Supplementary Table S1. List of 282 genes targeted for sequencing

ABL1	*CD83*	*FGFR3*	*KIK3R1*	*PAX5*	*SGK1*
ACD	*CDK4*	*FLT3*	*KIT*	*PDCD1LG2*	*SH2B3*
AKT1	*CDK6*	*FOXO1*	*KLF2*	*PDGFRA*	*SMARCA4*
ALK	*CDKN1B*	*FOXP1*	*KLHL6*	*PDGFRB*	*SMARCB1*
ANKRD26	*CDKN2A*	*GATA1*	*KMT2A*	*PDS5B*	*SMC1A*
APC	*CDKN2B*	*GATA2*	*KMT2C*	*PHF6*	*SMC3*
ARAF	*CDKN2C*	*GATA3*	*KMT2D*	*PIGA*	*SOCS1*
ARID1A	*CEBPA*	*GNA13*	*KRAS*	*PIK3CB*	*SOCS3*
ARID1B	*CHEK2*	*GNAS*	*LCK*	*PIK3CD*	*SPEN*
ARID2	*CIITA*	*GPR34*	*LMO2*	*PIK3CA*	*SPIB*
ASXL1	*CKS1B*	*GTF21*	*LRRFIP1*	*PIM1*	*SRC*
ASXL2	*CNOT3*	*HDAC9*	*LTB*	*PLCG2*	*SRSF2*
ASXL3	*CRBN*	*HIST1H1B*	*MAP2K1*	*POT1*	*SRSF3*
ATM	*CREBBP*	*HIST1H1C*	*MAP2K4*	*POU2AF1*	*STAG2*
ATRX	*CSF1R*	*HIST1H1D*	*MAP3K1*	*POU2F2*	*STAT1*
B2M	*CSF3R*	*HIST1H1E*	*MAP3K13*	*PPM1D*	*STAT3*
BCL10	*CTCF*	*HIST1H2AC*	*MAPK10*	*PRDM1*	*STAT5A*
BCL11A	*CTNNB1*	*HIST1H2AG*	*MCL1*	*PRKCB*	*STAT5B*
BCL2	*CUX1*	*HIST1H2AM*	*MECOM*	*PRPF8*	*STAT6*
BCL6	*CXCR4*	*HIST1H2BC*	*MED12*	*PTCH1*	*STK11*
BCL7A	*CYLD*	*HIST1H2BD*	*MEF2B*	*PTEN*	*SUZ12*
BCOR	*DDX3X*	*HIST1H2BG*	*MET*	*PTK2B*	*SYK*
BCORL1	*DDX41*	*HIST1H2BK*	*MGA*	*PTPN11*	*TBL1XR1*
BIRC2	*DIS3*	*HIST1H3B*	*MPEG1*	*PTPN2*	*TCF3*
BIRC3	*DNMT3A*	*HIST1H3G*	*MPL*	*PTPN23*	*TENT5C*
BLM	*DNMTA*	*HLA-A*	*MSH2*	*PTPN4*	*TERC*
BRAF	*DTX1*	*HLA-B*	*MSH6*	*PTPN6*	*TERT*
BTG1	*EBF1*	*HLA-C*	*MSN*	*PTPRC*	*TET1*
BTG2	*ECSIT*	*HRAS*	*MTOR*	*PTPRD*	*TET2*
BTK	*EGFR*	*ID3*	*MYB*	*PTPRK*	*THRAP3*
CALR	*EGR1*	*IDH1*	*MYC*	*RAD21*	*TLR2*
CARD11	*EGR2*	*IDH2*	*MYD88*	*RAD51*	*TMEM30A*
CASP8	*ELANE*	*IGH*	*NF1*	*RASA2*	*TMSB4X*
CBFB	*EP300*	*IKBKB*	*NF2*	*RB1*	*TNF*
CBL	*ERBB2*	*IKZF1*	*NFE2*	*RCOR1*	*TNFAIP2*
CCND1	*ERBB3*	*IKZF3*	*NFKB1*	*REL*	*TNFAIP3*
CCND2	*ETNK1*	*IL2RG*	*NFKB2*	*RHOA*	*TNFRSF14*
CCND3	*ETV6*	*IL7R*	*NFKBIA*	*ROS1*	*TP53*
CCNE1	*EZH2*	*INPP5D*	*NFKBIE*	*RPS15*	*TRAF3*
CCR6	*FAS*	*IRF1*	*NFKBIZ*	*RUNX1*	*U2AF1*
CD22	*FAT1*	*IRF4*	*NOTCH1*	*SAMD9*	*U2AF2*
CD274	*FAT3*	*IRF8*	*NOTCH2*	*SAMD9L*	*UBR5*
CD28	*FAT4*	*ITPKB*	*NPM1*	*SETBP1*	*VAV1*
CD58	*FBX011*	*JAK1*	*NRAS*	*SETD2*	*WT1*
CD70	*FBXW7*	*JAK2*	*NSD2*	*SETDB1*	*XPO1*
CD79A	*FGFR1*	*JAK3*	*NTRK1*	*SF1*	*ZFP36L1*
CD79B	*FGFR2*	*KDM6A*	*P2RY8*	*SF3B1*	*ZRSR2*

Supplementary Table S2. Sequencing quality and depth of coverage of each sample

Study ID[a]	On Target (%)	Mean Target Depth (×)	50× (%)	100× (%)
A1	39	494	90	80
A2	75	833	97	90
A3	48	624	90	82
A4	49	609	91	83
A5	62	690	96	88
A6	73	937	97	91
A7	51	691	98	92
A8	57	744	98	93
A9	58	472	91	82
A10	44	555	93	84
A11	63	851	99	95
A12	70	832	98	93
A13	66	950	98	95
A14	54	786	98	92
A15	65	772	97	90
E1	49	704	97	90
E2	62	717	97	89
E3	76	831	94	87
E4	34	464	92	82
E5	55	703	98	91

[a] Study subjects were assigned unique identification numbers, which correspond to the order of samples (*x*-axis) in Figure 1.

Supplementary Table S3. Comparison of SNVs/indels between ANKL and ENKTL-BM

	ANKL (n=15)	ENKTL-BM (n=5)	*P* value[a]
SNV/indel[b]			
Single gene			
DDX3X	3 (20.0%)	1 (20.0%)	1.000
FGFR3	2 (13.3%)	0 (0.0%)	1.000
SETD2	2 (13.3%)	0 (0.0%)	1.000
PIK3R1	3 (20.0%)	0 (0.0%)	0.539
PIK3CB	2 (13.3%)	0 (0.0%)	1.000
PDGFRB	3 (20.0%)	0 (0.0%)	0.539
ERBB2	3 (20.0%)	0 (0.0%)	0.539
IKZF3	3 (20.0%)	0 (0.0%)	0.539
PTPN11	2 (13.3%)	0 (0.0%)	1.000
NFKB1	2 (13.3%)	0 (0.0%)	1.000
ASXL3	2 (13.3%)	0 (0.0%)	1.000
MAP2K1	2 (13.3%)	0 (0.0%)	1.000
IRF1	1 (6.7%)	1 (20.0%)	0.447
TET2	1 (6.7%)	0 (0.0%)	1.000
GATA1	0 (0.0%)	1 (20.0%)	0.25
UBR5	3 (20.0%)	2 (40.0%)	0.560
BCORL1	3 (20.0%)	0 (0.0%)	0.539
BCOR	2 (13.3%)	0 (0.0%)	1.000
DNMT3A	2 (13.3%)	1 (20.0%)	1.000
MGA	3 (20.0%)	0 (0.0%)	0.539
EP300	2 (13.3%)	1 (20.0%)	1.000
SPEN	3 (20.0%)	0 (0.0%)	0.539
PRDM1	1 (6.7%)	0 (0.0%)	1.000
APC	4 (26.7%)	1 (20.0%)	1.000
TP53	4 (26.7%)	0 (0.0%)	0.530
NOTCH1	1 (6.7%)	0 (0.0%)	1.000
FAS	2 (13.3%)	0 (0.0%)	1.000
CREBBP	1 (6.7%)	0 (0.0%)	1.000
CIITA	3 (20.0%)	0 (0.0%)	0.539
INPP5D	2 (13.3%)	0 (0.0%)	1.000
PRPF8	2 (13.3%)	0 (0.0%)	1.000
CTNNB1	0 (0.0%)	1 (20.0%)	0.250
Family/pathway			
DDX family	3 (20.0%)	2 (40.0%)	0.560
FGFR family	3 (20.0%)	1 (20.0%)	1.000
SETD family	3 (20.0%)	1 (20.0%)	1.000
PIK3 family	4 (26.7%)	0 (0.0%)	0.530
PDGFR family	3 (20.0%)	1 (20.0%)	1.000
ERBB family	3 (20.0%)	0 (0.0%)	0.539
IKZF family	3 (20.0%)	0 (0.0%)	0.539
PTP family	4 (26.7%)	0 (0.0%)	0.530
NFKB family	3 (20.0%)	1 (20.0%)	1.000
ASXL family	2 (13.3%)	0 (0.0%)	1.000
RAS-MAPK pathway	3 (20.0%)	0 (0.0%)	0.539
BCOR-BCORL1	5 (33.3%)	0 (0.0%)	0.266
Epigenetic modifiers	12 (80.0%)	3 (60.0%)	0.560
Tumor suppressor genes	8 (53.3%)	1 (20.0%)	0.319

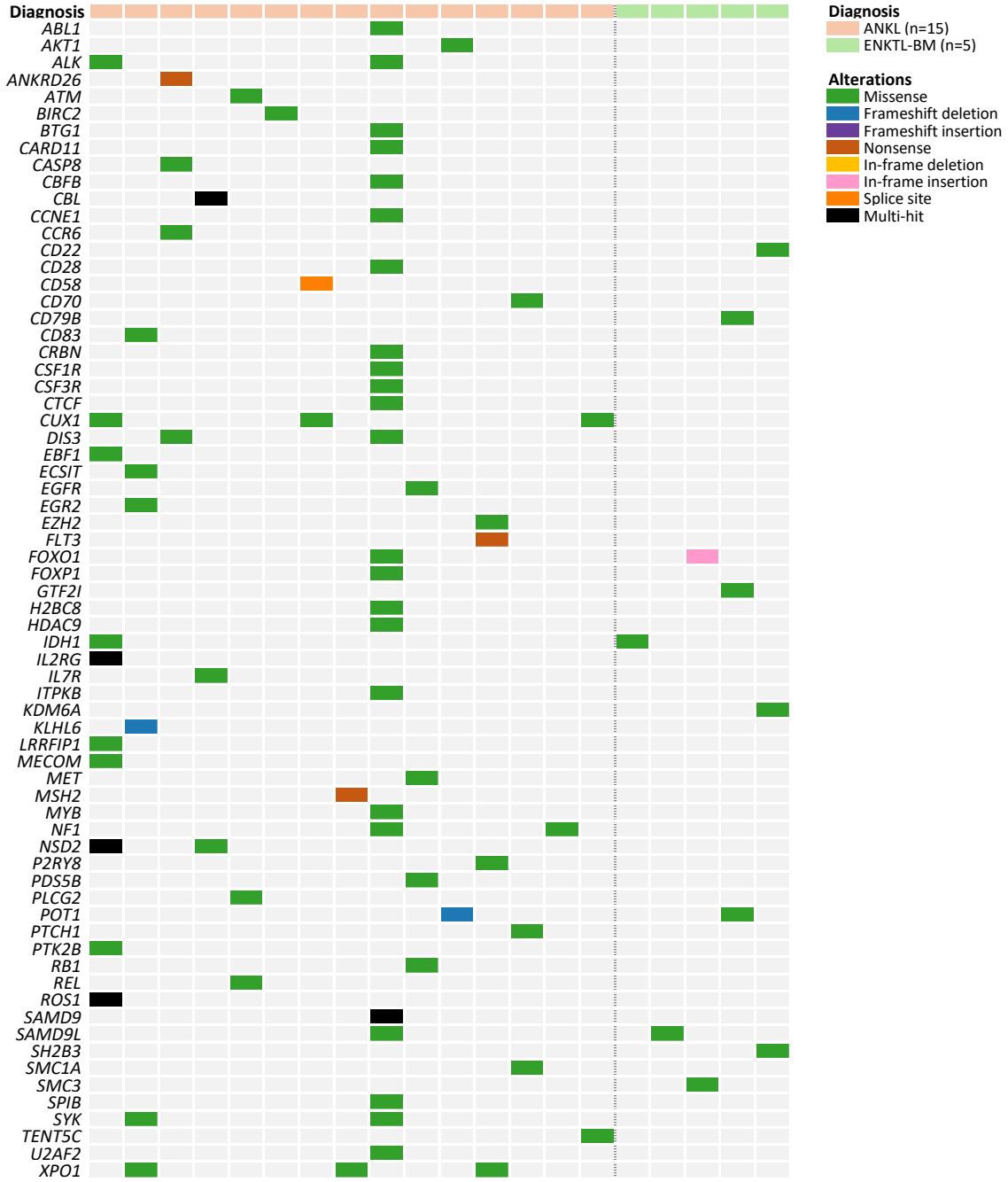
[a] Statistical significance was analyzed using Fisher's exact test for categorical variables and Mann–Whitney U test for continuous variables. Frequencies of categorical variables and median values with

interquartile ranges for continuous variables are presented. *P* value < 0.05 was considered statistically significant.

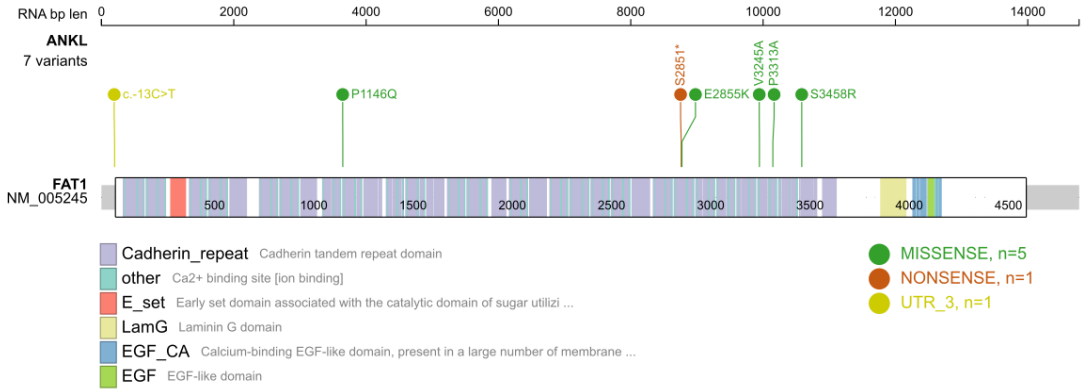
[b] The order of genes and families/pathways is consistent with that in Figure 1. For single genes, those with high frequencies of mutations and previously reported in the literature were selected for display.

Abbreviations: ANKL, aggressive NK-cell leukemia; ENKTL-BM, extranodal NK/T-cell lymphoma with bone marrow involvement; SNV, single nucleotide variant; indel, small insertion or deletion

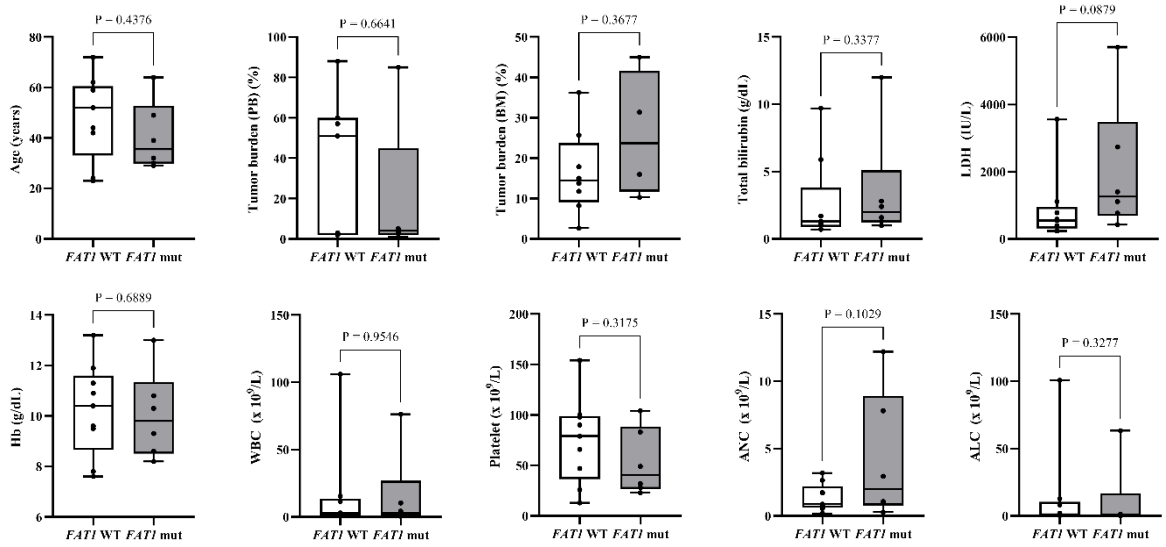
Supplementary Figure S1. The remaining part of the oncoplot not shown in Figure 1. The order of the study subjects (*x*-axis) is the same as in Figure 1. In total, 68 genes are listed in alphabetical order. Abbreviations: ANKL, aggressive NK-cell leukemia; ENKTL-BM, extranodal NK/T-cell lymphoma with bone marrow involvement



Supplementary Figure S2. Lollipop plot of FAT atypical cadherin 1 (*FAT1*) gene. Among 7 SNVs detected in the *FAT1* gene, 6 SNVs (85.7%) were located in the cadherin tandem repeat domain. This plot was generated using the visualization tool ProteinPaint from St. Jude Children's Research Hospital. Abbreviations: ANKL, aggressive NK-cell leukemia; SNV, single nucleotide variant



Supplementary Figure S3. Comparison of age, tumor burden, total bilirubin, LDH, and CBC between WT *FAT1* (n=9) and mutated *FAT1* (n=6) in ANKL. No significant difference was observed between the two groups. Mann–Whitney U test was used for group comparisons and P value < 0.05 was considered statistically significant. Abbreviations: WT, wild type; mut, mutated; PB, peripheral blood; BM, bone marrow; LDH, lactate dehydrogenase; Hb, hemoglobin; WBC, white blood cell; ANC, absolute neutrophil count; ALC, absolute lymphocyte count; CBC, complete blood count



Supplementary Figure S4. Kaplan–Meier survival curves of all (n=20) patients according to mutations in (A) *FAT1*, (B) *FAT3*, (C) *FAT4*, (D) *FAT* family, (E) *ARID1A*, and (F) *ARID* family. *FAT* family included *FAT1*, *FAT3*, and *FAT4*. *ARID* family included *ARID1A*, *ARID1B*, and *ARID2*. Survival analyses of patients with *ARID1B* and *ARID2* mutations could not be performed due to the small number of samples. *P* value < 0.05 was considered statistically significant for the Log-rank test. Abbreviations: mut, mutated; WT, wild type