211,040	78,181,864	58.971
B-31	18	149,885	75,946,870	75.797
B-31	21	10,039,984	46,924,583	36.885
B-31	23	1,911,310	57,324,660	55.413
B-32	21	23,126,095	23,223,686	0.098
B-32	21	23,634,269	46,894,358	23.260
B-32	23	159,978	31,916,674	31.757
B-33	23	1,911,310	32,980,939	31.070
B-35	5	110,419,790	180,629,495	70.210
B-35	14	19,526,274	22,029,666	2.503
B-35	14	22,069,902	105,685,710	83.616
B-36	14	19,285,288	106,312,036	87.027
B-36	21	10,039,984	46,924,583	36.885
B-37	21	10,039,984	46,924,583	36.885
B-40	7	73,559,909	158,605,053	85.045
B-43	2	34,148,652	34,386,124	0.237
B-44	1	143,140,453	244,850,724	101.710
B-47	1	185,649,343	185,758,880	0.110
B-47	3	35,796,249	35,916,128	0.120
B-54	2	43,841,634	43,842,267	0.001
B-54	6	150,610	47,433,570	47.283
B-54	10	2,283,989	22,566,131	20.282
B-54	12	108,913,407	123,828,884	14.915
B-54	16	77,648,829	77,649,348	0.001
B-55	8	73,906,603	73,910,715	0.004
B-55	9	20,638,805	39,005,654	18.367
B-61	1	142,694,585	245,120,412	102.426
B-61	5	260,504	180,003,855	179.743
B-61	6	28,574,967	170,770,193	142.195
B-61	7	1,307,029	158,554,645	157.248
B-61	9	130,736,916	138,166,210	7.429
B-61	13	18,042,610	43,561,145	25.519
B-61	13	44,117,895	114,051,465	69.934
B-61	14	19,285,288	106,312,036	87.027
B-61	17	451,209	64,346,267	63.895

B-61	17	64,644,947	78,181,864	13.537
B-61	19	341,341	63,437,743	63.096
B-61	21	10,039,984	46,924,583	36.885
B-61	22	15,263,131	48,983,486	33.720
T-1	17	27,888,812	31,460,104	3.571
T-1	17	31,923,810	78,599,918	46.676
T-2	13	18,042,610	49,543,165	31.501
T-2	13	50,441,141	114,051,465	63.610
T-3	8	112,530,420	146,263,538	33.733
T-3	12	7,850,883	8,008,336	0.157
T-3	13	54,865,809	55,464,860	0.599
T-3	13	55,583,840	55,721,381	0.138
T-3	19	2,784,431	2,797,782	0.013
T-4	8	43,232,092	43,820,269	0.588
T-5	14	93,493,789	106,356,482	12.863
T-5	17	21,641,572	78,599,918	56.958
T-6	1	74,356,475	75,831,618	1.475
T-6	4	166,154,498	167,771,280	1.617
T-7	5	26,358,425	46,419,092	20.061
T-7	19	32,651,846	33,928,074	1.276
T-7	19	33,934,258	35,965,262	2.031
T-8	3	11,820,285	12,019,704	0.199
T-8	13	17,960,319	49,033,464	31.073
T-8	13	52,051,564	114,092,980	62.041
T-10	20	12,572,679	12,582,137	0.009
T-10	20	12,757,182	12,837,747	0.081
T-11	21	31,008,125	31,141,251	0.133
T-12	19	20,643,736	20,777,265	0.134
T-13	5	128,026,678	128,529,519	0.503
T-13	7	69,410,843	69,754,537	0.344

Online Supplementary Table S6. Chromosomal regions of amplifications in adult ALL samples.

Case #	Location	Physical localization		Size (Mb)	Gene(s) in the region
		Proximal	Distal		
B-26	2	59,727,570	63,267,171	3.5	>10 genes including *BCL11A, REL*
T-7	19	35,986,840	45,571,967	9.6	>10 genes including *AKT2*

Amplified genomic regions (≥5 copies) in adult ALL samples are displayed.

Online Supplementary Table S7. Chromosomal regions of copy-number neutral loss of heterozygosity in adult ALL samples.

Case #	Chr.	Physical localization		Size (Mb)	# of SNPs	Gene(s) in the region
		Proximal	Distal			
B-1	16	205,160	9,346,193	9.141	140	>10 genes including *TSC2, CREBBP and USP7*
B-2	9	97,152,922	138,166,210	41.013	679	>10 genes including *PTCH1, XPA, NR4A3, ALDOB, TAL2, KLF4, TXN, LPAR1, TNFSF15, TNC, DAB2IP, HSPA5, SET, PPP2R4, PRRX2, FNBP1, ABL1, NUP214, TSC1 and NOTCH1*
B-13	9	239,391	21,204,877	20.965	758	>10 genes including *JAK2, RLN2, KDM4C, PTPRD, PSIP1, SH3GL2 and MLLT3*
B-13	9	22,404,640	38,111,300	15.707	468	>10 genes including *TEK, TOPORS, BAG1, FANCG, PAX5 and SHB*
B-14	9	30,910	37,488,334	37.457	5177	>10 genes including *JAK2, RLN2, KDM4C, PTPRD, PSIP1, SH3GL2, MLLT3, CDKN2A, TEK, TOPORS, BAG1, FANCG and PAX5*
B-15	22	15,271,316	48,859,864	33.589	349	>10 genes including *CLTCL1, SEPT5, IGL, BCR, MMP11, SMARCB1, MN1, CHEK2, EWSR1, NF2, MYH9, RAC2, PDGFB, ATF4, MKL1, RBX1 and EP300*

B-21	9	30,910	21,775,018	21.744	3430	>10 genes including *JAK2, RLN2, KDM4C, PTPRD, PSIP1, SH3GL2 and MLLT3*
B-21	9	22,850,886	38,014,458	15.164	1676	>10 genes including *TEK, TOPORS, BAG1, FANCG, PAX5 and SHB*
B-26	2	24,049	242,717,659	242.694	22215	>10 genes including *E2F6, MYCN, SDC1, RHOB, ALK, NLRC4, BIRC6, STRN, EML4, EPCAM, MSH2, MSH6, LHCGR, RTN4, BCL11A, REL, LOXL3, KCMF1, CAPG, IGK, AFF3, FHL2, RANBP2, BCL2L11, MERTK, IL1B, PAX8, BIN1, ERCC3, ACVR2A, ATF2, MIR10B, DIRC1, PMS1, HSPD1, CFLAR, ADAM23, IKZF2, BARD1, ATIC, DIRC3, PAX3, PTMA, CXCR7, SEP2 and BOK*
B-26	13	17,960,319	114,092,980	96.133	11117	>10 genes including *ZMYM2, CDX2, FLT3, HSPH1, STARD13, LHFP, LOC646982, FOXO1, LCP1, RB1, INTS6, KLF5, POU4F1, RAP2A and ERCC5*
B-26	18	210,071	3,538,692	3.329	401	>10 genes including *YES1*
B-26	18	3,651,485	5,979,848	2.328	295	*DLGAP1, LOC642597, LOC339290, ZFP161, EPB41L3, TMEM200C* and *L3MBTL4*

B-26	18	8,440,613	8,882,906	0.442	76	*RAB12, KIAA0802*
B-26	18	12,967,206	17,740,723	4.774	187	>10 genes
B-26	18	18,312,106	25,138,544	6.826	648	>10 genes including *ROCK1, RBBP8 and SS18*
B-26	18	31,328,729	36,410,642	5.082	494	>10 genes
B-26	18	37,406,044	40,744,907	3.339	369	*KC6, PIK3C3 and RIT2*
B-26	18	41,925,238	44,638,071	2.713	232	>10 genes including *SMAD2*
B-26	18	45,807,493	48,412,486	2.605	323	>10 genes including *MAPK4 and SMAD4*
B-26	18	52,002,040	56,251,380	4.249	490	>10 genes including *TCF4*
B-29	6	99,536	37,252,382	37.153	836	>10 genes including *IRF4, CAGE1, TFAP2A, DEK, ID4, E2F3, SOX4, HFE, IER3, LTA, TNF, DAXX, HMGA1, PPARD, FANCE, MAPK13, CDKN1A and PIM1*
B-31	5	91,924,473	180,003,855	88.079	2273	>10 genes including *APC, LOX, FNIP1, IL3, IRF1, AFF4, TGFBI, HDAC3, ARHGAP26, SPINK7, CSNK1A1, CSF1R, PDGFRB, ITK, PTTG1, TLX3, NPM1, NKX2-5, NSD1, MAPK9, GNB2L, FER, FMS, FGFR4 and FLT4*
B-38	3	48,603	55,005,160	54.957	285715	>10 genes including *FANCD2, VHL, GHRL, PPARG, RAF1, XPC, SATB1, MLH1, CTNNB1, CCR9, MAP4, CDC25A, PLXNB1, NCKIPSD, RHOA, TCTA, MST1R, RBM5, SEMA3F,*

						SEMA3B, HYAL1, HYAL2, RASSF1, BAP1 and PRKCD
B-39	4	68,177,070	191,306,043	123.129	12322	>10 genes including *AREG, RCHY1, HNRNPD, MAPK10, PTPN13, AFF1, SPP1, RAP1GDS1, NFKB1, SYNPO2, MAD2L1, EPHA5, FGA7, NR3C2, ING2 and SORBS2*
B-40	17	18,901	13,185,172	13.166	888	>10 genes including *HIC1, ALOX15, USP6, XAF1, ALOX12, TP53, GAS7, ELAC2, TNK1 and RYKps*
B-52	9	239,391	28,372,826	28.133	1001	>10 genes including *JAK2, RLN2, KDM4C, PTPRD, PSIP1, SH3GL2, MLLT3, CDKN2A and TEK*
B-61	2	100,819	241,601,632	241.501	5271	>10 genes including *E2F6, MYCN, SDC1, RHOB, ALK, NLRC4, BIRC6, STRN, EML4, EPCAM, MSH2, MSH6, LHCGR, RTN4, BCL11A, REL, LOXL3, KCMF1, CAPG, IGK, AFF3, FHL2, RANBP2, BCL2L11, MERTK, IL1B, PAX8, BIN1, ERCC3, ACVR2A, ATF2, MIR10B, DIRC1, PMS1, HSPD1, CFLAR, ADAM23, IKZF2, BARD1, ATIC, DIRC3, PAX3, PTMA, CXCR7, SEP2 and BOK*

T-1	7	70,551,875	158,605,053	88.053	7204	>10 genes including *BCL7B, CLDN4, LIMK1, HIP1, HSPB1, DMTF1, ABCB1, STEAP1, AKAP9, ERVWE1, COL1A2, TAC1, ASNS, MUC17, HBP1, NRCAM, CAV1, EPHB6, EPHA1, MET, NRF1, CREB3L2, TRIM24, BRAF, TRB, TRPV6, EPHA1, SHH and MNX1*
T-1	12	108,346,094	132,387,995	24.042	2020	>10 genes including *ALDH2, PTPN11, PEBP1, PRKAB1, P2RX7, DENR, RAN, EP400 and CHFR*
T-2	10	259,695	29,377,894	29.118	690	>10 genes including *KLF6, AKR1C3, NET1, MLLT10, BMI1 and ABI1*
T-3	2	24,049	27,006,493	26.982	2796	>10 genes including *E2F6, MYCN, SDC1 and RHOB*
T-4	19	212,033	13,505,719	13.294	375	>10 genes including *FSTL3, STK11, TCF3, SH3GL1, MLLT1, VAV1, ELAVL1, MUC16, DNMT1, INSR, TYK2, CTK, AXL, ICAM1, SMARCA4, JUNB, GADD45GIP1 and LYL1*
T-7	5	81,949	26,357,418	26.275	2931	>10 genes including *PDCD6*

Chromosomal regions with loss of heterozygosity and normal copy-number status, called copy-number neutral LOH (CNN-LOH) in adult ALL samples are summarized. The frequency of CNN-LOH for each chromosome is compared between pediatric and adult cases in *Online Supplementary Figure S6*. Four samples (B-13, -14, -21 and -52) showed 9p CNN-LOH which was the most common CNN-LOH. Genes in the region are listed when there are less than ten: selected genes are listed when more than ten genes are located in

the region based on information from the Atlas of Genetics and Cytogenetics in Oncology and Haematology http://atlasgeneticsoncology.org/.

Online Supplementary Table S8. Comparison of adult and pediatric ALL (with and without hyperdiploidy)

a. Abnormalities in pediatric ALL (all cases).

	Pediatric ALL (all), 397 cases			
Abnormalities	N.	Per sample	*P-value (versus adult)*	
Homozygous deletion	59	0.1	1.00	
Heterozygous deletion	761	1.9	2.63E-06	**
Duplication	1204	3.0	1.00	
Amplification	19	0.05	1.00	
CNN-LOH	218	0.6	1.00	
Total	2261	5.7	1.00	

b. Abnormalities in pediatric ALL (non-hyperdiploid cases)

	non-hyperdiploid-pediatric ALL, 282 cases			
Abnormalities	N.	per sample	*P-value (versus adult)*	
Homozygous deletion	56	0.2	1.00	
Heterozygous deletion	679	2.4	1.07E-02	*
Duplication	265	0.9	0.09	
Amplification	8	0.03	1.00	
CNN-LOH	94	0.3	1.00	
Total	1102	3.9	1.30E-02	*

c. Abnormalities in pediatric ALL (hyperdiploid cases)

	hyperdiploid-pediatric ALL, 115 cases			
Abnormalities	N.	per sample	*P-value (versus adult)*	
Homozygous deletion	3	0.03	3.96E-03	**
Heterozygous deletion	83	0.7	9.93E-15	**
Duplication	923	8.0	1.05E-27	**
Amplification	11	0.1	1.00	
CNN-LOH	118	1.0	0.13	
Total	1138	10.0	7.83E-06	**

(a) Copy number changes in 75 adult and 397 pediatric ALL[3] were compared using a threshold of 141 kb per lesion. The pediatric ALL cases were separated into two groups: (b) non-hyperdiploid (282 samples) or (c) hyperdiploid (115 samples). Chromosomal alterations

are summarized including homozygous deletions (0 copy of gene dosage) and heterozygous deletions (1 copy), duplications (3-4 copies), amplifications (≥5 copies) and CNN-LOH (2 copies). Differences *versus* adult ALL are noted; *, $P<0.05$; **, $P<0.01$.

Online Supplementary Table S9. Comparison of genomic changes between adult ALL and non-hyperdiploid (HD)-pediatric ALL

Chromosomal sites	Type of abnormality	Candidate genes	Adult, (total, n=75)		Child (non-HD, n=282)		*P-value* (vs. adult)	
			[n]	[%]	[n]	[%]		
1q	Duplication		7	9%	25	9%	0.82	
1q	Deletion		6	8%	13	5%	0.25	
3p21	Deletion		4	5%	14	5%	1.00	
3p14.2	Deletion	*FHIT*	5	7%	12	4%	0.37	
3q26.3	**Deletion**	***TBL1XR1***	**0**	**0%**	**16**	**6%**	**0.03**	*
4q31	Deletion		2	3%	14	5%	0.54	
5q33.3	**Deletion**	***EBF***	**5**	**7%**	**4**	**1%**	**0.02**	*
6q	Deletion		13	17%	42	15%	0.59	
7p12.2	**Deletion**	***IKZF1***	**9**	**12%**	**13**	**5%**	**0.03**	*
8p	Deletion		5	7%	12	4%	0.37	
8q	Duplication		8	11%	17	6%	0.20	
8q24	Duplication	*MYC*	7	9%	15	5%	0.28	
9p21.3	Deletion	*CDKN2A/B*	23	31%	107	38%	0.28	
9p13.2	Deletion	*PAX5*	15	20%	50	18%	0.62	
9q	Duplication	*ABL*	5	7%	10	4%	0.33	
10p	Duplication		3	4%	16	6%	0.77	
10q24	Deletion		2	3%	5	2%	0.64	
11q	Deletion		8	11%	20	7%	0.33	
12p	Duplication		5	7%	14	5%	0.57	
12p13.2	**Deletion**	***ETV6***	**5**	**7%**	**84**	**30%**	**0.00001**	**
13q14.2	Deletion	*RB1*	7	9%	18	6%	0.44	
13q14.3	Deletion	*miR-15a, miR-16-1*	6	8%	18	6%	0.61	
15q	Deletion		5	7%	14	5%	0.57	
17p	**Deletion**	***TP53***	**8**	**11%**	**7**	**2%**	**0.005**	**
17q	**Duplication**		**7**	**9%**	**4**	**1%**	**0.002**	**
17q11.2	Deletion	*NF1*	2	3%	8	3%	1.00	
20p12.2	Deletion		2	3%	9	3%	1.00	
20q	Deletion		2	3%	20	7%	0.19	
21or 21q	Duplication		7	9%	44	16%	0.20	

Copy number changes in 75 adult and 282 non-HD-pediatric[3] ALL samples were compared.

Differences between them (χ^2 test) are noted: *, $P<0.05$; **, $P<0.01$

Online Supplementary Table S10. Comparison of genomic changes between adult ALL and hyperdiploid (HD)-pediatric ALL

Chromosomal sites	Type of abnormality	Candidate genes	Adult, (total, n=75)		Child (HD, n=115)		*P-value* (vs. adult)	
			[n]	[%]	[n]	[%]		
1q	**Duplication**		**7**	**9%**	**27**	**24%**	**0.02**	*
1q	Deletion		6	8%	6	5%	0.54	
3p21	Deletion		4	5%	1	1%	0.08	
3p14.2	**Deletion**	***FHIT***	**5**	**7%**	**1**	**1%**	**0.04**	*
3q26.3	Deletion	*TBL1XR1*	0	0%	0	0%	1.00	
4q31	Deletion		2	3%	1	1%	0.56	
5q33.3	**Deletion**	***EBF***	**5**	**7%**	**0**	**0%**	**0.01**	**
6q	**Deletion**		**13**	**17%**	**0**	**0%**	**2.85E-06**	**
7p12.2	**Deletion**	***IKZF1***	**9**	**12%**	**4**	**4%**	**0.04**	*
8p	Deletion		5	7%	3	3%	0.27	
8q	**Duplication**		**8**	**11%**	**39**	**34%**	**2.61E-04**	**
8q24	**Duplication**	***MYC***	**7**	**9%**	**39**	**34%**	**1.06E-04**	**
9p21.3	**Deletion**	***CDKN2A/B***	**23**	**31%**	**9**	**8%**	**5.70E-05**	**
9p13.2	**Deletion**	***PAX5***	**15**	**20%**	**3**	**3%**	**1.55E-04**	**
9q	**Duplication**	***ABL***	**5**	**7%**	**24**	**21%**	**0.01**	**
10p	**Duplication**		**3**	**4%**	**83**	**73%**	**8.86E-23**	**
10q24	Deletion		2	3%	3	3%	1.00	
11q	**Deletion**		**8**	**11%**	**2**	**2%**	**1.51E-02**	*
12p	Duplication		5	7%	19	17%	0.07	
12p13.2	Deletion	*ETV6*	5	7%	9	8%	1.00	
13q14.2	Deletion	*RB1*	7	9%	3	3%	0.05	
13q14.3	Deletion	*miR-15a, miR-16-1*	6	8%	2	2%	0.06	
15q	Deletion		5	7%	6	5%	0.75	
17p	**Deletion**	***TP53***	**8**	**11%**	**1**	**1%**	**2.82E-03**	**
17q	**Duplication**		**7**	**9%**	**86**	**75%**	**4.11E-20**	**
17q11.2	Deletion	*NF1*	2	3%	0	0%	0.15	
20p12.2	Deletion		2	3%	1	1%	0.56	
20q	Deletion		2	3%	1	1%	0.56	
21or 21q	**Duplication**		**7**	**9%**	**113**	**99%**	**1.08E-40**	**

Copy number changes in 75 adult and 115 HD-pediatric[3] ALL samples were compared. Differences between them (χ^2 square test) are noted: *, $P<0.05$; **, $P<0.01$.

Online Supplementary Table S11. Comparison of genomic changes between adult ALL and pediatric ALL (total)

Chromosomal sites	Type of abnormality	Candidate genes	Adult, (total, n=75)		Child (total, n=397)		*P-value* (vs. adult)	
			[n]	[%]	[n]	[%]		
1q	Duplication		7	9%	52	13%	0.45	
1q	Deletion		6	8%	19	5%	0.26	
3p21	Deletion		4	5%	15	4%	0.52	
3p14.2	Deletion	*FHIT*	5	7%	13	3%	0.18	
3q26.3	**Deletion**	***TBL1XR1***	**0**	**0%**	**16**	**4%**	**0.09**	*
4q31	Deletion		2	3%	15	4%	1.00	
5q33.3	**Deletion**	***EBF***	**5**	**7%**	**4**	**1%**	**0.01**	**
6q	Deletion		13	17%	42	11%	0.11	
7p12.2	**Deletion**	***IKZF1***	**9**	**12%**	**17**	**4%**	**0.01**	*
8p	Deletion		5	7%	15	4%	0.34	
8q	Duplication		8	11%	56	14%	0.58	
8q24	Duplication	*MYC*	7	9%	54	14%	0.35	
9p21.3	Deletion	*CDKN2A/B*	23	31%	116	29%	0.78	
9p13.2	Deletion	*PAX5*	15	20%	53	13%	0.15	
9q	Duplication	*ABL*	5	7%	34	9%	0.82	
10p	**Duplication**		**3**	**4%**	**99**	**25%**	**1.08E-05**	**
10q24	Deletion		2	3%	8	2%	0.66	
11q	Deletion		8	11%	22	6%	0.12	
12p	Duplication		5	7%	33	8%	0.82	
12p13.2	**Deletion**	***ETV6***	**5**	**7%**	**93**	**23%**	**5.43E-04**	**
13q14.2	Deletion	*RB1*	7	9%	21	5%	0.18	
13q14.3	Deletion	*miR-15a, miR-16-1*	6	8%	20	5%	0.28	
15q	Deletion		5	7%	20	5%	0.57	
17p	**Deletion**	***TP53***	**8**	**11%**	**8**	**2%**	**1.26E-03**	**
17q	**Duplication**		**7**	**9%**	**90**	**23%**	**0.01**	**
17q11.2	Deletion	*NF1*	2	3%	8	2%	0.66	
20p12.2	Deletion		2	3%	10	3%	1.00	
20q	Deletion		2	3%	21	5%	0.56	
21or 21q	**Duplication**		**7**	**9%**	**157**	**40%**	**6.75E-08**	**

Copy number changes in 75 adult and 397 pediatric[3] ALL samples were compared. Differences between them (χ^2 square test) are noted: *, $P<0.05$; **, $P<0.01$.

Online Supplementary Table S12. Comparison of genomic changes between non-hyperdiploid (HD)-pediatric ALL and HD-pediatric ALL

Chromosomal sites	Type of abnormality	Candidate genes	Children (non-HD, n=282)		Children (HD, n=115)		*P-value* (non-HD vs. HD)	
			[n]	[%]	[n]	[%]		
1q	**Duplication**		**25**	**9%**	**27**	**24%**	**1.8E-04**	**
1q	Deletion		13	5%	6	5%	1.0E+00	
3p21	Deletion		14	5%	1	1%	9.9E-02	
3p14.2	Deletion	*FHIT*	12	4%	1	1%	1.6E-01	
3q26.3	**Deletion**	***TBL1XR1***	**16**	**6%**	**0**	**0%**	**2.0E-02**	**
4q31	Deletion		14	5%	1	1%	9.9E-02	
5q33.3	Deletion	*EBF*	4	1%	0	0%	4.7E-01	
6q	**Deletion**		**42**	**15%**	**0**	**0%**	**2.7E-05**	**
7p12.2	Deletion	*IKZF1*	13	5%	4	4%	8.2E-01	
8p	Deletion		12	4%	3	3%	6.2E-01	
8q	**Duplication**		**17**	**6%**	**39**	**34%**	**1.4E-12**	**
8q24	**Duplication**	***MYC***	**15**	**5%**	**39**	**34%**	**1.6E-13**	**
9p21.3	**Deletion**	***CDKN2A/B***	**107**	**38%**	**9**	**8%**	**4.5E-09**	**
9p13.2	**Deletion**	***PAX5***	**50**	**18%**	**3**	**3%**	**1.2E-04**	**
9q	**Duplication**	***ABL***	**10**	**4%**	**24**	**21%**	**6.8E-08**	**
10p	**Duplication**		**16**	**6%**	**83**	**73%**	**4.2E-43**	**
10q24	Deletion		5	2%	3	3%	8.9E-01	
11q	**Deletion**		**20**	**7%**	**2**	**2%**	**6.1E-02**	*
12p	**Duplication**		**14**	**5%**	**19**	**17%**	**3.4E-04**	**
12p13.2	**Deletion**	***ETV6***	**84**	**30%**	**9**	**8%**	**5.2E-06**	**
13q14.2	Deletion	*RB1*	18	6%	3	3%	2.0E-01	
13q14.3	Deletion	*miR-15a, miR-16-1*	18	6%	2	2%	9.6E-02	
15q	Deletion		14	5%	6	5%	8.8E-01	
17p	Deletion	*TP53*	7	2%	1	1%	5.2E-01	
17q	**Duplication**		**4**	**1%**	**86**	**75%**	**1.4E-55**	**
17q11.2	Deletion	*NF1*	8	3%	0	0%	1.5E-01	
20p12.2	Deletion		9	3%	1	1%	3.2E-01	
20q	**Deletion**		**20**	**7%**	**1**	**1%**	**2.3E-02**	*
21or 21q	**Duplication**		**44**	**16%**	**113**	**99%**	**5.9E-52**	**

Copy number changes in 282 non-HD- and 115 HD-pediatric[3] ALL samples were compared. Differences between them (χ^2 square test) are noted: *, $P<0.05$; **, $P<0.01$.

Online Supplementary Table S13. Comparison of genomic changes in adult ALL by age.

a. Comparison of the adolescents (younger than 21 years old) *versus* adult (older than 21 years old and above) patients.

Abnormalities	9 cases (<21 years old) N.	per sample	66 cases (>21 years old) N.	per sample	*P-value*
Homozygous deletion	2	0.2	17	0.3	0.73
Heterozygous deletion	32	3.6	317	4.8	0.68
Duplication	6	0.7	163	2.5	0.19
Amplification	0	0	2	0.03	0.25
CNN-LOH	3	0.3	30	0.5	0.73
Total	43	4.8	529	8.0	0.97

b. Comparison of patients younger or older than 60 years of age.

Abnormalities	51 cases (<60 years old) N.	per sample	24 cases (>60 years old) N.	per sample	*P-value*
Homozygous deletion	10	0.2	9	0.4	0.29
Heterozygous deletion	239	4.7	110	4.6	0.73
Duplication	102	2	67	2.8	0.53
Amplification	1	0.02	1	0.04	1.00
CNN-LOH	12	0.2	21	0.9	0.21
Total	364	7.1	208	8.7	0.93

Genomic changes in 75 adult ALL were compared by age. Adult patients with ALL were separated into those younger or older than either 21 or 60 years old. The alterations include homozygous deletions (0 copy of gene dosage) and heterozygous deletions (1 copy), duplications (3-4 copies), amplifications (≥5 copies) and CNN-LOH (2 copies).

Online Supplementary Table S14. Comparison of genomic changes in adult ALL by ethnic group.

Abnormalities	Asian, 41 cases		Caucasian,34 cases		
	N.	per sample	N.	per sample	*P-value*
Homozygous deletion	6	0.1	7	0.2	0.58
Heterozygous deletion	120	2.9	126	3.7	0.82
Duplication	60	1.5	86	2.5	0.76
Amplification	0	0	2	0.1	0.20
CNN-LOH	10	0.2	23	0.7	0.41
Total	196	4.8	244	7.2	0.78

Copy number changes in 75 adults of Asian or Caucasian ethnicity were compared. To adjust the SNP-array platform, abnormalities sized >141 kb were calculated. Chromosomal alterations are summarized including homozygous deletions (0 copy of gene dosage) and heterozygous deletions (1 copy), duplications (3-4 copies), amplifications (≥5 copies) and CNN-LOH (2 copies). Differences *versus* adult ALL are noted; *, $P<0.05$; **, $P<0.01$.

Online Supplementary Table S15. Primer sequences.

Target region	Sequences		Melting temperature for qPCR (°C)
CDKN2A/B	Forward	5'-GTG CCA AAG TGC TCC TGA AGC TG-3'	79
(primer c)	Reverse	5'-AGC AAA TCT GTT TGG AGG TCTG-3’	
CDKN2A	Forward	5'-AGT TAA GGG GGC AGG AGT G-3’	91
exon 1 beta	Reverse	5'-GGA GGG TCA CCA AGA ACC TG-3’	
CDKN2B	Forward	5'-GCG GAT TTC CAG GGA TAT TT-3’	83
exon 2	Reverse	5'-CAC CAG GTC CAG TCA AGG AT-3’	
2p21	Forward	5'-GGC AAT CCT GGC TGC GGA TCA AGA-3'	81
(control)	Reverse	5'-ATT TCT GAA CTT CTT GGC TGC C-3'	
REL	Forward	5'-AGA GGG GAA TGC GTT TTA GAT AC-3'	81
	Reverse	5'-ACC TGG ATA GAA GGG TAT GTT CG-3'	
BCL11A	Forward	5'-TGT GGT TTA TGA TGC ACG TTG-3'	83
	Reverse	5'-GTG GGG ATT AGA GCT CCA TGT-3'	
AKT2	Forward	5'-TTC GAC TAT CTC AAA CTC CTT GG-3'	85
	Reverse	5'-AGG ATC TTC ATG GCG TAG TAG C-3'	
PTPRD-B4	Forward	5'-GGC CCG TGA TAT TCC AGT TA-3'	85
(primer a)	Reverse	5'-CAC ATC TTG TGT CAT GGG AAA-3'	
FOXO3	Forward	5'-GGA CAA ACG GCT CAC TCT GT-3'	88
(expression)	Reverse	5'-CCA GTT CCC TCA TTC TGG AC-3'	
rs10481545	Forward	5'-CCC TCA AAA AGT GGA GAC GA-3'	81
(primer b)	Reverse	5'-ATT CTT GGG GCA CCT CTC TT-3'	
rs10810528	Forward	5'-TGC CTC TGC TCT GTC ATC TG-3'	-
	Reverse	5'-TGA TTG GCA CCA AAC TCA TC-3'	
PAX5 primer	Forward	5'-ATC AAC AGG ATC ATC CGG AC -3'	
ETV6 primer	Reverse	5'-CTT CAG AAT ATG CTG AAG GA-3'	
FOXO3	Forward	5’-TTA GGT TAG GAA AGG GGA GAA GAG-3’	
(methylation)	Reverse	5’-CCT AAA AAA ACA CCA AAA AAA AAA A -3’	