

Supplementary Table 1. Primer sets	
<i>mouse cDNA primers</i>	<i>Sequence</i>
Utx-F	TCCAAGACCACCATCCTCAC
Utx-R	GGAGGAAAGAAAGCATCACG
Jmjd3-F	ACGAGCCTGCCTACTACTGC
Jmjd3-R	CTCGCAGTGCACCAGGTA
Hes1-F	GCGAAGGGCAAGAATAAATG
Hes1-R	TGTCTGCCTTCTCTAGCTTGG
Il7ra-F	CATTTCACTCGTAAAAGAGCCC
Il7ra-R	TGGAAGTGGATGGAAGTCAA
Suz12-F	TGATGGCTTATCATTTTTGTGG
Suz12-R	GAGAAAATGAAAGGAGAGCAAGA
<i>mouse ChIP Primers</i>	
Hes1 promoter-F	AAGTTTCACACGAGCCGTTTC
Hes1 promoter-R	TGTATCAGCACCAGCTCCA
Jmjd3 promoter-F	CGCAGCTTCCCAGAAGTTAG
Jmjd3 promoter-R	ACCAAGTTCCTCCAGCTCCT
<i>human cDNA primers</i>	
NRARP-F	CGCTGTGCTGGTGTCTAA
NRARP-R	CATTGACCACGCAGTGTTTT
NOTCH1-F	CGGGGCTAACAAAGATATGC
NOTCH1-R	AGTGGTCCAGCAGCACCTT
MYC-F	GCTGCTTAGACGCTGGATTT
MYC-R	CGAGGTCATAGTTCCTGTTGG
MAZ-F	GACCACATGAAGGTGCACAG
MAZ-R	GTCCTTACC CGTGGAT
HEY1-F	ATTTTGCCAGAAAAAGACG
HEY1-R	CTGGGTACCAGCCTTCTCAG
JMJD3-F	GGGAAGAAAATCGCTTACCAG
JMJD3-R	TCACTTGTACGAACAGGATG
UTX-F	ACTTGGAAAAC TTTGTGGTGTCT
UTX-R	CAAGATGAGGCGGATGGTA
<i>human ChIP primers</i>	
NRARP locus-F	ACCAACTGCGAGTTCAACG
NRARP locus-R	TTGACCAGCAGCTTACAG
NOTCH1 locus-1F	CAGACACTTTGAAGCCCTCAG
NOTCH1 locus-1R	CGCCTTTGTGCTTCTGTCT
NOTCH1 locus-2F	CCTCCTCTTCCCTCGTGT
NOTCH1 locus-2R	CAGACTGAGCACCCGTCTCT
NOTCH1 locus-3F	AGGCTGGCAGCTCTATTACAG
NOTCH1 locus-3R	CGTGGCAGAGTCTGGAAGT
MYC locus 1F	GGTCCGACATTCTGCTTTA
MYC locus 1R	CAAGGAGCTCAGGATGCAA
MAZ locus-1F	GTCTCCCTCCCTCCTGTGT
MAZ locus-1R	AAATTTGAAAAGGCGGAGTG
MAZ locus-2F	ATCTTCGGGGAACGACTCA
MAZ locus-2R	CTTCGGCTTCCGCTTTTT
HEY1 locus-F	TGGGGACATGGAACCTAGAG
HEY1 locus-R	GCGACCTCTCAGATCACCTC
RBBP6 locus-1F	TATGGTGCTGGTGGCTGTTA
RBBP6 locus-1R	GCTGCTGCTTCCAATAAACTG
RBBP6 locus-2F	TGAGCCTGGCAATGTTGTTA
RBBP6 locus-2R	CCGCTGCCAAGAAGTATA
JMJD3 locus (NFkB binding) 2.1AF	GTGGGCTGAGGAGTTGTGTC
JMJD3 locus (NFkB binding) 2.1AR	CCAGAAAACCTTCCCCTCTT
JMJD3 locus (NFkB binding) 2.1BF	GTGGGCTGAGGAGTTGTGTC
JMJD3 locus (NFkB binding) 2.1BR	CGTGAGTCACCCAGAAAACC

Supplementary Table 2. Details on the frameshift mutations identified in pediatric T-ALL (Sanger sequencing)
flanking sequence[wt sequence>mutant sequence]flanking sequence
SJTALL037: R1111fs, TGCTTTGTG[C----->GGGGCGTAA]GTGTCGTATC
SJTALL177: V1113fs, GTGCGTGTGG[----->GGTGTGG]TATCAGCAGG
SJTALL189: V1112fs, TTGTGCGTGT[CGTATCA-->GGCTAATAG]CAGGAAATCT

Supplementary Table 3. Overlap between gene expression changes in knock-downs, GSKJ4 and Utx knockout genotype

GENES	LIST-A	LIST-B	INTERSECTION	EXPECTED	P-VALUE	LIST-A	LIST-B
20414	749	3682	373	135.1	6.53E-91	<i>shJMJD3</i> specific.down	<i>CEM shJMJD3</i> specific.down
20414	297	1636	62	23.8	2.01E-12	<i>shJMJD3</i> specific.up	<i>CEM shJMJD3</i> specific.up
20414	749	486	97	17.8	4.88E-44	<i>shJMJD3</i> specific.down	GSKJ4 vs untreated.down
20414	297	486	17	7.1	8.18E-04	<i>shJMJD3</i> specific.up	GSKJ4 vs untreated.down
20414	749	1751	74	64.2	1.11E-01	<i>shJMJD3</i> specific.down	GSKJ4 vs untreated.up
20414	297	1751	79	25.5	2.57E-20	<i>shJMJD3</i> specific.up	GSKJ4 vs untreated.up
20414	46	486	7	1.1	9.95E-05	<i>shUTX</i> specific.down	GSKJ4 vs untreated.down
20414	189	486	24	4.5	2.51E-11	<i>shUTX</i> specific.up	GSKJ4 vs untreated.down
20414	46	1751	11	3.9	1.43E-03	<i>shUTX</i> specific.down	GSKJ4 vs untreated.up
20414	189	1751	29	16.2	1.54E-03	<i>shUTX</i> specific.up	GSKJ4 vs untreated.up
20414	1472	486	48	35	1.66E-02	<i>UTXKO</i> down	GSKJ4.down
20414	1789	486	83	42.6	2.49E-09	<i>UTXKO</i> up	GSKJ4.down
20414	1472	1751	167	126.3	8.95E-05	<i>UTXKO</i> down	GSKJ4.up
20414	1789	1751	210	153.5	1.02E-06	<i>UTXKO</i> up	GSKJ4.up

Supplementary Table 4. Reproducibility Summary of High-throughput Sequencing data	
RNA-Seq reproducibility Summary	<i>Spearman correlation coefficient</i>
CUTLL1.GSKJ4_24h	0.915
CUTLL1.GSKJ4_48h	0.91
CUTLL1.GSKJ4_72h	0.916
CUTLL1sh <i>Renilla</i>	0.845
CUTLL1.sh <i>JMJD3</i>	0.834
CUTLL1.sh <i>UTX</i>	0.91
CEM.sh <i>Renilla</i>	0.923
CEM.sh <i>JMJD3</i>	0.916
CEM.sh <i>UTX</i>	0.925
	0.753
ChIP-Seq reproducibility Summary	
	<i>genome-wide analysis</i>
CUTLL1-H3K27me3-sh <i>JMJD3</i>	0.642
CUTLL1-H3K27me3-GSKJ4_6h	0.68
CUTLL1-H3K27me3-sh <i>Renilla</i>	0.716
	<i>TSS-based analysis</i>
CUTLL1-H3K27me3-sh <i>Renilla</i>	0.852
CUTLL1-H3K27me3-sh <i>JMJD3</i>	0.85
CUTLL1-H3K27me3-GSKJ4_6h	0.827
CUTLL1-JMJD3-GSKJ5 (control)	0.753