SUPPORTING INFORMATION

SUPPLEMENTAL METHODS

Clinical samples

Bone marrow lymphoblast samples from 26 T-ALL patients carrying t(8;14)(q24,q11) translocation were collected from 9 different centers under local informed consent. Criteria of inclusion were the presence of t(8;14)(q24;q11) translocation and the patients age (0-18 years-old) (**Table S1**). FISH analyses to confirm *TRA/TRD-MYC* rearrangement were performed at leukemia diagnosis in the respective centers. Primary T-ALL samples (n=15) carrying *TAL1-LMO2* rearrangements were acquired by informed consent from the Department of Pediatric Hemato-Oncology at Ghent University Hospital.

Cell lines

T-ALL cell lines were purchased from the DSMZ repository (Braunschweig, Germany) and cultured at 37°C (5% CO_2) in RPMI-1640 medium (Life Technologies, Carlsbad, CA, USA; 52400-025) supplemented with 10% or 20% fetal bovine serum (FBS), 2mM L-glutamine (Life Technologies, 25030081), 100U/mL penicillin and 100 μg/mL streptomycin (Life Technologies, 15140163).

Array comparative genomic hybridization

Patient DNA was profiled on the 180K custom-designed oligonucleotide array platform (Agilent SurePrint G3 Human CGH microarrays, G4449A, design ID: 022060). Genomic DNA from patients and standard controls was labeled using random prime labeling with Cy3 and

Cy5 dyes (Perkin Elmer, Waltham, MA, USA). Hybridization was performed according to the manufacturer's instructions (Agilent Technologies, Santa Clara, CA, USA) and then the data were analyzed using the ViVar arrayCGHbase tool (Sante *et al*, 2014). Array CGH data have been deposited in the GEO database (GEO accession number: GSE106773).

Mutation screening

DNA from T-ALL patients carrying t(8;14)(q24,q11) was amplified by PCR using specific primers to study *NOTCH1, PTEN, FBXW7, LEF1* genes (**Table S2**). Amplified material was analyzed by Sanger sequencing and mutation analysis was performed using DNAdynamo tool.

RNA sequencing analyses

Total RNA samples from 5 T-ALLs carrying the t(8;14)(q24,q11) rearrangement were isolated using miRNeasy mini kit (Qiagen, Hilden, Germany). Total RNA from 8 *TAL1-LMO2* T-ALL samples was provided by the Department of Pediatric Hemato-Oncology at Ghent University Hospital. RNA quality was evaluated by Experion analyses (Bio-Rad, Hercules, CA, USA).

RNA sequencing was performed on a NextSeq 500 instrument (Illumina, San Diego, CA, USA). Reads were aligned to the reference genome GRCh38 using STAR-2.4.2a with default settings (Dobin et al, 2013). STAR was used for gene expression quantification on the Ensembl GTF file version 84. Differential expression analysis was performed using DESeq2 in R (version 3.3.1) a two-condition design was implemented (Love et al, 2014). TAL1-LMO2 *T-ALL* cases (n=8) were compared to TRA/TRD-*MYC* translocated ones (n=5). Using this design, two patients from *TAL1-LMO2* group clustered with TRA/TRD-*MYC* translocated samples in unsupervised hierarchical clustering analyses. Next, a supervised analysis was performed including these two patients in the TRA/TRD-*MYC* translocated group (n=7) versus the other *TAL1-LMO2*

cases (n=6). The computational resources and services used in this work were provided by the VSC (Flemish Supercomputer Center), funded by the Research Foundation - Flanders (FWO) and the Flemish Government – department EWI. RNA sequencing data have been deposited in the GEO database (GEO accession number GSE106699).

Quantitative real-time polymerase chain reactions (qRT-PCR)

Total RNA was isolated using the miRNeasy mini kit (Qiagen) and iScript cDNA synthesis kit (Bio-Rad) was used to synthesize cDNA. Quantitative real-time polymerase chain reactions were performed using the SsoAdvanced SYBR Green Supermix (Bio-Rad). LightCycler 480 instrument (Roche, Pleasanton, CA, USA) was used for amplification and detection. Every sample was analyzed in duplicate and the gene expression was standardized against at least 3 housekeeping genes. qBasePLUS software (Biogazelle, Zwijnaarde, Belgium) was used for analysis. Primer sequences are listed in **Table S2**.

ChIP-seq and ChIP-qPCR

MOLT16 cells ($2x10^7$) were cross-linked with methanol-free formaldehyde (1% final concentration) at room temperature for 7 min and cross-linking reaction was quenched with glycine (125 mM final concentration, Sigma-Aldrich, Saint Louis, MO, USA, G-8790). Nuclei were isolated and chromatin was purified by chemical lysis (truChIP Chromatin Shearing Reagent KIT, Covaris, Woburn, MA, USA, PN520154). Next, the purified chromatin was fragmented to 200–300 bp fragments by sonication (Covaris, M220, Focused-ultrasonicator). Chromatin immunoprecipitation was performed by incubation of the chromatin fraction overnight with 40 µl of Protein A UltraLink™ Resin (Thermo-Scientific, Waltham, MA, USA; 53139) and 4 µg Anti-Histone H3 (acetyl K27) antibody - ChIP Grade (Abcam, Cambridge,

United Kingdom, ab4729). The next day, beads were washed to remove non-specific binding events and enriched chromatin fragments were eluted from the beads, followed by reverse cross-linking by incubation at 65 °C overnight. Input sample (from 1.6 x10^6 cells) was also included. DNA was subsequently purified (Chromatin IP DNA Purification Kit, Active-Motif, Carlsbad, CA, USA, 58002). DNA obtained from the ChIP assays was adaptor ligated and amplified using NEBNext Ultra DNA library Prep Kit (New England Biolabs, Ipswich, MA, USA, E73370S) and sequenced by NextSeq 500 instrument (Illumina, San Diego, CA, USA). After quality control with FastQC, raw sequencing data were mapped to the human reference genome (GRCh38) using Bowtie2 v2.3.3.1 with default settings. Peak calling was performed using MACS 2.1.1 using input sample as control. Rose (Young Lab) was used for Super enhancer calling, excluding promoters from the analysis. ChIP sequencing data have been deposited in the GEO database (GEO accession number GSE106939).

Chromatin immunoprecipitation was performed in MOLT16 cell line (3×10^7) after treatment with JQ1 (2μM) or DMSO for 7 hours. Once treated, cells were crosslinked and ChIP protocol was performed as described above. In parallel, chromatin immunoprecipitation was performed on a chromatin fraction incubated overnight with IgG 4μg IgG XP® Isotype Control (DA1E) (Cell Signaling Technology, Danvers, MA, USA 3900). Input sample was also included. For qRT-PCR analysis specific primers were designed for the putative *TRA/TRD* enhancer region (H3K27ac positive region from ChIPseq data). Negative regions downstream the target sequences were used as control (chr14:22,626,300-22,626,420). Signals obtained either from H3K27ac or IgG ChIP DNA were normalized on signals obtained from the relative input samples, after being adjusted to the amount of chromatin used in the ChIP. Yield were calculated as 2^(-ΔΔCt). Yield averages were calculated on 4 replicates for H3K27ac and IgG

ChIP and final percentage, relative to input, reported both for putative positive (enhancer regions) and negative regions. Primer sequences are listed in **Table S2**.

Western blotting

Cells were lysed with radioimmunoprecipitation assay (RIPA) buffer and protein concentration was measured with the Pierce BCA protein assay kit (Thermo-Scientific, 23227). Denatured protein was loaded on a 10% polyacrylamide gel and the sodium dodecyl sulfate-polyacrylamide gel electrophoresis was run followed by western blotting on a nitrocellulose membrane. Primary antibodies: cMYC N262 (sc-764, SantaCruz; 1:1000), AKT S473 (4060, Cell Signaling Technology; 1:1000), AKT (9272, Cell Signaling Technology; 1:1000), Cleaved NOTCH1 (4147, Cell Signaling Technology; 1:1000), PTEN (9552, Cell Signaling Technology; 1:1000) and β–ACTIN antibody (A2228, Sigma-Aldrich; 1:10000). Secondary antibodies: anti-rabbit IgG, HRP-linked Antibody (7074, Cell Signaling Technology) and anti-mouse IgG, HRP-linked Antibody (7076, Cell Signaling Technology). The detection of the blots was done with ChemiDoc-It Imaging System (UVP, Upland, CA, USA).

T-ALL cell lines drug screening

A panel of T-ALL cell lines (MOLT16, KE-37, ALL-SIL, JURKAT, HPB-ALL, LOUCY, KOPTK1) was plated at 50.000 cells per well in 96-well plates. The cells were incubated for 72 hours in 100 μL medium with 20% FBS and 5 μL of the appropriate drug dilution (JQ1 compound (BPS Bioscience, San Diego, CA, USA; 27401) or dimethylsulfoxide (DMSO) was added. Cell viability was evaluated by means of Celltiter-Glo Luminescent Cell Viability Assay (Promega, Madison, WI, USA) according to the manufacturer's instructions. To determine the half maximal inhibitory concentration (IC_{50}), scalar concentration points were chosen for each cell line. The

IC_{50} values were calculated using the CalcuSyn software (Biosoft, Cambridge, MA). The experiment was performed 3 times independently in duplicate.

MOLT16 and KE-37 cell lines were seeded at a density of 1×10^6 cells/ml and treated for 6, 12 and 72 hours with either DMSO or JQ1 compound (1 μM). Cells were harvested at the indicated time point and RNA or protein isolation was performed as described above.

TRA/TRD-*MYC* rearranged T-ALL xenograft models and *in vivo* treatment

Xenograft models were established from primary t(8;14)(q24;q11) positive T-ALL patient cells. Animal experiments were approved by the ethical committee on animal welfare at Ghent University Hospital. Ten non-obese diabetic/severe combined immunodeficient γ (NSG) mice were injected at 6 weeks of age by retro-orbital injection with 200 μL phosphate-buffered saline containing $2x10^6$ leukemic primary cells from t(8;14)(q24,q11) patients. At regular time points, leukemia engraftment was monitored by staining lymphocytes from murine peripheral blood with human CD45 antibody (PE-labeled antibody for human CD45 (Miltenyi Biotec, Bergisch Gladbach, Germany; 130-098-141)). Presence of human leukoblasts was analyzed using FACS analysis with the S3 cell sorter (Bio-Rad). Upon full establishment of leukemia, human leukemic cells were isolated from the spleen and re-transplanted into 10 secondary recipients. Once human CD45 positive leukemic blasts were detected in peripheral blood, the mice were randomly divided into 2 groups and treated with JQ1 (50mg/kg) or with vehicle twice a day by intraperitoneal injection. (+)-JQ1 (MedChem Express, South Brunswick Township, NJ, USA) was formulated in 10% DMSO and 90% of a 10% 2-hydroxypropyl-β-cyclodextrin solution. After 14 days of treatment, the percentage of human CD45-positive

leukemic blasts was determined by FACS in peripheral blood and bone marrow. Spleens were analyzed for size and weight.

Statistical analysis

GraphPad Prism 5.04 (La Jolla, CA) was used for statistical analyses.

SUPPLEMENTAL REFERENCES

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- Love, M.I., Huber, W. & Anders, S. (2014) Moderated estimation of fold change and dispersion for RNA-seq data with DESeq2. *Genome Biology*, **15**:550.
- Sante, T., Vergult, S., Volders, P.J., Kloosterman, W.P., Trooskens, G., De Preter, K., Dheedene, A., Speleman, F., De Meyer, T., Menten, B. (2014) ViVar: a comprehensive platform for the analysis and visualization of structural genomic variation. *PLOS ONE*, **9**(12):e113800.

SUPPLEMENTAL TABLES

Table S1. Biological and clinical characteristics of 26 studied T-ALLs carrying t(8;14)(q24,q11) translocation.

Patient	Sex	Age at diagnosis (years)	Karyotype	WBC Count ($x10^9$/L)	Relapse	Death (cause)
1	M	6	46,XY,t(8;14)[2]/46,XY [10]	223	Yes	Yes
2	F	16	46,XX,del(6)(q13q21),t(8,14)(q24,q11),del(9)(p22)	86.3	No	Yes (infection)
3	M	13	46,XY,t(8,14)(q24,q11) [14]	128.9	Yes	Yes
4	M	8	46,XY,del(6)(q21q25),t(8;14)(q24;q11.2)[15]/46,XY[5]	363	No	No
5	M	15	46,Y,der(X)t(X;17)(q28;q11.2),t(8;14)(q24;q11.2)[15]/46,XY[5]	380	Yes	Yes
6	F	1	46,XX,t(8;14)(q24;q11.2)[6]/46,XX[2]	254	Yes	Yes
7	F	3	46,XX,t(8;14)(q24;q11)[6]/46,XX[4]	650	No	No
8	M	8	46,XY,t(8;14)(q24;q11)[2]/46,XY[6]	168	No	No
9	M	11	46,XY,t(8;14)(q24;q11)[18]/46,XY[1]	NA	Yes	yes
10	M	13	46,XY,del(6)(q21q26),t(8;14)(q24;q11)[22]/46,XY[3]	NA	No	Yes (Treatment-related mortality)
11	M	13	46,XY,t(8;14)(q24;q11)/idem,i(17p)/46,XY	382	No	No
12	M	4	47,XY,t(8;14)(q24;q11),del(12)(p11p13)	201	No	Yes (toxicity)
13	F	16	46,XX,t(8;14)(q24;q11)[23]/46,XX[2]	139	Yes	Yes (leukemia progression)
14	F	1	46,XX,t(8;14)(q24.1;q11.2)[20]	446.1	No	No
15	F	12	46,XX,t(8;14)(q24.1;q11.2)[2]/46,XX[7]	411	No	No
16	F	7	46,XX,t(8;14)(q24.1;q11.2)[7]/46,XX[13]	176	No	No
17	M	11	46,XY,t(2;11)(p16;p14)[11]/46,idem,t(8;14)(q24;q11.2)[8]/46,XY[1]	718.8	Yes	No
18	F	9	46,XX,del(9)(p21.3)[7]/46,idem,del(6)(q12q21)[9]/46,idem,del(6)(q12q21),t(8;14)(q24;q11.2)[7]	472	Yes	Yes (leukemia progression)
19	F	9	47,XX,t(8;14)(q24.1;q11.2),+17[20]	587.8	No	No
20	F	12	46,XX,del(6)(q21q25),t(8;14)(q24.1;q11.2)[20]/45,idem,-14,der(16)t(14;16)(q12.1;q11.2)[3]/46,XX[2]	128.5	No	No
21	F	3	46,XX,del(7)(q34q36),t(8;14)(q24.1;q11.2)[9]/46,XX,-4,del(7)(q34q36),der(8)t(8;9)(q24.1;q22),der(9)t(4;9)(q21;q34),+mar[7]/46,XX[4]	186.1	No	Yes (leukemia progression)
22	F	0	46,XX,del(6)(q23q25),dup(7)(q31q32),t(8;14)(q24;q11.2)[6]/46,XX[9]	1087.6	NA	Yes (leukemia progression)
23	F	18	46,XX,t(8;14)(q24.1;q11.2)[9]/47,idem,+8[2]/47,XX,+8[2]/46,XX[7]	81.4	No	No
24	M	NA	NA	70	NA	No
25	F	3	47,XX,t(8;14)(q24;q11),inv(9)(p13p24),i(17)(q10),+i(17)(p10)[15]	NA	No	No
26	M	2	46,XY,t(8;14)(q24;q11),del(9)(p21)[18]	NA	No	Yes (second tumor)

NA= Not Available

Table S2. Primers used for mutation screening, qRT-PCR and ChIP qPCR analyses.

Sanger Sequencing Primers (5'>3')	
PTEN exon1 F	AGCTTCTGCCATCTCTCTC
PTEN exon1 R	TTTCGCATCCGTCTACTC
PTEN exon2 F	ACATTGACCACCTTTTATTACTC
PTEN exon2 R	GGTAAGCCAAAAAATGATTATAG
PTEN exon3 F	ATGGTGGCTTTTTGTTTGT
PTEN exon3 R	GCTCTTGGACTTCTTGACTTA
PTEN exon4 F	TCAGGCAATGTTTGTTAGTATT
PTEN exon4 R	ATCGGGTTTAAGTTATACAACATA
PTEN exon5 F	TTGTATGCAACATTTCTAAAGTT
PTEN exon5 R	ATCTGTTTTCCAATAAATTCTCA
PTEN exon6 F	ACGACCCAGTTACCATAGC
PTEN exon6 R	TAGCCCAATGAGTTGAACA
PTEN exon7 F	AATCGTTTTTGACAGTTTGAC
PTEN exon7 R	TCACCAATGCCAGAGTAAG
PTEN exon8 F	GATTGCCTTATAATAGTCTTTGTG
PTEN exon8 R	TTTTTGACGCTGTGTACATT
PTEN exon9 F	GCCTCTTAAAGATCATGTTTG
PTEN exon9 R	GGTCCATTTTCAGTTTATTCA
NOTCH1 exon26 F	AGGAAGGCGGCCTGAGCGTGT
NOTCH1 exon26 R	AGAGTTGCGGGGATTGACCGT
NOTCH1 exon27 F	GTGGCGTCATGGGCCTCA
NOTCH1 exon27 R	GCACAAACAGCCAGCGTGT
NOTCH1 exon28 F	GATCGGTGTCATGTGAAGT
NOTCH1 exon28 R	TCCCGGTGAGGATGCTCGG
NOTCH1 exon34a F	CTTCCTCTGGTGATGGAACCT
NOTCH1 exon34a R	CATCCCAGGCAGGTGGTTGA
NOTCH1 exon34b F	GCCCTCCCCGTTCCAGCAGTCT
NOTCH1 exon34b R	GCCTGGCTCGGCTCTCCACTCA
NOTCH1 exon34c F	AGCCGCACCTTGGCGTGAGC
NOTCH1 exon34c R	TGGTCGGCCCTGGCATCCAC
FBXW7 exon7 F	TTTATGCCTTCATTTTTCTCTT
FBXW7 exon7 R	GGGGAAAAAAGCTAAGTTATG
FBXW7 exon8 F	TTTTCCAGTGTCTGAGAACAT
FBXW7 exon8 R	CCCAAATTCACCAATAATAGA
FBXW7 exon9 F	TAAACGTGGGTTTTTTTGTT
FBXW7 exon9 R	TCAGCAATTTGACAGTGATT
FBXW7 exon10 F	CCTGGCATTACCTGTTTC
FBXW7 exon10 R	AGGCTCCATATTTCTCTTGA
FBXW7 exon11 F	GGACATGGGTTTCTAAATATGTA
FBXW7 exon11 R	CTGCACCACTGAGAACAAG

LEF1 exon1 F	ACCCTTCCAACTCTCCTTTCC
LEF1 exon1 R	AACGAGGGATCTACTCGGGAC
LEF1 exon2 F	CTTTGAATTACCAGCGCACAC
LEF1 exon2 R	CCAAGGGTCCCTAACTCATTC
LEF1 exon3 F	TGGTTTGCTGCTAAGCTATTTAAG
LEF1 exon3 R	AAGGTGGCCATTCCTCATAAC
LEF1 exon4 F	GACTGGTTACTGCTGCTGTGTG
LEF1 exon4 R	ATCCACCCAGTGACATGGAG
LEF1 exon5 F	TCCTGTTCCTTGGATCTGGTG
LEF1 exon5 R	AGCACCTTGCTTGTTGATGTG
LEF1 exon6 F	TGACACTTTGATTGGGTGGAG
LEF1 exon6 R	ACACATGGCTGAGGTATGCAC
LEF1 exon7 F	TGCTTCTGTGCGTAAAGATGTG
LEF1 exon7 R	TGTTGCAAAGGAGCAACAGTG
LEF1 exon8 F	TTGTCGCCATCCTGAGTGTAG
LEF1 exon8 R	CCTGATATGGGATTAAATTGGG
LEF1 exon9 F	CACTTGGCACTTGGTCTTCTG
LEF1 exon9 R	AATGCAATATATCCATGAAATCCTT
LEF1 exon10 F	CCACCTGCCTGTACTTCCAC
LEF1 exon10 R	GATTCCAGGTGACAGGGTTTG
LEF1 exon11 F	CATCAGTGAGGTCCCATTTATTT
LEF1 exon11 R	TTCACAAGCAAGTGCCTCTTT
PCR protocol: 95°C 10 min; 40 cycles (96°C 15 sec, 57°C 1 min, 72°C 1 min); 72°C 10 min. KAPA2G Robust PCR kit was used (KapaBiosystems, Inc., Wilmington, MA, USA).	

qRT-PCR primers	
cMYC F	GCCACGTCTCCACACATCAG
cMYC R	TGGTGCATTTTCGGTTGTTG
Reference Genes	
HPRT1 F	TGACACTGGCAAAACAATGCA
HPRT1 R	GGTCCTTTTCACCAGCAAGCT
TBP F	CACGAACCACGGCACTGATT
TBP R	TTTTCTTGCTGCCAGTCTGGAC
UBC F	ATTTGGGTCGCGGTTCTTG
UBC R	TGCCTTGACATTCTCGATGGT
YWHAZ-F	ACTTTTGGTACATTGTGGCTTCAA
YWHAZ-F	CCGCCAGGACAAACCAGTAT

ChIP-qPCR primers	
TRA/TRD_H3K27ac positive region_F	TTTGAGTTGGCTGCAGTGAC
TRA/TRD_H3K27ac positive region_R	CTCTGAGGTTCTTGGAGGGG
MYC_H3K27ac positive region_F	CCCTCCCATATTCTCCCGTC
MYC_H3K27ac positive region_R	TCCCAATTTCTCAGCCAGGT
TRA/TRD_H3K27ac negative region_F	ATTCTAAGCACCCCGAACCA
TRA/TRD _H3K27ac negative region_R	GCATGTCTGACCACCCATTC
MYC_H3K27ac negative region_F	ATTGGTCACAGAGGTCAGGG
MYC_H3K27ac negative region_R	CGTCCGTATTTGTGCTAGCC

SUPPLEMENTAL FIGURES

Figure S1

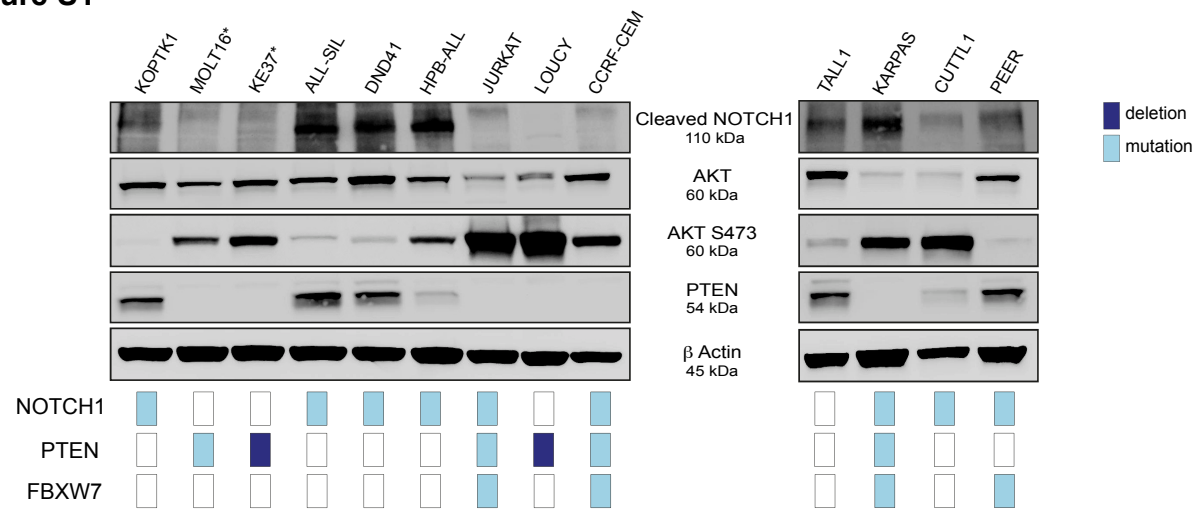


Figure S2

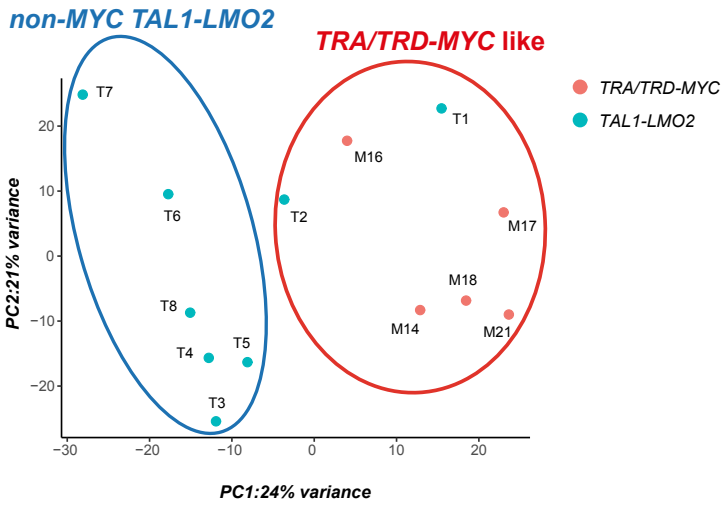


Figure S3

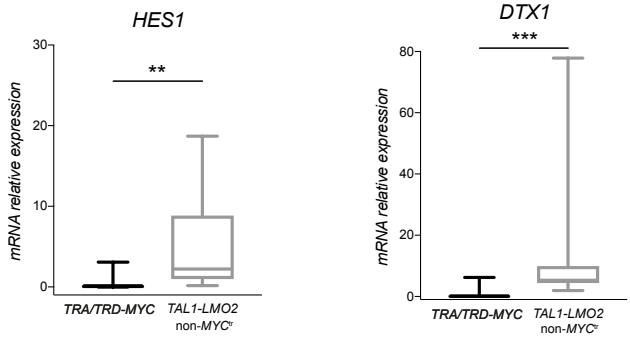
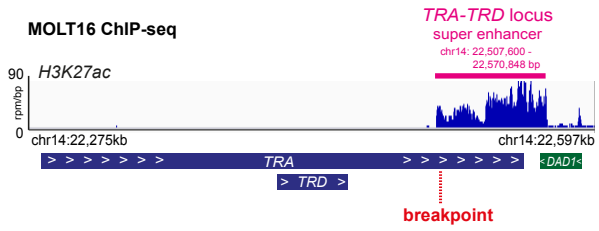


Figure S4



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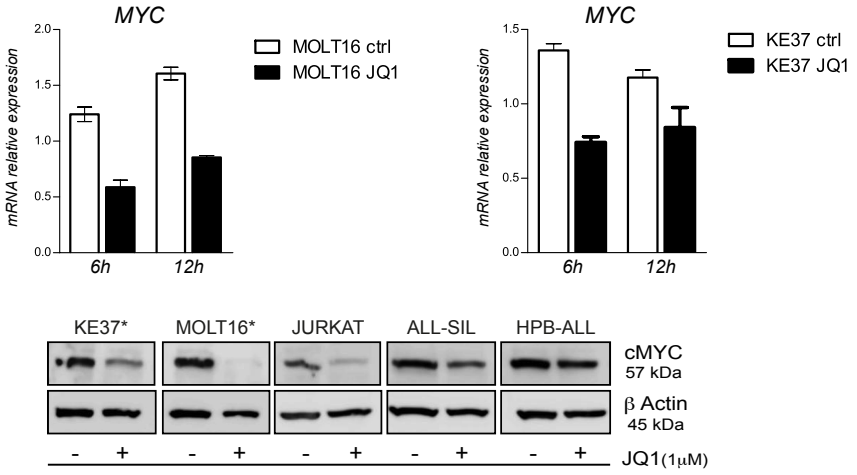


Figure S6

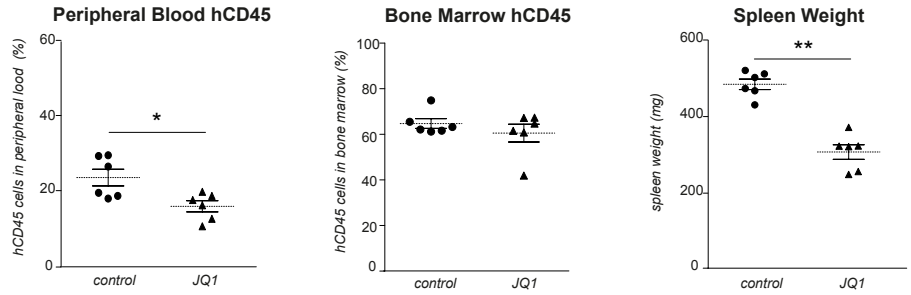
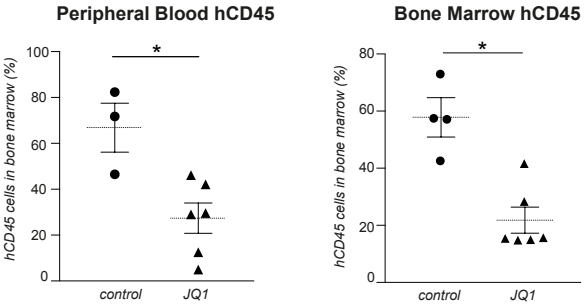


Figure S7



SUPPLEMENTAL FIGURE LEGENDS

Figure S1. T-ALL cell lines screening for cleaved NOTCH1, AKT and PTEN protein expression or activation. Among the cell line panel, MOLT16 and KE-37 are *TRA/TRD-MYC* translocated cells (*) presenting *NOTCH1* and *FBXW7* wild-type, *PTEN* deletion or mutation and pAKT activation. Deletion and mutation are reported in dark and light blue, respectively.

Figure S2. Transcriptomic profiling by RNA-seq analysis of *TRA/TRD-MYC* translocated T-ALLs (n=5) and *TAL1-LMO2* T-ALLs (n=8). Unsupervised clustering of the two T-ALL subsets revealed the presence of two clusters of leukemias, including one group that consisted of all 5 *TRA/TRD-MYC* positive T-ALLs and 2 additional *TRA/TRD-MYC* negative leukemias, named *TRA/TRD-MYC* like.

Figure S3. *NOTCH1* target genes validation in an independent set of *TRA/TRD-MYC* translocated T-ALLs (n=16) and *TAL1-LMO2* T-ALLs (n=7). *HES1* and *DTX1* expression was assessed by qRT-PCR in the studied T-ALL subgroups. Mann–Whitney test was performed to compare the different groups (**P<0.01, ***P<0.001). Horizontal lines represent the median for each group.

Figure S4. Schematic representation of *TRA/TRD* locus in MOLT16 cell line detected by H3K27ac CHIP sequencing analyses (chr14:22,275-22,597kb, GRCh38). In pink, *TRA/TRD* enhancer elements (chr14:22,507,600-22,570,848 bp) identified by high level of H3K27ac and reported in the Hockey-stick plot (Figure 2A, red dot).

Figure S5. MYC mRNA and protein downregulation after JQ1 treatment (1μM) in MOLT16 and KE-37 cell lines. Control cells were treated with dimethylsulfoxide. MYC mRNA expression was analyzed after JQ1 treatment at 6 and 12 hours. MYC protein expression was studied after 72 hours upon JQ1 treatment for MOLT16, KE37, JURKAT, ALL-SIL and HPB-ALL cell lines. Protein downregulation was confirmed after JQ1 treatment in both t(8;14)(q24;q11) positive cell lines (*). Minor effects at protein level were observed in less sensitive cell lines, such as ALL-SIL and HPB-ALL.

Figure S6. NSG mice xenotransplanted with primary *TRA/TRD-MYC* T-ALL cells and treated with JQ1 (50mg/kg) once/day for 14 days. Percentage of hCD45 leukemic cells in peripheral blood and in bone marrow. Xenografts spleen weight (mg). Mann–Whitney test was used to compare the treatment groups (*P<0.05, **P<0.01).

Figure S7. NSG mice xenotransplanted with primary *TRA/TRD-MYC* T-ALL cells (from patient 17, see Table S1) and treated with JQ1 (50mg/kg) twice/day for 14 days. Percentage of hCD45 leukemic cells in peripheral blood and in bone marrow. Mann–Whitney test was used to compare the treatment groups (*P<0.05).