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

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Running heads: Pediatric BPDCN with *MYB* rearrangement

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Blastic plasmacytoid dendritic cell neoplasm (BPDCN) is a rare, aggressive hematologic malignancy of plasmacytoid dendritic cells (pDCs); recent data support skin-based transformation influenced by ultraviolet exposure. [1] Pediatric BPDCN is uncommon (<100 reported cases), and typically presents in children and adolescents without the strong male predominance and clonal myeloid neoplasm association seen in adults.[2-4] Although many children achieve remission with ALL-type regimens, relapses and central nervous system (CNS) disease remain clinically relevant and have motivated incorporation of venetoclax, CD123-targeted therapies, and hematopoietic stem cell transplantation (HSCT) in selected cases. [2, 5-7] Diagnosis relies on pDC-associated markers such as TCF4, CD303, and TCL1, with variable expression of lineage-associated antigens alongside CD4, CD56, and CD123.[2, 4, 8] Genetically, pediatric BPDCN frequently shows copy-number abnormalities involving 13q14 (*RB*1), 9p21.3 (*CDKN2A/B*), 12p13 (*ETV*6, *CDKN1B*), and 7p12 (*IKZF1*).[9] Importantly, *MYB* rearrangements are more prevalent in pediatric BPDCN (~90%) than in adult disease (~44%).[10] However, the full spectrum of *MYB* alterations and cooperating lesions—particularly across skin and bone marrow compartments—remains incompletely defined.

We identified pediatric patients with BPDCN diagnosed between 2000 and 2025 and reviewed clinical records, pathology materials, and ancillary studies. Cases were confirmed by integrated morphologic and immunophenotypic assessment using pDC-associated markers, when available, with exclusion of alternative lineage-defining neoplasms. Clinical involvement at diagnosis (skin, bone marrow [BM], lymph node [LN], CNS), treatment exposures, and outcomes were abstracted. Available molecular testing included RNA-seq, WES/WGS, and/or targeted DNA-based NGS performed on involved tissue or BM; structural variants, somatic SNV/indels, and copy-number alterations were annotated and summarized (Supplementary Figure S1 and Supplementary Table S1).

The study was conducted with institutional review board approval in accordance with the Declaration of Helsinki.

The cohort comprised 21 patients (12 males, 9 females) with a median age at diagnosis of 12 years (range, 5–18 years). No patient had a documented prior myeloid neoplasm. At presentation, cutaneous involvement was documented in 16/20 evaluable cases (80%), with BM involvement in 9/16 (56%), LN involvement in 8/14 (57%), and CNS involvement in 5/11 (45%). Site-stratified clinical characteristics are summarized in Table 1. Among adequately staged cases, presentations were categorized as skin-only (3/15, 20%), skin plus systemic (BM and/or other extramedullary disease; 8/15, 53%), or systemic-only disease (4/15, 27%). No association was observed between clinical presentation and *MYB* rearrangements. Representative paired skin and BM morphology from case 1 is shown in Figure 1.

MYB-region alterations defined pediatric BPDCN in this cohort and expanded the spectrum of reported events. Eighteen cases underwent RNA-seq or RNA fusion panel testing, but only 12 yielded informative results for *assessing MYB or MYBL1* rearrangements; 11 of these 12 informative cases harbored *MYB* or *MYBL1* alterations. Detected events included *MYB::DCPS* (n=4), *MYB::PLEKHO1* (n=2), *MYB::ZFAT* (n=1), truncating *MYB* structural variants without a defined 3' partner (n=2), a peri-*MYB HBS1L::UGCG* fusion (n=1), and *MYBL1::MTFR1* (n=1). In the pediatric literature reviewed in Supplementary Table S2, peri-*MYB HBS1L::UGCG* and *MYBL1::MTFR1* were not previously reported. Case 5 also showed a truncating *ETV6* rearrangement predicted to disrupt exon 3 in the context of a concurrent *MYB::DCPS* fusion. Breakpoints were heterogeneous; genomic coordinates are provided when available in Supplementary Table S1.

The *MYB* fusions and truncations observed are predicted to preserve the DNA-binding and transactivation domains while lacking the C-terminal negative regulatory domain (NRD). NRD loss is associated with constitutive *MYB* activity and deregulation of oncogenic targets, including *MYC, BCL2, KIT*, and *ERBB2*.[7, 10] Truncated *MYB* alleles uniformly lacked the NRD, supporting NRD loss as a shared oncogenic mechanism across diverse *MYB* structural variants. Functional studies by Booth et al. demonstrated that BPDCN-associated *MYB* fusions redirect transcriptional programs away from normal dendritic cell differentiation toward aberrant G2/M cell-cycle regulation and are sufficient to induce a myeloid-dendritic leukemia phenotype in vivo.[11] The peri-*MYB HBS1L::UGCG* event was located upstream of *MYB* and is most consistent with a cis-regulatory alteration affecting *MYB*. After normalization, this case showed *MYB* expression comparable to that in *MYB*-altered cases and higher than in other tumors tested in our laboratory.

Somatic oncogenic variants were identified in a subset of cases, with activating RAS-pathway alterations representing the most frequent cooperating events (*NRAS*, n=6 [43%]; *KRAS*, n=2 [14%]; Supplementary Figure S1). Additional point mutations involved *RB1* and *KMT2C/KMT2D* (2 cases each; 14%) and single cases of *CDKN1C*, *IKZF1*, *NF1*, and *TP53* (7% each). Copy-number alterations were most frequent in *IKZF1*, *CDKN2A*, and *CDKN2B* (3/7, 43% each), followed by *ETV6* and *JAK1/2* (2/7; 28% each), and *TCF4* and *TP53* (1/7; 14% each). Recurrent chromosomal losses involved 12p (6/7, 86%), 13q (6/7, 86%), 9q (6/7, 86%), 17p (4/7, 57%), and 6q (3/7, 43%). *TP53* disruption was observed in Case 5, with concurrent mutation and 17p loss. These patterns are consistent with prior pediatric BPDCN reports and underscore convergence on key pathways regulating cell-cycle control (*RB1*; *CDKN2A/B*), transcriptional regulation (*IKZF1*; *ETV6*), and signaling pathways (*RAS*). [9, 10]

We observed monoallelic *TCF4* deletion in one case (Case 2; Supplementary Figure S1). *TCF4* is a lineage-survival oncogene and a reliable diagnostic immunophenotypic marker; experimental downregulation disrupts super-enhancer–associated transcription and induces apoptosis in BPDCN models. [8] Beyond its oncogenic role, *TCF4* is required for pDC lineage specification, raising the possibility that haploinsufficiency may influence differentiation state or therapeutic vulnerability.

Paired-site molecular profiling was available in one patient (Case 1). In this case, the skin lesion harbored *MYB::PLEKHO1* and *KRAS* G12C, whereas concurrent bone marrow RNA-seq, WES, and WGS did not detect these alterations. *RAS*-pathway alterations were also detected in the bone marrow in a subset of cases, underscoring the value of multi-compartment profiling when feasible. These findings are consistent with adult studies linking *RAS*-pathway alterations to systemic disease and sun-exposure history [12, 13], and with pediatric reports identifying *NRAS* and other signaling mutations in skin/lymph node or bone marrow, depending on disease presentation. [5, 6]

Review of published pediatric BPDCN cases with molecular characterization (≤20 years; n=25, Supplementary Table S2) showed predominant skin involvement: reported skin-only disease (5, 20%), skin plus systemic (15, 60%), and systemic-only disease (5, 20%). In contrast to adult cohorts, which are enriched for *TET2*, *ASXL1*, *ZRSR2*, and other splicing factor mutations and may show clonal relationships to myeloid neoplasms, pediatric *MYB*-rearranged cases have fewer documented cooperating mutations, with recurrent alterations involving *ETV6*, *KMT2C*/*KMT2D*, *IKZF1*, *NRAS*, and *CDKN2A*.[3, 12, 14] Together, these findings support *MYB* rearrangements as dominant initiating lesions in pediatric BPDCN, with subsequent acquisition of cooperating alterations (including *RAS*-pathway lesions) that may influence tissue dissemination and clinical phenotype (Figure 2).

Pediatric BPDCN is typically treated with ALL-like multiagent chemotherapy, including intrathecal CNS prophylaxis; radiotherapy is generally avoided. [2, 4] In our cohort, 16/17 evaluable patients received ALL-like therapy (venetoclax added in three), and one received an AML-like regimen; no patient received frontline tagraxofusp. All evaluable patients achieved remission; however, two relapsed—both with systemic-only presentation at diagnosis (Cases 5 and 17). Case 17 relapsed after AML-like therapy and died of progressive disease. Case 5 developed early CNS and bone marrow relapse, was refractory to venetoclax-based salvage, CD123-directed cellular therapy, and tagraxofusp. Sequencing of relapse bone marrow identified an acquired *TP53* variant. One additional patient discontinued therapy but was alive at last contact. Outcome data were available for 17 patients: 15 were alive at last follow-up, one died of progressive disease, and one died of treatment-related infection; four additional cases lacked adequate follow-up. Thirteen patients remained alive and event-free at a median follow-up of 48 months (range, 5-168), consistent with prior reports of more favorable outcomes in pediatric compared with adult BPDCN.[2, 4]

Similarly, published pediatric cases with evaluable BM status and outcomes (Supplementary Table S2) suggested that BM involvement was associated with adverse outcomes, although these differences did not reach statistical significance (relapse: 7/14 [50%] vs 1/6 [16.7%]; p=0.324; death: 6/16 (37%) vs 0/8 (0%); p=0.066). In contrast, reported skin-only disease had no relapse or death. Molecular findings among refractory or deceased cases were heterogeneous (including *MYB*-fusion–only disease and cases with additional cooperating lesions), limiting inference about genotype-specific risk. BM-involved cases demonstrated a broader spectrum of cooperating alterations (e.g., *KMT2C*/*KMT2D* or *ETV6/TET2*) in addition to *MYB* fusions. In contrast, BM-negative, skin-predominant cases more often exhibited *MYB*-driven disease with fewer additional

alterations or lesions, such as *KMT2*/*IKZF* family genes. Outcomes in these cases, including those with cooperating *RAS*-pathway mutations, were generally favorable, although staging and follow-up were heterogeneous.

In adult BPDCN, activated signaling lesions—including *RAS*-pathway mutations—are enriched in patients with systemic involvement, and overt marrow involvement (≥5% BPDCN in BM) is independently associated with inferior overall survival. In this context, *NRAS* appears to track with systemic disease/organ involvement rather than serving as a stand-alone risk marker. [13, 14] *TP53* alterations appear uncommon across cohorts (e.g., ~4% in a 50-case clinical cohort) [14]; however, integrative profiling suggests *TP53* represents a key lesion shared between BPDCN and AML, but not chronic myelomonocytic leukemia, and may exert transcriptomic “trans” effects that shape malignant programs, consistent with a higher-risk, AML-like biology (Figure 2). [12, 14, 15]

In our pediatric BPDCN cohort, *NRAS*/*KRAS* alterations were relatively frequent and observed across involved anatomic sites, supporting their role as common cooperating events rather than primary drivers. Despite this, relapse and refractory disease were uncommon. Notably, the only patient with early relapse harbored multiple high-risk genomic features at diagnosis, including an *ETV6* rearrangement, deletions of *CDKN2A* and *CDKN2B*, an *RB1* mutation, and a high–variant allele frequency *TP53* alteration, suggesting a more complex, higher-risk biology. These findings indicate that, in contrast to adult BPDCN, *RAS*-pathway mutations in pediatric disease were not clearly associated with adverse outcomes, whereas composite genomic disruption—particularly involving *TP53*—may be associated with aggressive clinical behavior. However, given the limited sample size, these observations should be interpreted with caution.

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Table 1. Site-stratified clinical characteristics of pediatric BPDCN

Characteristics	Overall cohort	Skin-only	Skin + systemic	Systemic-only
Patient, *n*	21	3	8	4
Age at diagnosis (years, median and range)	12 (5-18)	7 (6-12)	14 (6-18)	13 (7-16)
Gender, Male, n/*N* (%)	12/21 (57)	3/3 (100)	5/8 (62)	2/4 (50)
Initial BM involvement, *n/N* (%)	9/16 (56)	0/3 (0)	5/7 (71)	4/4 (100)
Initial LN involvement, *n/N* (%)	8/14 (57)	0/3 (0)	6/8 (75)	2/3 (66)
CNS involvement, *n/N* (%)	5/11 (45)	0/2 (0)	3/5 (60)	2/3 (66)
Remission during therapy, *n/N* (%)	17/17 (100)	3/3 (100)	7/7 (100)	4/4 (100)
Relapse, *n/N* (%)	2/16 (12)	0/3 (0)	0/7 (0)	2/3 (66)
ALL-type therapy, *n/N* (%)	16/17 (94)	3/3 (100)	7/7 (100)	3/4 (75)
Hematopoietic stem cell transplant, *n/N* (%)	2/17 (12)	1/3 (33)	1/7 (14)	0/4 (0)
Alive at last follow-up, *n/N* (%)	15/17 (88)	3/3 (100)	6/7 (86)	3/4 (75)
Follow-up, months (median, range)	48 (5-168)	12 (5-168)	17 (8-132)	35.5 (17-108)
MYB/peri-*MYB*/*MYBL1* rearrangement among informative tumors, *n/N* (%)	11/12 (92)	2/2 (100)	4/5 (80)	2/2 (100)

Denominators reflect cases with available data. Site-stratified columns include the 15 sufficiently staged cases described in the text. Abbreviations: ALL, acute lymphoblastic leukemia; BM, bone marrow; BPDCN, blastic plasmacytoid dendritic cell neoplasm; CNS, central nervous system; LN, lymph node

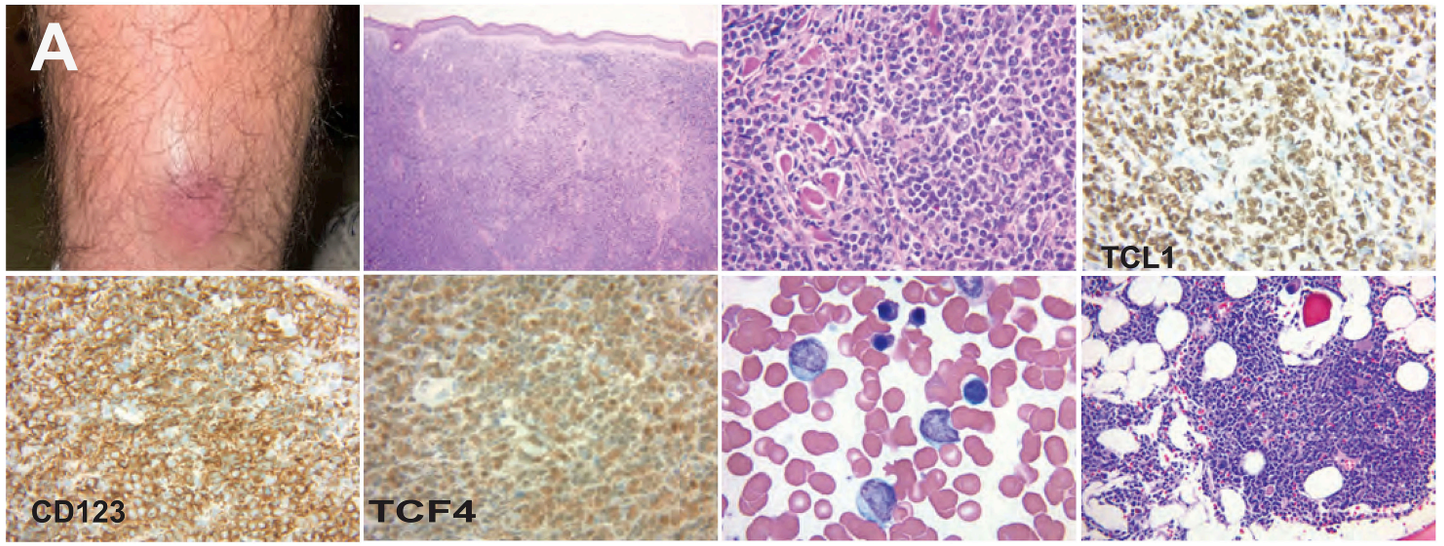
Figure 1. Clinical, histologic, and immunohistochemical findings of skin tumor with concurrent bone marrow histology and flow cytometry immunophenotypic findings.

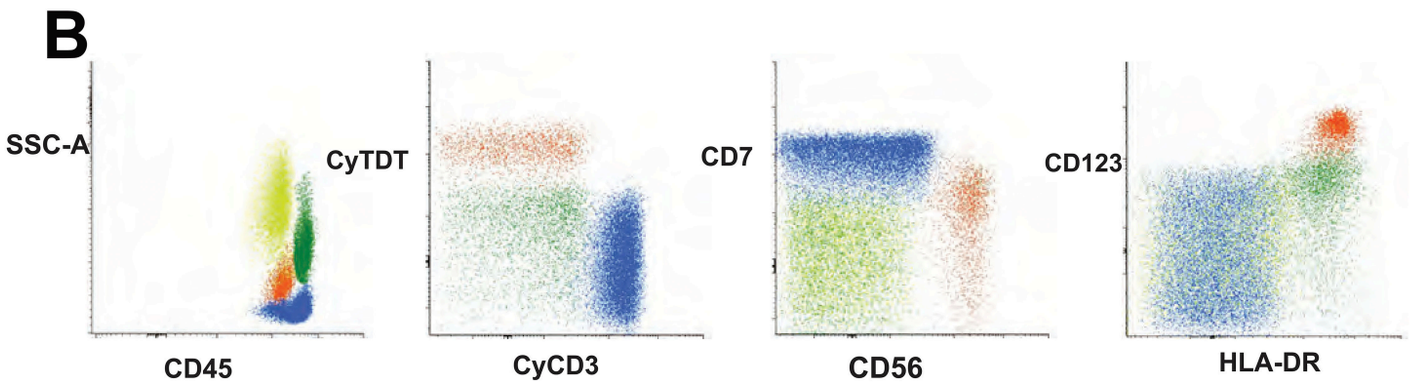
A: Clinical photograph of a cutaneous lesion in a 17-year-old male with no significant past medical history, presenting with a progressively enlarging, mobile mass on the left lower extremity measuring approximately 6.0 × 6.0 cm. The lesion was non-draining at presentation. Excisional biopsy demonstrating cutaneous involvement by BPDCN. The dermis is diffusely infiltrated by immature neoplastic cells with blastoid morphology, extending from the superficial to the deep dermis with involvement of the subcutis, while the epidermis is spared (skin; hematoxylin and eosin, ×40 and ×400). Immunohistochemistry shows tumor cell expression of TCL1, CD123, and TCF4 (×400). Bone marrow involvement by BPDCN. Wright–Giemsa–stained aspirate smears demonstrate neoplastic cells with lightly basophilic, agranular cytoplasm and blastoid nuclei with open chromatin and a prominent nucleolus (×600). The bone marrow biopsy (trephine) shows diffuse infiltration by tumor cells (hematoxylin and eosin, ×400).
B: Flow cytometry immunophenotyping in bone marrow aspirate shows neoplastic cells (red) have bright CD45 expression on CD45 expression/side scatter plots. Neoplastic cells are positive for HLA-DR, CD123, CD56, CD7, and CyTdT, and negative for CyCD3.
C: Schematic representation of the *MYB::PLEKHO1* fusion. The fusion results from juxtaposition of *MYB* on chromosome 6 (breakpoint: chr6:135,196,002) and *PLEKHO1* on chromosome 1 (breakpoint: chr1:150,158,819). The predicted fusion protein retains the *MYB* DNA-binding domain (green) and the LMSTEN motif (purple). Abbreviations: BPDCN, blastic plasmacytoid dendritic cell neoplasm; BM Asp, bone marrow aspirate; BM BX, bone marrow biopsy; Cy, cytoplasmic.

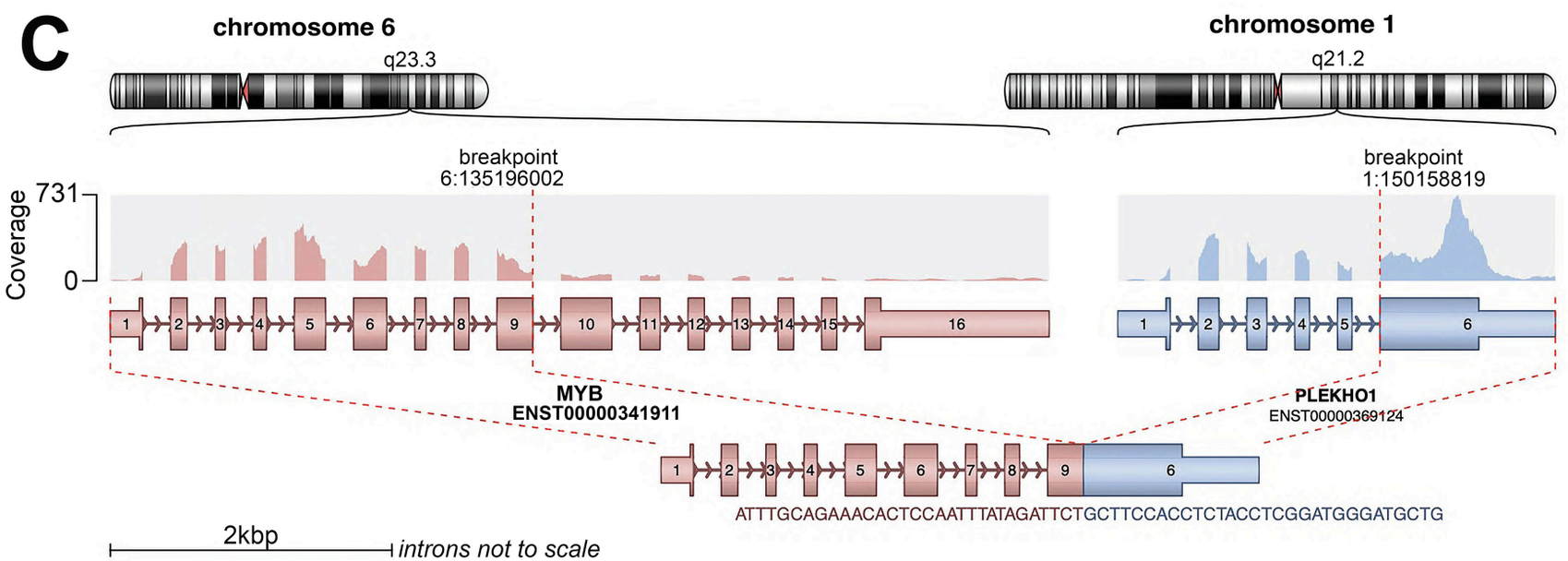
Figure 2. Conceptual model of pediatric versus adult BPDCN molecular evolution.

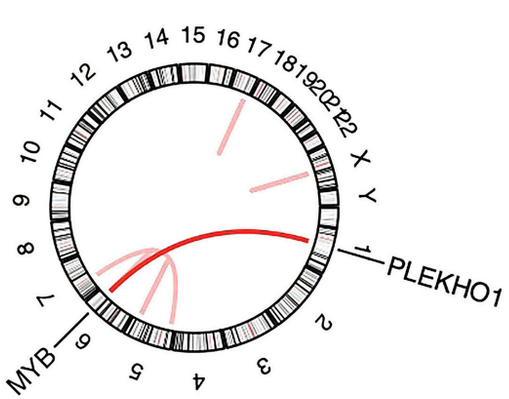
This schematic summarizes published observations indicating that adult BPDCN frequently harbors clonal hematopoiesis–associated mutations (e.g., *TET2*, *ASXL1*, *ZRSR2*, and other splicing factors) and may share a clonal origin with myeloid neoplasms. In contrast, pediatric BPDCN is predominantly characterized by *MYB*-region rearrangements with fewer recurrent cooperating lesions. This model is hypothesis-generating and is not directly derived from the present cohort. [3, 12, 14, 15]

Abbreviation: BPDCN, blastic plasmacytoid dendritic cell neoplasm.

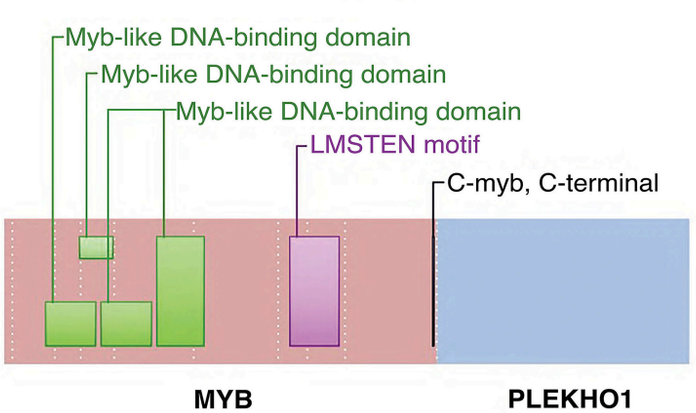








RETAINED PROTEIN DOMAINS
in-frame fusion

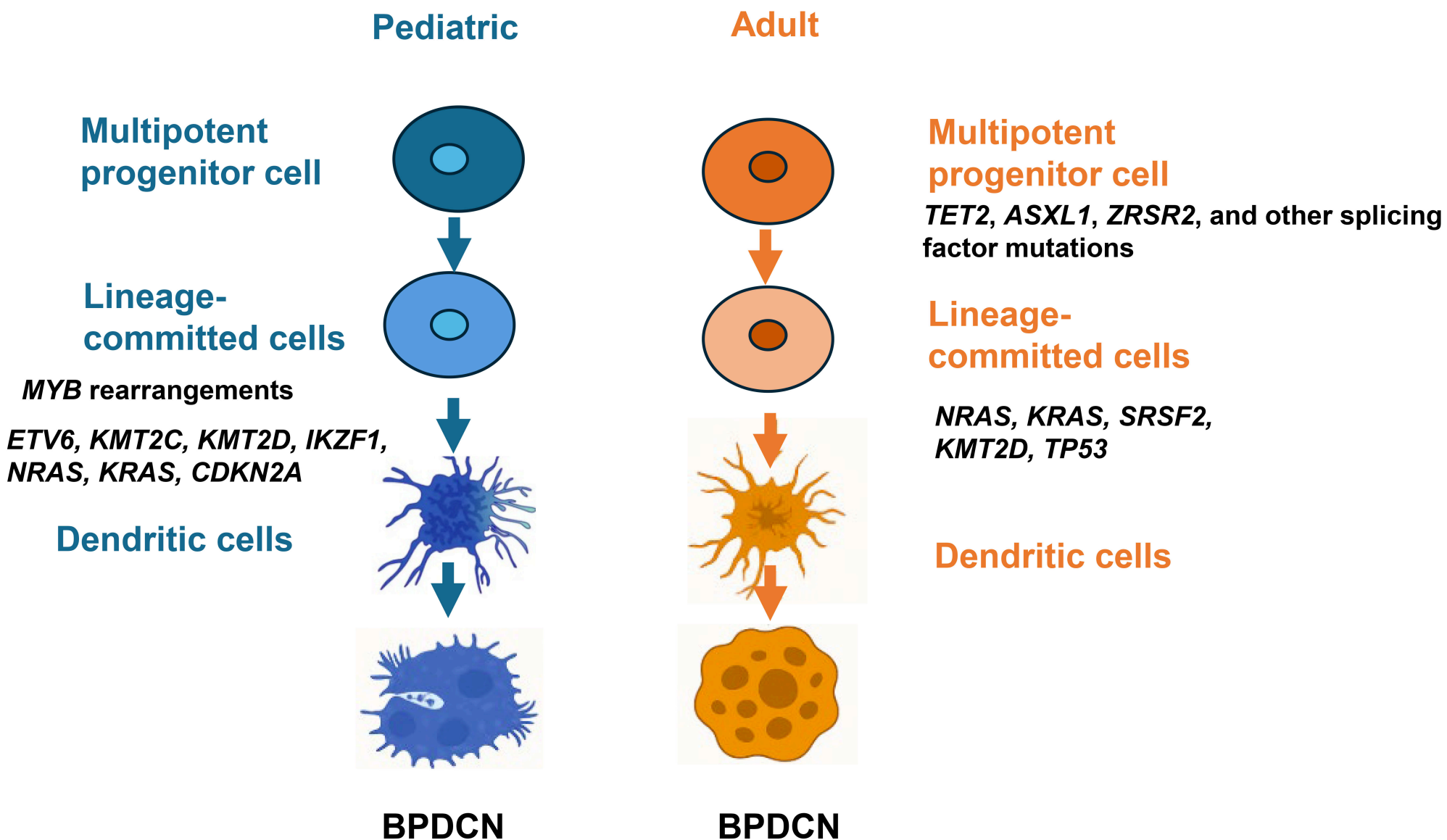


SUPPORTING READ COUNT

Split reads in MYB = 1

Split reads in PLEKHO1 = 4

Discordant mates = 0

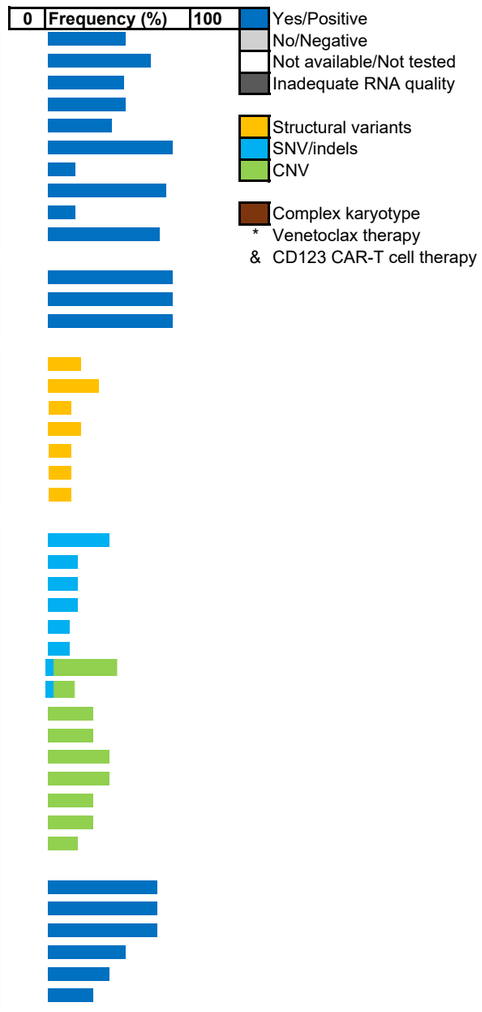

Pediatric
Adult
Multipotent progenitor cell
Lineage-committed cells
MYB rearrangements
ETV6, KMT2C, KMT2D, IKZF1, NRAS, KRAS, CDKN2A
Dendritic cells
BPDCN
Multipotent progenitor cell
TET2, ASXL1, ZRSR2, and other splicing factor mutations
Lineage-committed cells
NRAS, KRAS, SRSF2, KMT2D, TP53
Dendritic cells
BPDCN

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.