Supplementary Figure Legends

Supplementary Figure 1. Biological replicates of Annexin-V staining studies by flow cytometry. Propidium iodide (PI) and Annexin-V (AV) staining of cells treated with 500 nM JQ1 for 48 hours.

Supplementary Figure 2. LC3 immunoblotting to measure inhibition of autophagy. MUTZ-5 cells treated with 500 nM JQ1 for 1, 2, 3, and 4 days. Chloroquine was used as a control for autophagy inhibition.

Supplementary Figure 3. Replicate BRD4 ChIP experiment at the *MYC* locus. Enrichment with a BRD4 antibody at two sites within the *MYC* locus in cells treated with 500 nM JQ1 for four hours. Enrichment is shown as the percentage of total input DNA. The negative control region primers amplify within a gene desert ~1 Mb upstream of *MYC*. Error bars represent +/- SEM of three qPCR reactions; (*$p < 0.1$, **$p < 0.01$).

Supplementary Figure 4. *P* values of expression changes of multiplexed expression data and correlation between biological replicates. (A) *P* values for both MHH-CALL4 and MUTZ-5 gene expression datasets (*$p < 0.1$, **$p < 0.01$; unpaired t test). (B) Scatterplots of Nanostring multiplexed expression data between biological replicates for MHH-CALL4 and MUTZ-5 cells treated with 500 nM JQ1 for 4 hours. Expression for each gene is shown as the log value relative to the average of three housekeeping gene controls. R^2 values were determined by nonlinear regression analysis.

Supplementary Figure 5. Clustering of the combined multiplexed gene expression analysis. Unsupervised heirarchical clustering of the combined expression data of c-MYC target genes across both MHH-CALL4 and MUTZ-5 cell lines treated with 500 nM JQ1 for 4 hours.

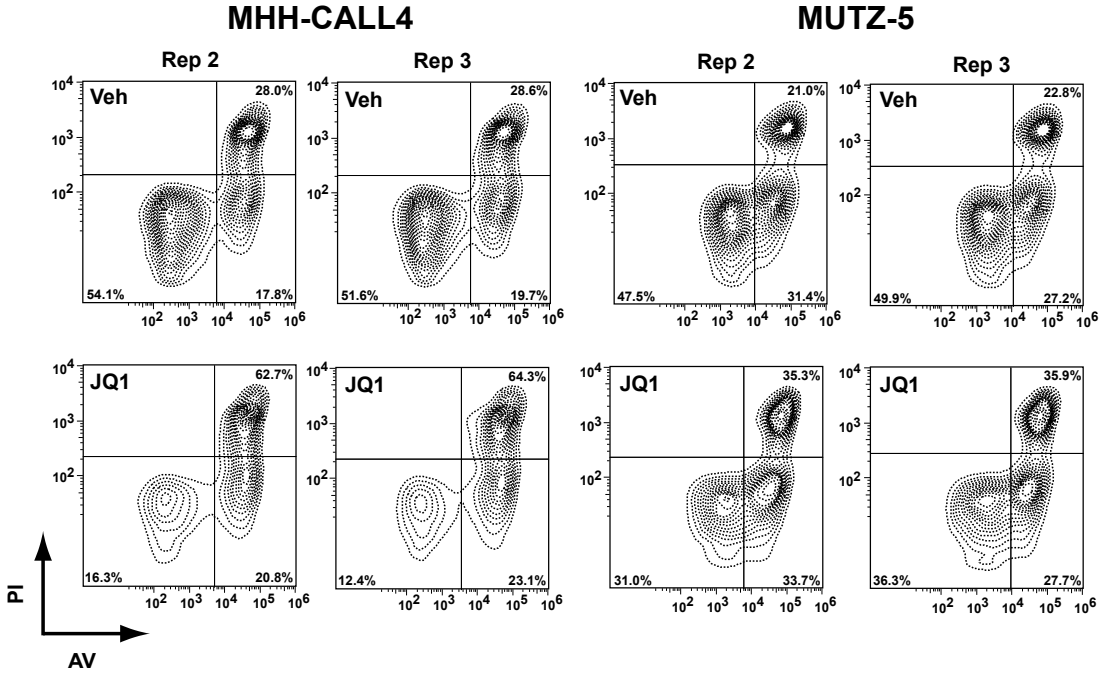
Supplementary Figure 6. Replicate flow cytometry for CRLF2 and IL7R. Histograms of a replicate flow cytometry experiment for detection of CRLF2 and IL7R expression. Cells were treated with 500 nM JQ1 for 8 and 24 hours.

Supplementary Figure 7. Replicate BRD4 ChIP experiment at the *IL7R* locus. Enrichment with a BRD4 antibody at two sites of the *IL7R* locus in cells treated with 500 nM JQ1 for four hours. Enrichment is shown as the percentage of total input DNA. Negative control region primers amplify within a gene desert region ~70 db downstream of *IL7R*. Error bars represent +/- SEM of three qPCR reactions; (**$p < 0.01$).

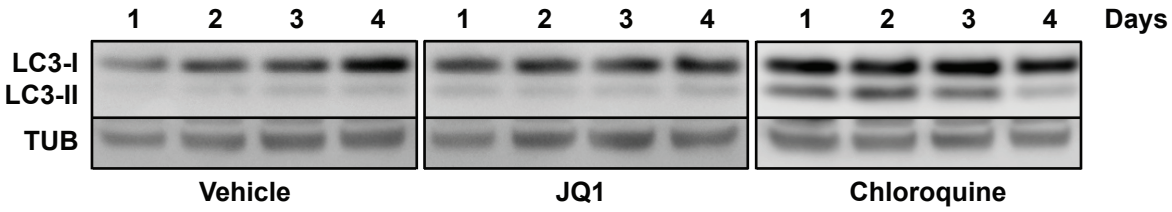
Supplementary Figure 8. *IL7R* expression analysis in the Cancer Cell Line Encyclopedia. Box plots of RMA-normalized expression values across a range of cancer cell lineages (ref. 43; www.broadinstitute.org/ccle). Cancer type is listed below the graph and the number of cell lines per cancer type is in parentheses.

Supplementary Figure 9. Analysis of primary human leukemia engraftment in NSG mice. Bone marrow samples were harvested from sentinel mice and assayed by flow cytometry for human CD45 positivity. In the bone marrow sample shown, 83.7% of cells were hCD45+, indicating substantial primary leukemia cell engraftment.

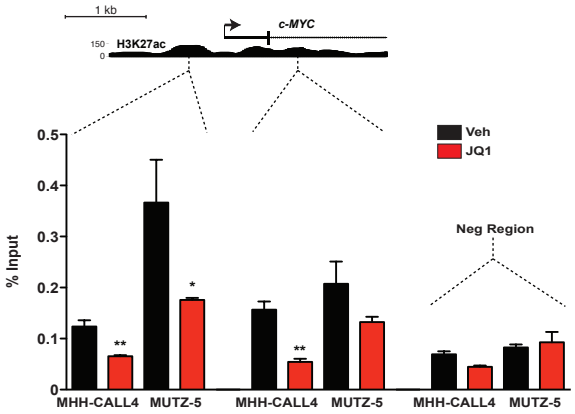
Supplementary Figure 10. CRLF2 expression analysis in JQ1-treated mice. Flow cytometry for CRLF2 from splenic cells harvested from mice treated for 5 days with Vehicle (Veh) or JQ1. Scatter plots on the left show overall CRLF2 expression versus hCD45 positivity. The histogram on the right is quantification of total CRLF2 expression in the sample.



Supplementary Figure 1



Supplementary Figure 2

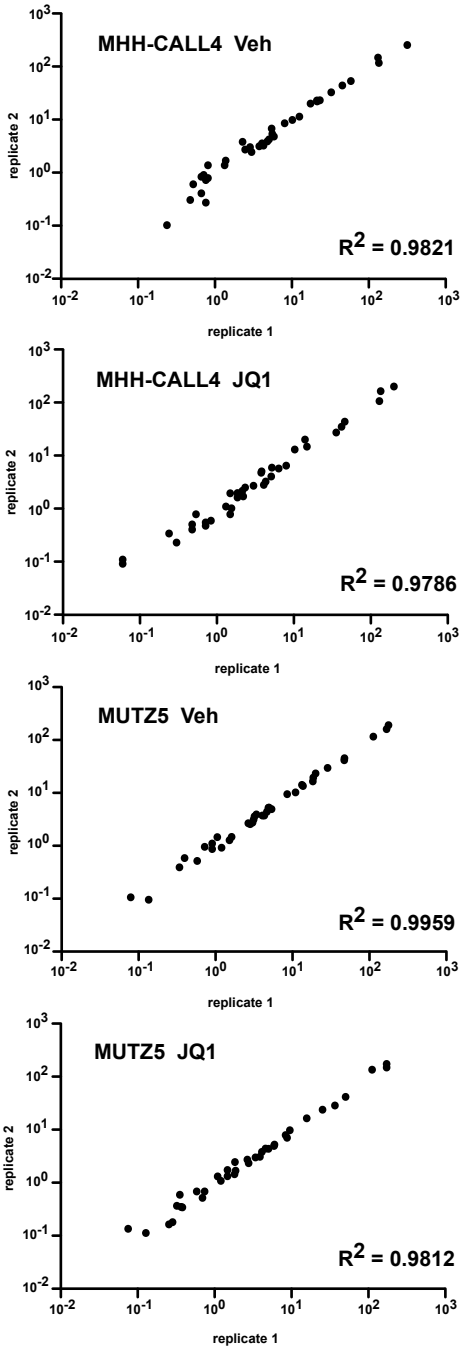


Supplementary Figure 3

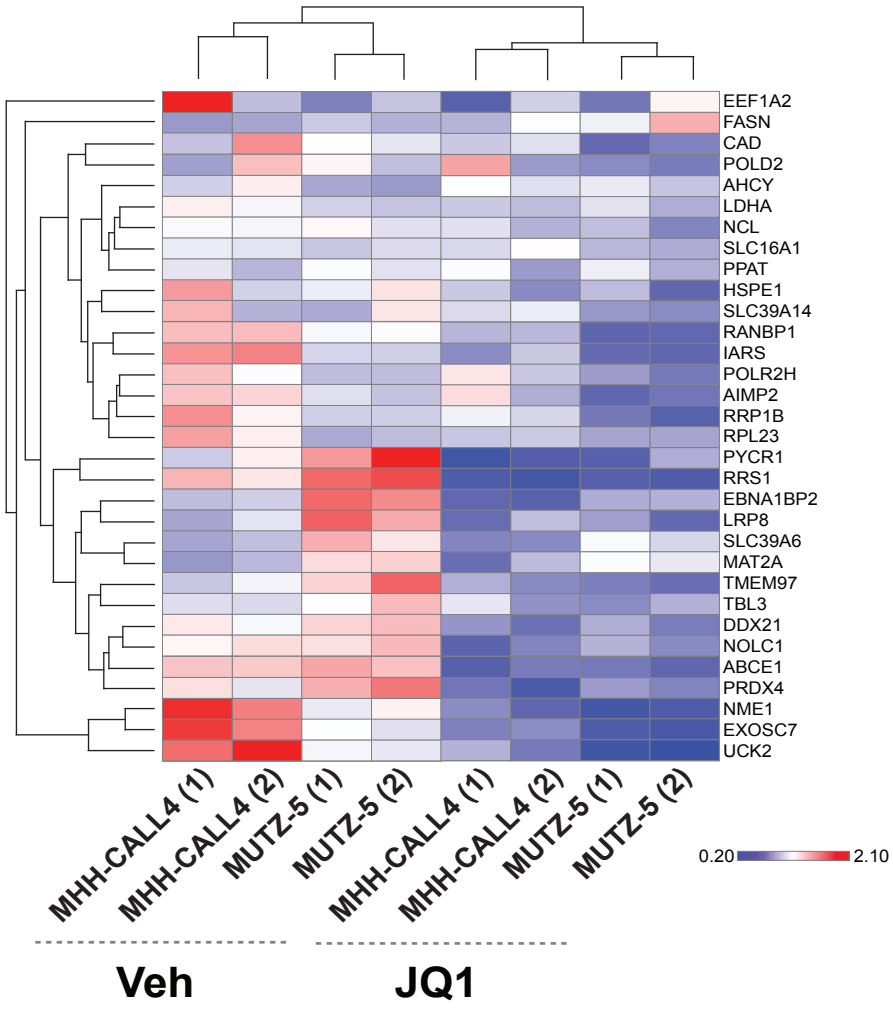
A

	MHH-CALL4	MUTZ-5
GAPDH	0.6057	0.8354
ACTB	0.6301	0.5392
TUBB	0.7857	*0.0796
MYC	**0.0035	**0.0054
DDX21	*0.0348	*0.0272
AIMP2	0.3397	*0.0294
MAT2A	0.6604	*0.0385
POLR2H	0.4745	0.1123
NCL	0.1871	0.1373
LDHA	*0.0562	0.9220
EXOSC7	*0.0198	**0.0077
PRDX4	*0.0587	0.2070
NOLC1	*0.0209	*0.0346
TBL3	0.5388	*0.081
TMEM97	0.1554	*0.0555
RRS1	*0.0107	**0.0026
CAD	0.5036	*0.0262
FASN	0.2649	0.1943
SLC39A14	0.7480	0.2979
SLC16A1	0.8262	0.1179
EBNA1BP2	*0.0142	**0.0069
LRP8	0.4586	*0.0347
AHCY	0.9340	0.1077
UCK2	*0.0373	**0.0052
NME1	*0.027	*0.0102
IARS	*0.0218	**0.0025
RANBP1	**<0.0001	**0.0021
EEF1A2	0.3580	0.7429
HSPE1	0.2900	0.1510
POLD2	0.9351	0.1326
SLC39A6	*0.0852	0.1395
RRP1B	0.2183	*0.0321
RPL23	0.1053	0.2456
PPAT	0.9783	0.4388
PYCR1	*0.0449	0.7910
ABCE1	*0.0125	**0.007

B

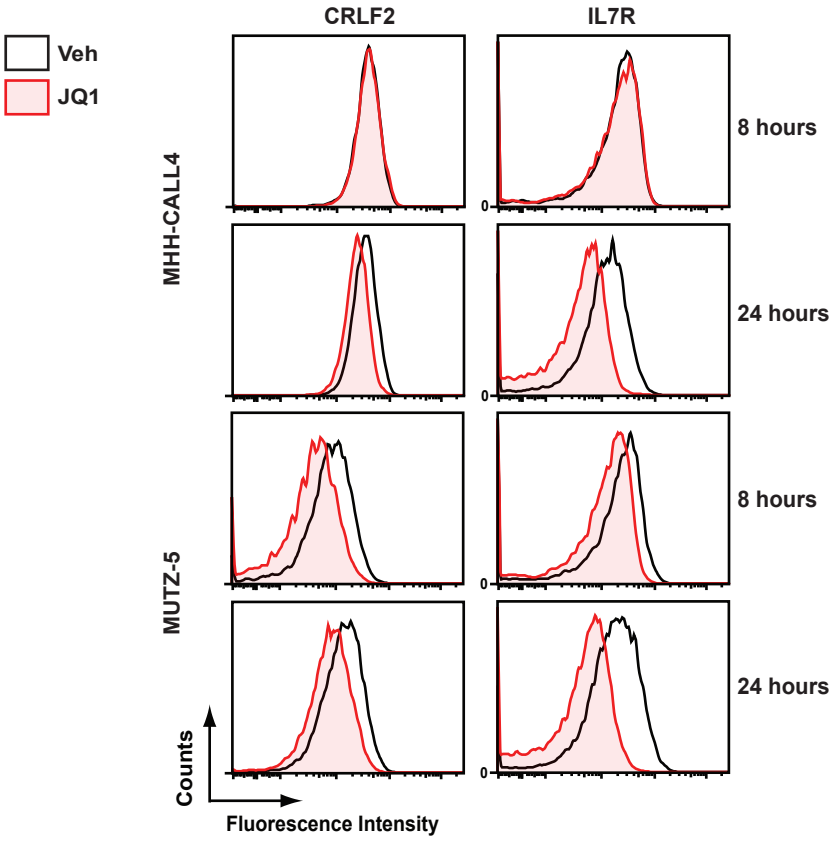


Supplementary Figure 4



Supplementary Figure 5

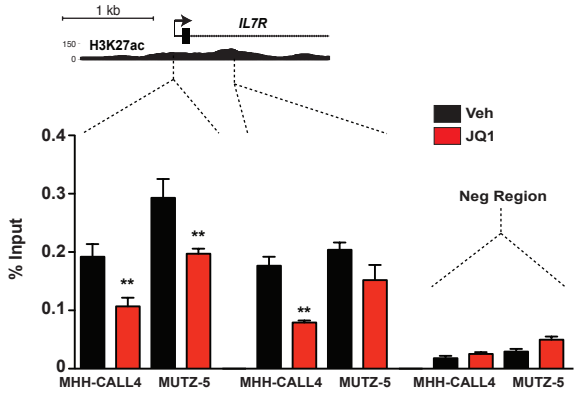
A



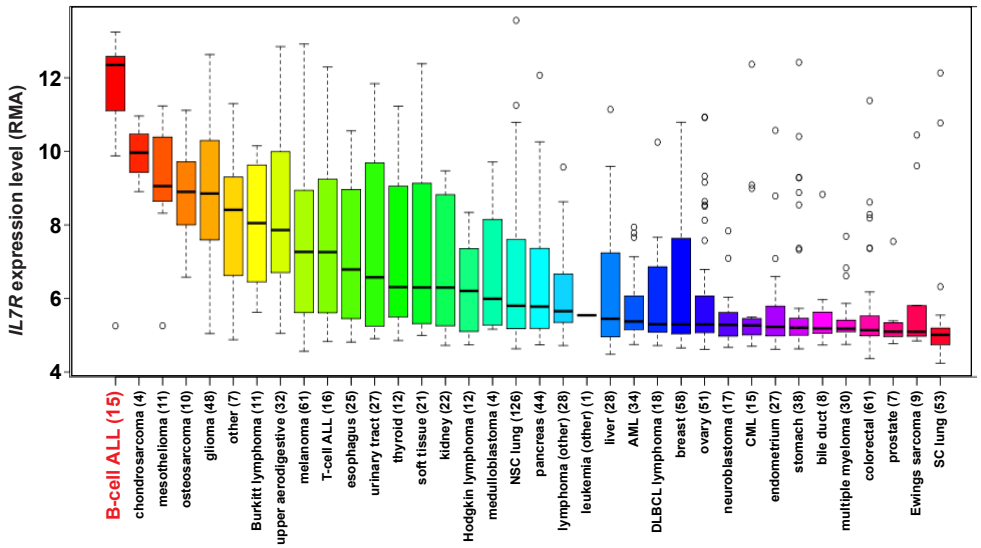
B

	CRLF2	IL7R
	% fluorescence relative to vehicle Mean (SEM) *p*-value	% fluorescence relative to vehicle Mean (SEM) *p*-value
MHH-CALL4 (8h)	108.2 (4.8) *p*=0.2762	86.4 (11.7) *p*=0.3773
MUTZ-5 (8h)	45.7 (13.2) *p*=0.1409	50.7 (8.6) *p*=0.0990
MHH-CALL4 (24h)	71.5 (0.6) *p*=0.0025	36.9 (1.9) *p*=0.0053
MUTZ-5 (24h)	61.3 (0.8) *p*=0.0026	28.1 (1.0) *p*=0.0003

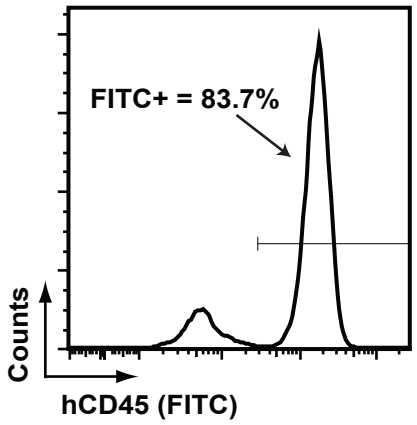
Supplementary Figure 6



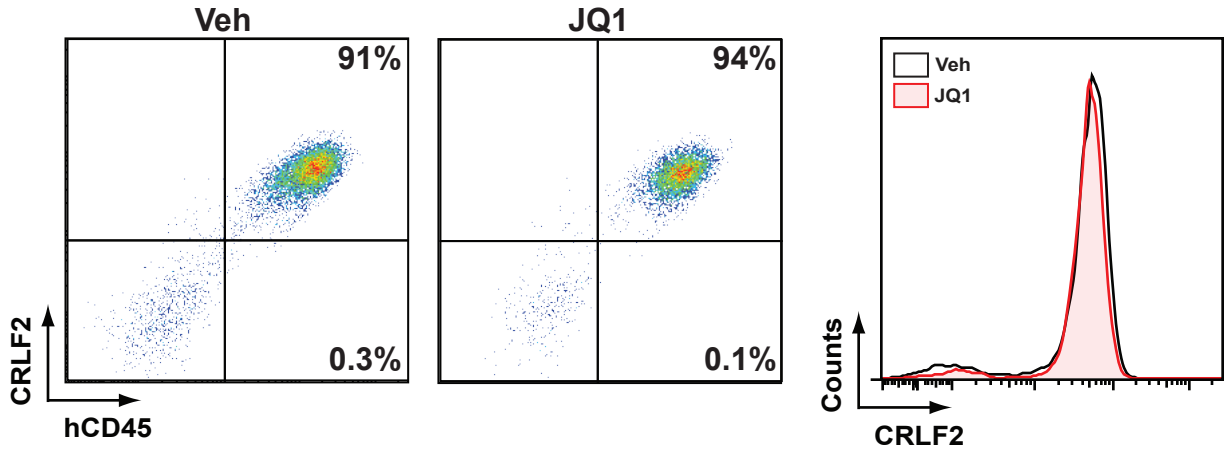
Supplementary Figure 7



Supplementary Figure 8



Supplementary Figure 9



Supplementary Figure 10