Supplemental data

Plasmacytoid dendritic cell expansion defines a distinct subset of *RUNX1* mutated acute myeloid leukemia

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Supplemental Methods

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Patients

A cohort of AML patients without pDC expansion was reported previously[1]. A cohort of patients with BPDCN was also identified through similar natural language search. The normal control cohort was previously described with addition of negative marrow specimens (by flow cytometry and morphology) from patients of lymphoma staging[1]. Written informed consent was received from participants prior to inclusion in the study.

Human Cells

Umbilical cord blood samples from healthy neonates were obtained from the New York Blood Center under an agreement that includes approval for ethical laboratory research use. Mononuclear cells were separated by density centrifugation using Ficoll-Paque (GE Healthcare) and ammonium chloride red cell lysis. CD34 positive cells were positively selected by magnetic microbeads purchased from Miltenyi. Cryopreserved bone marrow aspirate or peripheral blood mononuclear cell specimens collected at diagnosis were retrieved from our institutional, IRB-approved biospecimen bank.

Cell culture

10,000 flow cytometry-sorted CD34 positive cells were cultured for 14 days in StemSpan serum free culture medium (StemCell Technologies) supplemented with β-mercaptoethanol and penicillin/streptomycin at 37 °C, together with the following cytokines (Peprotech): human fms-like tyrosine kinase 3 ligand (hFLT3L) (100 ng/mL), human stem cell factor (hSCF) (10 ng/mL), human thrombopoietin (hTPO) (50 ng/mL), and Stemregenin 1 (SR1) (1 μg/mL). Human IL-7 was also included in some experiments. Half of the medium containing the cytokine cocktail was replaced every 3-4 days.

Patient-derived xenograft models and tagraxofusp administration

NOD/SCID/IL-2Rg-null female mice were purchased from Taconic and maintained under specific pathogen-free conditions. Mice ages 6–7 weeks were sub-lethally irradiated (2 Gy) up to 24 hr before intravenous (i.v.) injection of various numbers of unsorted human PBMCs, unsorted bone marrow cells or 500,000 sorted leukemic blasts or pDCs. In the treatment

experiments, tagraxofusp (gift from Stemline Therapeutics) was diluted in PBS to 10 μg/mL and was administered intraperitoneally (i.p.) at 0.1 mg/kg/d (low dose cohort) or 0.2 mg/kg/d (high dose cohort) for 5 days. Mice were monitored every 1–2 weeks by peripheral blood sampling. All experiments involving mice were performed in accordance with national and institutional guidelines for animal care and were approved by IACUC at MSK.

Flow cytometry and Cell sorting

For clinical samples, multiparameter flow cytometry was performed on bone marrow aspirates at diagnosis and/or relapse. Briefly, up to 1.5 million cells from freshly drawn bone marrow aspirate were stained with 4-6 10-"color" panels as previously reported, washed, and acquired on a Canto-10 cytometer (BD Biosciences, San Jose, CA)[1]. pDC tubes were described in supplemental Table 1. The results were analyzed with custom Woodlist software (generous gift of Wood BL, University of Washington). Cryopreserved live cells were sorted into myeloid blasts, pDCs, monocytes and T cells (as somatic controls) using FACS-Aria Fusion cell sorter (BD Biosciences, San Jose, CA). For cell cultures and PDX samples, similar sample preparation processes were followed. The samples were acquired on a Fortessa cytometry (BD Biosciences, San Jose, CA). The results were analyzed with FlowJo™ Software version 10.6.1 (Ashland, OR: Becton, Dickinson and Company; 2019). The bone marrow cells from PDX mice were sorted using SH800S cell sorter (Sony Biotechnology, San Jose, CA).

Chromosome and FISH analysis:

Conventional chromosome analysis of bone marrow, peripheral blood or fresh tissue was performed following standard procedures with overnight short-term culturing without mitogen. At least 20 metaphase cells were analyzed for a complete chromosome study. The chromosome abnormalities were recorded as per ISCN (2016). In most cases, FISH analysis was performed for recurring chromosome abnormalities in AML and ALL, including t(9;22), MLL, and t(12;21), and in a few cases with inadequate chromosome analysis, extensive FISH tests for t(8;21),

inv(16), t(6;9) and IKZF1 were also performed. All FISH probes were from Abbott Molecular (Des Plaines, IL), and its quality and performance were validated in the laboratory.

Sequencing studies

Bone marrow samples obtained were submitted to a 28-gene amplicon capture-based next-generation sequencing (NGS) assay (RainDance) or a larger 400-gene amplicon capture-based next-generation sequencing assay (MSK IMPACT) as previously described. Sorted cells of specific populations from pDC-AML patients were submitted for MSK IMPACT testing. Variants were detected through our clinical workflow.

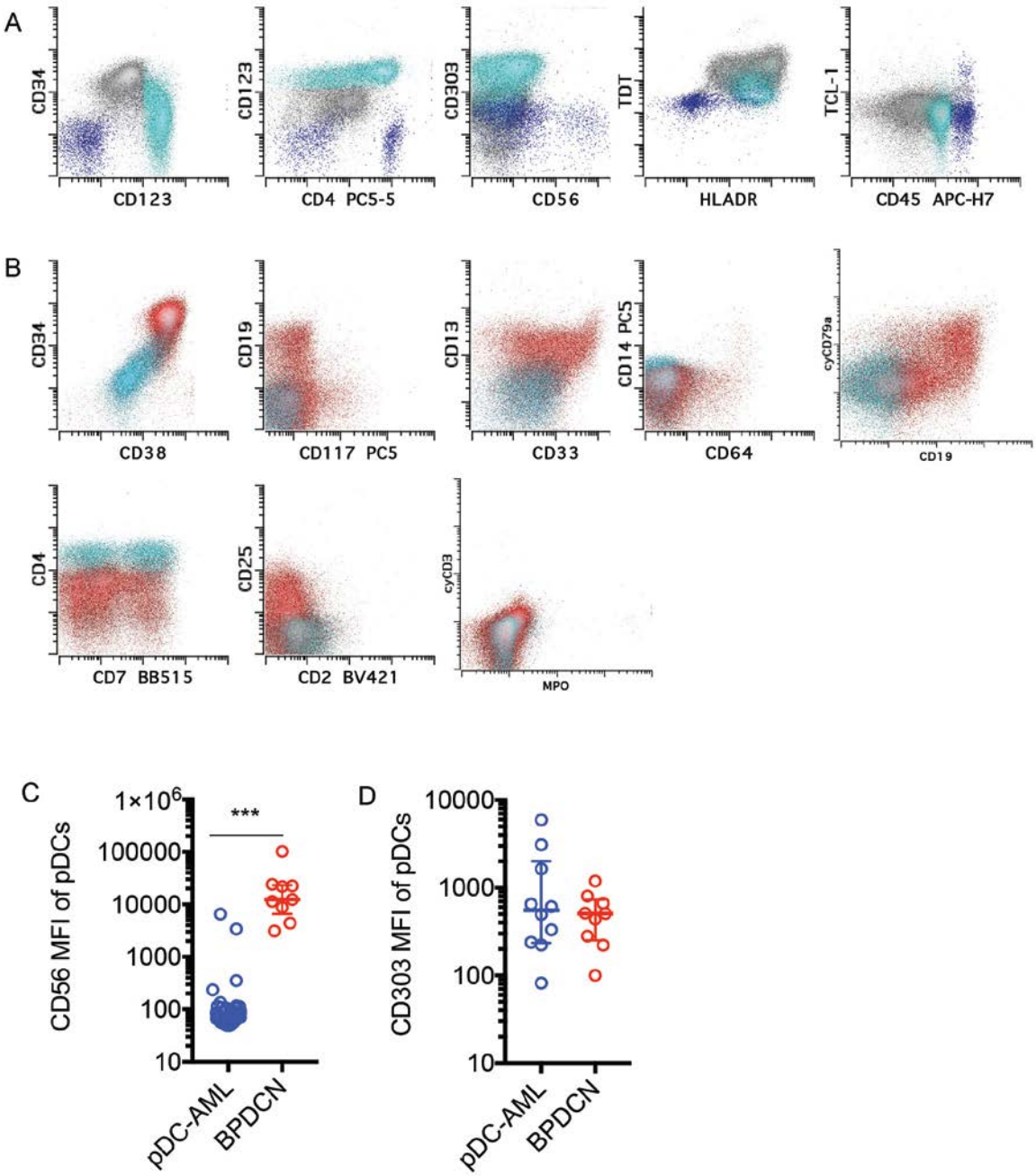
CD34+ blasts or pDCs were sorted from AML patients or healthy controls into RNA lysis buffer. Total RNA was isolated and RNA integrity and concentration were assessed using a BioAnalyzer. RNA sequencing libraries were generated using SMARTerAmpSeq. Multiplexed libraries were sequenced at the Memorial Sloan Kettering Cancer Center's core sequencing facility. Approximately 20-30 million paired-end 50 bp reads were sequenced per sample on a Hi-Seq 4000. Fastq files were mapped to the human genome (hg38) and genome wide transcript counting was performed using featureCounts. Differentially expressed genes (DEGs) were identified with DESeq2 and genes with an FDR of 5% were used for downstream analysis. Gene ontology analysis was performed using clusterProfiler. Normalized ssGSEA scores were calculated using normalized expression values and previously published pDC gene sets as input. The algorithm gene set variation analysis (GSVA) was applied[2-4].

Statistics

Statistical analyses were performed using Prism software (GraphPad) or DEseq2 for RNA-seq, as indicated. Data are plotted as mean ± SD, except as where indicated in legends. Statistical significance calculations on pairwise comparisons were performed using 2-tailed t tests. Survival analyses were performed on curves generated using the Kaplan-Meier method and groups were compared using the log-rank test. Cox proportional hazards regression models were used to estimate the hazard ratios (HR) and 95% confidence intervals (CIs), for high level of pDC (2%

cutoff), on the risk of mortality, without (univariate) and with adjusting for age at diagnosis (years, continuous) and ELN risk. A p value less than 0.05 was considered significant.

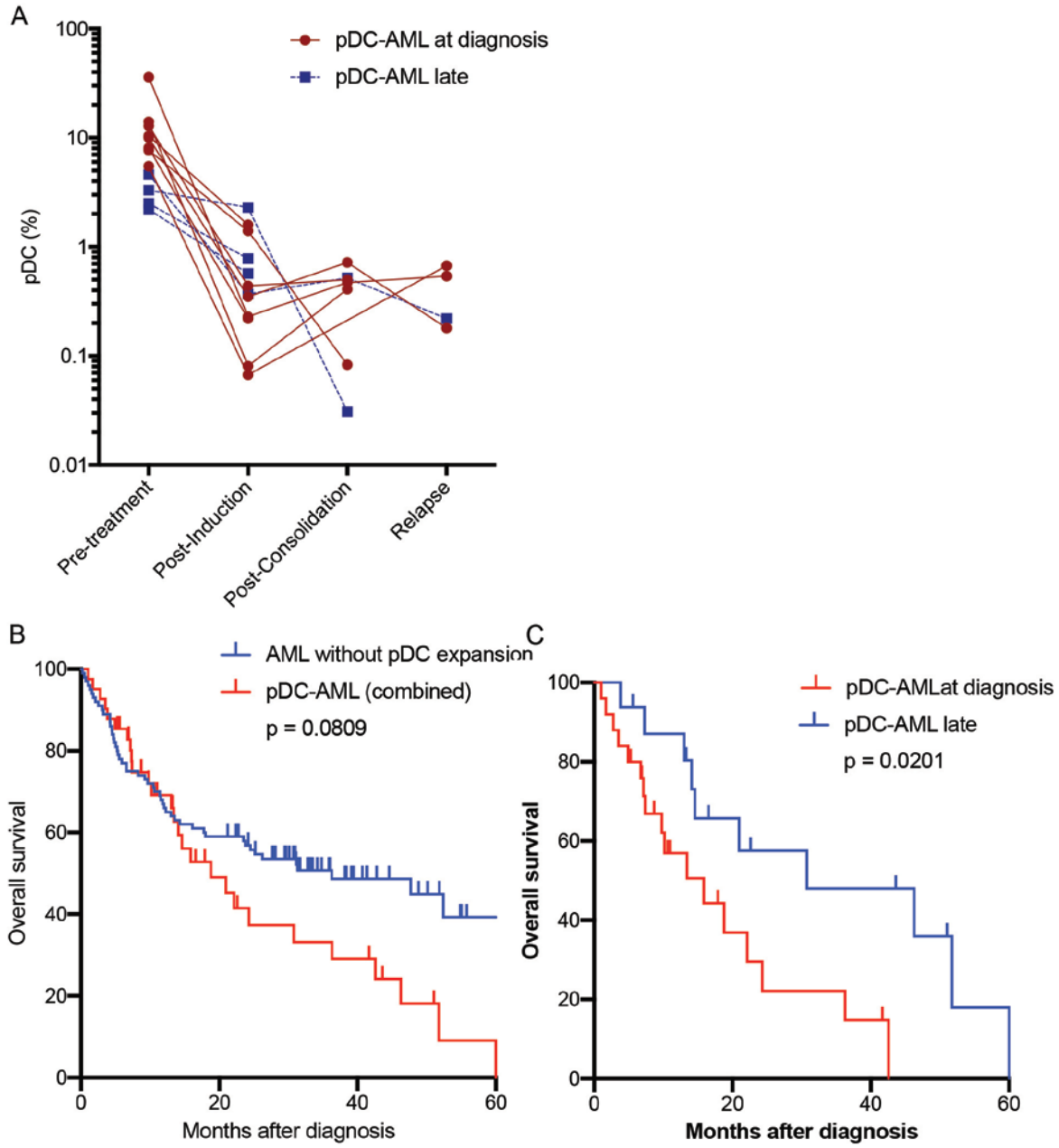
Fig S1



Supplemental Figure 1. Detailed immunophenotype of pDCs and leukemic blasts from a representative pDC-AML patient. A. Flow plots of DC tubes (aqua, pDCs; grey, blasts; blue, lymphocytes). B. Flow plots of myeloid and intracytoplasmic tubes (aqua, pDCs; red, blasts). The pDCs are positive for CD123, CD4, HAL-DR, dim CD45, dim CD34, dim CD38, CD7 (subset) and dim CD33, but negative for CD56, TCL-1, TdT, CD117, CD2, CD5(not shown), CD8 (not shown), CD25, CD13, CD14, CD64, CD19, cyCD79a, cyCD3 and MPO. The blasts are positive for CD34, CD38, HLA-DR, CD117 (minor subset), intermediate CD123, intermediate CD4, dim TdT, CD13, CD33, CD7 (subset), CD25 (subset), CD19 (subset) and cyCD79 (subset), but negative for CD303, CD56, CD14, CD2, cyCD3, MPO and TCL-1. The blasts show myeloid and B lineage mixed phenotype. C, CD56 expression on pDCs of pDC-AML and BPDCN. 4 patients had MFI>200 (2 of them had MFI>1000). In contrast, 9/9 BPDCN patients had MFI>1000. The two pDC-

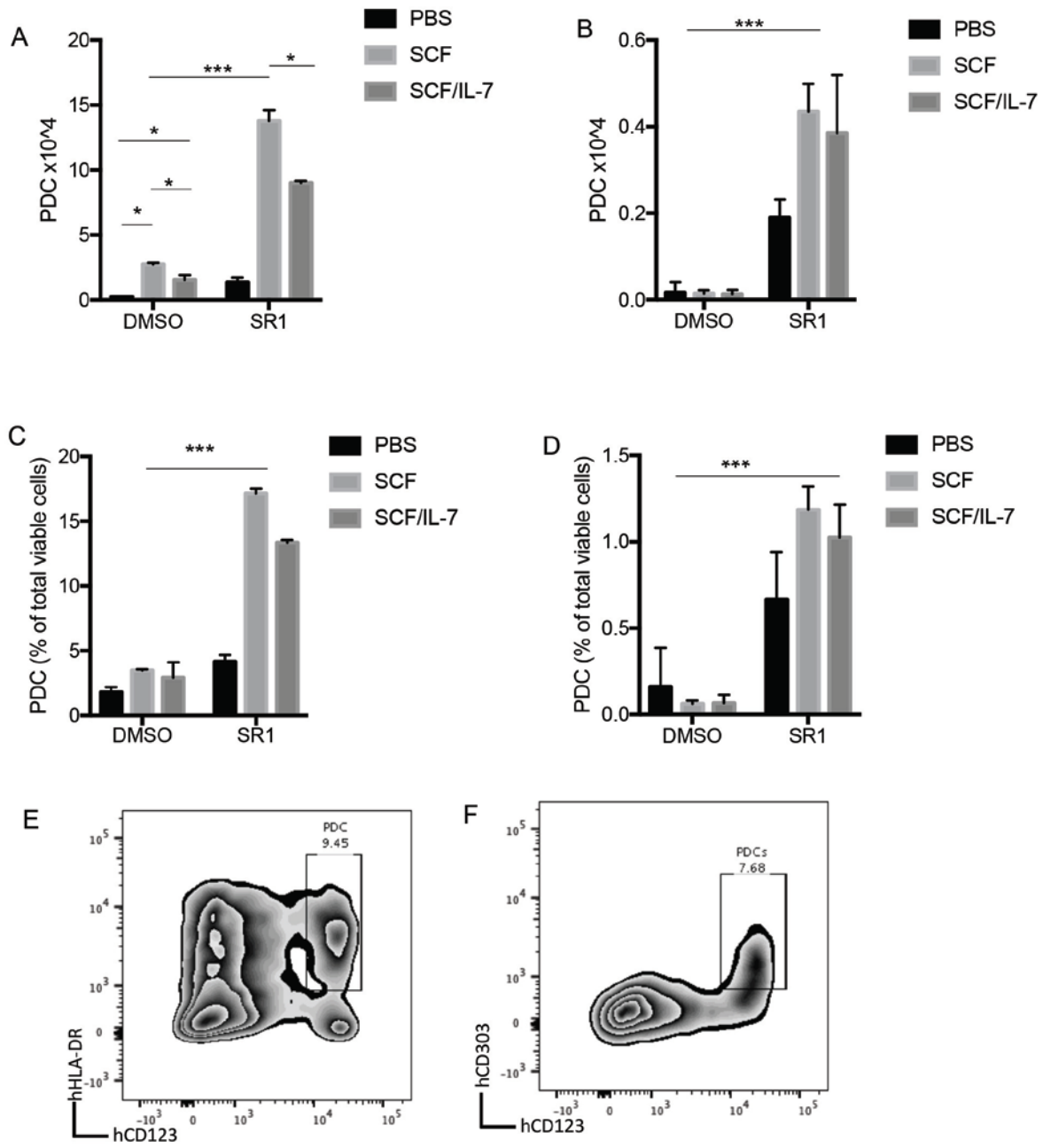
AML patients with CD56>1000 had pDCs of 7% and 13% in the marrow. One had history of CMML and was negative for RUNX1 mutation. Neither had skin involvement. D, CD303 expression on pDCs of pDC-AML and BPDCN. CD303 is expressed in 7/10 pDC-AML and 6/9 BPDCN (MFI 300 was chosen as cutoff).

Fig S2



Supplemental Figure 2. Dynamics of pDC after treatment (A) and Kaplan-Meier survival curve (B and C).

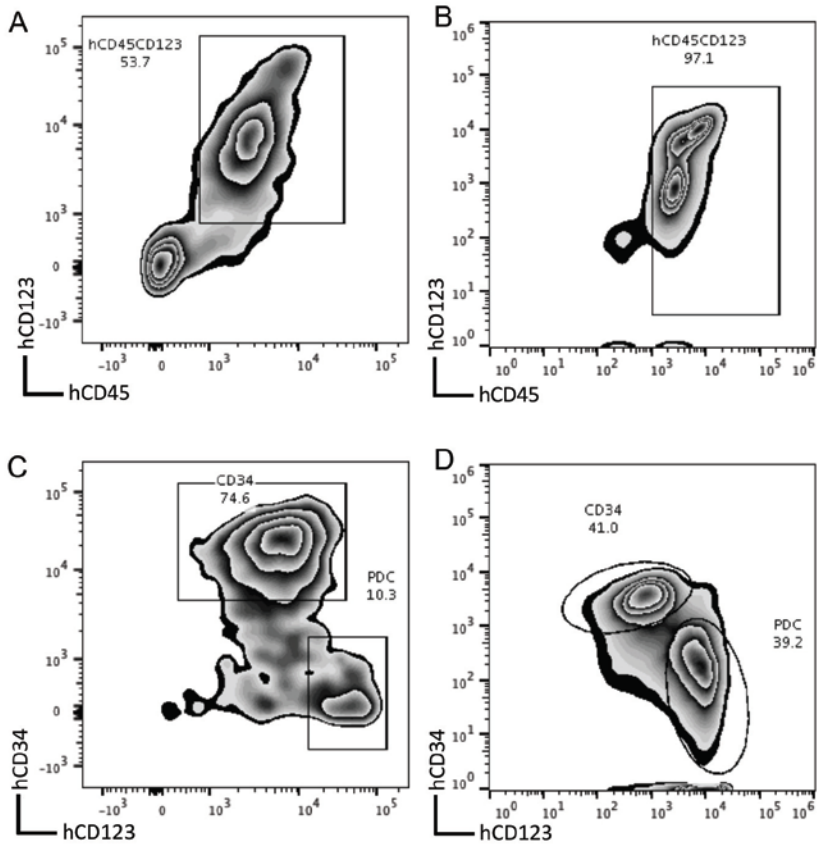
Fig S3



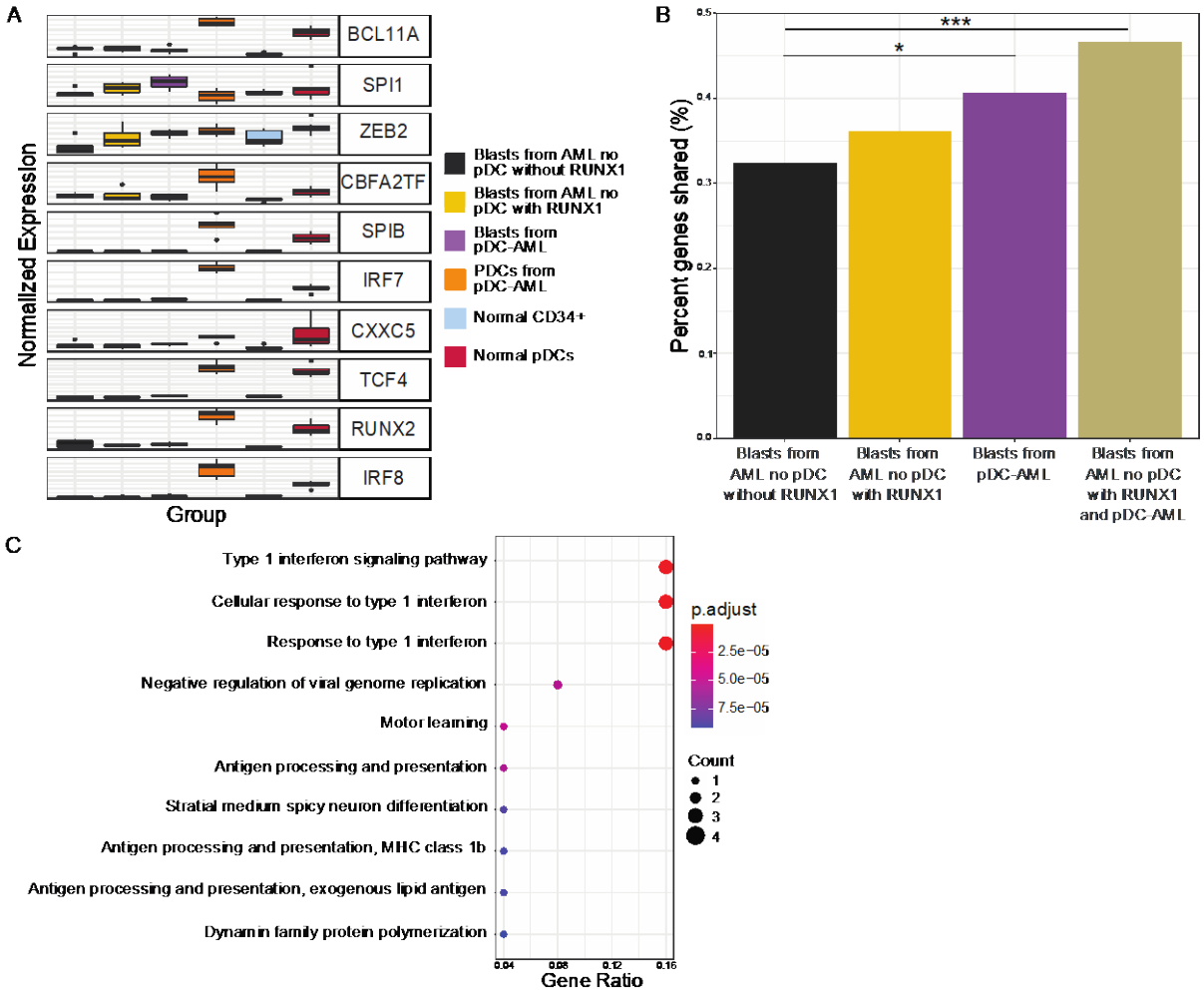
Supplemental Figure 3. pDC differentiation facilitated by SR1. A-B, Purified CD34 positive cells from cord blood (A and C) and G-CSF mobilized peripheral blood mononuclear cells (B and D) were cultured in STEMSPAN serum free medium with hFLT3L 100ng/ml, hTPO 50 ng/ml and cytokines (SCF 10 ng/ml or IL-7 10 ng/ml) or SR1 (1 μM) as indicated for 2 weeks. E-F, Cells cultured in vitro for 2 weeks (from panel A) with addition of SR1 and SCF 10 ng/ml were immunophenotyped by flow cytometry. pDCs were identified as DAPI-CD3-CD19-CD56-CD14-FceRI-CD123+HLA-DR+CD303+ population. Under these conditions we were able to efficiently differentiate pDCs from cord blood and peripheral blood CD34 positive cells. pDC output from cord blood CD34 positive cells was increased by nearly 10-fold by adding SR1 **(A,C)**. pDC output from G-CSF mobilized peripheral blood CD34 positive HSPC was 10-fold

lower that that from cord blood HSPC (**B,D**). The pDCs differentiated from cord blood cells showed characteristic surface expression of CD123, HLA-DR and CD303 (**E-F**) and plasmacytoid cytomorphology (data not shown).

Fig S4

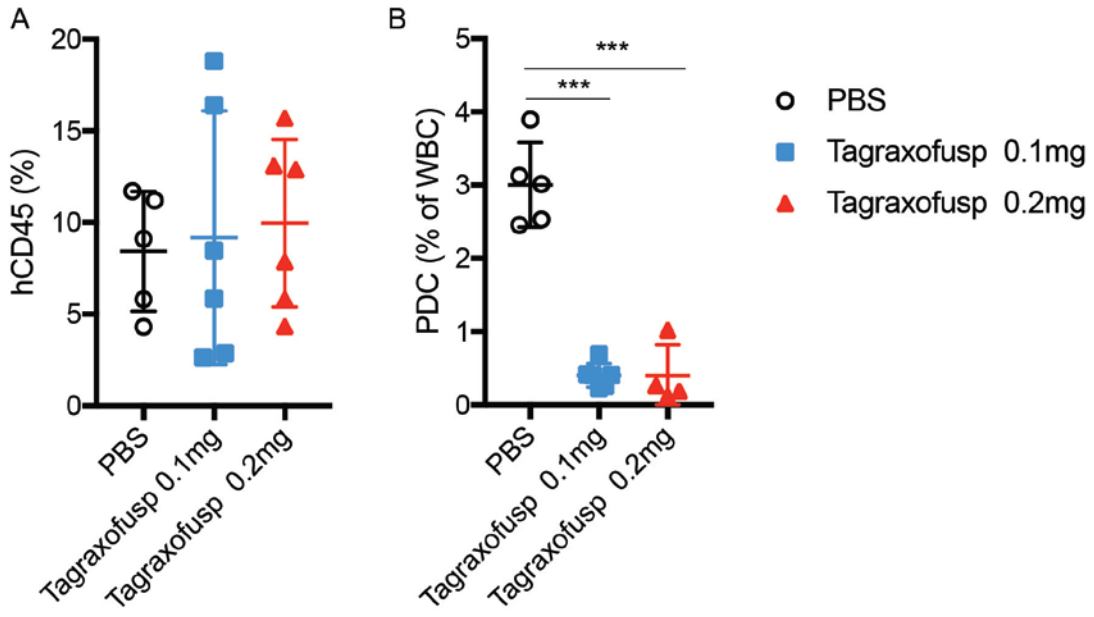


Supplemental Figure 4. Immunophenotype of primary NSG mice mice receiving pDC-AML cells. A and B, hCD45 engraftment in peripheral blood (A) and bone marrow (B) 6 months after transplant. C and D, Leukemic blasts and pDCs in hCD45 positive cells from peripheral blood (C) and bone marrow (D).



Supplemental Figure 5. A, Expression levels of key pDC genes. B, Shared pDC transcriptional program for each group. C, Gene ontology analysis showing upregulated pathways in the subset of 30 genes from Figure 5C.

Fig S6



Supplemental Figure 6. Tagraxofusp treatment eliminates pDCs in secondary NSG recipients. A, hCD45 positive cells in bone marrow prior to treatment were comparable between 3 cohorts. B, pDC proportions in total WBC of peripheral blood were nearly eliminated by one cycle of tagraxofusp treatment. mean±SD. ***$p<0.0001$

Supplemental Table 1 List of antibodies for pDC-AML immunophenotype by flow cytometry

M1 Tube	M2 Tube	M3 Tube	Intra Tube	pDC1 Tube	pDC2 Tube	pDC3 Tube
CD15 FITC (80H5, BC)	CD64 FITC (22, BC)	CD7 BB515 (M-T701, BD)	cytoplasmic MPO FITC (CLB-MPO-1, BC)	CD303 (BCDA-2) PE (AC144, Miltenyi)	cytoplasmic TdT control FITC (Supertechs)	cytoplasmic TdT FITC (Supertechs)
CD33 PE (D3HL60.251, BC)	CD123 PE (9F5, BD)	CD56 PE (N901 [HLDA6], BC)	cytoplasmic CD79a PE (HM47, BC)	CD123 APC (9F5, BD)	CD34 PERCP-CY5.5 (8G12, BD)	CD34 PERCP-CY5.5 (8G12, BD)
CD117 PC5 (104D2D1, BC)	CD14 PC5 (RMO052, BC)	CD5 Percp-cy 5.5 (L17F12, BD)	cytoplasmic CD3 APC (UCHT1, BC)	CD56 PC7 (N901 [HLDA6], BC)	CD123 APC (9F5, BD)	CD123 APC (9F5, BD)
CD13 PE-CY7 (L138, BD)	CD13 PE-CY7 (L138, BD)	CD34 APC (581, BC)	CD34 PERCP-CY5.5 (8G12, BD)	CD4 PC5.5 (13B8.2, BC)	CD45 APC-H7 (2D1, BD)	CD45 APC-H7 (2D1, BD)
CD34 APC (581, BC)	CD34 APC (581, BC)	CD33 PC7 (D3HL60.251, BC)	CD19 PC7 (J3-119, BC)	CD45 APC-H7 (2D1, BD)	HLADR PACIFIC BLUE (Immu-357, BC)	HLADR PACIFIC BLUE (Immu-357, BC)
CD71 APC-A700 (YDJ1.2.2, BD)	CD16 APC -A700 (3G8, BC)	CD4 APC-A700 (13B8.2, BC)	CD45 APC-H7 (2D1, BD)	HLADR PACIFIC BLUE (Immu-357, BC)		
CD38 APC-A750 (LS198-4-3, BC)	CD38 APC-A750 (LS198-4-3, BC)	CD38 APC-A750 (LS198-4-3, BC)	CD3 BV421 (UCHT1, BD)			
HLADR PACIFIC BLUE (Immu-357, BC)	HLADR PACIFIC BLUE (Immu-357, BC)	CD2 BV421 (RPA-2.10, BD)				
CD45 V500c (2D1, BD)	CD45 V500c (2D1, BD)	CD45 V500c (2D1, BD)				
CD19 BV605 (HIB19, BioL)	CD11b BV605 (1CRF44, BioL)	CD25 BV605 (BC96, BioL)				

BC: Beckman Coulter, Miami, FL; BD: BD Biosciences, San Jose, CA; BioL: BioLegend, San Jose, CA; Miltenyi: Miltenyi Biotec, San Jose, CA; Supertechs: Supertechs, Inc., Rockville, MD

Supplemental Table 2 Immunophenotype of pDC in pDC-AML

Markers	pDC-AML at diagnosis (n = 26) (FC available n = 25)	pDC-AML late (n=16) (FC available n = 16)	pDC-AML (combined) (n=42) (FC available n = 41)	BPDCN[a]	Normal pDCs[a]
CD4	20/20 (100%)	9/9 (100%)	29/29 (100%)	37/37 (100%)	21/21 (100%)
CD123	25/25 (100%)	15/15 (100%)	41/41 (100%)	37/37 (100%)	21/21 (100%)
HLA-DR	25/25 (100%)	15/15 (100%)	41/41 (100%)	37/37 (100%)	21/21 (100%)
CD303	5/8 (63%)	2/2 (100%)	7/10 (70%)	7/16 (44%)	21/21 (100%)
CD56	3/21 (14%)	1/9 (11%)	4/30 (13%)	36/37 (97%)	Small population
TCL-1	1/7 (14%)	2/2 (100%)	3/9 (33%)		
TdT	4/8 (50%)	0/2 0%)	4/10 (40%)	4/16 (25%)	
CD34	14/25 (56%)	11/16 (69%)	25/41 (61%)	0/27 (0)	
CD38	24/25 (96%)	16/16 (100%)	40/41 (98%)	30/34 (88%)	21/21 (100%)
CD2	6/20 (30%)	2/9 (22%)	8/29 (28%)	5/27 (19%)	21/21 (100%)
CD5	3/20 (15%)	2/9 (22%)	5/29 (17%)	1/30 (3%)	
CD7	8/20 (40%)	4/9 (44%)	12/29 (41%)	21/33 (64%)	21/21 (100%)
CD13	9/25 (36%)	8/16 (50%)	17/41 (41%)	0/30 (0)	
CD14	0/25 (0%)	0/16 (0%)	0/41 (0%)		
CD33	4/21 (19%)	7/12 (58%)	11/33 (33%)	16/33 (48%)	21/21 (100%)
CD64	0/25 (0%)	1/16 (6%)	1/41 (2%)		

[a] Data were extracted from Wang, W., et al. (2020). "Immunophenotypic characterization of reactive and neoplastic plasmacytoid dendritic cells permits establishment of a 10-color flow cytometric panel for initial workup and residual disease evaluation of blastic plasmacytoid dendritic cell neoplasm." Haematologica: haematol.2020.247569.

Supplemental Table 3 Immunophenotype of blasts in pDC-AML

Markers	**pDC-AML at diagnosis (n = 26) (FC available n = 25)**	**pDC-AML late (n=16) (FC available n = 16)**	**pDC-AML (combined) (n=42) (FC available n = 41)**
Cross lineage antigen expression	6 (24%)	7 (44%)	13 (32%)
T-cell markers[a] (≥2 aberrantly expressed)	4 (16%)	5 (31%)	9 (22%)
B-cell markers[b] (≥2 aberrantly expressed)	2 (8%)	2 (13%)	4 (10%)
Meets MPAL criteria	5 (20%)	3 (19%)	8 (20%)
T-cell markers Number abnormal / number tested (%)			
CD2	4/25 (16%)	2/16 (13%)	6/41 (15%)
CD3 (cytoplasmic)	0/19 (0%)	2/5 (40%)	2/24 (8%)
CD5	2/25 (8%)	2/16 (13%)	4/41 (10%)
CD7	10/25 (40%)	9/16 (56%)	19/41 (46%)
B-cell markers			
CD10	0/24 (0%)	2/5 (40%)	2/29 (7%)
CD19	7/25 (28%)	4/16 (25%)	11/41 (27%)
CD79a (cytoplasmic)	4/14 (29%)	2/5 (40%)	6/19 (32%)
Other markers			
CD4	2/25 (8%)	0/16 (0%)	2/41 (5%)
CD11b	11/25 (44%)	4/16 (25%)	15/41 (37%)
CD13	24/25 (96%)	11/16 (69%)	35/41 (85%)
CD14	0/25 (0%)	0/16 (0%)	0/41 (0%)
CD15	13/25 (52%)	2/16 (13%)	15/41 (37%)
CD25	10/25 (40%)	5/16 (31%)	15/41 (37%)
CD33	23/25 (92%)	14/16 (88%)	37/41 (90%)
CD34	17/25 (68%)	12/16 (75%)	19/41 (46%)
CD38	14/25 (56%)	8/16 (50%)	22/41 (54%)
CD56	3/25 (12%)	3/16 (19%)	6/41 (15%)
CD64	4/25 (16%)	2/16 (13%)	6/41 (15%)
CD117	24/25 (96%)	14/16 (88%)	38/41 (93%)
CD123	21/25 (84%)	10/16 (63%)	31/41 (76%)
HLA-DR	20/25 (80%)	12/16 (75%)	32/41 (78%)

Supplemental Table 4 Clinicopathologic features of 42 patients with pDC-AML

Patient	Sex	Age	Diagnosis (WHO Category)	Known MDS	Known CMML	Extramedullary Disease	Flowp pDCs (%)	Karyotype	Survival status	Overall Survival
Patient 01	M	78	AML-MRC	yes	no	No	2.3%	45,XY,-7[4]/46,XY[17]	Died	15.9
Patient 02	M	77	AML NOS	no	no	No	3.5%	47,XY,+13[2]/48,idem,+19[14]/46,XY[4]	Died	13.4
Patient 03	F	73	AML NOS	no	no	Leukemia cutis	3.7%	not performed	Died	6.7
Patient 04	M	67	AML NOS	no	no	Leukemia cutis	14.0%	47,XY,+13 [14]/46,XY [6]	Alive	41.7
Patient 05	M	80	AML NOS	yes	no	No	3.7%	45,X,-Y[19]/46,XY[1]	Died	24.3
Patient 06	M	72	AML NOS	no	no	No	20.5%	46,XY[20]	Died	1.0
Patient 07	M	77	AML NOS	no	no	No	5.1%	45,X,-Y,del(2)(p13p21)[21]	Died	3.5
Patient 08	M	47	AML-MRC	no	no	Leukemia cutis	5.5%	46,XY,add(7)(q32)[6]/ 92,XXYY[5]/46,XY[9]	Alive	9.8
Patient 09	M	74	AML-MRC	no	no	No	35.9%	46,XY,del(20)(q11.2q13.1)[16]/46,idem,der(7)t(1;7)(q21;q22)[5]	Died	18.8
Patient 10	M	72	AML-MRC	no	no	No	5.8%	48,XY,+8,+21[3]/46,XY[17]	Died	2.8
Patient 11	M	79	AML-MRC	yes	no	No	14.0%	46,XY[20]	Alive	6.9
Patient 12	F	62	AML-MRC	yes	no	No	4.1%	46,XX,t(8;21)(q11.2;q22)[2]/46,idem,del(3)(q12q29),del(17)(p11.2)[4]/46,XX[13]	Alive	0.0
Patient 13	F	44	AML NOS	no	no	No	7.7%	46,XX[20]	Alive	10.6
Patient 14	M	72	t-AML	no	no	No	2.6%	46,XY[1]/Outside 11/12/2018: 45,X-Y[3]/[46,XY[17]	Alive	5.3
Patient 15	F	76	AML-MRC	yes	no	No	9.8%	46,XX,t(15;21)(q21;q22)[17]/46,XX[3]	Died	4.9
Patient 16	M	74	AML NOS	no	no	No	2.5%	46,XY[20]	Died	36.3
Patient 17	F	14	t-AML	tMDS	no	No	10.4%	46,XX,del(5)(q22q35) [20]	Died	7.1
Patient 18	M	61	AML NOS	no	no	No	12.9%	46,XY[20]	Alive	8.7
Patient 19	M	68	AML NOS	no	no	No	8.1%	79-88<4n>,XXYY,-3,del(5)(q23q35)x2,-7,-7,-11,-16,-17,-21,inc[cp2]/46,XY[12]	Died	7.4
Patient 20	M	75	AML-MRC	yes	no	Leukemia cutis	8.2%	46,XY[20]	Died	9.8
Patient 21	M	81	AML NOS	no	no	No	5.4%	47,XY,t(4;6)(q31;q27),+13[1]/90~92,idemx2,inc[2]/46,XY[11]	Died	1.7
Patient 22	M	70	AML-MRC	yes	no	No	10.0%	46,XY[20]	Died	42.6
Patient 23	M	65	AML-MRC	yes	no	No	4.8%	46,XY,inv(4)(p15q21) [4]/46,XY [5]	Died	22.1
Patient 24	F	66	AML NOS	yes	yes	Lymph Node	13.2%	47,XX,+8[12]/46,XX[8]	Died	10.2
Patient 25	F	77	AML-MRC	no	no	No	2.1%	46,XX[20]	Alive	17.9
Patient 26	M	63	AML-MRC	yes	yes	Leukemia cutis		46,XY[20]	Alive	11.0
Patient 27	M	71	AML NOS	no	no	No	6.3%	46,XY[20]	Died	21.0
Patient 28	M	58	AML NOS	no	no	No	26.3%	46,XY[15]	Died	3.8
Patient 29	M	56	AML MRC	no	no	Lymph Node	3.5%	46,XY,+X,-7[16]/46,XY[4]	Alive	5.6
Patient 30	M	65	AML MRC	yes	no	No	5.9%	46,XY,del(9)(q22q32)[6]/46,idem,t(18;19)(q21;p13.3)[1]/46,idem,del(1)(q32)[1]/46,XY,del(9)(q12q34)[1]/46,XY[11]	Alive	16.6
Patient 31	F	68	AML NOS	no	no	No	4.6%	karyotype failure	Died	30.8
Patient 32	M	54	t-AML	no	no	No	3.0%	45,XY,-7[14]	Died	14.1
Patient 33	M	15	AML MRC	yes	no	No	7.7%	46,XY,dup(1)(q22q42)[8]/46,idem,add(6)(p23)[6]	Died	46.3
Patient 34	M	76	AML MRC	yes	no	No	2.2%	46,XY[14] use this was 46,XY,+1,der(1;7)(q10;p10)[8/12]	Died	51.8
Patient 35	M	78	AML MRC	yes	no	No	2.5%	46,XY[20]	Died	7.3
Patient 36	M	9	AML MRC	no	no	No	2.9%	45,XY,-7 [20]	Died	96.6
Patient 37	M	59	t-AML	no	no	No	3.3%	46,XY[20]	Alive	22.6

Patient 38	M	45	AML NOS	no	no	No	2.2%	46,XY[20]	Alive	43.6
Patient 39	F	76	AML NOS	no	no	No	9.2%	46,XX[20]	Died	13.0
Patient 40	F	65	AML NOS	no	no	No	2.5%	46,XX[20]	Died	14.6
Patient 41	M	29	AML NOS	no	no	No	4.4%	46,XY,?del(12)(p12)[3]/46,XY[22]	Alive	51.0
Patient 42	F	31	AML w NPM1	no	no	No	2.8%	46,XY[20]	Alive	13.3

Patients 1-26 were pDC-AML at diagnosis. Patients 27-42 were pDC-AML late (after diagnosis).

Supplemental Table 5. Mutational annotation of pDC-AML

PT#	Ploatform	Tm	chr	start pos	Gene	TxID	cDNA_annotation	AA_annotation	VAF	Annotation
1	RD	D	20	31022615	ASXL1	NM_015338	c.2101delC	p.P701fs	18.80%	Likely ONCOGENIC
1	RD	D	X	133551212	PHF6	NM_032458	c.848G>T	p.C283F	31.70%	Likely ONCOGENIC
1	RD	D	21	36259172	RUNX1	NM_001754	c.319C>T	p.R107C	14.40%	Likely ONCOGENIC
1	RD	D	X	133551305	PHF6	NM_032458	c.941T>C	p.I314T	15.00%	Likely ONCOGENIC
1	RD	D	4	106157989	TET2	NM_001127208	c.2890C>T	p.Q964X	18.40%	Likely ONCOGENIC
1	RD	F#1	20	31022615	ASXL1	NM_015338	c.2101delC	p.P701fs	41.50%	Likely ONCOGENIC
1	RD	F#1	X	133551212	PHF6	NM_032458	c.848G>T	p.C283F	70.40%	Likely ONCOGENIC
1	RD	F#1	21	36259172	RUNX1	NM_001754	c.319C>T	p.R107C	32.90%	Likely ONCOGENIC
1	RD	F#1	12	111856098	SH2B3	NM_005475	c.149G>A	p.R50Q	6.10%	UNKNOWN
1	RD	F#1	4	106157989	TET2	NM_001127208	c.2890C>T	p.Q964X	32.80%	Likely ONCOGENIC
2	RD	D	2	209113112	IDH1	NM_005896	c.395G>A	p.R132H	13.80%	ONCOGENIC
2	RD	D	21	36171683	RUNX1	NM_001754	c.881delC	p.P294fs	75.20%	Likely ONCOGENIC
3	RD	D	21	36231864	RUNX1	NM_001754	c.520A>C	p.T174P	36.90%	Likely ONCOGENIC
4	IMPACT	D	21	36164571	RUNX1	NM_001754	c.1303dupG	p.A435Gfs*165	6.50%	Likely ONCOGENIC
5	RD	D	20	31022989	ASXL1	NM_015338	c.2475_2476delAG	p.G826Nfs*6	24.73%	Likely ONCOGENIC
6	IMPACT	D	21	36259198	RUNX1	NM_001754	c.292delC	p.L98Sfs*24	53.80%	Likely ONCOGENIC
6	IMPACT	D	2	25467449	DNMT3A	NM_022552	c.1627G>T	p.G543C	42.70%	Likely ONCOGENIC
6	IMPACT	D	2	25463539	DNMT3A	NM_022552	c.2142_2143insGGTCAAACAAGCCC	p.I715Gfs*69	19.70%	Likely ONCOGENIC
7	RD	D	21	36259138	RUNX1	NM_001754	c.351+2T>C	Splicing	42.62%	Likely ONCOGENIC
7	RD	D	21	36259186	RUNX1	NM_001754	c.305T>C	p.L102P	10.31%	Likely ONCOGENIC
7	RD	D	17	30274671	SUZ12	NM_015355	c.422T>C	p.V141A	55.05%	UNKNOWN
8	IMPACT	D	1	115258747	NRAS	NM_002524	c.35G>C	p.G12A	2.40%	ONCOGENIC
8	IMPACT	D	21	36164685	RUNX1	NM_001754	c.1189delC	p.Q397Kfs*197	22.70%	Likely ONCOGENIC
8	IMPACT	D	17	74732959	SRSF2	NM_003016	c.284C>T	p.P95L	6.20%	ONCOGENIC
8	IMPACT	D	12	112888199	PTPN11	NM_002834	c.215C>G	p.A72G	16.70%	Likely ONCOGENIC
9	IMPACT	D	2	25966453	ASXL2	NM_015338	c.2752_2753delinsGGT	p.S918Gfs*8	17.00%	Likely ONCOGENIC
9	IMPACT	D	X	133511704	PHF6	NM_032458	c.59_70delinsTT	p.C20Ffs*10	33.40%	Likely ONCOGENIC
10	RD	D	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	16.10%	ONCOGENIC

10	RD	D	7	148514354	EZH2	NM_004456	c.1370G>A	p.C457Y	38.30%	UNKNOWN
10	RD	D	20	31023408	ASXL1	NM_015338	c.2893C>T	p.R965*	18.90%	ONCOGENIC
10	RD	D	21	36231783	RUNX1	NM_001754	c.601C>T	p.R201*	18.30%	ONCOGENIC
10	RD	F#1	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	10.95%	ONCOGENIC
10	RD	F#1	7	148514354	EZH2	NM_004456	c.1370G>A	p.C457Y	7.60%	UNKNOWN
10	RD	F#1	20	31023408	ASXL1	NM_015338	c.2893C>T	p.R965*	1.00%	ONCOGENIC
10	RD	F#1	9	5073770	JAK2	NM_004972	c.G1849T	p.V617F	0.10%	ONCOGENIC
10	RD	F#2	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	25.37%	ONCOGENIC
10	RD	F#2	7	148514354	EZH2	NM_004456	c.1370G>A	p.C457Y	44.25%	UNKNOWN
10	RD	F#2	20	31023408	ASXL1	NM_015338	c.2893C>T	p.R965*	18.04%	ONCOGENIC
10	RD	F#2	21	36231783	RUNX1	NM_001754	c.601C>T	p.R201*	7.67%	ONCOGENIC
10	RD	F#3	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	38.70%	ONCOGENIC
10	RD	F#3	7	148514354	EZH2	NM_004456	c.1370G>A	p.C457Y	70.51%	UNKNOWN
10	RD	F#3	20	31023408	ASXL1	NM_015338	c.2893C>T	p.R965*	26.94%	ONCOGENIC
10	RD	F#3	21	36231783	RUNX1	NM_001754	c.601C>T	p.R201*	37.43%	ONCOGENIC
10	RD	F#3	21	36259152	RUNX1	NM_001754	c.338_339insGCAG	p.I114Qfs*25	15.35%	Likely ONCOGENIC
10	RD	F#4	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	50.15%	ONCOGENIC
10	RD	F#4	7	148514354	EZH2	NM_004456	c.1370G>A	p.C457Y	92.35%	UNKNOWN
10	RD	F#4	13	28608260	FLT3	NM_004119	c.1795_1796insCCCTTGATTTCAGAGAATATGAAT	p.E598_Y599insSLDFREYE	3.10%	ONCOGENIC
10	RD	F#4	20	31023408	ASXL1	NM_015338	c.2893C>T	p.R965*	62.16%	ONCOGENIC
10	RD	F#4	21	36231783	RUNX1	NM_001754	c.601C>T	p.R201*	68.92%	ONCOGENIC
10	RD	F#4	21	36259152	RUNX1	NM_001754	c.338_339insGCAG	p.I114Qfs*25	48.17%	Likely ONCOGENIC
11	RD	D	7	148544353	EZH2	NM_004456	c.26_36delinsG	p.E9Gfs*8	24.79%	UNKNOWN
11	RD	D	7	148508721	EZH2	NM_004456	c.1943G>C	p.G648A	6.56%	UNKNOWN
11	RD	D	9	139399237	NOTCH1	NM_017617	c.4906G>A	p.E1636K	66.46%	UNKNOWN
11	RD	D	20	31022497	ASXL1	NM_015338	c.1982_1990delinsCTCT	p.R661Tfs*5	25.63%	Likely ONCOGENIC
11	RD	D	X	123211892	STAG2	NM_001042749	c.2759_2760insAA	p.L921Ifs*11	26.49%	Likely ONCOGENIC
11	RD	F#1	7	148544353	EZH2	NM_004456	c.26_36delinsG	p.E9Gfs*8	42.16%	UNKNOWN
11	RD	F#1	7	14850872	EZH2	NM_004456	c.1943G>C	p.G648A	31.14%	UNKNOWN

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11	RD	F#1	9	139399237	NOTCH1	NM_017617	c.4906G>A	p.E1636K	66.01%	UNKNOWN
11	RD	F#1	20	31022497	ASXL1	NM_015338	c.1982_1990delinsCTCT	p.R661Tfs*5	41.13%	Likely ONCOGENIC
11	RD	F#1	X	123211892	STAG2	NM_001042749	c.2759_2760insAA	p.L921Ifs*11	41.95%	Likely ONCOGENIC
12	IMPACT	D	21	36171718	RUNX1	NM_001754	c.847C>T	p.Q283*	76.00%	Likely ONCOGENIC
12	IMPACT	D	13	28592642	FLT3	NM_004119	c.2503G>T	p.D835Y	54.10%	ONCOGENIC
12	IMPACT	D	4	106158000	TET2	NM_001127208	c.2905delC	p.Q969Kfs*38	42.90%	Likely ONCOGENIC
12	IMPACT	D	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	46.80%	ONCOGENIC
12	IMPACT	D	17	7577099	TP53	NM_000546	c.839G>C	p.R280T	3.50%	ONCOGENIC
12	IMPACT	D	1	115256529	NRAS	NM_002524	c.182A>G	p.Q61R	38.50%	ONCOGENIC
12	IMPACT	D	X	39932146	BCOR	NM_001123385	c.2452_2453insGTCTCCTG	p.D818Gfs*41	70.80%	Likely ONCOGENIC
12	IMPACT	D	18	42531913	SETBP1	NM_015559	c.2608G>A	p.G870S	4.70%	ONCOGENIC
12	IMPACT	D	2	198267371	SF3B1	NM_012433	c.1986C>A	p.H662Q	47.70%	Likely ONCOGENIC
12	IMPACT	D	20	31022468	ASXL1	NM_015338	c.1955dupG	p.G653Rfs*5	40.00%	Likely ONCOGENIC
13	RD	D	17	74732935	SRSF2	NM_003016	c.284_307delCCCCGGACTCACACCACAGCCGCC	p.P95_R102del	39.48%	ONCOGENIC
13	RD	D	X	39922106	BCOR	NM_001123385	c.4066A>T	p.K1356*	65.99%	ONCOGENIC
13	RD	D	21	36252878	RUNX1	NM_001754	c.484A>G	p.R162G	58.40%	Likely ONCOGENIC
14	RD	D	1	115258747	NRAS	NM_002524	c.35G>A	p.G12D	36.40%	ONCOGENIC
14	RD	D	21	36231791	RUNX1	NM_001754	c.593A>G	p.D198G	44.40%	Likely ONCOGENIC
15	RD	D	2	25464525	DNMT3A	NM_022552	c.1988C>T	p.S663L	11.00%	UNKNOWN
15	RD	D	21	44524456	U2AF1	NM_006758	c.101C>T	p.S34F	37.00%	ONCOGENIC
15	RD	D	21	36259175	RUNX1	NM_001754	c.314_315delAC	p.H105Lfs*32	26.50%	Likely ONCOGENIC
16	IMPACT	D	X	133551305	PHF6	NM_032458	c.941T>C	p.I314T	26.19%	Likely ONCOGENIC
16	IMPACT	D	13	28608320	FLT3	NM_004119	c.1736T>A	p.V579E	18.84%	Likely ONCOGENIC
16	IMPACT	D	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	44.85%	Likely ONCOGENIC
16	IMPACT	D	X	133551305	PHF6	NM_032458	c.941T>C	p.I314T	63.88%	Likely ONCOGENIC
17	RD	D	20	31022547	ASXL1	NM_015338	c.2036delG	p.G679Efs*24	12.68%	Likely ONCOGENIC
17	RD	D	21	36259198	RUNX1	NM_001754	c.292delC	p.L98Sfs*24	5.41%	Likely ONCOGENIC
17	RD	F#1	20	31022547	ASXL1	NM_015338	c.2036delG	p.G679Efs*24	28.29%	Likely ONCOGENIC

17	RD	F#1	21	36259198	RUNX1	NM_001754	c.292delC	p.L98Sfs*24	25.53%	Likely ONCOGENIC
17	RD	F#1	21	36252865	RUNX1	NM_001754	c.497G>T	p.R166L	7.11%	LIKELY ONCOGENIC
17	RD	F#1	21	36252877	RUNX1	NM_001754	c.485G>A	p.R162K	10.48%	Likely ONCOGENIC
17	RD	F#1	X	44938515	KDM6A	NM_021140	c.3063G>A	p.W1021*	31.87%	UNKNOWN
17	RD	F#1	4	106156042	TET2	NM_001127208	c.945delC	p.Q317Rfs*30	11.50%	Likely ONCOGENIC
17	RD	F#1	4	106164866	TET2	NM_001127208	c.3734A>G	p.Y1245C	12.25%	Likely ONCOGENIC
17	RD	F#1	21	36206762	RUNX1	NM_001754	c.749_750insGTTGACCC	p.A251Lfs*6	58.92%	Likely ONCOGENIC
17	RD	F#1	X	39931909	BCOR	NM_001123385	c.2690C>A	p.S897*	69.72%	ONCOGENIC
18	IMPACT	D	1	115258674	NRAS	NM_002524	c.108A>G	p.I36M	46.60%	UNKNOWN
18	IMPACT	D	20	31022441	ASXL1	NM_015338	c.1934dupG	p.G646Wfs*12	35.10%	ONCOGENIC
18	IMPACT	D	21	36171751	RUNX1	NM_001754	c.814C>T	p.Q272*	34.90%	Likely ONCOGENIC
18	IMPACT	D	X	39922119	BCOR	NM_001123385	c.4051_4052delAC	p.T1351Rfs*57	86.40%	Likely ONCOGENIC
18	IMPACT	D	X	133559265	PHF6	NM_032458	c.1003A>T	p.R335*	91.60%	ONCOGENIC
18	IMPACT	D	X	39922124	BCOR	NM_001123385	c.4048T>A	p.Y1350N	87.90%	UNKNOWN
19	IMPACT	D	12	49428194	KMT2D	NM_003482	c.10505_10506insTTTACCC	p.N3503Lfs*4	7.62%	Likely ONCOGENIC
19	IMPACT	D	2	198267705	SF3B1	NM_012433	c.1774G>A	p.E592K	18.93%	UNKNOWN
19	IMPACT	D	20	31022402	ASXL1	NM_015338	c.1900_1922delAGAGAGGCGGCCACCACTGCCAT	p.E635Rfs*15	19.79%	Likely ONCOGENIC
19	IMPACT	D	21	36252865	RUNX1	NM_001754	c.497G>A	p.R166Q	17.55%	LIKELY ONCOGENIC
19	IMPACT	D	4	106190860	TET2	NM_001127208	c.4138C>T	p.H1380Y	17.10%	Likely ONCOGENIC
19	IMPACT	D	8	117874082	RAD21	NM_006265	c.371_372insTGAGGGCGGA	p.L124Ffs*6	5.66%	UNKNOWN
19	IMPACT	D	X	133547940	PHF6	NM_032458	c.673C>T	p.R225*	20.24%	ONCOGENIC
20	IMPACT	D	1	115258747	NRAS	NM_002524	c.35G>T	p.G12V	13.40%	ONCOGENIC
20	IMPACT	D	12	25398285	KRAS	NM_033360	c.34G>C	p.G12R	2.40%	ONCOGENIC
20	IMPACT	D	4	106193931	TET2	NM_001127208	c.4393C>T	p.R1465*	16.00%	Likely ONCOGENIC
20	IMPACT	D	4	106157326	TET2	NM_001127208	c.2227C>T	p.Q743*	52.90%	Likely ONCOGENIC
20	IMPACT	D	11	119148919	CBL	NM_005188	c.1139T>C	p.L380P	21.50%	Likely ONCOGENIC
20	IMPACT	D	17	74732959	SRSF2	NM_003016	c.284C>T	p.P95L	34.00%	Likely ONCOGENIC
21	OSH	D	1	115258747	NRAS	NM_002524	c.35G>T	p.G12V	37.00%	ONCOGENIC

21	OSH	D	21	36171607	RUNX1	NM_001754	c.958C>T	p.R320*	17.00%	Likely ONCOGENIC
21	OSH	D	21	36259172	RUNX1	NM_001754	c.319C>T	p.R107C	16.50%	Likely ONCOGENIC
21	OSH	D	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	42.00%	ONCOGENIC
21	OSH	D	20	31022402	ASXL1	NM_015338	c.1900_1922delAGAGAGGCGGCCACCACTGCCAT	p.E635fs*15	26.00%	Likely ONCOGENIC
22	RD	D	2	198267359	SF3B1	NM_012433	c.1998G>T	p.K666N	46.90%	Likely ONCOGENIC
22	RD	D	21	36231774	RUNX1	NM_001754	c.610C>T	p.R204*	50.00%	Likely ONCOGENIC
22	RD	D	13	28592642	FLT3	NM_004119	c.2503G>T	p.D835Y	2.10%	ONCOGENIC
22	RD	D	2	25469964	DNMT3A	NM_022552	c.1078A>G	p.N360D	10.00%	UNKNOWN
23	IMPACT	D	21	36231782	RUNX1	NM_001754	c.602G>A	p.R201Q	14.40%	ONCOGENIC
23	IMPACT	D	2	25464537	DNMT3A	NM_022552	c.1976G>A	p.R659H	31.80%	Likely ONCOGENIC
23	IMPACT	D	2	25468159	DNMT3A	NM_022552	c.1513_1516delGAAC	p.E505Tfs*145	19.50%	Likely ONCOGENIC
23	IMPACT	D	21	44514777	U2AF1	NM_006758	c.470A>G	p.Q157R	13.60%	ONCOGENIC
23	IMPACT	D	14	81558933	TSHR	NM_000369	c.526T>C	p.C176R	14.50%	UNKNOWN
23	IMPACT	D	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	15.30%	ONCOGENIC
24	RD	D	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	36.40%	ONCOGENIC
24	RD	D	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	34.80%	ONCOGENIC
24	RD	D	21	36171710	RUNX1	NM_001754	c.855C>G	p.Y285X	28.70%	ONCOGENIC
24	RD	F#1	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	23.70%	ONCOGENIC
24	RD	F#1	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	33.80%	ONCOGENIC
24	RD	F#1	21	36171710	RUNX1	NM_001754	c.855C>G	p.Y285X	16.70%	ONCOGENIC
24	RD	F#1	21	36252954	RUNX1	NM_001754	c.408T>G	p.N136K	33.20%	Likely ONCOGENIC
24	RD	F#2	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	41.80%	ONCOGENIC
24	RD	F#2	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	43.60%	ONCOGENIC
24	RD	F#2	21	36171710	RUNX1	NM_001754	c.C855G	p.Y285X	25.20%	ONCOGENIC
24	RD	F#2	21	36252954	RUNX1	NM_001754	c.408T>G	p.N136K	44.90%	Likely ONCOGENIC
24	RD	F#3	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	46.80%	ONCOGENIC
24	RD	F#3	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	47.40%	ONCOGENIC
24	RD	F#3	21	36171710	RUNX1	NM_001754	c.855C>G	p.Y285X	24.50%	ONCOGENIC
24	RD	F#3	21	36252954	RUNX1	NM_001754	c.408T>G	p.N136K	48.10%	Likely ONCOGENIC

24	RD	F#4	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	17.60%	ONCOGENIC
24	RD	F#4	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	22.20%	ONCOGENIC
24	RD	F#4	21	36171710	RUNX1	NM_001754	c.855C>G	p.Y285X	7.00%	ONCOGENIC
24	RD	F#4	21	36252954	RUNX1	NM_001754	c.408T>G	p.N136K	13.80%	Likely ONCOGENIC
24	RD	F#5	2	25457243	DNMT3A	NM_022552	c.C2644T	p.R882C	46.01%	ONCOGENIC
24	RD	F#5	15	90631934	IDH2	NM_002168	c.G419A	p.R140Q	47.45%	ONCOGENIC
24	RD	F#5	21	36252954	RUNX1	NM_001754	c.408T>G	p.N136K	41.02%	Likely ONCOGENIC
25	RD	D	2	209113113	IDH1	NM_005896	c.394C>T	p.R132C	41.41%	ONCOGENIC
25	RD	D	2	25457242	DNMT3A	NM_022552	c.2645G>A	p.R882H	41.72%	Likely ONCOGENIC
25	RD	D	2	25464516	DNMT3A	NM_022552	c.1997G>A	p.C666Y	40.78%	UNKNOWN
25	RD	D	11	32456486	WT1	NM_024426	c.406C>T	p.P136S	27.75%	UNKNOWN
25	RD	D	11	32456248	WT1	NM_024426	c.643_644insCG	p.Q215fs	34.95%	UNKNOWN
25	RD	D	13	28592642	FLT3	NM_004119	c.2503G>C	p.D835H	38.39%	ONCOGENIC
25	RD	D	19	33792937	CEBPA	NM_004364	c.383dupC	p.P129fs	29.58%	Likely ONCOGENIC
25	RD	D	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	26.06%	Likely ONCOGENIC
25	RD	F#1	2	209113113	IDH1	NM_005896	c.394C>T	p.R132C	18.99%	ONCOGENIC
25	RD	F#1	2	25457242	DNMT3A	NM_022552	c.2645G>A	p.R882H	26.53%	Likely ONCOGENIC
25	RD	F#1	2	25464516	DNMT3A	NM_022552	c.1997G>A	p.C666Y	27.08%	UNKNOWN
25	RD	F#1	11	32456486	WT1	NM_024426	c.406C>T	p.P136S	33.60%	UNKNOWN
25	RD	F#1	11	32456248	WT1	NM_024426	c.643_644insCG	p.Q215fs	12.85%	UNKNOWN
25	RD	F#1	13	28592642	FLT3	NM_004119	c.2503G>C	p.D835H	11.95%	ONCOGENIC
25	RD	F#1	19	33792937	CEBPA	NM_004364	c.383dupC	p.P129fs	9.72%	Likely ONCOGENIC
25	RD	F#1	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	10.12%	Likely ONCOGENIC
25	RD	F#2	2	209113113	IDH1	NM_005896	c.394C>T	p.R132C	44.85%	ONCOGENIC
25	RD	F#2	2	25457242	DNMT3A	NM_022552	c.2645G>A	p.R882H	37.30%	Likely ONCOGENIC
25	RD	F#2	2	25464516	DNMT3A	NM_022552	c.1997G>A	p.C666Y	51.25%	UNKNOWN
25	RD	F#2	11	32456486	WT1	NM_024426	c.406C>T	p.P136S	46.80%	UNKNOWN
25	RD	F#2	11	32456248	WT1	NM_024426	c.643_644insCG	p.Q215fs	41.55%	UNKNOWN
25	RD	F#2	13	28592642	FLT3	NM_004119	c.2503G>C	p.D835H	37.46%	ONCOGENIC
25	RD	F#2	19	33792937	CEBPA	NM_004364	c.383dupC	p.P129fs	46.26%	Likely ONCOGENIC

25	RD	F#2	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	36.74%	Likely ONCOGENIC
25	RD	F#3	2	209113113	IDH1	NM_005896	c.394C>T	p.R132C	43.29%	ONCOGENIC
25	RD	F#3	2	25457242	DNMT3A	NM_022552	c.2645G>A	p.R882H	41.15%	Likely ONCOGENIC
25	RD	F#3	2	25464516	DNMT3A	NM_022552	c.1997G>A	p.C666Y	40.46%	UNKNOWN
25	RD	F#3	11	32456486	WT1	NM_024426	c.406C>T	p.P136S	34.81%	UNKNOWN
25	RD	F#3	11	32456248	WT1	NM_024426	c.643_644insCG	p.Q215fs	38.68%	UNKNOWN
25	RD	F#3	13	28592642	FLT3	NM_004119	c.2503G>C	p.D835H	37.28%	ONCOGENIC
25	RD	F#3	19	33792937	CEBPA	NM_004364	c.383dupC	p.P129fs	27.99%	Likely ONCOGENIC
25	RD	F#3	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	29.87%	Likely ONCOGENIC
25	RD	F#4	2	209113113	IDH1	NM_005896	c.394C>T	p.R132C	44.88%	ONCOGENIC
25	RD	F#4	2	25457242	DNMT3A	NM_022552	c.2645G>A	p.R882H	52.79%	Likely ONCOGENIC
25	RD	F#4	2	25464516	DNMT3A	NM_022552	c.1997G>A	p.C666Y	43.93%	UNKNOWN
25	RD	F#4	11	32456486	WT1	NM_024426	c.406C>T	p.P136S	29.57%	UNKNOWN
25	RD	F#4	11	32456248	WT1	NM_024426	c.643_644insCG	p.Q215fs	47.15%	UNKNOWN
25	RD	F#4	13	28592642	FLT3	NM_004119	c.2503G>C	p.D835H	46.57%	ONCOGENIC
25	RD	F#4	19	33792937	CEBPA	NM_004364	c.383dupC	p.P129fs	44.76%	Likely ONCOGENIC
25	RD	F#4	21	36252994	RUNX1	NM_001754	c.366_367dupGG	p.D123Gfs*11	32.76%	Likely ONCOGENIC
26	RD	F#1	21	36252865	RUNX1	NM_001754	c.497G>A	p.R166Q	41.20%	Likely ONCOGENIC
27	RD	F#1	2	209113113	IDH1	NM_005896	c.394C>A	p.R132S	29.37%	Likely ONCOGENIC
27	RD	F#1	2	25467408	DNMT3A	NM_022552	c.1667+1G>A	p.X556_splice	89.10%	ONCOGENIC
27	RD	F#1	17	7577091	TP53	NM_000546	c.847C>T	p.R283C	65.57%	ONCOGENIC
27	RD	F#1	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	43.85%	ONCOGENIC
27	RD	F#1	X	53430498	SMC1A	NM_006306	c.2420G>A	p.R807H	10.94%	UNKNOWN
28	RD	F#1	1	115258748	NRAS	NM_002524	c.34G>A	p.G12S	6.32%	ONCOGENIC
28	RD	F#1	4	55599321	KIT	NM_000222	c.2447A>T	p.D816V	10.08%	ONCOGENIC
28	RD	F#1	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	47.38%	ONCOGENIC
29	RD	F#1	21	36164485	RUNX1	NM_004364	c.1390A>T	p.T464S	9.50%	UNKNOWN
30	RD	F#1	4	106156364	TET2	NM_001127208	c.1270dupA	p.S424Kfs*19	38.97%	Likely ONCOGENIC
30	RD	F#1	4	106182916	TET2	NM_001127208	c.3957delA	p.E1320Rfs*43	44.09%	Likely ONCOGENIC
30	RD	F#1	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	4.52%	ONCOGENIC

30	RD	F#1	X	123197782	STAG2	NM_001042749	c.1907dupA	p.Y636*	5.80%	Likely ONCOGENIC
30	RD	F#1	X	133511705	PHF6	NM_032458	c.58T>A	p.C20S	89.86%	UNKNOWN
31	RD	F#1	21	44524456	U2AF1	NM_006758	c.101C>T	p.S34F	12.34%	ONCOGENIC
31	RD	F#1	21	36252878	RUNX1	NM_001754	c.484A>G	p.R162G	7.03%	Likely ONCOGENIC
31	RD	F#1	21	36231774	RUNX1	NM_001754	c.593_609delATGGGCCCCGAGAACCT	p.D198Afs*9	6.21%	ONCOGENIC
32	RD	F#1	17	7578404	TP53	NM_000546	c.526T>G	p.C176G	2.15%	ONCOGENIC
32	RD	F#1	17	7578406	TP53	NM_000546	c.524G>A	p.R175H	4.28%	ONCOGENIC
32	RD	F#1	17	74732959	SRSF2	NM_003016	c.284C>T	p.P95L	12.02%	Likely ONCOGENIC
32	RD	F#1	21	36231797	RUNX1	NM_001754	c.587C>A	p.T196K	16.21%	Likely ONCOGENIC
32	RD	F#1	18	42531907	SETBP1	NM_015559	c.2602G>A	p.D868N	4.74%	ONCOGENIC
33	RD	F#1	12	25398285	KRAS	NM_033360	c.34G>A	p.G12S	9.41%	ONCOGENIC
33	RD	F#1	21	36231782	RUNX1	NM_001754	c.602G>A	p.R201Q	11.07%	ONCOGENIC
33	RD	F#1	12	11992079	ETV6	NM_001987	c.169C>T	p.Q57*	6.22%	UNKNOWN
33	RD	F#1	19	13054704	CALR	NM_004343	c.1231G>A	p.G411S	44.64%	UNKNOWN
33	RD	F#1	2	25463286	DNMT3A	NM_022552	c.2207G>A	p.R736H	8.04%	Likely ONCOGENIC
33	RD	F#1	20	31023691	ASXL1	NM_015338	c.3178dupG	p.V1060Gfs*27	5.66%	Likely ONCOGENIC
33	RD	F#1	4	106164741	TET2	NM_001127208	c.3609C>G	p.S1203R	39.81%	UNKNOWN
33	RD	F#1	7	148544291	EZH2	NM_004456	c.100C>T	p.R34*	23.27%	UNKNOWN
33	RD	F#1	7	148543659	EZH2	NM_004456	c.149T>C	p.L50S	25.90%	UNKNOWN
34	IMPACT	F#1	21	36231791	RUNX1	NM_001754	c.593A>G	p.D198G	2.80%	Likely ONCOGENIC
34	IMPACT	F#1	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	5.40%	ONCOGENIC
34	IMPACT	F#1	4	106193748	TET2	NM_001127208	c.4210C>T	p.R1404*	5.30%	Likely ONCOGENIC
34	IMPACT	F#1	20	31022441	ASXL1	NM_015338	c.1934dupG	p.G646Wfs*12	22.20%	Likely ONCOGENIC
35	IMPACT	F#1	21	36259325	RUNX1	NM_001754	c.165delG	p.L56Cfs*16	2.00%	Likely ONCOGENIC
35	IMPACT	F#1	4	106158198	TET2	NM_001127208	c.2482delT	p.C828Afs*13	43.40%	Likely ONCOGENIC
35	IMPACT	F#1	4	106157580	TET2	NM_001127208	c.3100delC	p.Q1034Sfs*21	3.00%	Likely ONCOGENIC
35	IMPACT	F#1	4	187541413	FAT1	NM_005245	c.6327C>G	p.D2109E	9.20%	UNKNOWN
35	IMPACT	F#1	1	1:43818431	MPL	NM_005373	c.1896G>T	p.W632C	5.50%	UNKNOWN
35	IMPACT	F#1	12	112888189	PTPN11	NM_002834	c.205G>A	p.E69K	12.30%	Likely ONCOGENIC
35	IMPACT	F#1	17	74732959	SRSF2	NM_003016	c.284C>G	p.P95R	13.10%	Likely ONCOGENIC

36	IMPACT	F#1	20	31022441	ASXL1	NM_015338	c.1934dupG	p.G646Wfs*12	17.30%	Likely ONCOGENIC
37	IMPACT	F#1	4	106196487	TET2	NM_001127208	c.4823_4824delAT	p.Y1608Ffs*5	45.10%	Likely ONCOGENIC
37	IMPACT	F#1	17	7578208	TP53	NM_000546	c.641A>G	p.H214R	39.70%	Likely ONCOGENIC
37	IMPACT	F#1	17	74732959	SRSF2	NM_003016	c.284C>A	p.P95H	44.60%	ONCOGENIC
38	RD	F#1	21	36164448	RUNX1	NM_001754	c.1427A>C	p.V476A	1.20%	UNKNOWN
38	RD	F#1	1	36932040	CSF3R	NM_000760	c.2429A>G	p.D810G	46.10%	UNKNOWN
38	RD	F#1	5	170837543	NPMI	NM_002520	c.860_863dupTCTG	p.W288Cfs*12	3.30%	Likely ONCOGENIC
38	RD	F#1	2	209113113	IDH1	NM_005896	c.394C>A	p.R132S	2.40%	Likely ONCOGENIC
39	IMPACT	F#1	6	15374449	JARID2	NM_004973	c.148_149insCG	E50Afs*8	87.00%	Likely ONCOGENIC

RD, raindance; D, diagnosis; F, follow-up.

Supplemental Table 6 Summary of primary PDX mice

Patients	NSG mice	Cells injected/mouse	hCD45 (%) in PB		hCD45 (%) in BM	Leukemic blasts	pDCs	Lymphocytes	Transplantable in 2° PDX mice
			3 months	6 months					
001	1	1.3 million	2.86	59.2	99	Y	Y	N	Y
	2	1.3 million	4.44	55.9	95	Y	Y	N	Y
	3	1.3 million	7.28	53.7	97.1	Y	Y	N	Y
002	1	374 000	15.3	16	5	N	N	Y	N
	2	374 000	43.9		35	N	N	Y	N
003	1	300 000	0.39	2.59	0.9	N	N	Y	N
	2	300 000	0.36	5.98	1.0	N	N	Y	N
004	1	186 000		1.85	0.5	N	N	Y	N
	2	186 000		1.80	0.4	N	N	Y	N
005	1	600 000	0.15		0.09	N	N	Y	N
	2	600 000	0.16		0.2	N	N	Y	N
	3	600 000	0.18		0.1	N	N	Y	N
006	1	2 million	10		4.22	N	Y (0.2%)	Y	N
	2	2 million	5.1[a]						
	3	2 million	24.5		7.64	N	Y (1.8%)	Y	N
	4	2 million	70		18.9	N	Y (2.6%)	Y	N
	5	2 million	10.3[a]						
	6	2 million	8.3[a]						
	7	2 million	died						

a: mice died after 3 months evaluation.

Reference

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