Evaluation of acute myeloid leukemia using genomic proximity mapping-based next generation cytogenomics

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SUPPLEMENTAL METHODS

Illumina Whole Genome Sequencing

Three hundred ng of DNA from cryopreserved specimens, quantified with the Qubit 2.0 Fluorometer (ThermoFisher, Waltham, MA), were used for the study. Libraries were prepared with the Illumina DNA PCR-Free Prep, Tagmentation, and Illumina DNA/RNA UD Indexes, Tagmentation (Illumina, San Diego, CA). Library quantification was performed using the QuantStudio5 real-time PCR system from Applied Biosystems (ThermoFisher Scientific, Waltham, MA) with the KAPA Library Quantification Kit for Illumina (Roche Diagnostics Corporation, Indianapolis, IN). Equimolar concentrations of individual libraries were pooled. Sequencing was performed on the Illumina NovaSeq 6000 (Illumina, Inc, San Diego, CA) with a paired-end, 150-base read length sequencing configuration. Four S4-300 flow cells were employed. The average sequencing output per library was 861.2.4M read pairs (range 595M-1124.8M).

Data analysis was conducted with the DRAGEN Somatic analysis pipeline v4.3.6 in tumor-only mode, implemented in BaseSpace (Illumina, San Deigo, CA). The hg38 human genome assembly was used as a reference. Illumina's filters were used to filter artifacts in the analysis: systematic noise filters for single nucleotide variants (SNV SomaticSystematic Noise v2.0.0) and structural variants (SV Systematic Noise Baseline Collection v3.0.0). Nirvana Variant Annotation and DUX4 rearrangement callers were implemented.

Supplementary Table 1. Post-sequencing quality control results. Post-sequencing quality control analysis of GPM library preparations showed acceptable performance for all libraries.

Sample #	% duplicate reads	% intercontig pairs HQ	% pairs on same strand HQ	Total read pairs	Total read pairs HQ
1	0.268	0.3843	0.4683	128138316	66756524
2	0.1595	0.3485	0.4671	158198178	97018854
3	0.2919	0.2957	0.4807	255791964	130213089
4	0.3254	0.3129	0.4753	171906050	82798933
5	0.2977	0.383	0.4767	139929729	70352432
6	0.2774	0.3034	0.4819	308417004	160210996
7	0.2896	0.2662	0.476	187717273	95437230
8	0.2996	0.31	0.4717	306884855	155358240
9	0.2114	0.2396	0.466	284307270	161045018
10	0.2278	0.3071	0.4669	261342993	148199028
11	0.1929	0.4692	0.4536	238220727	134518042
12	0.2407	0.303	0.4714	408779334	228990767
13	0.1391	0.6086	0.3449	311895105	194610052
14	0.1912	0.2924	0.4671	194916399	115308883
15	0.2035	0.2787	0.4699	233983297	135128096
16	0.1866	0.2816	0.4682	194097094	116218179
17	0.2306	0.3166	0.464	234451225	131271273
18	0.1145	0.516	0.3991	74235391	47263475
19	0.1719	0.4902	0.4716	143506049	86668251
20	0.1774	0.3201	0.4765	180468720	109404100
21	0.284	0.3621	0.4737	141391492	74694588
22	0.2724	0.4978	0.4701	288961236	150095993
23	0.2776	0.3227	0.475	195732656	100742735
24	0.28	0.3703	0.469	89535264	45514809
25	0.2959	0.3684	0.4756	213516744	107490569
26	0.2874	0.3781	0.4759	61608272	31941310
27	0.2483	0.2857	0.4793	117674331	62947370
28	0.2826	0.3609	0.4695	147586536	77203129
29	0.277	0.3551	0.4717	185706559	97588610
30	0.2899	0.3279	0.4791	192816245	100354469
31	0.2968	0.3682	0.477	195825713	98791628
32	0.3101	0.3761	0.4713	359911424	182650007
33	0.1638	0.3246	0.4756	111336166	69489188
34	0.1763	0.2911	0.4709	255236310	153930933
35	0.2823	0.386	0.4775	308994411	157363877
36	0.2843	0.33	0.4826	197568214	100152984
37	0.2681	0.533	0.4627	202344451	106492243
38	0.2728	0.3567	0.4759	284225164	150362784
39	0.2802	0.4159	0.4736	107191740	55762051
40	0.2696	0.3847	0.4745	292759260	152203548
41	0.286	0.4191	0.4698	356567893	181951672
42	0.2947	0.3826	0.4724	241731837	122552004

43	0.282	0.3379	0.4767	232292327	118715458
44	0.2905	0.3671	0.4764	296885773	151746852
45	0.2884	0.3312	0.4769	242870427	123639428
46	0.1942	0.3506	0.4645	231639007	134835553
47	0.18	0.3232	0.4709	174546387	103768875
48	0.184	0.205	0.4737	188608507	111095087

Abbreviations: GPM: Genomic Proximity Mapping™

Supplemental Table 2. Inter-chromosomal variants identified by GPM compared with the corresponding clinical cytogenetic presentation. "Discordant" means the given abnormality was reported by clinical cytogenetics but missed or reported differently by GPM. "Added" means the given variant was reported by GPM but not by clinical cytogenetics.

Patient #	GPM findings	Clinical cytogenetics ISCN	Structural Aberrations	ELN class-defining variant?	Concordance between GPM and clinical cytogenetics
13	gpm 45,X,t(8;21)(q21.3;q22.12),dup(10)(q21.1)[0.6]	45,X,-Y,t(8;21)(q22;q22)[19]/46,XY[1].nuc ish(RUNX1T1,RUNX1)x3(RUNX1T1 con RUNX1x2)[180/200]	t(8;21)(q21.3;q22.12)	Yes	Concordant
18	gpm 46,XX,del(6)(p24.1p24.1),t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),dup(9)(p21.1p13.3)[0.3]	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q21)[5]/47,sdl,+13[10]/46,XX[2]	t(6;9)(p22.3;q34.12)	Yes	Concordant
			t(6;15)(p24.2p24.1;q21.1)	No	Concordant
32	gpm 46,XX,t(6;11)(q27;q23.3),dup(9)(q32)	46,XX,t(6;11)(q27;q23)[20].nuc ish(MLLx2)(5'MLL sep 3'MLLx1)[152/200]	t(6;11)(q27;q23.3)	Yes	Concordant
8	gpm 46,XX,del(6)(p23p22.3),t(6;7)(p23;q36.3),del(7)(q36.3),inv(12)(p13.32p13.2)	46,XX,t(6;7)(p2?2;q36)[20].arr[GRCh38] 6p23p22.3(15,138,707_15,564,800)x1[0.85],7q36.3(157,093,285_157,944,041)x1[0.85]	t(6;7)(p23;q36.3	No	Concordant
26	gpm 46,XX,t(10;17)(p11.2;q11.2)*[0.2]	46,XX,add(17)(p13)[2]/46,sl,del(10)(q24)[2]/46,XX,t(10;17)(p10;p10)[5]/46,XX[11].nuc ish(TP53,CEP17)x2[200]	t(10;17)(p10;p10)	No	Discordant
24	gpm 46,XY	46,XY,t(2;19)(q35;p13.3)[5]/45,XY,-21[3]/46,XY[12]	t(2;19)(q35;p13.3)	No	Discordant
40	gpm 51,XY,+4,+8,t(11;12)(p15.4;p13.33),+12,+16[0.6] [0.8]	51,XY,+4,+6,+8,+12,+16[13]/46,XY[7]	t(11;12)(p15.4;p13.33)	No	Added
42	gpm	47,XY,+X[4]/46,XY[16]	ins(13;5)(q12.13;q31.3q31.1)	No	Added

	46,XY,dup(3)(q26.31q26.31),ins(13;5)(q12.13;q31.3q31.1)[0.5]				
48	gpm 45,XY,t(5;14)(q35.1;q23.1),t(5;17)(q14.3;p13.3),t(5;18)(q35.1;q21.1),-7,t(9;14)(q33.3;q23.1),t(14;18)(q23.1;q21.1),t(17;18)(p13.3;q21.1),dup(21)(q22.12)[0.5]	45,XY,-7[14]/45,sl,del(5)(q22q35)[4]/44,sdl,t(X;9)(p11.2;p22),t(2;11)(p21;q13),?inv(10)(p11.2q11.2),del(13)(q14q31),der(13;22)(q10;q10)[2],nuc ish(D5S23x2,EGR1x1)[128/200],(D7Z1,D7S486)x1[190/200]	t(5;17)(q14.3;p13.3)	No	Added
			t(5;18)(q35.1;q21.1)	No	Added
			t(5;14)(q35.1;q23.1)	No	Added
			t(9;14)(q33.3;q23.1)	No	Added
			t(14;18)(q23.1;q21.1)	No	Added
			t(17;18)(p13.3;q21.1)	No	Added

* Retrospectively observed

Note: Blank rows indicate longitudinal cases within the histories of the patient represented in the most recent occupied row.

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, ELN: European Leukemia Network

Supplementary Table 3. Intra-chromosomal abnormalities detected by GPM compared with the corresponding clinical cytogenetic presentation. "Discordant" means the given abnormality was reported by clinical cytogenetics but missed or reported differently by GPM. "Added" means the given variant was reported by GPM but not by clinical cytogenetics.

Patient #	GPM findings	Clinical cytogenetics ISCN	Inversion	ELN class-defining variant?	Other Risk	Concordance between GPM and clinical cytogenetics
2	gpm 46,XY,inv(16)(p13.11q22.1)[0.8]	46,XY,inv(16)(p13.1q22)[13]/92<4N>,slx2[7].nuc ish(CBFBx2)(5'CBFB sep 3'CBFBx1)[119/200]/(CBFBx4)(5'CBFB sep 3'CBFBx2)[44/200]	inv(16)(p13.11q22.1)	Yes		Concordant
7	gpm 45,XY,inv(3)(p24.3q26.2),-7[0.8]	45,XY,-7[11]/46,XY[9]	inv(3)(p24.3q26.2)	Yes		Added
16	gpm 46,XY,del(7)(q22.1q36.1),dup(8)(p23.3),dup(12)(p13.31),inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),+22[3].nuc ish(D7Z1x2,D7S486x1)[189/200]	inv(16)(p13.11q22.1)	Yes		Concordant
38	gpm 46,XX,inv(16)(p13.11q22.1)[0.8]	46,XX,inv(16)(p13.1q22)[16]/46,XX[4]	inv(16)(p13.11q22.1)	Yes		Concordant
47	gpm 45,XY,der(3)del(3)(q21.3)inv(3)(q21.3q26.1)del(3)(q26.1q26.2),dup(4)(q32.2q32.2)?c,-7	45,XY,inv(3)(q21q26.2),-7[16]/45,sl,del(6)(p23)[4]	inv(3)(q21.3q26.1)	Yes		Concordant
8	gpm 46,XX,del(6)(p23p22.3),t(6;7)(p23;q36.3),del(7)(q36.3),inv(12)(p13.32p13.2)	46,XX,t(6;7)(p2?2;q36)[20].arr[GRCh38] 6p23p22.3(15,138,707_15,564,800)x1[0.85],7q36.3(157,093,285_157,944,041)x1[0.85]	inv(12)(p13.32p13.2)	No	No	Added
9	gpm 46,XY,dup(1)(p36.22p36.22)?c,inv(9)(p13.3p13.1)	46,XY[20].arr[GRCh38]13q12.13qter(27,055,669_114,338,054)x2 hmz[0.75]	inv(9)(p13.3p13.1)	No	No	Added
15	gpm 48,XX,+8,inv(9)(p13.3p13.1),ins(12;12)(p13.31;p11.21p11.21),inv(16)(p13.11q22.1),+22	48,XX,+8,inv(16)(p13.1q22),+22[20]	inv(9)(p13.3p13.1)	No	No	Added
			ins(12)(9320000-9390000)<-(12)(31140000-31260000)	No	Yes	Added

	inv(16)(p13.11q22.1)	Yes	Concordant

* Retrospectively observed

Note: Blank rows indicate longitudinal cases within the histories of the patient represented in the most recent occupied row.

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, ELN: European Leukemia Network

Supplementary Table 4. Copy number variant (CNV) abnormalities detected by GPM compared with the corresponding clinical cytogenetic presentation. "Discordant" means the given abnormality was reported by clinical cytogenetics but missed or reported differently by GPM. "Added" means the given variant was reported by GPM but not by clinical cytogenetics.

Patient #	GPM findings	Clinical cytogenetics ISCN	CNV	ELN class-defining variant?	Other Risk	Concordance between GPM and clinical cytogenetics
6	gpm 46,XX,dup(7)(q35q35)?c	46,XX[20]	dup(7)(q35q35)	No	No	Added
8	gpm 46,XX,del(6)(p23p22.3),t(6;7)(p23;q36.3),del(7)(q36.3),inv(12)(p13.32p13.2)	46,XX,t(6;7)(p2?2;q36)[20].arr[GRCh38] 6p23p22.3(15,138,707_15,564,800)x1[0.85],7q36.3(157,093,285_157,944,041)x1[0.85]	del(6)(p23p22.3)	No	No	Concordant
			del(7)(q36.3)	No	No	Concordant
9	gpm 46,XY,dup(1)(p36.22p36.22)?c,inv(9)(p13.3p13.1)	46,XY[20]	dup(1)(p36.22p36.22)	No	No	Added
11	gpm 46,XY,del(4)(q24q24)	47,XY,+22[2]/46,XY[18]	del(4)(q24q24)	No	Yes	Added
12	gpm 46,XY,del(4)(q24q24)[0.8]	46,XX[20]	del(4)(q24q24)	No	Yes	Added
13	gpm 45,X,t(8;21)(q21.3;q22.12),dup(10)(q21.1q21.1)[0.6]	45,X,-Y,t(8;21)(q22;q22)[19]/46,XY[1].nuc ish(RUNX1T1,RUNX1)x3(RUNX1T1 con RUNX1x2)[180/200]	dup(10)(q21.1)	No	No	Added
14	gpm 46,XY,dup(2)(p22.3p22.3)?c	46,XY[20].arr[GRCh38] 6pterp22.1(1_30,006,723)x2hmz[0.9]	dup(2)(p22.3p22.3)	No	No	Added
16	gpm 46,XY,del(7)(q22.1q36.1),dup(8)(p23.3p23.3),dup(12)(p13.31p13.31),inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),+22[3].nuc ish(D7Z1x2,D7S486x1)[189/200]	del(7)(q22.1q36.1)	No	No	Concordant
			dup(8)(p23.3p23.3)	No	No	Added
			dup(12)(p13.31p13.31)	No	No	Added

17	gpm 46,XY,dup(17)(q25.1q25.1)[0.6]	46,XY[20].arr[GRCh38] 3p21.31(46,531,828_47,287,254)x1[0.65],9q21.32(83,766,899_84,002,350)x1[0.65]	dup(17)(q25.1q25.1)	No	No	Added
			3p21.31(46,531,828_47,287,254)	No	No	Discordant
			9q21.32(83,766,899_84,002,350)	No	No	Discordant
18	gpm 46,XX,del(6)(p24.1p24.1),t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),dup(9)(p21.1p13.3)[0.3]	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q21)[5]/47,sdl,+13[10]/46,XX[2]	del(6)(p24.1)	No	No	Added
			dup(9)(p21.1p13.3)	No	No	Added
20	gpm 46,XY,del(9)(q21.11q31.1)	46,XY,del(9)(q22;q34)[33]/46,idem,t(6;14)(q21;q32)[2] ** on a different day				FALSE
25	gpm 47,XY,+13,dup(15)(q13.3q13.3)[0.8]	47,XY,+13[16]/46,XY[4]	dup(15)(q13.3q13.3)	No	No	Added
26	gpm 46,XX,t(10;17)(p11.2;q11.2)*[0.2]	46,XX,add(17)(p13)[2]/46,sl,del(10)(q24)[2]/46,XX,t(10;17)(p10;p10)[5]/46,XX[11]. nuc ish(TP53,CEP17)x2[200]	del(10)(q24)[2]	No	No	Discordant
27	gpm 46,XX,del(2)(p23.3p23.3),del(16)(p13.11p12.3),(13)x2 hmz	46,XX[20].arr[GRCh37] 2p23.3(24,587,652_26,417,829)x1, 13q12.11qter(19,814,912_115,103,529)x2 hmz, 16p13.13p12.3(12,040,511_18,539,704)x1	del(2)(p23.3p23.3)	No	No	Concordant
			del(16)(p13.13p12.3)	No	No	Concordant
29	gpm 46,XY,dup(11)(q22.3q22.3)?c	46,XY[20].nuc ish(MECOMx2)[200],(DEK,NUP214)x2[200],(MLLx2)[200].arr(1-22)x2,(X,Y)x1	dup(11)(q22.3q22.3)?c	No	No	Added

30	gpm 46,XY,del(2)(p23.3p23.3)[0.8]	46,XY[20].nuc ish(MECOMx2)[200],(DEK,NUP214)x2[200],(RUNX1T1,RUNX1)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200],(RARAx2)[200].arr[GRCh37] 2p23.3(24,190,632_25,989,981)x1	del(2)(p23.3)	No	No	Concordant
31	gpm 46,XX,dup(12)(p13.31p13.31)?c	46,XX[20]	dup(12)(p13.31p13.31)?c	No	No	Added
32	gpm 46,XX,t(6;11)(q27;q23.3),dup(9)(q32q32)	46,XX,t(6;11)(q27;q23)[20].nuc ish(MLLx2)(5'MLL sep 3'MLLx1)[152/200]	dup(9)(q32)	No	No	Added
34	gpm 46,XX	46,XX,del(7)(q31)[5]/46,XX[15]	del(7)(q31)[5/20]	No	No	Discordant
37	gpm 46,XY,dup(3)(q26.31q26.31)[0.3]	46,XY[20].nuc ish(MECOMx2)[200],(DEK,NUP214)x2[200],(RUNX1T1,RUNX1)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200].arr(1-22)x2,(X,Y)x1	dup(3)(q26.31)	No	No	Added
41	gpm 46,XY,dup(20)(p13p13)?c	46,XY[20].nuc ish(MECOMx2)[200],(DEK,NUP214)x2[200],(RUNX1T1,RUNX1)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200].arr(1-22)x2,(X,Y)x1	dup(20)(p13p13)	No	No	Added
42	gpm 46,XY,dup(3)(q26.31q26.31),ins(13;5)(q12.13;q31.3q31.1)[0.5]	47,XY,+X[4]/46,XY[16]	dup(3)(q26.31q26.31)	No	No	Added
44	gpm 46,XX,dup(11)(q14.2q14.3)?c	46,XX[20].nuc ish(MECOMx2)[200],(DEK,NUP214)x2[200],(RUNX1T1,RUNX1)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200].arr(1-	dup(11)(q14.2q14.3)?c	No	No	Added

		22,X)x2				
45	gpm 46,XX,dup(3)(q26.31q26.31)?c,dup(8)(q12.1q12.1)?c	46,XX[20].nucish(MECOMx2)[200],(DEK,NUP214)x2[200],(RUNX1T1,RUNX1)x2[200],(ABL1,ASS1,BCR)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200]	dup(3)(q26.31q26.31)	No	No	Added
			dup(8)(q12.1q12.1)	No	No	Added
46	gpm 47,XY,dup(1)(q41q41)?c,dup(12)(p13.33p13.33)?c,del(19)(q13.11q13.12),+21	47,XY,+21c[20].nucish(MECOMx2)[200],(D5S23,EGR1)x2[200],(DEK,NUP214)x2[200],(D7Z1,D7S486)x2[200],(RUNX1T1x2,RUNX1x3)[147/200],(ABL1,ASS1,BCR)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200],(TP53,CEP17)x2[200].arr[GRCh37]19q13.11q13.12(33,503,646_37,428,465)x1[0.95],(21)x3c	dup(1)(q41q41)?c	No	No	Added
			dup(12)(p13.33p13.33)?c	No	No	Added
			del(19)(q13.11q13.12)	No	No	Concordant
47	gpm 45,XY,der(3)del(3)(q21.3)inv(3)(q21.3q26.1)del(3)(q26.1q26.2),dup(4)(q32.2q32.2)?c,-7	45,XY,inv(3)(q21q26.2),-7[16]/45,sl,del(6)(p23)[4]	del(3)(q21.3)	No	No	Added
			del(3)(q26.1q26.2)	No	No	Added
			dup(4)(q32.2)	No	No	Added
			del(6)(p23)[4/20]	No	No	Discordant
48	gpm 45,XY,t(5;14)(q35.1;q23.1),t(5;17)(q14.3;p13.3),t(5;18)(q35.1;q21.1),-7,t(9;14)(q33.3;q23.1),t(14;18)(q23.1	45,XY,-7[14]/45,sl,del(5)(q22q35)[4]/44,sdl,t(X;9)(p11.2;p22),t(2;11)(p21;q13),?inv(10)(p11	dup(21)(q22.12)	No	No	Added

;q21.1),t(17;18)(p13.3;q21.1),dup(21)(q22.12)[0.5]	.2q11.2),del(13)(q14q31),der(13;22)(q10;q10)[2].nuc ish(D5S23x2,EGR1x1)[128/200],(D7Z1,D7S486)x1[190/200]			
		del(5)(q22q35)	Yes	Concordant

* Retrospectively observed

** Due to complex multi-chromosomal unbalanced translocations

Note: Blank rows indicate longitudinal cases within the histories of the patient represented in the most recent occupied row.

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, ELN: European Leukemia Network, CNV: copy number variation

Supplementary Table 5. Aneuploidy variants detected by GPM compared with the corresponding clinical cytogenetic presentation. "Discordant" means the given abnormality was reported by clinical cytogenetics but missed or reported differently by GPM. "Added" means the given variant was reported by GPM but not by clinical cytogenetics.

Patient #	GPM findings	Clinical cytogenetics ISCN	Aneuploidy	ELN class-defining variant?	Other Risk	Concordance between GPM and clinical cytogenetics
7	gpm 45,XY,inv(3)(p24.3q26.2),-7[0.8]	45,XY,-7[11]/46,XY[9]	-7[11/20]	Yes		Concordant
47	gpm 45,XY,der(3)del(3)(q21.3)inv(3)(q21.3q26.1)del(3)(q26.1q26.2),dup(4)(q32.2q32.2)?c,-7	45,XY,inv(3)(q21q26.2),-7[16]/45,sl,del(6)(p23)[4]	-7[20/20]	Yes		Concordant
48	gpm 45,XY,t(5;14)(q35.1;q23.1),t(5;17)(q14.3;p13.3),t(5;18)(q35.1;q21.1),-7,t(9;14)(q33.3;q23.1),t(14;18)(q23.1;q21.1),t(17;18)(p13.3;q21.1),dup(21)(q22.12)[0.5]	45,XY,-7[14]/45,sl,del(5)(q22q35)[4]/44,sdl,t(X;9)(p11.2;p22),t(2;11)(p21;q13),?inv(10)(p11.2q11.2), del(13)(q14q31),der(13;22)(q10;q10)[2]	-7[20/20]	Yes		Concordant
2	gpm 46,XY,inv(16)(p13.11q22.1)	46,XY,inv(16)(p13.1q22)[13]/92<4N>,slx2[7].nuc ish(CBFBx2)(5'CBFB sep 3'CBFBx1)[119/200]/(CBFBx4)(5'CBFB sep 3'CBFBx2)[44/200]	tetraploid[7/20]	No		Discordant
3	gpm 46,XY	47,XY,+8[15]/46,XY[5]	+8[15/20]	No	No	Discordant
5	gpm 46,XY	47,XY,+8[5]/45,X,-Y[3]/46,XY[12]	+8[5/20]/-Y[3/20]	No	No	Discordant
11	gpm 46,XY,del(4)(q24q24)	47,XY,+22[2]/46,XY[18]	+22[2/20]	No	No	Discordant
15	gpm 48,XX,+8,inv(9)(p13.3p13.1),ins(12;12)(p13.31;p11.21p11.21),inv(16)(p13.11q22.1),+22	48,XX,+8,inv(16)(p13.1q22),+22[20]	+8,+22[20/20]	No	No	Concordant
16	gpm 46,XY,del(7)(q22.1q36.1),dup(8)(p23.3),dup(12)(p13.31),inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),+22[3]	+22[3/20]	No	No	Discordant
18	gpm	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q2	+13[10/20]	No	No	Discordant

	46,XX,del(6)(p24.1p24.1),t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),dup(9)(p21.1p13.3)[0.3]	1)[5]/47,sdl,+13[10]/46,XX[2]				
19	gpm 47,XY,+8	47,XY,+8[4]/46,sl,-Y[11]/46,XY[5]	+8[15/20]	No	No	Concordant
			-Y[11/20]	No	No	Discordant
24	gpm 46,XY	46,XY,t(2;19)(q35;p13.3)[5]/45,XY,-21[3]/46,XY[12]	-21[3/20]	No	No	Discordant
25	gpm 47,XY,+13,dup(15)(q13.3q13.3)[0.8]	47,XY,+13[16]/46,XY[4]	+13[16/20]	No	No	Concordant
35	gpm 47,XY,+8,(13)x2 hmz[0.8]	47,XY,+8[16]/46,XY[4].nuc ish(D8Z2x3)[161/200]	+8[16/20]	No	No	Concordant
40	gpm 51,XY,+4,+8,t(11;12)(p15.4;p13.33),+12,+16[0.6] [0.8]	51,XY,+4,+6,+8,+12,+16[13]/46,XY[7]	+4[13/20]	No	No	Concordant
			+6[13/20]	No	No	Concordant
			+8[13/20]	No	No	Concordant
			+12[13/20]	No	No	Concordant
			+16[13/20]	No	No	Concordant
46	gpm 47,XY,dup(1)(q41q41)?c,dup(12)(p13.33p13.33)?c,del(19)(q13.11q13.12),+21	47,XY,+21c[20].nuc ish(MECOMx2)[200],(D5S23,EGR1)x2[200],(DEK,NUP214)x2[200],(D7Z1,D7S486)x2[200],(RUNX1T1x2,RUNX1x3)[147/200],(ABL1,ASS1,BCR)x2[200],(MLLx2)[200],(PML,RARA)x2[200],(CBFBx2)[200],(TP53,CEP17)x2[200].arr[GRCh37] 19q13.11q13.12(33,503,646_37,428,465)x1[0.95],(21)x3c	+21[20/20]	No	No	Concordant
18	gpm 46,XX,del(6)(p24.1p24.1),t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),dup(9)(p21.1p13.3)[0.3]	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q21)[5]/47,sdl,+13[10]/46,XX[2]	+13[10/20]	No	No	Discordant

Note: Blank rows indicate longitudinal cases within the histories of the patient represented in the most recent occupied row.

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, ELN: European Leukemia Network

Supplementary Table 6. Copy-neutral loss of heterozygosity (cnLOH) abnormalities detected by GPM compared with the corresponding clinical cytogenetic presentation. "Discordant" means the given abnormality was reported by clinical cytogenetics but missed or reported differently by GPM. "Added" means the given variant was reported by GPM but not by clinical cytogenetics.

Patient #	GPM findings	Clinical cytogenetics ISCN	cnLOH	ELN class-defining variant?	Other risk	Concordance between GPM and clinical cytogenetics
14	gpm 46,XY,dup(2)(p22.3p22.3)?c	46,XY[20].arr[GRCh38] 6pterp22.1(1_30,006,723)x2 hmz[0.9]	6p cnLOH	No	No	Discordant
9	gpm 46,XY,dup(1)(p36.22p36.22) ?c,inv(9)(p13.3p13.1)	46,XY[20].arr[GRCh38]13q12.13qter(27,055,669_ 114,338,054)x2 hmz[0.75]	13q cnLOH	No	No	Discordant
27	gpm 46,XX,del(2)(p23.3p23.3),del (16)(p13.11p12.3),(13)x2 hmz *	46,XX[20].arr[GRCh37] 2p23.3(24,587,652_26,417,829)x1, 13q12.11qter(19,814,912_115,103,529)x2 hmz, 16p13.13p12.3(12,040,511_18,539,704)x1	13q cnLOH	No	No	Concordant
35	gpm 47,XY,+8,(13)x2 hmz *	47,XY,+8[16]/46,XY[4].nuc ish(D8Z2x3)[161/200]	13q cnLOH	No	No	Added

* cnLOH only detectable by newer version software

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, cnLOH: copy-neutral loss of heterozygosity, ELN: European Leukemia Network

Supplementary Table 7. Orthogonal evaluation of discordant copy number and structural variant calls by WGS testing, including whether WGS results support each sample's GPM results, clinically reported cytogenetics results, both, or neither. Constitutional abnormalities (indicated by "?c" per ISCN nomenclature) were not evaluated.

Patient #	GPM Findings (discordant calls bolded and underlined)	Clinical cytogenetics ISCN (discordant calls bolded and underlined)	Confirmation of presence/absence of discordant abnormality by Illumina WGS	Which platform's molecular presentation was corroborated by WGS?
2	gpm 46,XY,inv(16)(p13.11q22.1)	46,XY,inv(16)(p13.1q22)[13]/**92<4N>**,slx2[7].nuc ish(CBFBx2)(5'CBFB sep 3'CBFBx1)[119/200]/(CBFBx4)(5'CBFB sep 3'CBFBx2)[44/200]	Cannot confirm tetraploidy - cannot confirm GPM discrepancy	None
3	gpm 46,XY	47,XY,**+8**[15]/46,XY[5]	Low level trysomy 8 (roughly estimated <10%) present.	Clinical cytogenetics
5	gpm 46,XY	47,XY,**+8**[5]/45,X,-Y[3]/46,XY[12]	Unconfirmed +8	GPM
5	gpm 46,XY	47,XY,+8[5]/45,X,**-Y**[3]/46,XY[12]	Unconfirmed -Y	GPM
7	gpm 45,XY,**inv(3)(p24.3q26.2)**,-7[0.8]	45,XY,-7[11]/46,XY[9]	Confirmed inv(3)	GPM
11	gpm 46,XY,del(4)(q24q24)	47,XY,**+22**[2]/46,XY[18]	Unconfirmed trisomy 22	GPM
11	gpm 46,XY,**del(4)(q24q24)**	47,XY,+22[2]/46,XY[18]	Confirmed del(4)(q24q24)	GPM
16	gpm 46,XY,del(7)(q22.1q36.1),**dup(8)(p23.3)**,dup(12)(p13.31),inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),+22[3]	Confirmed by dup(8)(p23.3)	GPM
16	gpm 46,XY,del(7)(q22.1q36.1),dup(8)(p23.3),**dup(12)(p13.31)**,inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),+22[3]	Unconfirmed dup (12)	Clinical cytogenetics
16	gpm 46,XY,del(7)(q22.1q36.1),dup(8)(p23.3),dup(12)(p13.31),inv(16)(p13.11q22.1) [0.8]	46,XY,del(7)(q22q36),inv(16)(p13.1q22)[17]/47,XY,inv(16)(p13.1q22),**+22**[3]	Unconfirmed +22	GPM
18	gpm 46,XX,del(6)(p24.1p24.1),t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),**d**	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q21)[5]/47,sdl,+13[10]/46,XX[2]	Unconfirmed dup 9	Clinical cytogenetics

	up(9)(p21.1p13.3)[0.3]			
18	gpm 46,XX,**del(6)(p24.1p24.1)**,t(6;9)(p22.3;q34.12),t(6;15)(p24.2p24.1;q21.1),dup(9)(p21.1p13.3)[0.3]	46,XX,t(6;9)(p23;q34)[3]/46,sl,t(6;15)(p23;q21)[5]/47,sdl,+13[10]/46,XX[2]	Confirmed del(6)(p24.1p24.1)	GPM
19	gpm 47,XY,+8	47,XY,+8[4]/46,sl,**-Y**[11]/46,XY[5]	Confirmed -Y	Clinical cytogenetics
24	gpm 46,XY	46,XY,t(2;19)(q35;p13.3)[5]/45,XY,**-21**[3]/46,XY[12]	Unconfirmed -21	GPM
24	gpm 46,XY	46,XY,**t(2;19)(q35;p13.3)**[5]/45,XY,-21[3]/46,XY[12]	Unconfirmed t(2;19)(q34;p13.3)	GPM
26	gpm 46,XX,t(10;17)(p11.2;q11.2)*[0.2]	46,XX,**add(17)(p13)**[2]/46,sl,del(10)(q24)[2]/46,XX,t(10;17)(p10;p10)[5]/46,XX[11].nuc ish(TP53,CEP17)x2[200]	Unconfirmed add(17)(p13)	GPM
26	gpm 46,XX,t(10;17)(p11.2;q11.2)*[0.2]	46,XX,add(17)(p13)[2]/46,sl,**del(10)(q24)**[2]/46,XX,t(10;17)(p10;p10)[5]/46,XX[11].nuc ish(TP53,CEP17)x2[200]	Unconfirmed del(10)(q24)	GPM
34	gpm 46,XX	46,XX,**del(7)(q31)**[5]/46,XX[15]	Unconfirmed del(7)(q31)	GPM
47	gpm 45,XY,der(3)del(3)(q21.3)inv(3)(q21.3q26.1)del(3)(q26.1q26.2),dup(4)(q32.2q32.2)?c,-7	45,XY,inv(3)(q21q26.2),-7[16]/45,sl,**del(6)(p23)**[4]	Unconfirmed del(6)(p23)	GPM

Abbreviations: GPM: Genomic Proximity Mapping™, ISCN: International System for Human Cytogenomic Nomenclature, WGS: whole genome sequencing