

SUPPLEMENTAL MATERIAL

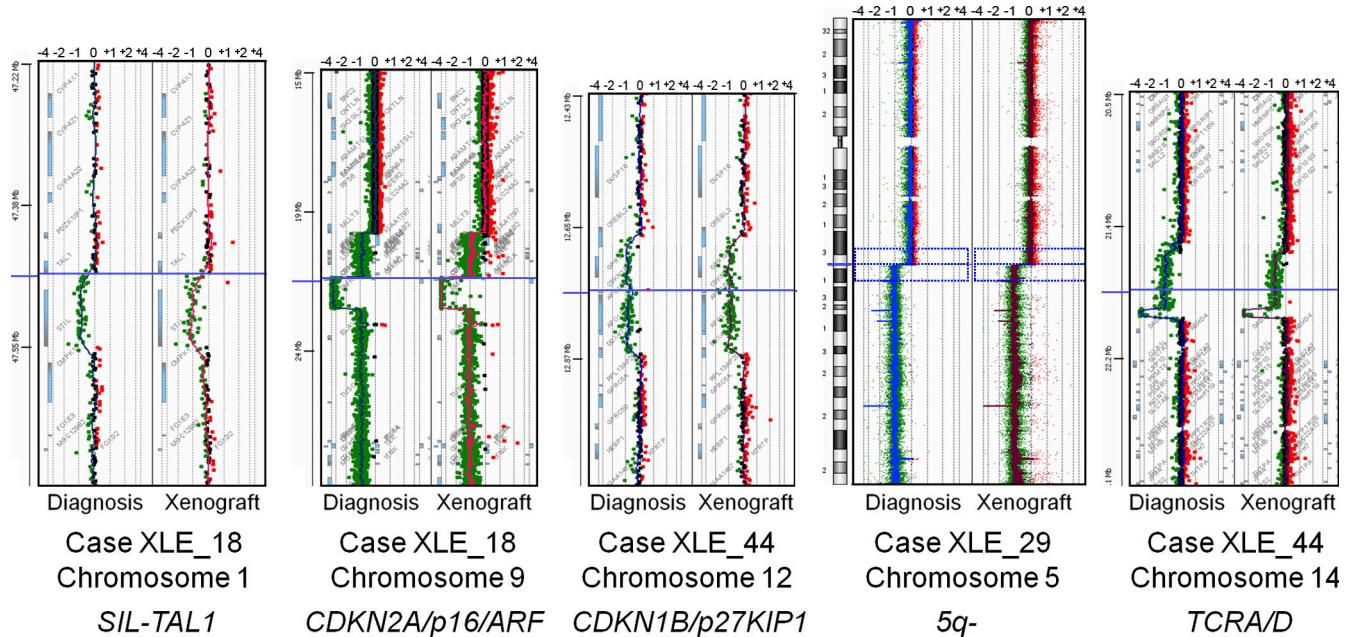
Clappier et al., <http://www.jem.org/cgi/content/full/jem.20110105/DC1>

Figure S1. Overall stability of genomic lesions between diagnosis and xenograft T-ALL samples. Examples of representative lesions as found by copy number analysis of both diagnosis and xenograft samples are shown. The complete list of the copy number lesions is shown in Table S2. TCR loci deletions caused by VDJ (variable, diverse, and joining) recombination are not considered as genomic lesions but can be used as clonality markers.

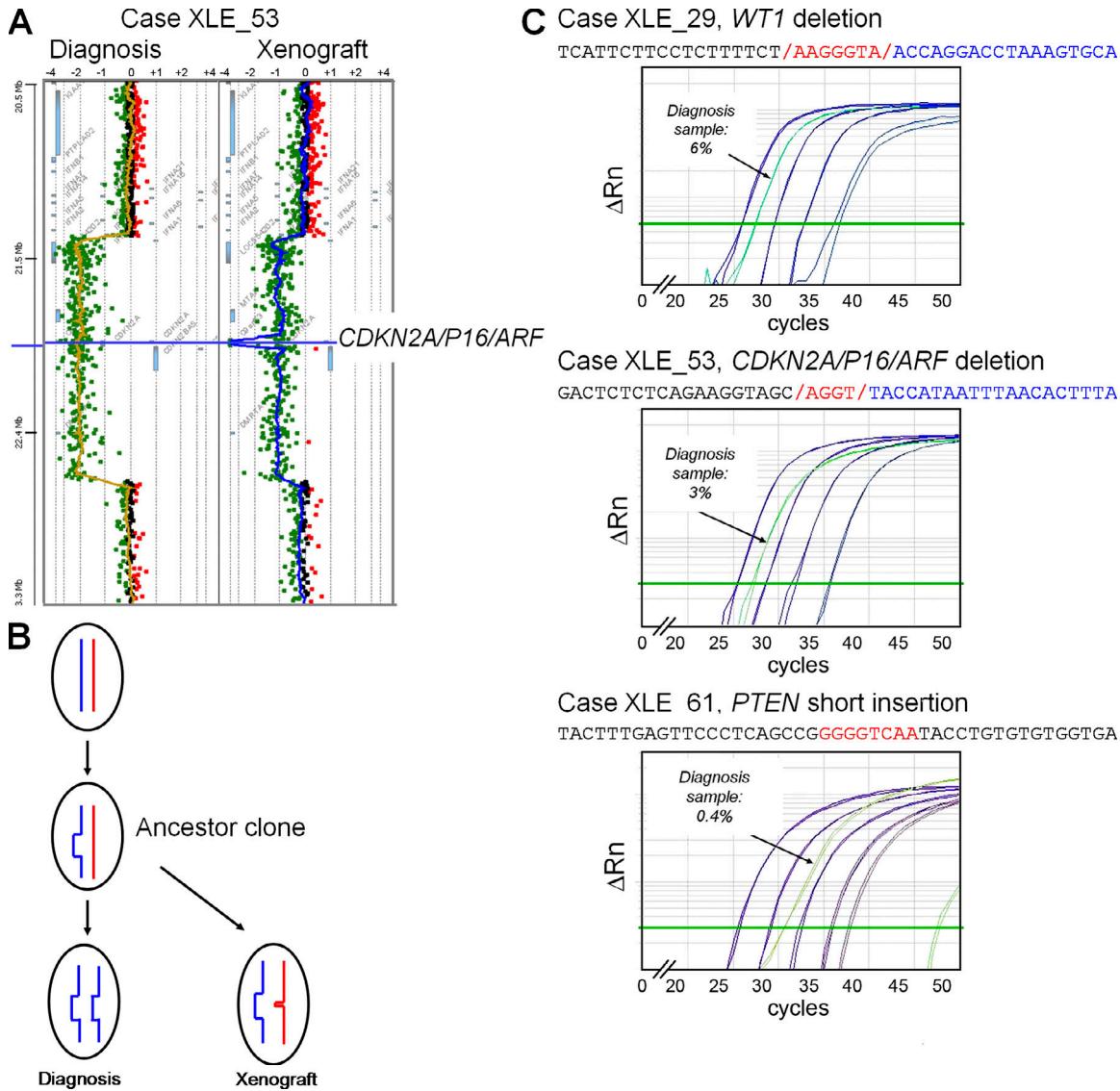


Figure S2. Common prediagnosis ancestor leukemia clone and backtracking in diagnosis samples of genomic abnormalities identified in xenograft samples. (A) Array CGH plots showing a large deletion at the 9p21.3 locus of the two alleles in the diagnosis sample (left) and the same deletion of one allele plus a focal deletion of CDKN2A on the other allele in the xenograft sample (right). (B) Schematic representation of the sequential acquisition of genomic deletions at the 9p21.3 locus shown in A. The two chromosomes 9 are represented in blue and red. (C) Breakpoint sequences of two genomic deletions (*WT1* and *CDKN2A* loci, cases XLE_29 and XLE_53, respectively) and sequence of a short insertion (*PTEN* gene, second allele of case XLE_61; *PTEN* deletion of the first allele is shown in Fig. 1 F) were used for specific backtracking. Nucleotides typed in black and blue are upstream and downstream of the breakpoints, respectively; slashes represent the breakpoints of the lesion; in red are nontemplate inserted nucleotides. Amplification curves of quantitative PCR experiments in duplicate are shown, with standard curves obtained by 10-fold dilutions from 10^{-1} to 10^{-4} of the xenograft DNA harboring the genomic lesion and of the diagnosis sample (indicated by arrows). The horizontal green lines indicate the threshold for PCR linearity.

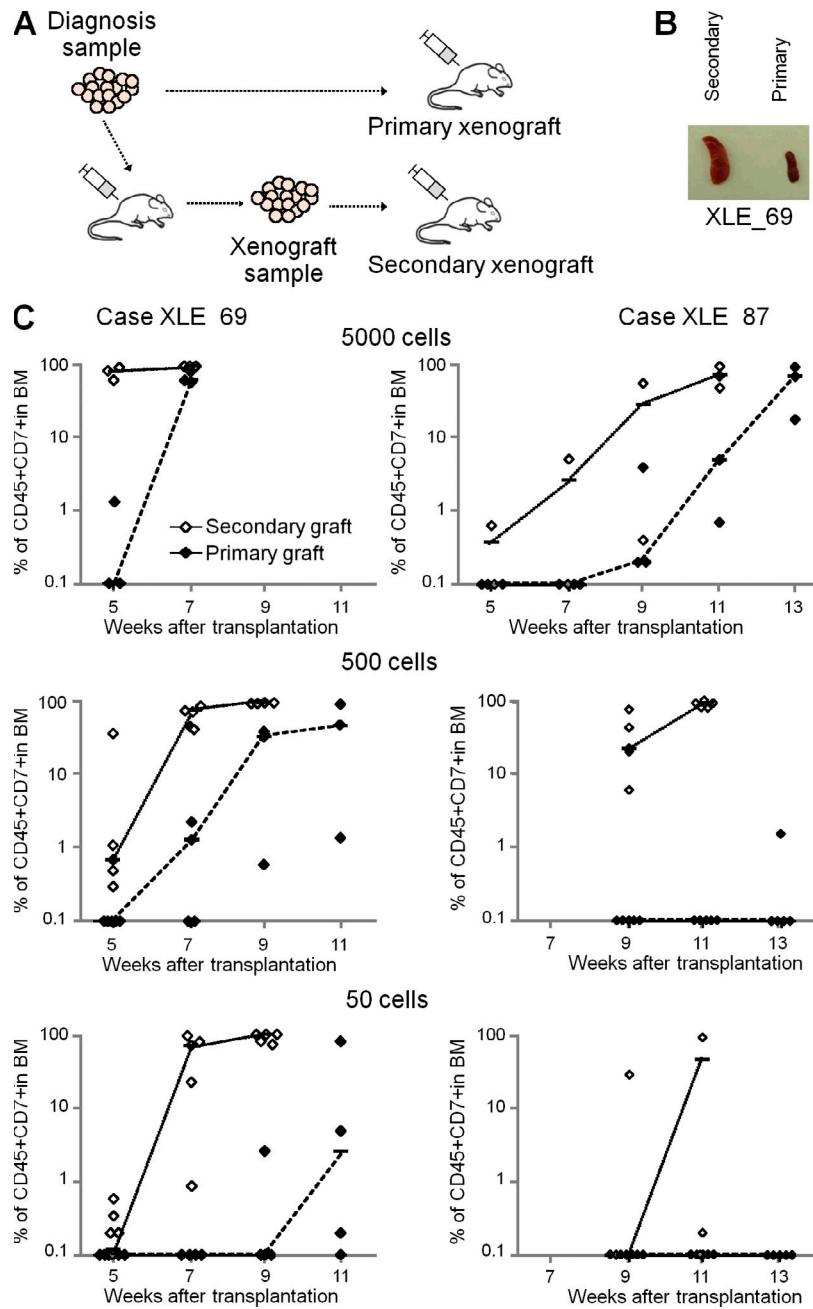


Figure S3. Xenografted leukemia cells have greater leukemia-initiating capacity than primary diagnosis cells. (A) Schematic of the experimental protocol for comparing primary versus secondary xenograft. (B) Representative pictures of the spleen of mice injected with 5,000 cells from case XLE_69 and sacrificed 7 wk after transplantation. (C) Kinetics of leukemia engraftment in primary and secondary recipient mice as measured by CD45⁺CD7⁺ cell percentages in the BM. Two T-ALL cases were tested; three cell doses were used for each sample; three to five mice were injected per cell dose. Each dot represents the data of one mouse, dashes represent medians, and lines connect the medians.

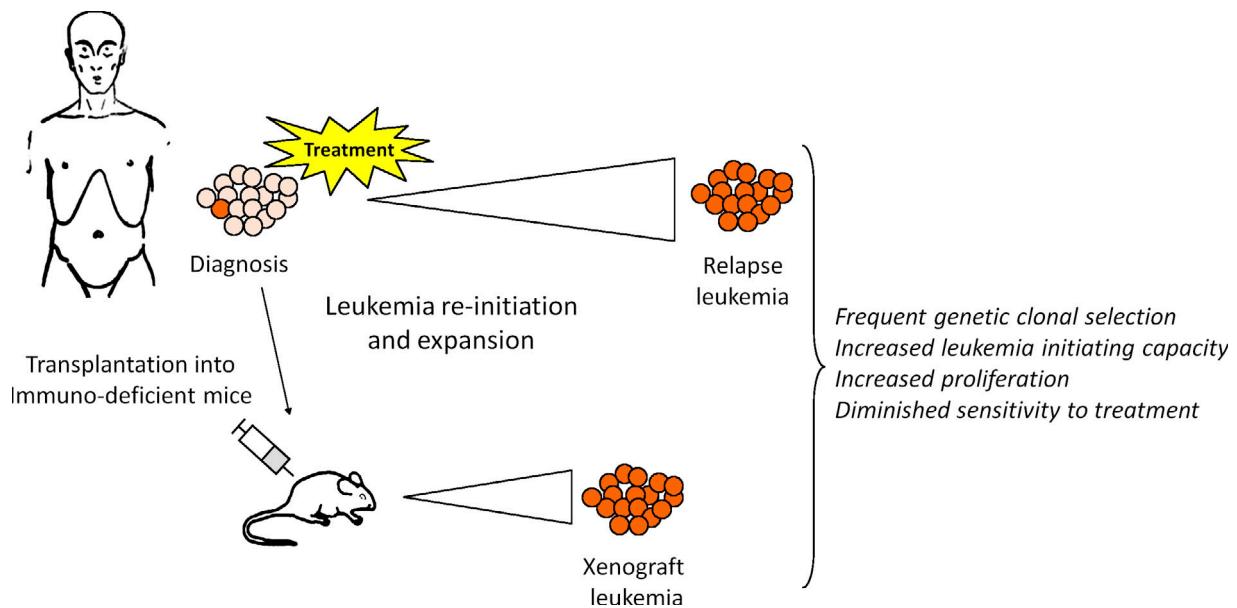


Figure S4. Clonal selection in xenografted human T-ALL recapitulates gain of malignancy at relapse: a model for clonal selection in patient and xenograft. After treatment in patients or injection into mice, leukemia can reinitiate and re-expand to an overt relapsing or xenografted leukemia, respectively. In both situations, a subclone with a higher selective advantage emerges, resulting in gain of malignancy. Clonal advantage is frequently driven by additional genomic lesions, although epigenetic mechanisms might also be involved.

Table S1. Enriched Gene Ontology terms in the overexpressed in T-ALL xenografts gene set compared with the paired diagnosis samples

Gene Ontology term	Gene Ontology accession number	P-value
Cell cycle process	GO:0022402	2.69×10^{-13}
Mitosis	GO:0007067	3.11×10^{-13}
M phase of mitotic cell cycle	GO:0000087	4.43×10^{-13}
Mitotic cell cycle	GO:0000278	7.18×10^{-13}
M phase	GO:0000279	3.09×10^{-11}
Cell cycle phase	GO:0022403	6.82×10^{-11}
Cell cycle	GO:0007049	1.47×10^{-9}
Regulation of mitosis	GO:0007088	1.57×10^{-8}
Chromosome segregation	GO:0007059	1.36×10^{-6}
Cytokinesis	GO:0000910	2.15×10^{-6}
Cell division	GO:0051301	3.69×10^{-6}
Mitotic sister chromatid segregation	GO:0000070	3.05×10^{-5}
Establishment of organelle localization	GO:0051656	3.95×10^{-5}
Sister chromatid segregation	GO:0000819	3.95×10^{-5}
Organelle localization	GO:0051640	1.66×10^{-4}
Chromosome condensation	GO:0030261	1.84×10^{-4}
Regulation of cell cycle	GO:0051726	2.28×10^{-4}
Microtubule cytoskeleton organization	GO:0000226	6.6×10^{-4}
Mitotic cell cycle checkpoint	GO:0007093	1.86×10^{-3}
Cell cycle checkpoint	GO:0000075	2.26×10^{-3}

Table S2, included as an Excel file, is a list of copy number aberrations in T-ALL samples (diagnosis, xenograft, and relapse samples). Table S3, included as an Excel file, is a list of *NOTCH1*, *FBXW7*, *PTEN*, and *WT1* mutations in the T-ALL samples (diagnosis, xenograft, and relapse samples).

The overexpressed in T-ALL xenografts gene set. The list of the genes overexpressed in the xenograft leukemia samples compared with the paired diagnosis samples are as follows: *ARHGAP19*, *ARL6IP1*, *ASPM*, *AURKA*, *BIRC5*, *BUB1*, *BUB1B*, *CASC5*, *CCNA2*, *CCNB1*, *CCNB2*, *CCNF*, *CDC25C*, *CDCA3*, *CDCA8*, *CDKN3*, *CENPA*, *CENPE*, *CENPF*, *CENPO*, *CKAP2*, *CKAP5*, *DEPDC1*, *DNMT3B*, *ESPL1*, *ETV5*, *FAM64A*, *GPSM2*, *GTSE1*, *HMMR*, *KIF14*, *KIF18A*, *KIF20A*, *KIF2C*, *KIFC1*, *MFAP4*, *MKI67*, *NCAPG*, *NEK2*, *NUCKS1*, *NUSAP1*, *PBK*, *PLK1*, *PLK4*, *PRC1*, *PROM1*, *PSRC1*, *PTTG1*, *RACGAP1*, *SHCBP1*, *SMC2*, *SMC4*, *SPAG5*, *TOP2A*, *TROAP*, *VPREB1*, and *WHSC1*.