Predisposed genomic instability in pre-treatment bone marrow evolves to therapy-related myeloid neoplasms in malignant lymphoma

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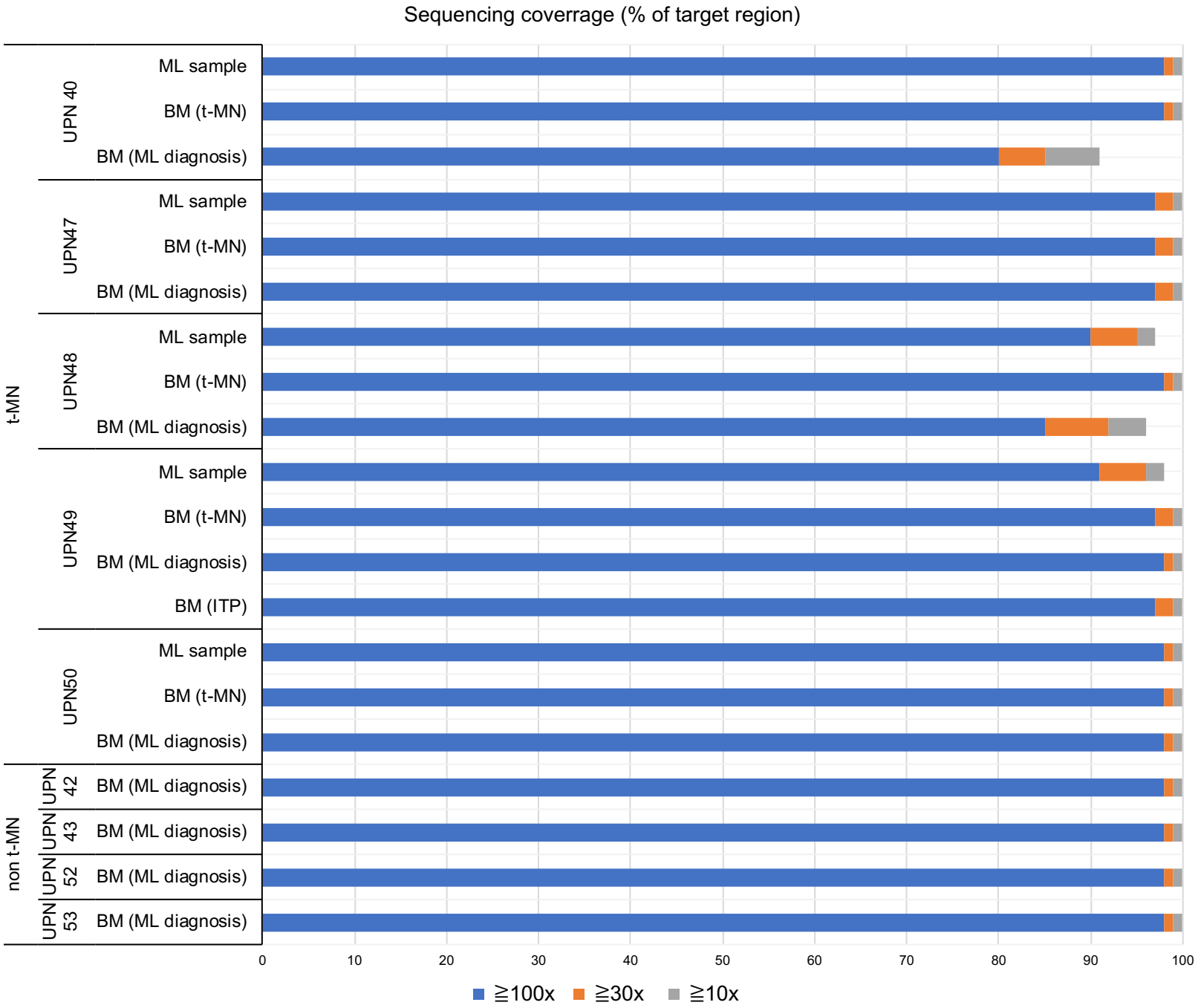
Supplemental Table 1: Summary of patient characteristics

	UPN	Gender	Malignant Lymphoma/ITP (UPN49) phase						Therapy-related myeloid neoplasm phase					
			Age (years)	Diagnosis	Karyotype of BM	Pre-leukemic mutations of BM		Therapy for ML	Age (years)	Diagnosis	Myeloblast of BM (%)	Pre-leukemic mutations of BM		Karyotype of BM
						Mutations	VAF					Mutations	VAF	
TMN patients	40	Female	38	DLBCL	46,XX【21】	not detected		8 cycles of R-CHOP RT 40Gy	42	t-AML	18	not detected		46,XX,inv(16)(p13;q22)【4】 /47,XX,idem,+22【18】
	47	Male	43	DLBCL	46,XY【16】/44,XY,-17,-18【2】 /45,XY,-18【2】/44,XY,-17【1】	not detected		8 cycles of R-CHOP 3 cycles of ESHAP Auto-PBSCT by MCVC	51	t-AML	47	*ZRSR2* R290*	0.431	48~52,XY,+8,del(20)(q11),+21,+20,-9,+21,+1~5m【10】
	48	Male	70	DLBCL	46,XY【21】	*TP53* T125M *DNMT3A* W753* *NRAS* Q61L	0.112 0.109 0.069	8 cycles of R-CHOP RT 40Gy	72	t-MDS	5.2	*TP53* R208S *TET2* R83*	0.378 0.153	40～46,XY,-5,-14,-3,-16,-17,-22,-6,-7,-10,-19,+1～4m【9】/86,XY,+X,+X,+11【1】
	49	Female	63	ITP	46,XX【21】	*RUNX1* R201* *TET2* R1359S *TET2* D545fs*10	0.406 0.4 0.29	none	71	t-AML	78.8	*RUNX1* R201* *TET2* R1359S *NRAS* Y64D *NF1* L1015Q	0.506 0.481 0.463 0.376	46,XX【21】/47,XX,+m【1】
			69	NSCHL	46,XX【21】	*RUNX1* R201* *TET2* R1359S *NRAS* Y64D	0.495 0.47 0.313	6 cycles of ABVD						
	50	Male	75	DLBCL	46,XY【21】	*DNMT3A* V567del *SF3B1* K666N	0.228 0.073	7 cycles of R-THPCOP	81	t-MDS	18	*TP53* R156_A159dup *SF3B1* K666N *RUNX1* S141*	0.39 0.386 0.092	47,XY,+6【17】, 46,XY【4】
Non-tMN patients	42	Male	64	DLBCL	46,XY【21】	not detected		6 cycles of R-CHOP						
	43	Male	70	FL	46,XY【21】	not detected		6 cycles of R-CHOP						
	52	Male	29	NSCHL	46,XY【21】	not detected		6 cycles of ABVD 3 cycles of ESHAP ASCT by MEAM						
	53	Male	35	ALK negative ALCL	46,XY【21】	not detected		7 cycles of R-THPCOP 1 cycles of ESHAP ASCT by MEAM						

Abbreviations: UPN: unique patient number, BM: bone marrow, ML: malignant lymphoma, VAF: variant allele frequency, ITP: idiopathic thrombocytopenic purpura, DLBCL: diffuse large B cell lymphoma, NSCHL: nodular scrolosis classical Hodgkin lymphoma, FL: follicular lymphoma, ALK: anaplastic lymphoma kinase, ALCL: anaplastic large cell lymphoma, R-CHOP: rituximab, cyclophosphamide, doxorubicin, vincristine, prednisolone, ABVD: doxorubicin, bleomycin, vinblastine, dacarbazine, ESHAP: etoposide, methylprednisolone, cytarabine, cisplatin, MEAM: ranimustine, etoposide, cytarabine, melphalan, ASCT: autologous hematopoietic stem cell transplantation, CHOEP: cyclophosphamide, doxorubicin, vincristine, etoposide, prednisolone, RT: radiation therapy, TMN: therapy-related myeloid neoplasm, t-AML: therapy-related acute myeloid leukemia, t-MDS: therapy-related myelodysplastic syndromes

Supplemental figure legends

Supplemental Figure 1. Sequencing depth and coverage in the bone marrow and malignant lymphoma samples of each case analyzed by targeted deep sequencing. The median percentage of target regions per case covered at depths of ≥100, ≥20, and ≥10 were 98%, 99%, and 100%, respectively. The median sequence depth was 1,790. UPN, unique patient number; BM, bone marrow; LN, lymph node; ML, malignant lymphoma; ITP, idiopathic thrombocytopenic purpura; tMN, therapy-related myeloid neoplasm.


Sequencing coverrage (% of target region)
t-MN
UPN 40
ML sample
BM (t-MN)
BM (ML diagnosis)
UPN47
ML sample
BM (t-MN)
BM (ML diagnosis)
UPN48
ML sample
BM (t-MN)
BM (ML diagnosis)
UPN49
ML sample
BM (t-MN)
BM (ML diagnosis)
BM (ITP)
UPN50
ML sample
BM (t-MN)
BM (ML diagnosis)
non t-MN
UPN 42
BM (ML diagnosis)
UPN 43
BM (ML diagnosis)
UPN 52
BM (ML diagnosis)
UPN 53
BM (ML diagnosis)
0
10
20
30
40
50
60
70
80
90
100
≧100x
≧30x
≧10x