Supplementary Materials

Supplementary Table S1. Clinically available data of B-ALL cohort. Principal component analysis of ancestry results: AMR = admixed American, EAS = east Asian, SAS = south Asian, EUR = European.

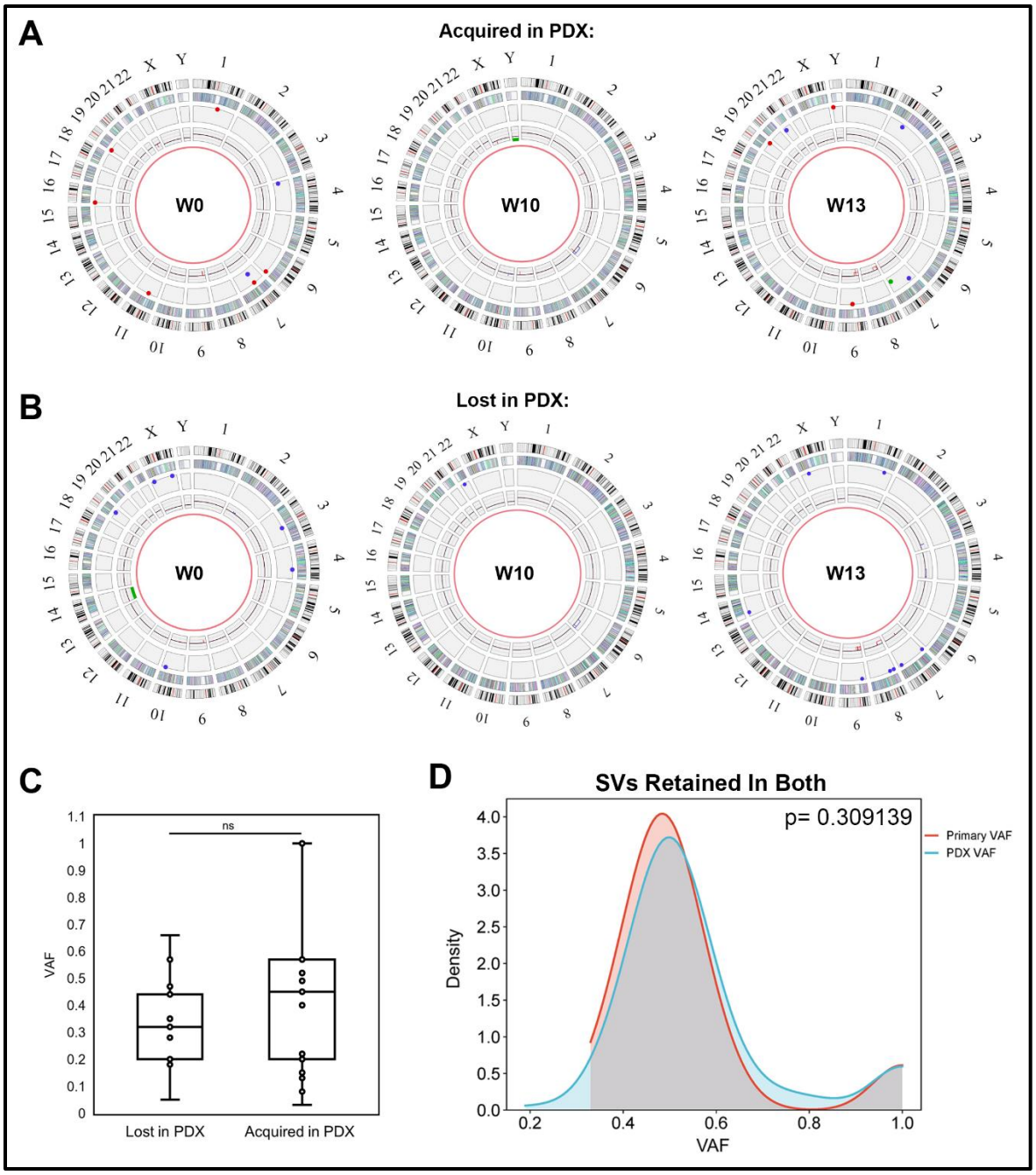
Individual	Leukemia Type	Self-reported race (if available)	PCA Ancestry Classification	Age (yrs)	Gender	Original cytogenetic features reported
W0	B-ALL	Hisp/Mex	AMR	10	M	CRLF2+ low. IKZF1del
W10	B-ALL	Hisp/Mex	AMR	18	M	CRLF2+ high, IKZF1 del
W31	B-ALL	Hisp/Mex	AMR	10	M	CRLF2+ IKZF1 wt
W13	B-ALL	Hisp/Mex	AMR	18	M	CRLF2- IKZF1 wt
G02	B-ALL	Hisp/Mex	AMR	9	F	CRLF2+ CD34+
E13	B-ALL	Hisp/Mex	AMR	6	F	CRLF2+ CD34+
K30	B-ALL	Hisp/Mex	AMR	12	F	CRLF2+ CD34+&CD34-
K09	B-ALL	Hisp/Mex	AMR		F	
PAVDRS	B-ALL		AMR	9	M	IGH-EPOR, CDKN2A, IKZF1, PAX5
ALL4364	B-ALL		AMR	4	M	JAK2 R683G, IGH-CRLF2
PAWFUU	B-ALL		AMR	18	F	RANBP2-ABL1
PAVCYL	B-ALL		AMR	8	M	ZMIZ1-ABL1
G2650	B-ALL		AMR	>20	M	
LAX7	B-ALL		AMR	>20	M	IKZF1 del CD10+CD19+
ICN1	B-ALL		EAS	14	F	BCR-ABL1
ALL-17	B-ALL		EAS	8	F	
PAVVIE	B-ALL		EUR	5	M	NUP153-ABL1
PVCRK	B-ALL		EUR	>20	M	IGH-EPOR, CDKN2A, IKZF1, JAK2
ALL-07	B-ALL		EUR	7	M	
ALL-11	B-ALL		EUR	3	F	
ALL-19	B-ALL		EUR	16	M	
ALL-25	B-ALL		EUR	12	M	
ALL-53	B-ALL		EUR	7	F	
ALL-57	B-ALL		EUR	5	F	
ALL-59	B-ALL		EUR	13	F	
ALL-82	B-ALL		EUR	5	F	
ALL-02	B-ALL		EUR	5	F	
ALL-58	B-ALL		EUR	2	F	
MXP3	B-ALL		SAS	13	M	

Supplementary Table S2. Comparison of WGS, OGM, Karyotyping, FISH, and RNA-Seq techniques for detection of SVs.

Variant type	WGS	OGM	Karyotype	FISH	RNA-Seq
SNV	✓	N/A	N/A	N/A	✓
Deletion	✓	>500 bp	>5-10 Mb	targeted	Expression-dependent
Duplication	✓	>500 bp	>5-10 Mb	targeted	Expression-dependent
Inversion	✓	>500 bp	>5-10 Mb	targeted	Expression-dependent
Insertion	small	>500 bp	>5-10 Mb	targeted	Expression-dependent
Translocation	✓	>500 bp	>5-10 Mb	targeted	Expression-dependent
Aneuploidy	✓	✓	✓	targeted	Expression-dependent
Repeat expansion	N/A	✓	N/A	N/A	N/A
Loss of heterozygosity	✓	✓	N/A	N/A	Expression-dependent

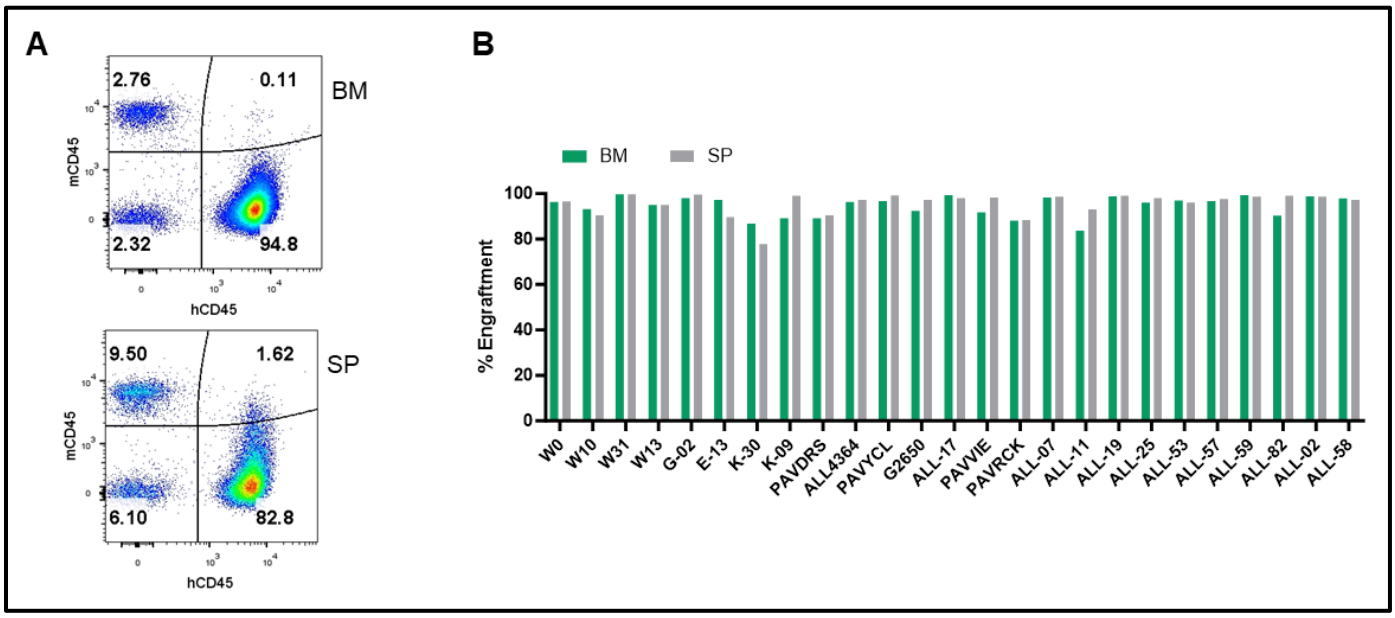
Supplementary Table S3. Novel putative gene-fusion events identified by WGS, OGM, or both. Novel fusions were not reported in ChimerDB 4.0, FusionGDB 2.0 databases or manual literature curation.

Fusion genes	Putative novel: not in FusionGDB, ChimerDB, or lit search	Previously reported	RNA-Seq expression (≥16 supporting reads)	Fusion genes (contd.)	Putative novel (contd.)	Previously reported (contd.)	RNA-Seq expression (contd.)
ABL1::NUP214		✓	✓	NCOA7::PHF20	✓		
ABL1::ZMIZ1		✓	✓	NKD2::ZCCHC16	✓		
ACOT13::SYN3		✓		NR3C1::DNM2	✓		✓
AGPAT4::PARK2		✓		PADI1::DCHS2	✓		
ARL8B::EDEM1	✓			PAGE2B::PAGE2	✓		
AUTS2::PAX5		✓		PAIP2B::FAM65B	✓		
BANP::PRKACA	✓		✓	PBX1::TCF3		✓	
BAZ2A::FSIP1		✓		PDGFRB::EBF1		✓	
BMP1::SAXO2	✓			PIGK::AK5	✓		✓
C12orf79::RNF17	✓			PRAMEF11::PRAMEF10	✓		
C7orf72::IKZF1	✓			RADIL::MMD2		✓	
CADPS2::VPS13A	✓			RAG1::C11orf74	✓		
CLOCK::SLC9B1	✓			RB1::RCBTB2		✓	
CMPK1::CLIC5		✓		RGPD6::RGPD5		✓	✓
CXorf23::MAP7D2	✓			RGPD6::RGPD8		✓	
DCDC5::ATRX		✓		RNASE13::CHD8	✓		
DCLRE1C::ACBD7	✓			SAFB::CATSPERD	✓		
DDX10::MRPL57		✓		SCD5::PCBD2	✓		
DOCK8::TMEM38B	✓		✓	SENP6::PTPRK	✓		✓
DPP10::SET	✓			SPAG17::OSBPL10	✓		
ETV6::RUNX1		✓	✓	SPOCK1::ETV6	✓		
FXR1::ATAD2	✓		✓	SPTBN1::CYB5D2	✓		
GPR56::CCDC135		✓		TACC1::HTRA4	✓		
HLF::TCF3		✓	✓	TMEM217::KMT5B	✓		✓
IKZF1::DDC		✓	✓	TRPM7::SPPL2A		✓	
ITPR2::TMTC1		✓		UBR4::ZFP37		✓	
KCTD5::SRRM2		✓		WAC::NRBF2	✓		
KIF18A::PRKACA	✓			WDHD1::SMEK1	✓		
KLF6::LINC00704	✓			WDR70::NXPH1	✓		
LETM2::ADAM5		✓		ZFP14::ZNF529	✓		
LHPP::FAM175B	✓			ZNF415::ZNF665	✓		
LINC02250::GRIK1	✓			ZSCAN26::ZKSCAN3	✓		
LRP1B::KCND2	✓						
MAP3K6::SERINC2	✓						



Supplementary Figure S1 Comparison of SVs in patient primary tumor and expanded PDX model from Bionano de novo analysis:

(A) Circos plots of SVs acquired in PDX model. SVs were originally not present/detectable in primary tumor but present/detectable in PDX. Track labels are as follows from outside to inside: chromosome number, cytoband, gene regions, SV (blue=deletion, red=insertion, pink=inversion, green=duplication), copy number, translocations. **(B)** Circos plots of SVs lost in PDX model, originally present/detectable in primary tumor, but not in PDX model. **(C)** Variant allele frequencies of SVs either lost or acquired in the PDX model compared to the primary tumor. Middle line represents median (p=0.13456, two-tailed T-test.) D) Density plot representing variant allele frequencies of SVs retained in both patient primary tumor and PDX model (p=0.309139, two-tailed T-test).



Supplementary Figure S2 Human CD45 cell engraftment in animal Bone marrow (BM) and Spleens (SP). Mice were terminated when sick or moribund post-injection of human cells or PDXs and their BM and SP were harvested. After tissue cell dissociation and processing, single cells were stained for mCD45 and hCD45. **(A)** A representative flow dot plot of BM (top) and SP(bottom) from PDX E-13 is shown. (**B)** The human CD45 cell engraftment data based on staining of mCD45 and hCD45 are presented in the bar graph. Human cell engraftment is defined as the percentage of human CD45+ cells divided by the percentage of total mouse and human CD45+ cells multiplied by 100.