Pediatric blastic plasmacytoid dendritic cell neoplasms are molecularly defined by recurrent *MYB* rearrangements: clinical and molecular insights

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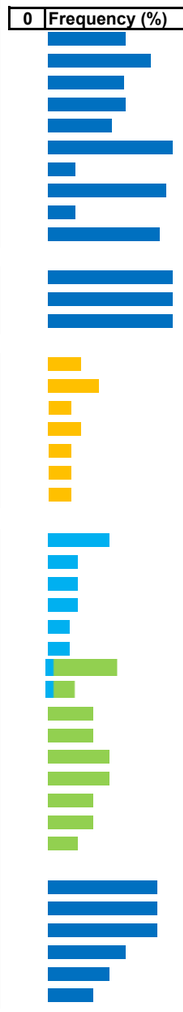
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Supplementary Figure S1. Integrated clinicogenomic landscape of pediatric BPDCN (n=21).

Columns represent individual cases. Tracks depict specimen type used for molecular testing, assays performed, clinical involvement at diagnosis (skin, bone marrow [BM], lymph node [LN], and central nervous system [CNS]), treatment exposures, response and relapse, immunophenotype, structural variants (including *MYB*-region alterations), selected somatic variants, and copy-number alterations and tumor ploidy. Colors and symbols are defined in the key; "*" denotes venetoclax exposure and "&" denotes CD123-directed CAR T-cell therapy. Percentages are calculated using cases with available data, and denominators vary by feature.

Abbreviations: BM, bone marrow; CNS, central nervous system; CN-LOH, copy-neutral loss of heterozygosity; CNV, copy-number variation; HSCT, hematopoietic stem cell transplant

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Specimen for molecular test																						
RNA sequencing/RNA fusion panel																						
Whole-exome/genome sequencing																						
Targeted sequencing (DNA-based)																						
Clinical information	**No./N (%)**																					
Gender, Male	12 (57)																					
Initial skin involvement	16 (80)																					
Initial BM involvement	9 (56)																					
Initial LN involvement	8 (57)																					
CNS involvement	5 (45)																					
Remission during therapy	17 (100)																					
Relapse	2 (12)																					
ALL-type therapy	16 (94)			*		*&	*															
HSCT	2 (12)																					
Outcome, alive	15 (88)																					
Immunophenotype																						
CD56+	21 (100)																					
CD123+	21 (100)																					
TCF4+	6 (100)																					
Rearrangements (tested cases, n=12)																						
MYB::PLEKHO1	2 (17)																					
MYB::DCPS	4 (33)																					
MYB::ZFAT	1 (8)																					
MYB trunc	2 (17)																					
MYBL1::MTFR1	1 (8)																					
ETV6 translocation/trunc	1 (8)																					
HBS1L::UGCG	1 (8)																					
Mutations (tested cases: SNV/indels, n= 14; CNV, n= 7)																						
NRAS	6 (43)																					
KRAS	2 (14)																					
RB1	2 (14)																					
KMT2C/KMT2D	2 (14)																					
CDKN1C	1 (7)																					
NF1	1 (7)																					
IKZF1	1 (7), 3 (43)																					
TP53	1 (7), 1 (14)																					
ABL1 deletion	2 (28)																					
ETV6 deletion	2 (28)																					
CDKN2A	3 (43)																					
CDKN2B	3 (43)																					
JAK1/2 deletion	2 (28)																					
NOTCH1 deletion	2 (28)																					
TCF4 deletion	1 (14)																					
Tumor ploidy& cytogenetics (tested cases, n=7)																						
9q deletion/monosomy	6 (86)																					
12p deletion	6 (86)																					
13q deletion/monosomy	6 (86)																					
17p deletion	4 (57)																					
6q deletion	3 (43)																					
5q deletion/gain	2 (28)																					



Bone marrow
Soft tissue
Skin

Yes/Positive
No/Negative
Not available/Not tested
Inadequate RNA quality

Structural variants
SNV/indels
CNV

Complex karyotype
* Venetoclax therapy
& CD123 CAR-T cell therapy

Supplementary Table S1. Clinical, cytogenetic, and molecular findings in the pediatric blastic plasmacytoid dendritic cell neoplasm cohort (n = 21).

Case no.	Treatment	Follow-up, mo	Response; Outcome	Specimen; Molecular test method	Fusion; Variants (SNV/indel; CNV)	Coordinates/description	Tumor ploidy (CNV/CN-LOH); Karyotype
Case 1	ALL-type therapy	10	Remission; Alive	Skin; RNA-seq, WES	*MYB::PLEKHO1* t(1;6)(q21.2;q23.3); *KRAS* G12C	chr6:135196002::chr1:150158819	
				Bone marrow; RNA-seq, WES, WGS	Not detected		
Case 2	ALL-type therapy	12	Remission; Alive	Skin; RNA-seq, WES	*MYB::PLEKHO1* t(1;6)(q21.2;q23.3); *CNOT3* E70K, *NRAS* Q61P, *RB1* c.-197G>A, TCF4 deletion (1 copy)	chr6:135517140::chr1:150131014	Loss: 5q23, chr. 9, 12p, chr.13, chr.Y; Gain: none; CN-LOH: none
Case 3	ALL-type therapy; Venetoclax	12	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	*MYB::DCPS* t(6;11)(q23.3;q24.2); Not detected		
Case 4	ALL-type therapy	50	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	*MYB* structural variant (truncated); *NRAS* Q61H	Structural variant involving *MYB* (C-terminal truncation of *MYB* after exon 9).	
Case 5	ALL-type therapy; Venetoclax; tagraxofusp	23	Remission/relapse; Alive with disease	Bone marrow; RNA-seq, WES, WGS	*MYB::DCPS* t(6;11)(q23.3;q24.2); *ETV6* trunc t(8;12)(q24.3;p13.2); *RB1* C712R, *TP53* P278S, *CDKN2A*/*CDKN2B* deletion (1 copy each), *NR3C1* del, *MUTYH* Ala385ProfsTer23 (germline)	chr6:135515600::chr11:126176465	Loss: 2q32.1-q37.3, 6q23.3-q27, 8p23.3-q13.1, 9q12-q31.3, 10p15.3-p11.22, 17p13.3-q11.2, 22q11.21-q13.33; Gain: 5q34-q35.3, 11q13.4-q24.2, 11q24.2-q25; CN-LOH: none; Karyotype: Complex; involving del(6)(q?23),del(12)(p?12),-17
Case 6	ALL-type therapy; Venetoclax	5	Remission; Alive, treatment abandoned	Skin; RNA-seq, WES	*HBS1L::UGCG* t(6;9)(q23.3;q31.3); *NRAS* G12S, *IKZF1* Q149*	chr6:135359170::chr9:114688664	
Case 7				Skin; RNA-seq, NGS (DNA-based)	*MYB::DCPS* t(6;11)(q23.3;q24.2); *NRAS* G12D, *KMT2D* Q5170*		
Case 8	ALL-type therapy	120	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	*MYB* structural variant (truncated); Not detected	Structural variant involving *MYB* (C-terminal truncation of *MYB* after exon 9).	
Case 9	ALL-type therapy	108	Remission; Alive	Bone marrow; RNA-seq	*MYB::ZFAT* t(6;8)(q23;q24)	chr6:135517140::chr8:135529901	46,XX,t(2;9)(q37;q13),add(3)(p25),add(12)(p11.2),del(13)(q12),del(14)(q13);46,XX(3)
Case 10				Skin; RNA-seq, NGS (DNA-based)	Not detected; Inadequate DNA quality		
Case 11	ALL-type therapy	72	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; *KRAS* Q61R		69-79 (unbanded)[7/41], 84-90 (unbanded)[2/11], 46,XY[8/47]
Case 12	ALL-type therapy	144	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; *CDKN1C* p.208_210del		
Case 13	ALL-type therapy	132	Remission; Alive	Skin; RNA-seq, NGS (DNA-based)	Inadequate RNA quality; *KMT2C* Q1186*		
Case 14	ALL-type therapy	84	Remission; Alive	Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		45,XY,-9,del(12)(p11.2),-13,del(17)(p11.2),+mar(20)
Case 15				Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		
Case 16	ALL-type therapy	168	Remission; Alive	Skin; RNA-seq; NGS (DNA-based)	Inadequate DNA& RNA quality		
Case 17	AML-type therapy	17	Remission/relapse; Died				
Case 18	ALL-type therapy	48	Remission; Alive				
Case 19	ALL-type therapy	8	Remission; Died (infection)	Bone marrow; NGS (DNA-based)			Loss: 1p (*JAK1*), 7p (*IKZF1*), 9q (*ABL1*& *NOTCH1*), 17p (*PRPF8*& *TP53*); Gain: Xq (*BRCC3*); Karyotype: 83~85,XXYY,-3,add(6)(q11),del(6)(q13q23),add(7)(p11.2),-8,-9,add(11)(p15),-12,-13,-13,-14,-15,-17,add(17)(p11.1),-18,+0~4mar[cp8]/46,XY[12]
Case 20	ALL-type therapy	17	Remission; Alive	Bone marrow; RNA fusion panel (Archer); NGS (DNA-based)	*MYB::DCPS; NRAS A146V, NF1 H586fs*		Loss: 7p (1 copy *IKZF1*), 9p (1 copy deletion *JAK2*, *CDKN2A*, *CDKN2B*); 9q (1 copy deletion *ABL1*, *NOTCH1*); 11q (1 copy deletion *ATM*, *KMT2A*, *CBL*), 12p (1 copy deletion *ETV6*); Karyotype: 43~44,XX,del(6)(q23q27),-9,del(11)(q21q23),der(12)t(12;14)(p13;q11.2),-13,-14,add(17)(p11.2),+0~1r[cp5]/46,XX[15]
Case 21				Nasal soft tissue; RNA fusion panel (Archer); NGS (DNA-based)	*MYBL1::MTFR1; NRAS G12A*		Loss: 7p (*IKZF1*), 9p (*CDKN2A*/*CDKN2B*/*MTAP*), 3p, 9q, 12p, 13q, and 17p

Abbreviations: CN-LOH, copy-neutral loss of heterozygosity; CNV, copy-number variation; mo, months; NGS, next-generation sequencing; RNA-seq, RNA sequencing; SNV, single-nucleotide variant; WES, whole-exome sequencing; WGS, whole-genome sequencing. When multiple specimens were tested for a case, the results are listed on separate rows (case 1).

Supplementary Table S2. Clinical and molecular findings in pediatric patients (≤ 20 years old) investigated by molecular tests: literature review. Patients with *MYB* alteration (including cases with presumptive *MYB* alteration of 6q abnormality based on cytogenetics) are highlighted in pink.

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Supplementary Table S2 is provided as a separate Excel file.