Table S1

	Total Reads	Human	Called peaks	DHS filter
EBNA3A	59,941,027	8,832,593 (15%)	1640	1064
EBNA3B	71,646,718	6,989,005 (10%)	3033	2648
EBNA3C	105,734,958	8,639,412 (8 %)	3588	1802
*EBNA2	12,947,095	4,883,146 (34%)	8592	7772
RBPJ Rep1	125,720,183	4,577,382 (36%)	4225	3329
*RBPJ Rep2	13,382,267	7,284,453 (54%)	8348	7526
RBPJ total			9938	8294

Table S1: Summary of ChIP-seq read alignment and peak calling.
For each ChIP-seq experiment, total reads, total reads aligned to human genome, and number of called peaks are indicated. Two of these datasets (indicated with an *) have been previously reported (42), but are reanalyzed here for comparison. The peaks called from initial data processing are further filtered based on their overlapping with the DNase hypersensitivity site (DHS) reported from ENCODE project.

Figure S1

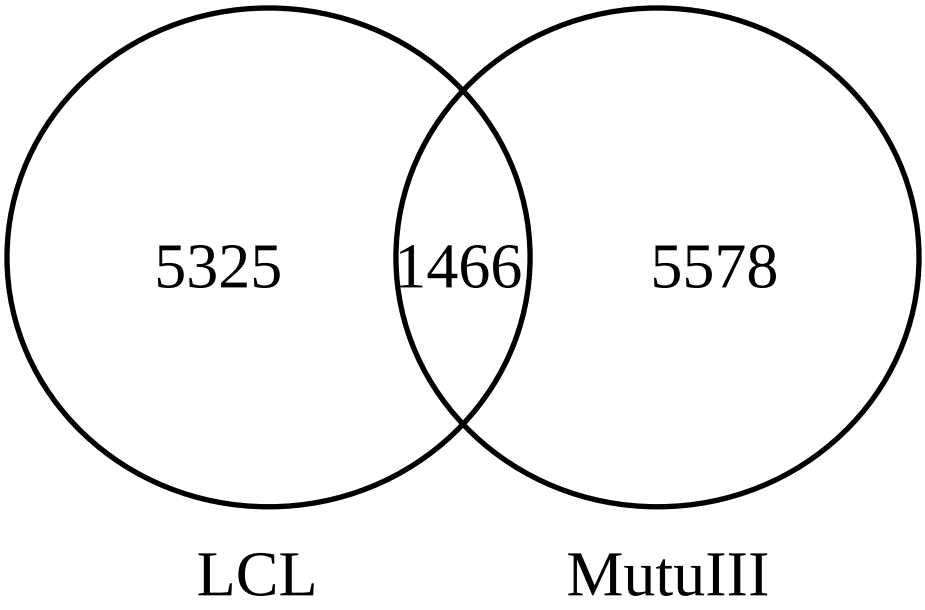


Figure S1: Overlap of EBNA3 binding peaks with previously published data.
Overlap between the 6791 EBNA3A, EBNA3B and EBNA3C bound sites (Table S2) identified by our ChIP-seq experiments (LCL) and the 7044 EBNA3 sites identified in MutuIII cells (33) is 1466 as indicated. Overlap was defined as sharing one or more 200 bp genomic bin.

Table S3

Gene	Primer sequence	
HDAC7	P1:CGAACCTGTCACTCCCAGAC	P2:CCCATTCCAAGGAGCCTAGC
EIF2AK3	P1:CTTCCGGACGCAATTACCAATGAG	P2:GTAGGAAAGGTATTCCGGGAACTG
METTL13	P1:AAAGCGTTTAGGTGTCTGCGACG	P2:TCAGCTAGTCATTGGTCGCTGCTT
C20orf24	P1:ACCGTTCTACCAAGATTGTCCCTC	P2:AAGCCATCCGAGTGAAACAGCGA
IL6R	P1:CAGTTGAGTCTGTGGGAACTC	P2:CCTGTTCCTCTTGCTCCTAATG
QSK	P1:GCTGTAGCAGGCAATACTCTCTTG	P2:GCAGCTGACTTTACATTGGGCAGA
HNRPLL	P1:GAACTGGGAAACCAAAAGAGCGGT	P2:GATGGCTTCCAGACTGTGGT
NFATC2	P1:CGCACAGCAGCCCAAATTAC	P2:ACCTGTCACCCCAATTAGCAG
ALOXE3	P1:CCGGATAGCTCAGTCGGTAG	P2:GCGGTACCCAAAAGCAAAGA
POU2F1	P1:TCTGGCGGCAGGAGAAA	P2:TGGCCCTTCGGTAGCTAAA
PIP5K1B	P1:AATGGGAATCCTAGGTCCCTGACT	P2:AGCTCCAGGTCTAGCTCCATCTTC
CTLA4	P1:CGTTGCAATAACATGGGGCAG	P2:GCATTCTGCCCAGCCTAATCT
CXCR5	P1:CACCACCCAGAAGACATGAA	P2:GCAAGGTGCTCTGGAAACTA
CCDC80	P1:TCTACCTCATGCTGCCCAAACTGT	P2:TTACCTCCTCTGTGGCTGCATTTG
ARHGAP25	P1:AGACAAGGGTAGTGGATGTTGCCT	P2:AGCATCACAGTAGCCACAGAACCT
JAK1	P1:TTCCTGCTTTGCACTTCAGCTCAG	P2:TGCTTCCCTCCCAAATACACCTCA
SHQ1	P1:GGTTTCATTTCCTCTGCCCAAACC	P2:GTCCTCTGTGATCAATTGTGGGCT
ROCK1	P1:ACCTAACAGAGTACAACCTGTC	P2:CCTCCTGAGAGTGCTTCTGTC
SYTL3	P1:ATCCTGGTGACTGCAGCCCCTT	P2:CCAGCGGAGGCCCTGCTATAC
BLK	P1:AAGGCACATGGAAGGAGAGCTGAA	P2:ACTAGACCCTAGCTCTGAAACGCC
BACH2	P1:AGCAGTAGTAGCAGTAGTAGCA	P2:ACCCAAACAGTGGTTCATAGAG
CDH1	P1:CAAAGGGAAACCCTGTCTCTAC	P2:TCCTGGACTCAAGGGATCTAC
CACNB4	P1:GTGGATGTCTTAGCAGTGATGA	P2:CTAGTGTGGATTGGCTCTGAAT
GSG2	P1:TTGCCCTGGTACAGGATAGT	P2:CCTGCTTGGTTTCATTGGTTTC
TMEM109	P1:AGCCACATTGGCCTTTCA	P2:ACATTGGAGGGTTTGAGACAG
SUB1	P1:GCAAAGAAGGGCAAGTCAAAG	P2:GCATCCTGTCCAATCTCATAGG
FOXO3	P1:GAAGCACGCATGTGCATTTA	P2:TTATGCACACATGACTAGGAGAC
ALPK2	P1:CTAGGAGTAAGCCCAACATAGTG	P2:CAGAGGGTCAGAGAAGCTAAAG
PARP9	P1:TGTCTGGCACCTTCTGTTAAG	P2:ACTGCCTTGAGGCAATTCA
TRIB2	P1:CATCTTGGCGACCATGGTATAG	P2:ACAAGGCATGCTATCTCTTTCA
PPIA	P1:GGGCCGAACGTGGTATAA	P2:CCATGGCTAATAGTACACGGTTT

Table S3: Primer pairs used for qPCR in this study.
For the indicated genomic loci sequences of the forward and reverse primers are indicated. PPIA primers are from a study by McClellan et al. (52).

Table S4

	Genes bound	EBNA2 co-bound	
EBNA3A	1731	600	35%
EBNA3B	2705	1340	50%
EBNA3C	3063	1081	35%
any EBNA3	5493	2014	37%

Table S4: Summary of the proportion of genes co-bound by EBNA3s and EBNA2 in LCLs.
For this analysis we assigned each bound site summarized in Table S2 to the nearest Ensembl annotated gene, regardless of strand. When this distance was zero for both genes, we considered them both bound. The number of annotated genes bound by each EBNA3 is indicated in the first column, number with EBNA2 co-binding and % EBNA2 co-binding is indicated in columns two and three.

Figure S2

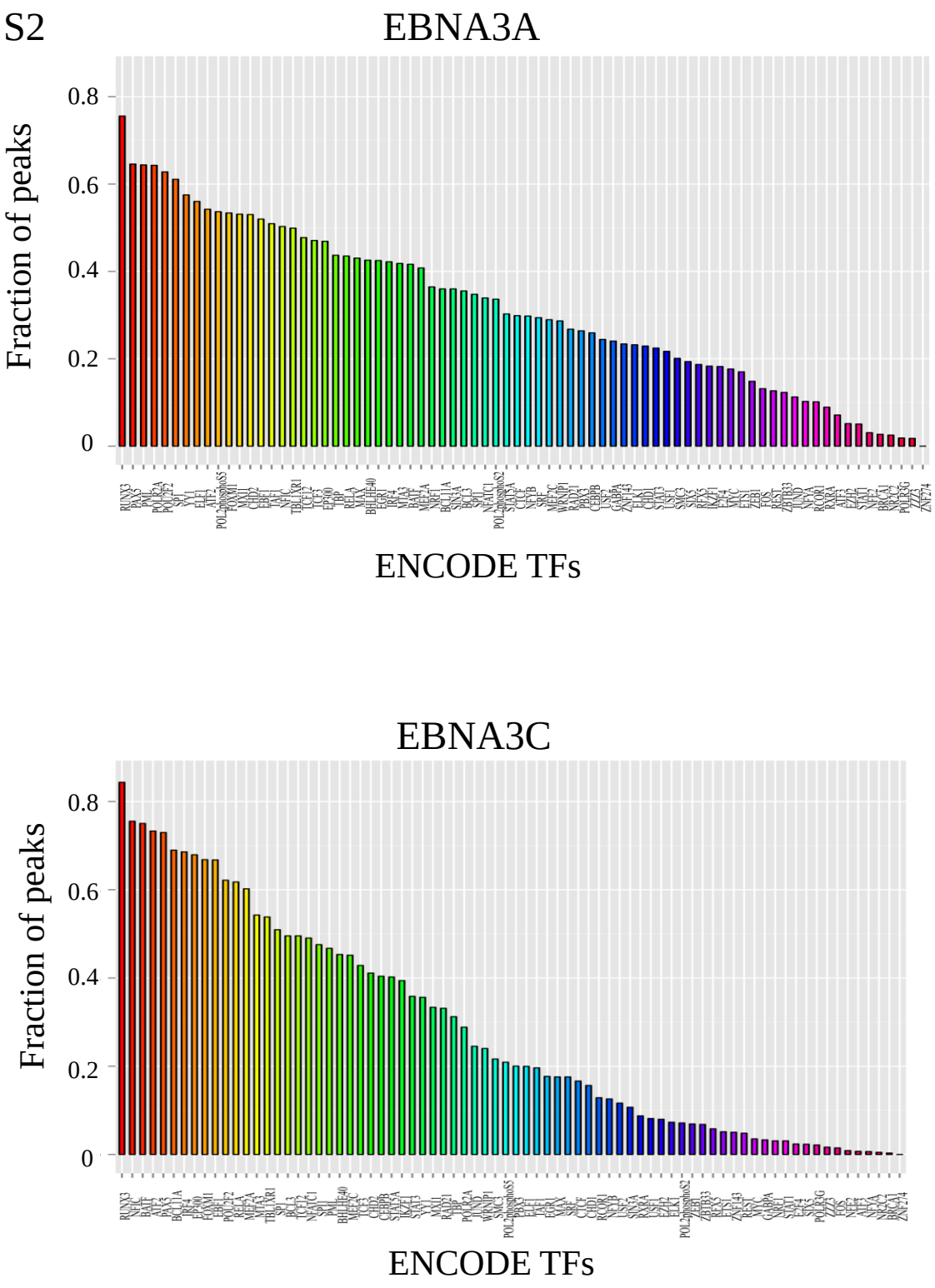


Figure S2: Transcription factor co-binding at EBNA3A and EBNA3C bound sites.
A) Bar plot showing the fraction of EBNA3A peaks co-associated with the indicated transcription factors (X-axis). Co-localization was defined as binding with 200 bp of EBNA3A bound sites and cell transcription factor binding locations were derived from ENCODE ChIP-seq data for 76 transcription factors in the GM12878 LCL. B) Bar plot as described for (A) showing the fraction of EBNA3C peaks co-associated with the indicated transcription factors.

Figure S3

EBNA3A

Motif sequence	P-value	Predicted TF
	3.2e-24	EGR1

EBNA3C

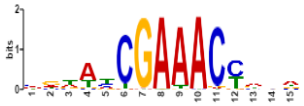
Motif sequence	P-value	Predicted TF
	1.2e-30	–
	2.3e-24	AP1 family
	6.0e-21	EICE
	1.2e-20	IRF4
	4.0e-20	RUNX
	3.7e-12	ETS family

Figure S3: Motif enrichment at EBNA3A and EBNA3C bound sites.
EBNA3A or EBNA3C bound sites were analyzed for enriched motifs using MEME-ChIP. Motifs with the lowest p-values are indicated as well as any transcription factors predicted to recognize them.

Figure S4

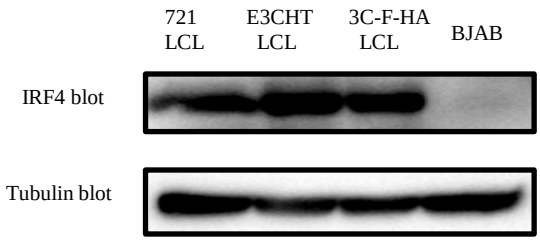


Figure S4: Western blot for IRF4 expression levels in multiple B cell lines. Western blots for IRF4 (top panel) and tubulin (bottom panel) were done on whole cell lysates from the indicated B cell lines to identify candidate cell lines lacking detectible IRF4 expression. Each lane represents whole cell lysates from 10^6 cells.

Figure S5

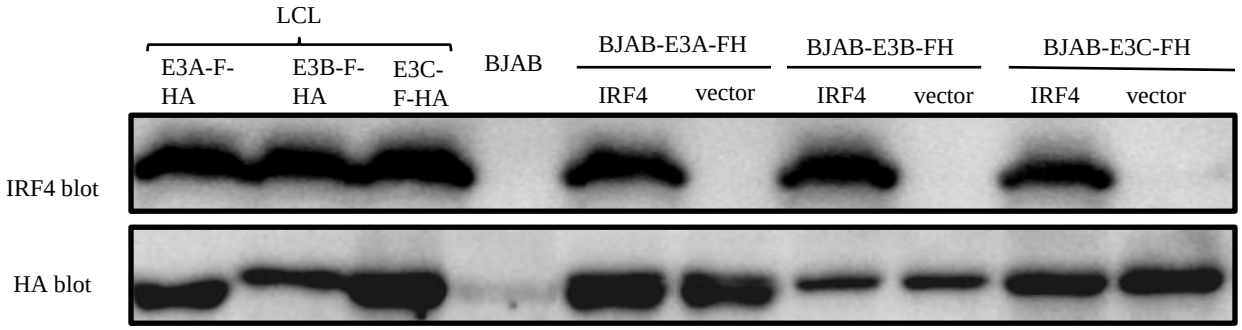


Figure S5: Characterization of BJAB stably expressing flag-HA tagged EBNA3A, EBNA3B, or EBNA3C with or without IRF4. Western blots for IRF4 (top panel) and HA (bottom panel) were done in BJAB clones expressing EBNA3A-FHA, EBNA3B-FHA, EBNA3C-FHA with either IRF4 or vector control. For comparison LCLs expressing EBNA3A-FHA, EBNA3B-FHA, EBNA3C-FHA are shown (left 3 lanes). Each lane represents whole cell lysate from 10^6 cells.