SUPPLEMENTAL MATERIAL

Kalchschmidt et al., http://www.jem.org/cgi/content/full/jem.20160120/DC1

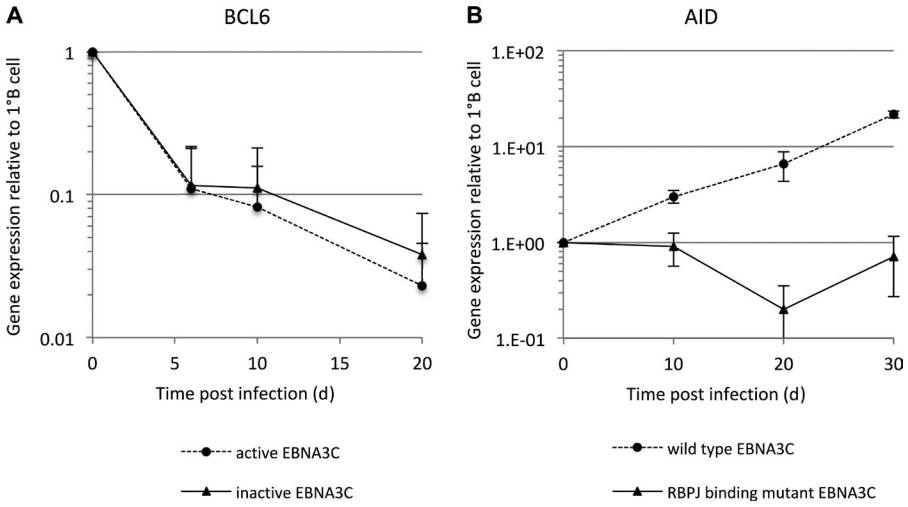

Figure S1. **Repression of BCL6 is independent of EBNA3C, and induction of AID is dependent on the ability of EBNA3C to interact with RBPJ.** (A) Infection of primary B cells with recombinant EBV expressing active (3CRev or 3CHT +HT) or inactive (3CKO or 3CHT −HT) EBNA3C. Gene expression of *BCL6* was normalized to *GAPDH* or GNB2L1 and is shown relative to uninfected primary B cells. (B) Infection of primary B cells with recombinant EBV with wild-type EBNA3C or encoding an EBNA3C mutant that is unable to bind to RBPJ (RBPJ-binding mutant EBNA3C). AID mRNA expression was normalized to *GNB2L1* and is shown relative to uninfected primary B cell. Results show mean ± SD of two biological replicates using B cells from different donors.

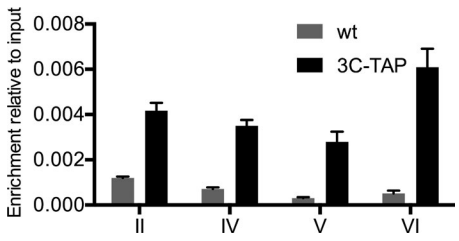

Figure S2. **ChIP-qPCR verification of EBNA3C occupancy at regulatory regions of *AICDA*.** Anti-Flag ChIP was performed on LCLs with either EBNA3C-TAP or untagged (wt) EBNA3C and determined by qPCR at the indicated regulatory regions of *AICDA*. ChIP values represent enrichment relative to input ± SD of triplicate qPCR reactions for ChIP and input of each sample. These are representative results of two biological replicates.

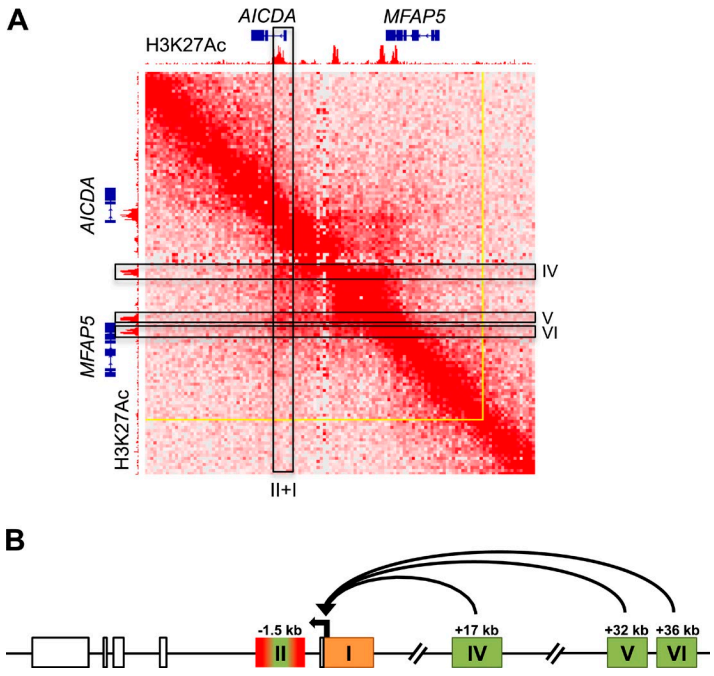

Figure S3. **Higher order chromatin structure of the *AICDA* locus in LCL GM12878.** (A) Juicebox was used to display GM12878 in situ MboI combined (4.9 B) Hi-C map at 1-kb resolution (Rao et al., 2014). The intensity of each pixel represents the normalized (balanced) observed number of contacts between a pair of loci. Gene location for *AICDA* and *MFAP5*, H3K27ac in LCL GM12878, topologically associating domain (yellow box), and locations of AID regulatory regions are indicated. (B) Schematic overview of higher order chromatin structure of the *AICDA* locus in LCL GM12878 with chromatin looping indicated by black arrows between the promoter region of *AICDA* and upstream enhancer elements IV, V, and VI.

Table S1. **Total number of sequencing reads and unique V-D-J rearrangements per sample**

Condition	Day	Technical replicate	Number of reads	Number of unique V-D-J rearrangements
−HT	0	A	198,362	11,219
		B	194,823	6,186
		C	149,604	8,850
		D	147,598	8,878
	15	A	201,034	9,582
	30	A	137,139	6,154
		B	184,503	3,756
	60	A	150,120	5,676
		B	164,873	3,156
+HT	15	A	179,405	9,541
	30	A	194,136	8,621
		B	191,113	3,613
	60	A	221,088	7,424
		B	187,481	3,559
		C	204,514	7,022

Table S2. **Characteristics of the four major clones according to the IMGT database**

Clone color	V gene	J gene	Nucleotide identity		Percentage of culture				
			V-region	J-region	−HT			+HT	
					d0	d30	d60	d30	d60
Blue	IGHV3-23*01	IGHJ4*02	205/222	25/30	29.8	53.4	45.4	45.3	33.7
Red	IGHV3-7*01	IGHJ4*02	200/219	31/31	31.3	39.6	54.5	39.7	65.9
Green	IGHV6-1*02	IGHJ4*02	228/228	27/31	15.2	2.5	0.01	9.3	0.03
Orange	IGHV7-4-1*02	IGHJ6*03	213/219	41/45	16.4	4.0	0.01	5.2	0.18

Table S3. **Sequences of RT-qPCR primers**

Gene	Primer sequence (5′–3′)	Reference
AICDA	Forward: AGCCGTTCTTATTGCGAAGA Reverse: TGATGAACCGGAGGAAGTTT	
BCL6	Forward: CTGCAGATGGAGCATGTTGT Reverse: TCTTCACGAGGAGGCTTGAT	Tran et al. (2010)
GNB2L1	Forward: GCTTGCAGTTAGCCAGGTTC Reverse: GAGTGTGGCCTTCTCCTCTG	Zhang et al. (2005)
GAPDH	Hs_GAPDH_2_SG QuantiTect primer assay, cat. no. QT01192646	QIAGEN

Table S4. **Sequences of ChIP primers**

Primer name	Primer sequence (5′–3′)	Reference
Region I	Forward: GAGGAAGGCCAGTGCAATCA Reverse: CAGGGAGGCAAGAAGACACT	
Region II	Forward: GCTAGTTAACTTTGTTGATC Reverse: CTACTCAGGACAGAAATGAC	
Region IV	Forward: TGGACACCAGCTAGATTGTTCA Reverse: TCACACTTTCACCCACACAGA	
Region V	Forward: CCTGTTCCTCTCCTTACCGC Reverse: ACGGAAGCCCTTGTATCTTTGA	
Region VI	Forward: CAGCAAGTTTCCTTCTGCGA Reverse: GCCATTTCTGACTCAGCAGC	
Control	Forward: GTCCTGTACAGTAACTAGAGAAAA Reverse: GCAAAGCAAGACGACAAAGGA	
GAPDH	Forward: CGCTCTCTGCTCCTCC Reverse: TTTCTCTCCGCCCGTCCAC	EMD Millipore
Myoglobin	Forward: GGAGAAAGAAGGGGAATCACA Reverse: GATAAATATAGCCAACGCCACA	Delbarre et al. (2010)

REFERENCES

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Tran, T.H., F.E. Utama, J. Lin, N. Yang, A.B. Sjolund, A. Ryder, K.J. Johnson, L.M. Neilson, C. Liu, K.L. Brill, et al. 2010. Prolactin inhibits BCL6 expression in breast cancer through a Stat5a-dependent mechanism. *Cancer Res.* 70:1711–1721. http://dx.doi.org/10.1158/0008-5472.CAN-09-2314

Zhang, X., L. Ding, and A.J. Sandford. 2005. Selection of reference genes for gene expression studies in human neutrophils by real-time PCR. *BMC Mol. Biol.* 6:4. http://dx.doi.org/10.1186/1471-2199-6-4