

Table S1. Analysis of genomic stability in DNA-PKcs-deficient ($D^{-/-}$ /HC/LC), Artemis-deficient ($A^{-/-}$ /HC/LC), and control (HC/LC) B cells activated for CSR with α -CD40/IL-4

Genotype	General genomic instability (T-FISH)				IgH locus-specific genomic instability (IgH FISH)			
	No. metaphases analyzed	No. metaphases with chromosomal aberrations (%)	No. chromosomal aberrations ^a (%)	Type of chromosomal aberrations ^b	No. metaphases analyzed	% metaphases with 3'5'Igh end dissociation	% Igh 3'5 end-dissociated IgH	No. translocated IgH locus breaks/total no. IgH locus breaks
HC/LC	30	1 (3.3%)	1 (3.3%)	1 dic	100	3	3	0/3
HC/LC	30	1 (3.3%)	1 (3.3%)	1 cb	100	1	1	1/1
HC/LC	30	3 (10%)	3 (10%)	3 CB	100	1	1	0/1
HC/LC	30	1 (3%)	1 (3%)	1 CB	100	0	0	-
HC/LC	30	3 (10%)	3 (10%)	2 CB, 1 cb	100	0	0	-
All HC/LC stimulations ($n = 5$) ^c		6.0 \pm 3.7	6.0 \pm 3.7			1.0 \pm 1.2	1.0 \pm 1.2	
$A^{-/-}$ /HC/LC	30	7 (23.3%)	10 (33.3%)	9 CB, 1 dic	100	10	10	3/10
$A^{-/-}$ /HC/LC	30	7 (23.3%)	7 (23.3%)	7 CB	100	7	7	3/7
$A^{-/-}$ /HC/LC	30	7 (23.2%)	8 (26.6%)	6 CB, 1 dic, 1RT	100	12	12	6/12
$A^{-/-}$ /HC/LC	30	7 (23%)	10 (33%)	7 CB, 3 dic	100	6	6	1/6
All $A^{-/-}$ /HC/LC stimulations ($n = 4$)		23.3 \pm 0.0	26.7 \pm 4.7			8.7 \pm 2.7	8.7 \pm 2.7	
$D^{-/-}$ /HC/LC	30	11 (36.6%)	11 (36.6%)	10 CB, 1 dic	100	24	30	2/30
$D^{-/-}$ /HC/LC	30	12 (40%)	16 (53.3%)	14 CB, 2 cb	100	17	17	7/17
$D^{-/-}$ /HC/LC	30	12 (40%)	16 (53.3%)	15 CB, 1 dic	100	22	24	2/24
$D^{-/-}$ /HC/LC	30	6 (20%)	8 (26%)	7 CB, 1 cb	100	15	16	4/16
All $D^{-/-}$ /HC/LC stimulations ($n = 4$)		34.2 \pm 9.6	42.5 \pm 13.2			19.5 \pm 4.2	21.7 \pm 6.5	

Metaphases were hybridized with either a telomere probe (T-FISH, for quantification of general chromosome breaks) or with BAC probes flanking the IgH locus (3' Igh and 5' Igh probes; two-color IgH FISH; for detection of chromosomal breaks specifically at Igh).

^aThe percentage of chromosomal aberrations was calculated as (total number of aberrations/total number of metaphases) \times 100.

^bCB, chromosome break; cb, chromatid break; dic, dicentric.

^cAverage and standard deviation of individual percentages.

Table S2. Analysis of genomic stability in DNA-PKcs^{-/-}/p53^{-/-} and control B cells after stimulation with LPS for 4 d

Genotype	General genomic instability (T-FISH)			IgH locus-specific genomic instability (IgH FISH)			
	No. metaphases analyzed	No. metaphases with aberrations (%)	No. aberrations ^a (%)	No. metaphases analyzed	No. metaphases with IgH locus breaks (%)	No. IgH locus breaks (%)	No. IgH locus breaks translocated/total no. IgH locus breaks
Stimulation 1							
DNAPKcs ^{+/+} /p53 ^{+/-}	30	0 (0%)	0 (0%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{+/+} /p53 ^{-/-}	30	0 (0%)	0 (0%)	50	1 (2%)	1 (2%)	1/1
DNAPKcs ^{-/-} /p53 ^{+/+}	30	3 (10%)	3 (10%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{-/-} /p53 ^{-/-}	30	9 (30%)	10 (33.3%)	50	9 (18%)	9 (18%)	1/9
Stimulation 2							
DNAPKcs ^{+/+} /p53 ^{-/-}	30	2 (6.7%)	3 (10%)	50	1 (2%)	1 (2%)	1/1
DNAPKcs ^{-/-} /p53 ^{-/-}	30	11 (36.7%)	12 (40%)	50	7 (14%)	7 (14%)	2/7
Stimulation 3							
DNAPKcs ^{+/+} /p53 ^{+/-}	30	3 (10%)	3 (10%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{+/+} /p53 ^{-/-}	30	1 (3.3%)	1 (3.3%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{-/-} /p53 ^{+/+}	30	2 (6.7%)	2 (6.7%)	50	1 (2%)	1 (2%)	0/1
DNAPKcs ^{-/-} /p53 ^{-/-}	30	11 (36.7%)	13 (43.3%)	50	5 (10%)	6 (12%)	1/6
Stimulation 4							
DNAPKcs ^{+/+} /p53 ^{+/-}	30	2 (6.7%)	2 (6.7%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{+/+} /p53 ^{-/-}	30	3 (10%)	3 (10%)	50	0 (0%)	0 (0%)	0/0
DNAPKcs ^{-/-} /p53 ^{+/+}	30	3 (10%)	3 (10%)	50	1 (2%)	1 (2%)	/1
DNAPKcs ^{-/-} /p53 ^{-/-}	30	14 (46.7%)	17 (56.7%)	50	7 (14%)	7 (14%)	/7
Stimulation 5							
DNAPKcs ^{+/+} /p53 ^{+/-}	30	0 (0%)	0 (0%)	50	1 (2%)	1 (2%)	/1
DNAPKcs ^{+/+} /p53 ^{-/-}	30	2 (6.7%)	2 (6.7%)	50	1 (2%)	1 (2%)	/1
DNAPKcs ^{-/-} /p53 ^{+/+}	30	4 (13.3%)	4 (13.3%)	50	2 (4%)	2 (4%)	/2
DNAPKcs ^{-/-} /p53 ^{-/-}	30	17 (56.7%)	20 (66.7%)	50	5 (10%)	5 (10%)	/5

Metaphases were hybridized with either a telomere probe (T-FISH, for quantification of general chromosome breaks) or with BAC probes flanking the IgH locus (3' IgH and 5' IgH probes; two-color IgH FISH; for detection of chromosomal breaks specifically at IgH).

^aThe percentage of chromosomal aberrations was calculated as (total number of aberrations/total number of metaphases) × 100.

Table S3. Effect of AID deficiency on genomic stability in B cells deficient for DNA-PKcs, Artemis, or AID

Mouse ID	Genotype	General genomic instability (T-FISH)				IgH locus-specific genomic instability (IgH FISH)			
		No. metaphases analyzed	No. metaphases with chromosomal aberrations (%)	No. chromosomal aberrations ^a (%)	Type of chromosomal aberrations ^b	No. metaphases analyzed	No. metaphases with 3'5' IgH dissociation (%)	No. IgH 3'5' end-dissociated IgH (%)	No. translocated IgH breaks/total no. IgH breaks
M#5	HC/LC	30	1 (3.3%)	1 (3.3%)	1 CB	50	2 (4%)	2 (4%)	1/2
M#79	HC/LC	30	0 (0%)	0 (0%)	-	50	1 (2%)	1 (2%)	0/1
M#83	AID ^{-/-} /HC/LC	30	1 (3.3%)	1 (3.3%)	1 CB	50	0 (0%)	0 (0%)	-
M#9	DNA-PKcs ^{-/-} /HC/LC	30	11 (36.7%)	13 (43.3%)	5CB,2 cb,6 dic	50	9 (18%)	9 (18%)	2/9
M#77	DNA-PKcs ^{-/-} /HC/LC	30	4 (13.3%)	3 (10%)	4 CB	50	8 (16%)	9 (18%)	1/9
M#67	DNA-PKcs ^{-/-} /AID ^{-/-} /HC/LC	30	4 (13.3%)	4 (13.3%)	3 CB, 1 RT	50	0 (0%)	0 (0%)	-
M#29	HC/LC	30	0 (0%)	0 (0%)	-	50	1 (2%)	1 (2%)	1/1
M#5A	AID ^{-/-} /HC/LC	30	0 (0%)	0 (0%)	-	50	0 (0%)	0 (0%)	-
M#2A	Artemis ^{-/-} /HC/LC	30	5 (16.6%)	6 (20%)	4 CB, 2 dic	50	5 (10%)	5 (10%)	2/5
M#2B	Artemis ^{-/-} /HC/LC	30	5 (16.6%)	5 (16.6%)	2 CB, 3 fg	50	5 (10%)	5 (10%)	1/5
M#5B	Artemis ^{-/-} /AID ^{-/-} /HC/LC	30	2 (6.6%)	3 (10%)	3 CB	50	0 (0%)	0 (0%)	-
wt	HC/LC	30	0 (0%)	0 (0%)	-	50	0 (0%)	0 (0%)	-
M#14	AID ^{-/-} /HC/LC	30	0 (0%)	0 (0%)	-	50	0 (0%)	0 (0%)	-
M#25	Artemis ^{-/-} /HC/LC	30	9 (30%)	10 (33.3%)	8 CB, 2 cb	50	5 (10%)	6 (12%)	0/6
M#34	Artemis ^{-/-} /HC/LC	30	12 (40%)	15 (50%)	14 CB,1 dic	50	7 (14%)	8 (16%)	4/8
M#33	Artemis ^{-/-} /AID ^{-/-} /HC/LC	30	3 (10%)	3 (10%)	2 fg, 1 dic	50	0 (0%)	0 (0%)	-
wt	HC/LC	30	0 (0%)	0 (0%)	-	50	0 (0%)	0 (0%)	-
M#75	AID ^{-/-} /HC/LC	30	1 (3.3%)	1 (3.3%)	1 fg	50	0 (0%)	0 (0%)	-
M#59	DNA-PKcs ^{-/-} /HC/LC	30	3 (10%)	3 (10%)	3 CB	50	6 (12%)	8 (16%)	0/8
M#58	DNA-PKcs ^{-/-} /AID ^{-/-} /HC/LC	30	4 (13.3%)	5 (16.7%)	2 CB, 3 dic	50	0 (0%)	0 (0%)	-
M#38	Artemis ^{-/-} /HC/LC	30	6 (20%)	6 (20%)	5 CB, 1 dic	50	3 (6%)	3 (6%)	1/3
M#24	Artemis ^{-/-} /HC/LC	30	3 (10%)	3 (10%)	2 CB, 1 dic	50	4 (8%)	4 (8%)	2/4
M#36	Artemis ^{-/-} /AID ^{-/-} /HC/LC	30	4 (13.3%)	4 (13.3%)	4 CB	50	0 (0%)	0 (0%)	-
Atm ko	ATM ^{-/-}	30	21 (70%)	36 (120%)	23 CB 8 cb, 5 dic	50	11 (22%)	12 (24%)	5/12
M#34	ATM ^{-/-} /AID ^{-/-}	30	21 (70%)	32 (106.7%)	20 CB,2cb, 10dic	50	3 (6%)	3 (6%)	1/3
M#5	wild-type					50	0 (0%)	0 (0%)	-
M#19	AID ^{-/-}					50	0 (0%)	0 (0%)	-
M#15	ATM ^{-/-}					50	9 (18%)	9 (18%)	2/9
M#19	ATM ^{-/-} /AID ^{-/-}					50	4 (8%)	4 (8%)	2/4
M#8	wild-type					50	0 (0%)	0 (0%)	-
M#13	ATM ^{-/-}					50	7 (14%)	8 (16%)	3/8
M#20	ATM ^{-/-} /AID ^{-/-}					50	5 (10%)	5 (10%)	2/5

B cells were activated for CSR with α -CD40/IL-4, and metaphases obtained at day 4 were hybridized with either a telomere probe (T-FISH, for quantification of general chromosome breaks) or with BAC probes flanking the IgH locus (3' IgH and 5' IgH probes; two-color IgH FISH; for detection of chromosomal breaks specifically at IgH).

^aThe percentage of chromosomal aberrations was calculated as (total number of aberrations/total number of metaphases) \times 100.

^bCB, chromosome break; cb, chromatid break; dic, dicentric; fg, fragment.