Supplemental files for Woodward *et al*: "Condensin II mutation causes T cell lymphoma through tissue-specific genome instability"

Figure S1: Missense mutations in *Caph2* induce thymic lymphoma

Figure S2: Absence of interphase chromatin decompaction in *Caph2*$^{nes/nes}$ T cells

Figure S3: Transcriptional response to *Caph2* mutation in premalignant DP cells

Figure S4: The *Caph2*$^{nes/nes}$ phenotype is reproduced in *ex vivo* primary T cell cultures.

Figure S5: *Caph2* mutation impairs ploidy maintenance in proliferating T, but not B cells.

Figure S6: Gating strategies for cell populations analysed in Figure 4 and Figure S5.

Figure S7: *Caph2* mutant thymocytes show DNA damage in early G1

Figure S8: *Caph2* mutation induces activation of P53-responsive genes

Figure S9: Copy number profiling of tumours from *Caph2* and *P53* mutant mice.

Figure S10: *Caph2*$^{nes/nes}$ tumours are near diploid, not tetraploid

Table S1: Full list of gene ontology terms for DP CD71+ transcriptome comparisons

Table S2: Full list of gene ontology terms for DP CD71- transcriptome comparisons

Table S3: P53 pathway qRT-PCR data

Table S4: Highest ranked deletions in *Caph2*$^{nes/nes}$ tumours

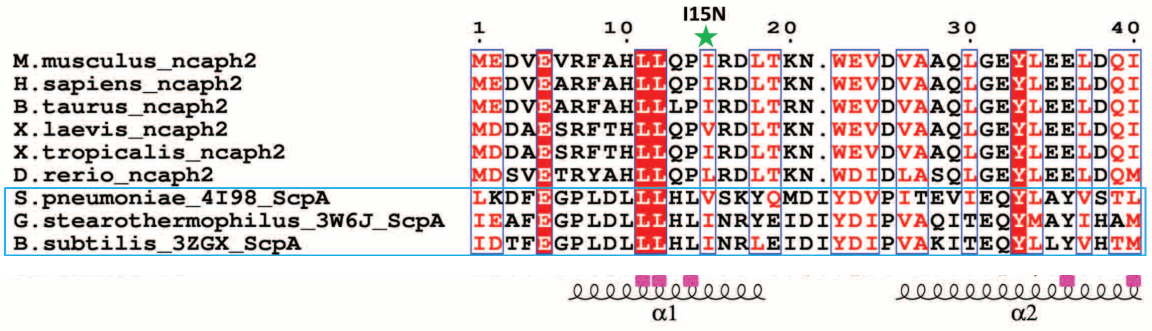
Table S5: Cell surface markers used to define haematopoietic cell populations

Table S6: Antibodies used in this study

Table S7: FISH probes and oligonucleotides used in this study

Table S8: Full list of gene ontology terms for *Caph2*$^{nes/nes}$ DP CD71-FSC^{lo} vs FSC^{hi} transcriptome comparisons

A



B

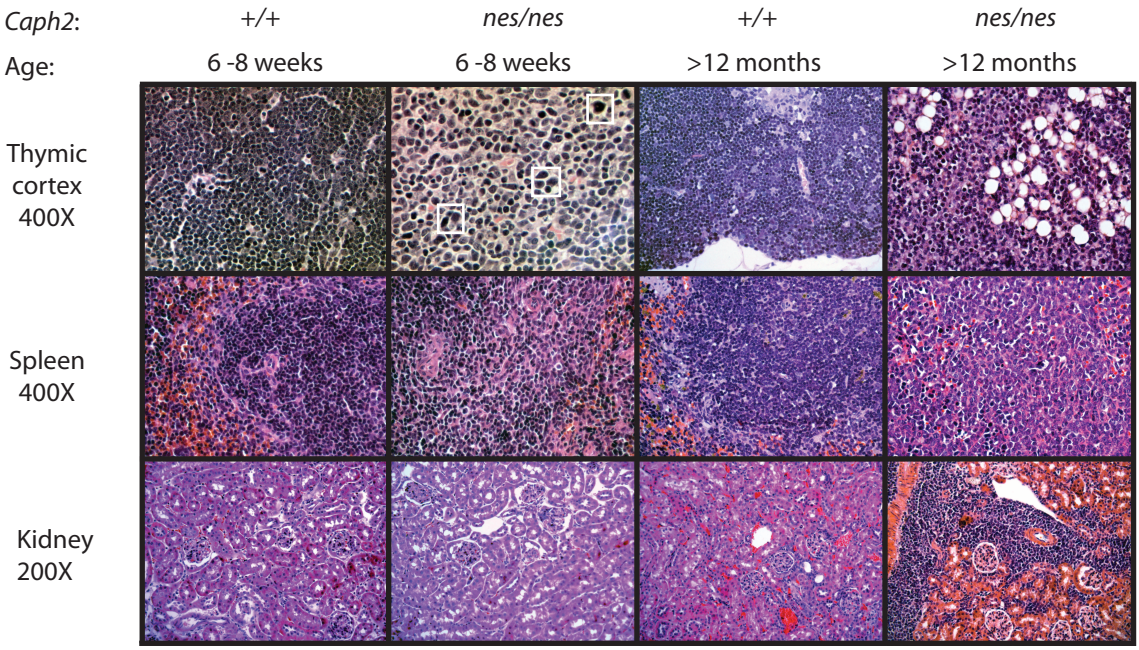


Figure S1: Missense mutations in *Caph2* induce thymic lymphoma
A. Multiple sequence alignment of the conserved N-terminal region from vertebrate Caph2 with bacterial ScpA sequences of known structure (within cyan box). The position of the mouse *Caph2*^{nes} mutation I15N is indicated (green star) and the residues involved in hydrophobic interactions with the equivalent I22 amino acid residue in *B. subtilis* (Bürmann et al. 2013) (Figure 1B) are shown with a solid pink block below the alignment. Positions of the two N-terminal alpha-helices are shown at the bottom. **B.** Haematoxylin and Eosin stained sections cut from formalin-fixed paraffin-embedded tissues from young adult wildtype and *Caph2*$^{nes/nes}$ animals. Note the accumulation of large, atypical nuclei (white boxes) in the *Caph2*$^{nes/nes}$ thymus in place of small $CD4^{+}CD8^{+}$ cell nuclei. Reduced density of mature T lymphocytes is also evident in the periarteriolar lymphoid sheaths of the spleen. In aged *Caph2*$^{nes/nes}$ animals, lymphoma cells can be clearly seen in the thymus (infiltrating adjacent fat), spleen (effacing the normal architecture), and infiltrating the kidney parenchyma. Images are representative of three or more animals.

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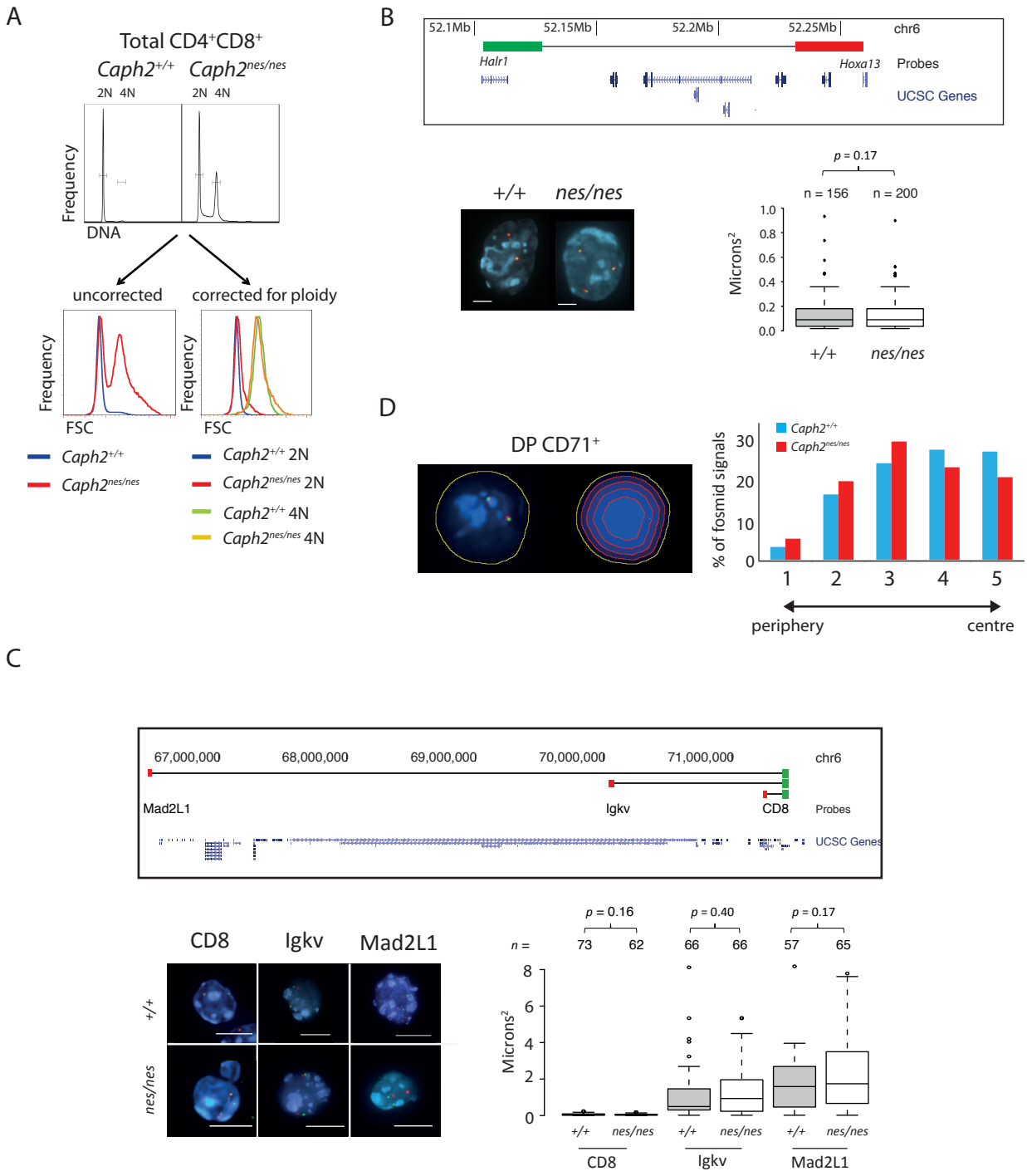
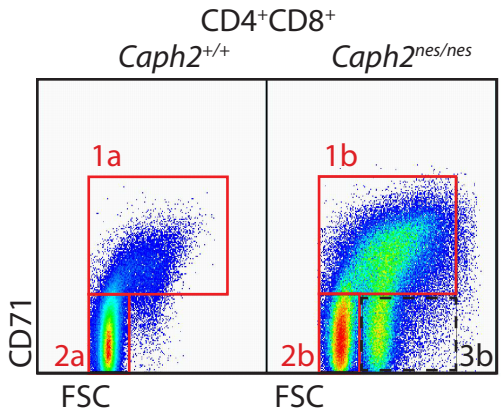

A
Total CD4+CD8+
Caph2+/+ Caph2nes/nes
2N 4N
2N 4N
Frequency
DNA
uncorrected
corrected for ploidy
Frequency
FSC
Frequency
FSC
Caph2+/+
Caph2nes/nes
Caph2+/+ 2N
Caph2nes/nes 2N
Caph2+/+ 4N
Caph2nes/nes 4N
B
52.1Mb
52.15Mb
52.2Mb
52.25Mb
chr6
Halr1
Hoxa13
Probes
UCSC Genes
+/+
nes/nes
p = 0.17
n = 156
n = 200
Microns2
1.0
0.8
0.6
0.4
0.2
0.0
+/+
nes/nes
D
DP CD71+
Caph2+/+
Caph2nes/nes
% of fosmid signals
30
20
10
0
1
2
3
4
5
periphery
centre
C
67,000,000
68,000,000
69,000,000
70,000,000
71,000,000
chr6
Mad2L1
Igkv
CD8
Probes
UCSC Genes
CD8
Igkv
Mad2L1
+/+
nes/nes
p = 0.16
p = 0.40
p = 0.17
n =
73
62
66
66
57
65
Microns2
8
6
4
2
0
+/+
nes/nes
+/+
nes/nes
+/+
nes/nes
CD8
Igkv
Mad2L1

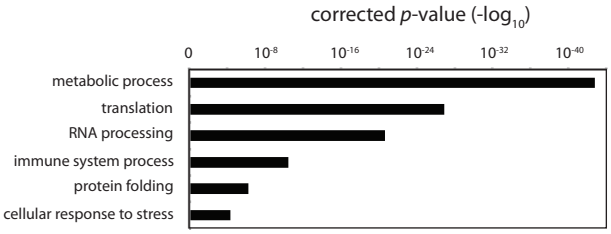
Figure S2: Absence of interphase chromatin decompaction in *Caph2*$^{nes/nes}$ T cells

A. Flow Cytometry DNA content histograms gated on total CD4^{+}CD8^{+} thymocytes, including both blast (CD71^{+}) and quiescent (CD71^{-}) subsets (top). Comparisons between Forward Scatter (FSC) profiles of wildtype and mutant cells are shown either for all cells (uncorrected), or for populations with identical DNA content (corrected for ploidy)(bottom). **B.** 3D FISH using pairs of fosmids spanning the *HoxA* locus (shown in UCSC browser track above the images) to probe FACS-purified DP CD71^{+} nuclei (middle) from wild-type or *Caph2*$^{nes/nes}$ mice. Scale bar = 2μM. Boxplots depict squared interprobe distances, including median, interquartile range, 95th percentile and outlier values. Probe details are listed in Table S7. *p*-values represent Mann-Whitney U-tests. **C.** Distribution of *HoxA* probe hybridisation signals across five concentric shells eroded from the nuclear periphery (shell 5) to the centre (shell 1) of DP CD71^{+} thymocytes (n = 100 chromosomes per genotype). Differences in the signal distribution were not significant (Chi^2 $P > 0.05$). **D.** 3D FISH using pairs of fosmids separated by 0.1Mb, 1Mb and 5Mb at the *CD8* locus. Scale bar = 5μM. Data are presented as described in panel B.

A

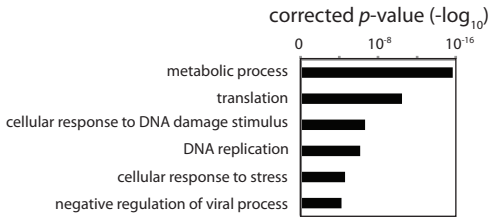


B



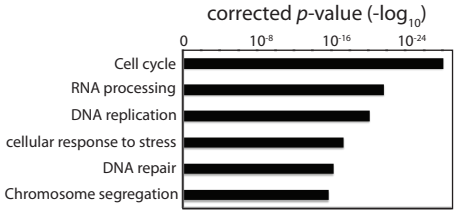
DP CD71+ (proliferative)
(1a versus 1b)

C



DP CD71- FSClo (quiescent)
(2a versus 2b)

D



DP CD71- FSChi versus FSClo (diploid versus tetraploid)
(2b versus 3b)

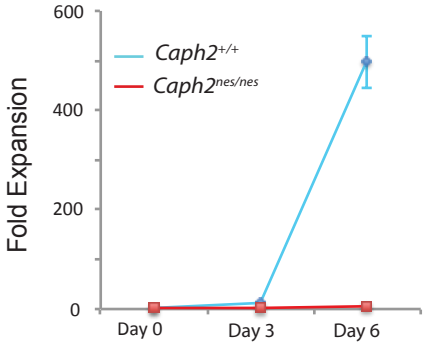
Figure S3

Transcriptional response to *Caph2* mutation in premalignant DP cells

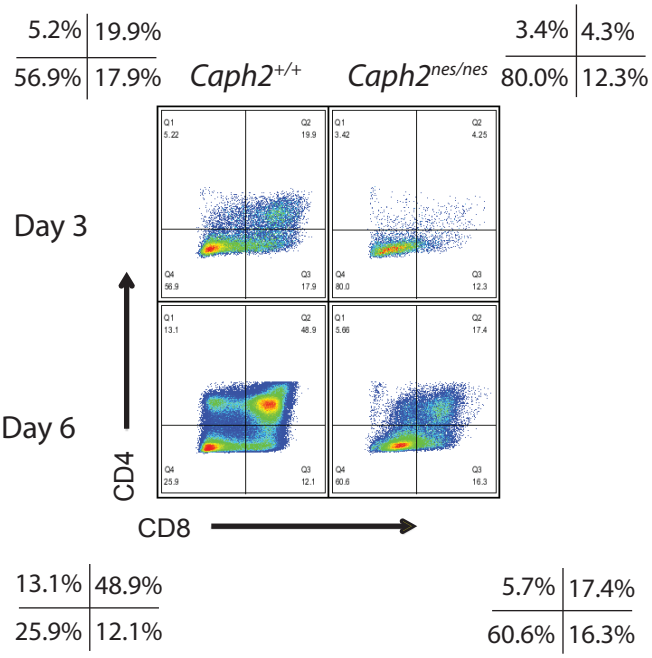
A. Flow cytometry dot plot, gated on $CD4^{+}CD8^{+}$ (DP) thymocytes, showing the gating scheme used to purify DP cell subsets for transcriptome studies. 1a and 1b correspond to proliferative ($CD71^{+}$) DP cells and 2a and 2b correspond to DP quiescent cells in a diploid G0 cell cycle phase. The $CD71^{lo}FSC^{hi}$ population present in the *Caph2* mutant, but not wildtype thymus, represents tetraploid cells which arise from mitotic failure, as shown in Figure 6. Because the microarray studies were designed to look for direct effects of *Caph2* mutation on transcription, rather than indirect transcriptional responses to mitotic failure, these tetraploid cells were excluded from gates 2a and 2b. However, $CD71^{lo}FSC^{hi}$ tetraploid cells from *Caph2*$^{nes/nes}$ thymus were also sorted separately (3b) for the identification of differentially expressed transcripts relative to $CD71^{lo}FSC^{lo}$ diploid cells from the same organ (panel D). Total DP $CD71^{-}$ cells were used to assess P53 pathway activation in Figure S8. **B**. Histograms showing representative gene ontology terms enriched among genes upregulated in stage-matched *Caph2*$^{nes/nes}$ versus *Caph2*$^{+/+}$ DP $CD71^{+}$ thymocytes, determined using the GOrilla tool. *p* values are corrected for multiple testing using the Benjamini-Hochberg method. **C**. Histograms presented as described above, showing gene ontology term enrichments among genes upregulated in DP $CD71^{-}FSC^{lo}$ thymocytes from *Caph2*$^{nes/nes}$ versus wildtype thymus. **D.** Histograms presented as above showing gene ontology term enrichment for genes upregulated in DP $CD71^{-}FSC^{lo}$ versus DP $CD71^{-}FSC^{hi}$ thymocytes from

Caph2$^{nes/nes}$ animals. Complete lists of enriched terms from gene ontology analyses depicted in panels B, C and D are given in Table S1, S2 and S8, respectively.

A


600
400
200
0
Fold Expansion
Caph2+/+
Caph2nes/nes
Day 0
Day 3
Day 6

B


5.2%
19.9%
56.9%
17.9%
Caph2+/+
Caph2nes/nes
3.4%
4.3%
80.0%
12.3%
Day 3
Day 6
CD4
CD8
13.1%
48.9%
25.9%
12.1%
5.7%
17.4%
60.6%
16.3%

C

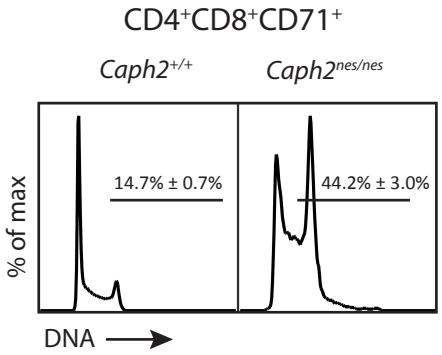

CD4+CD8+CD71+
Caph2+/+
Caph2nes/nes
% of max
14.7% ± 0.7%
44.2% ± 3.0%
DNA

Figure S4: The *Caph2*$^{nes/nes}$ phenotype is reproduced in *ex vivo* primary T cell cultures.

A. Proliferation curves for primary DN3 thymocytes cultured on monolayers of OP9-DL1 stromal cells (de Pooter and Zúñiga-Pflücker 2007). Error bars show SEM of $n = 3$ biological replicate experiments. **B.** Differentiation status of T cell cultures from panel A. Percentages represent mean values from biological triplicates. **C.** DNA content analysis of freshly isolated DP CD71^{+} thymocytes from neonatal *Caph2*$^{nes/nes}$ and control animals. The percentage of cells with 4N, or greater than 4N DNA content is indicated (± SEM, $n = 3$ biological replicates).

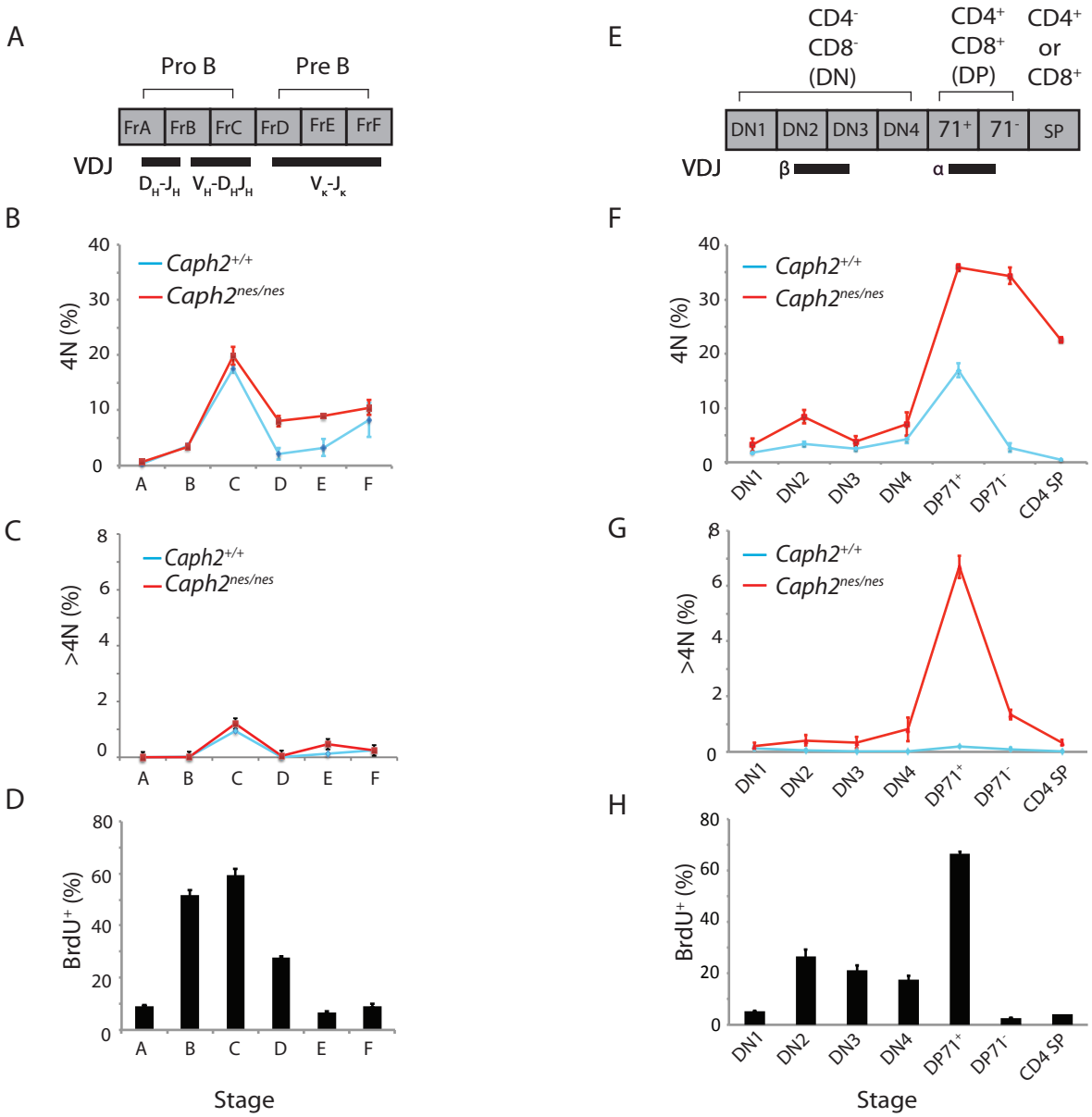
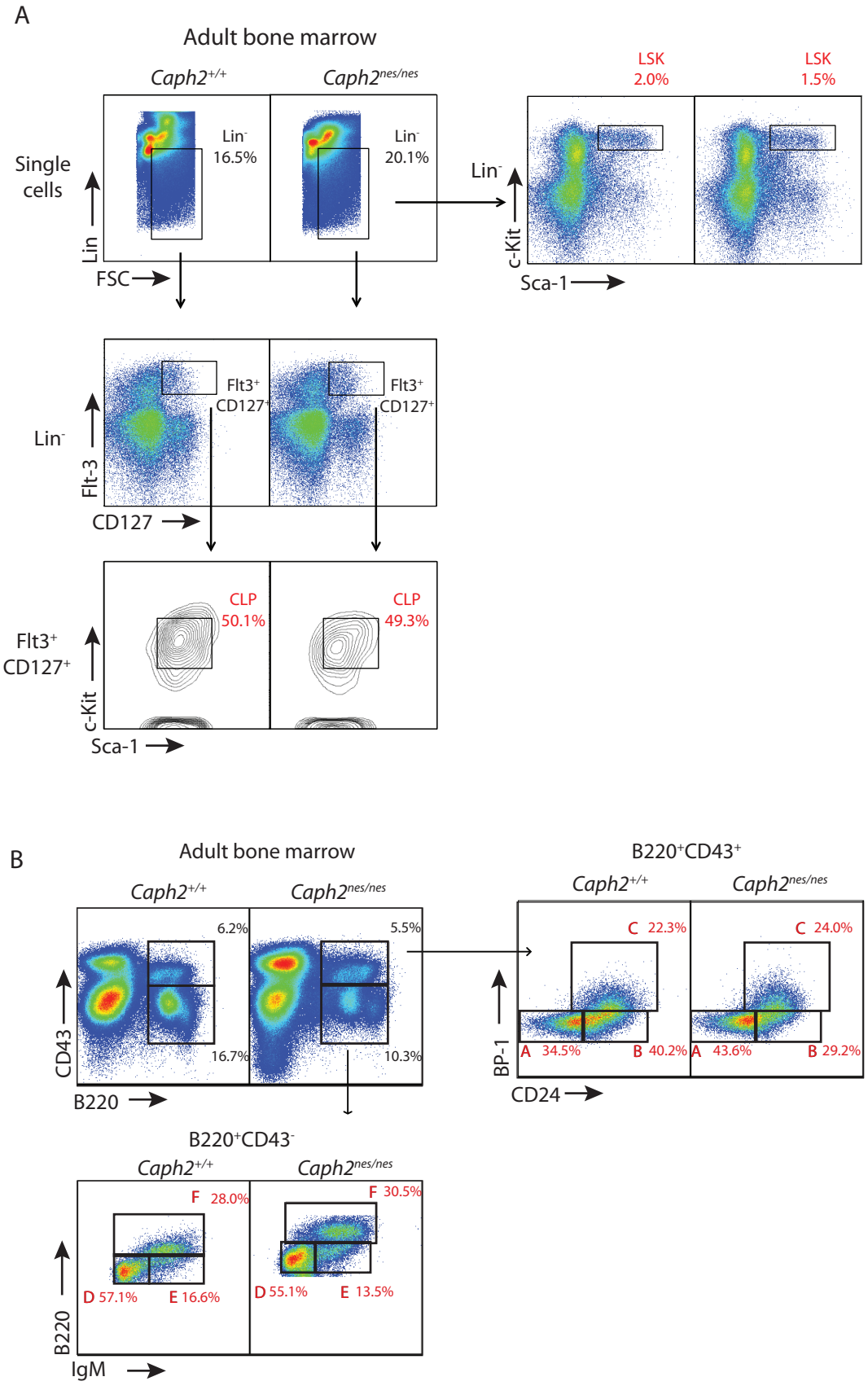

A
Pro B
Pre B
FrA
FrB
FrC
FrD
FrE
FrF
VDJ
D_H-J_H
V_H-D_HJ_H
$V_κ$-$J_κ$
B
4N (%)
Caph2+/+
Caph2nes/nes
A B C D E F
C
>4N (%)
D
BrdU+ (%)
Stage
E
CD4-
CD8-
(DN)
CD4+
CD8+
(DP)
CD4+
or
CD8+
DN1 DN2 DN3 DN4 71+ 71- SP
VDJ
β
α
F
G
H
DN1 DN2 DN3 DN4 DP71+ DP71- CD4 SP

Figure S5: *Caph2* mutation impairs ploidy maintenance in proliferating T, but not B cells.

A & E. Schematic of the major stages of bone marrow B (A) and thymic T (E) cell differentiation in young adult mice, arranged in chronological sequence. Horizontal black bars show the timing of VDJ recombination events. Cell surface marker and antibody combinations used to distinguish cell populations are listed in Tables S3 & S4, and gating schemes are in Figure S6. **B & F**. The percentage of *wildtype* (blue) and *Caph2*$^{nes/nes}$ (red) cells with 4N DNA content at each of the stages shown in panels A & E, as determined by flow cytometric (FC) quantification of DAPI fluorescence. DAPI histograms for each stage are shown in Figure 4. **C & G.** Percentage of cells with greater than 4N (hyperdiploid) DNA content during lymphocyte differentiation, depicted as above. **D & H.** The fraction of actively cycling cells at each stage of lymphocyte differentiation in wildtype animals, determined by FC quantification of BrdU 2 hours following intraperitoneal BrdU injection. Error bars represent SEM for ploidy (n = 4 biological replicates) and BrdU (n = 3 biological replicates for B cell populations, n = 6 biological replicates for T cells)


A
Adult bone marrow
Caph2+/+
Caph2nes/nes
Single cells
Lin
FSC
Lin- 16.5%
Lin- 20.1%
Lin-
c-Kit
Sca-1
LSK 2.0%
LSK 1.5%
Lin-
Flt-3
CD127
Flt3+ CD127+
Flt3+ CD127+
Flt3+ CD127+
c-Kit
Sca-1
CLP 50.1%
CLP 49.3%
B
Adult bone marrow
B220+CD43+
Caph2+/+
Caph2nes/nes
CD43
B220
6.2%
16.7%
5.5%
10.3%
BP-1
CD24
C 22.3%
A 34.5%
B 40.2%
C 24.0%
A 43.6%
B 29.2%
B220+CD43-
B220
IgM
F 28.0%
D 57.1%
E 16.6%
F 30.5%
D 55.1%
E 13.5%

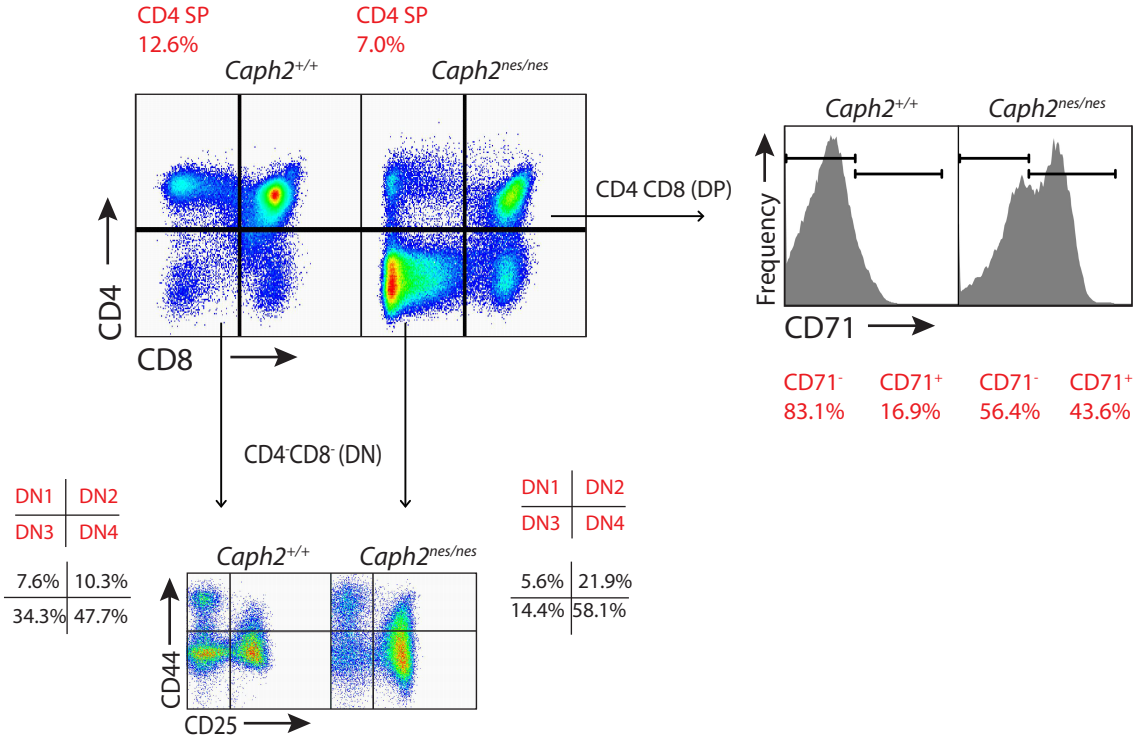
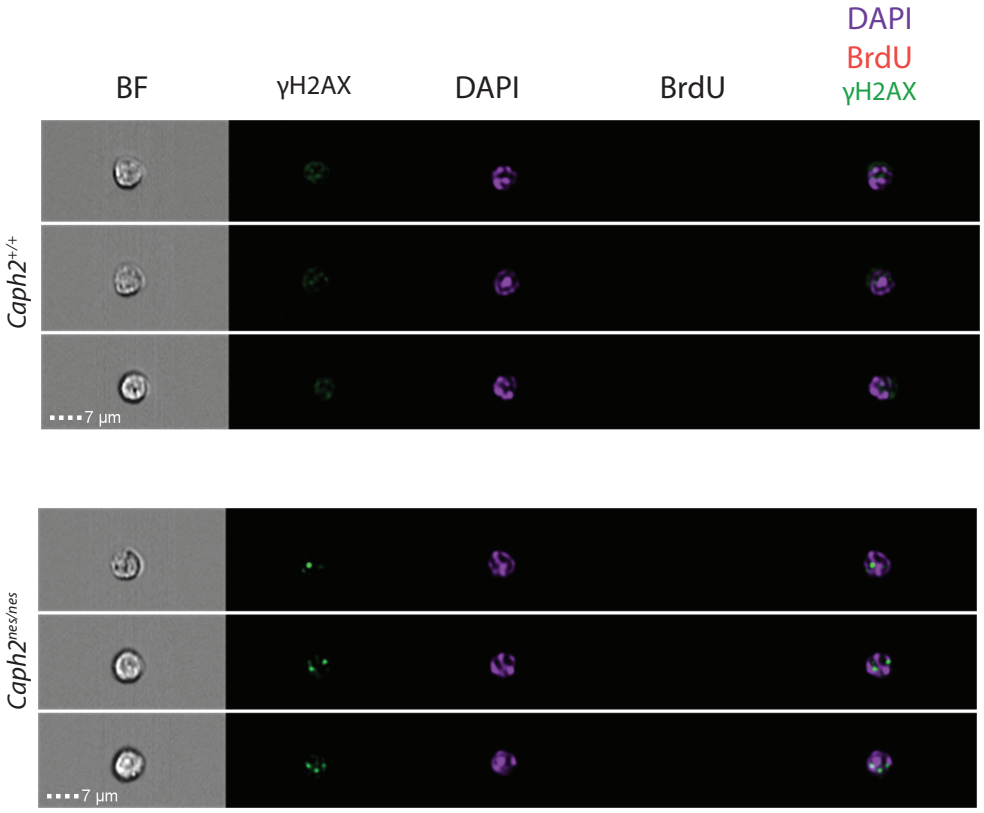

CD4 SP
12.6%
CD4 SP
7.0%
Caph2+/+
Caph2nes/nes
CD4
CD8
CD4 CD8 (DP)
CD4-CD8- (DN)
Caph2+/+
Caph2nes/nes
Frequency
CD71
CD71-
83.1%
CD71+
16.9%
CD71-
56.4%
CD71+
43.6%
DN1
DN2
DN3
DN4
7.6%
10.3%
34.3%
47.7%
DN1
DN2
DN3
DN4
5.6%
21.9%
14.4%
58.1%
Caph2+/+
Caph2nes/nes
CD44
CD25

Figure S6: Gating strategies for cell populations analysed in Figure 4 and Figure S5.

A. Multipotent haematopoietic progenitor populations: LSK (Lin^-, $Sca\text{-}1^+$, $c\text{-}kit^+$) and Common Lymphoid Progenitor (CLP). Dot plots are pre-gated on single cells from whole bone marrow tissue of young adult animals. **B.** Gating Strategy for bone marrow B cell populations. Dot plots are pre-gated on single cells from whole bone marrow tissue of young adult animals. **C.** Gating strategy for thymic T cell populations. Dot plots are pre-gated on single cells from whole thymic tissue of young adult animals. For panels A – C, mean percentages of parent population are shown, calculated from a minimum of 3 biological replicates in each case. Antibody details are listed in Table S6.

A


BF
γH2AX
DAPI
BrdU
DAPI
BrdU
γH2AX
Caph2+/+
7 μm
Caph2nes/nes
7 μm

B

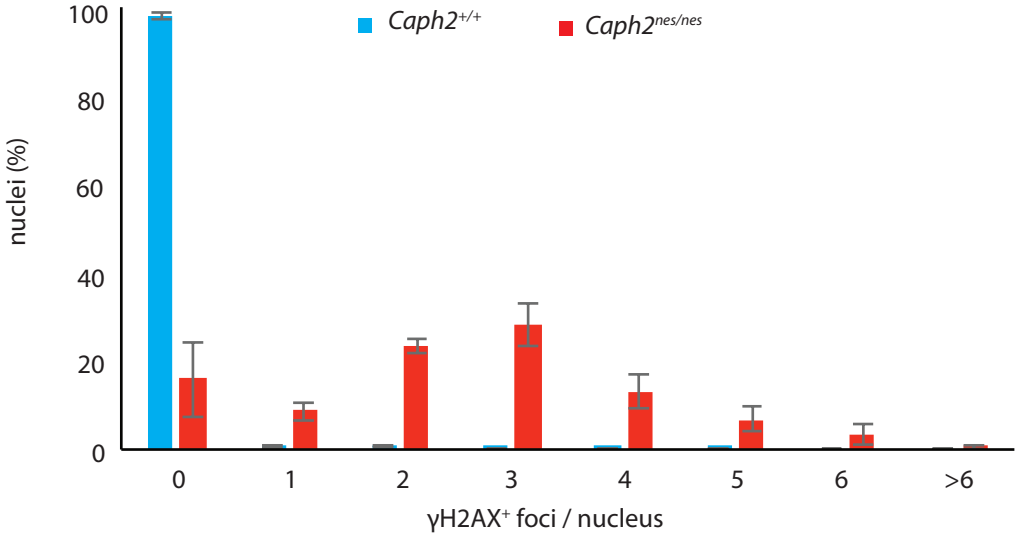
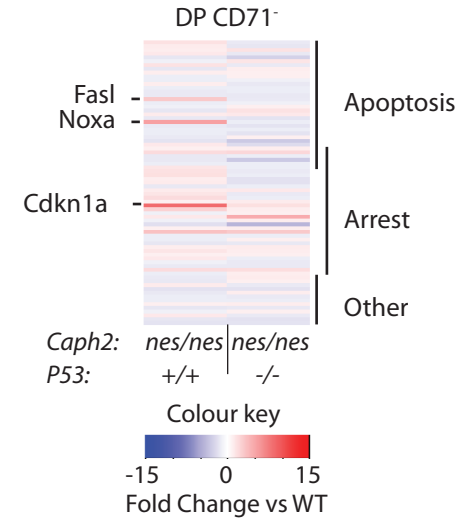

100
80
60
40
20
0
nuclei (%)
Caph2+/+
Caph2nes/nes
0
1
2
3
4
5
6
>6
γH2AX+ foci / nucleus

Figure S7: *Caph2* mutant thymocytes show DNA damage in early G1

A. Multispectral images showing representative cells from the smallest 25% of the G1 (2N, $BrdU^-$) thymocyte population. Images were acquired on an ImageStream Flow Cytometer using a 60X objective. **B**. Histogram shows the frequency of γH2AX foci per nucleus for the smallest 20% of G1 cells. Error bars show SEM of *n* = 3 biological replicate experiments, with the gated population comprising at least 450 cells per experiment.

A


DP CD71-
Fasl
Noxa
Cdkn1a
Apoptosis
Arrest
Other
Caph2: nes/nes nes/nes
P53: +/+ -/-
Colour key
-15 0 15
Fold Change vs WT

B

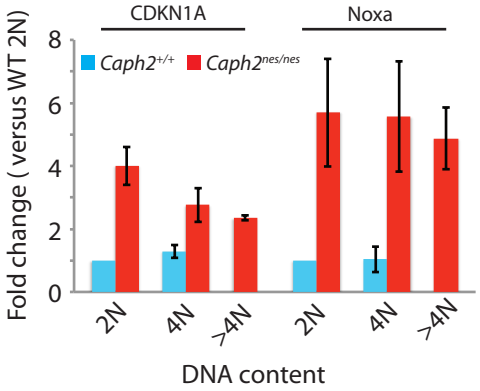
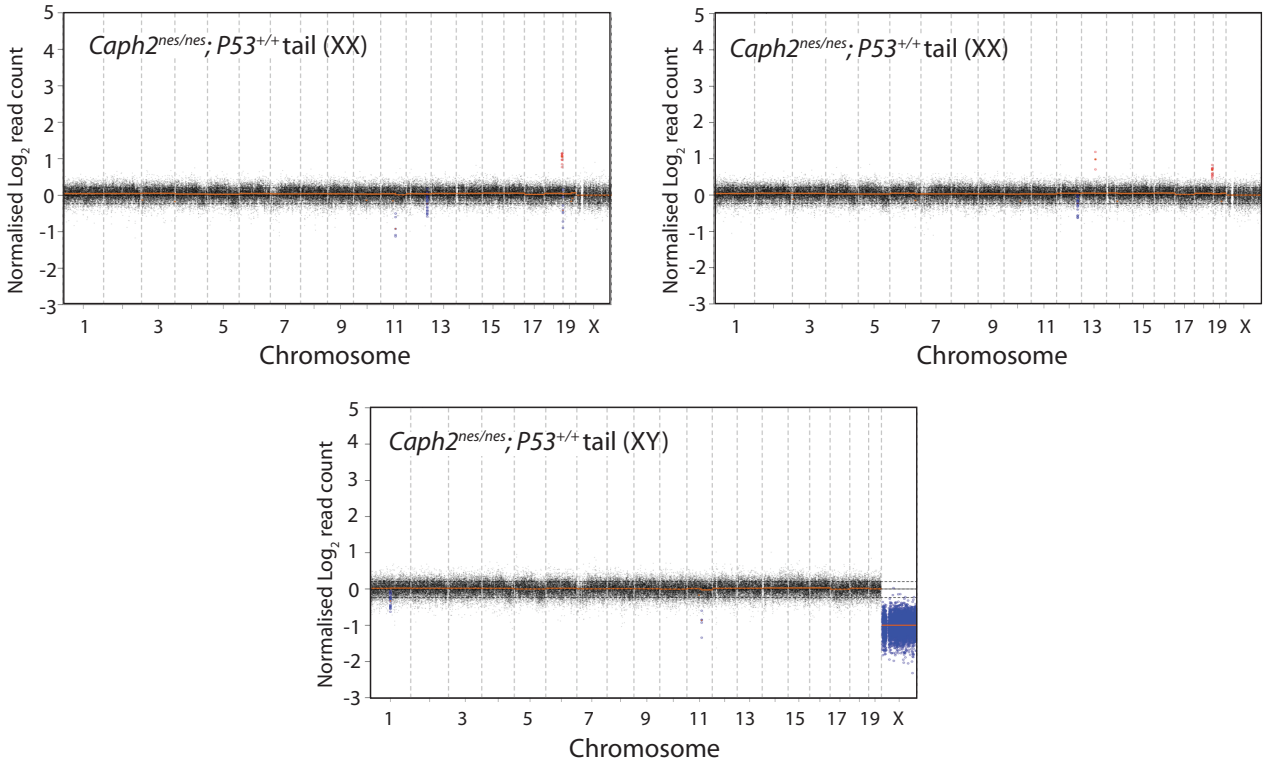

CDKN1A
Noxa
Caph2+/+
Caph2nes/nes
Fold change (versus WT 2N)
0
2
4
6
8
2N
4N
>4N
2N
4N
>4N
DNA content

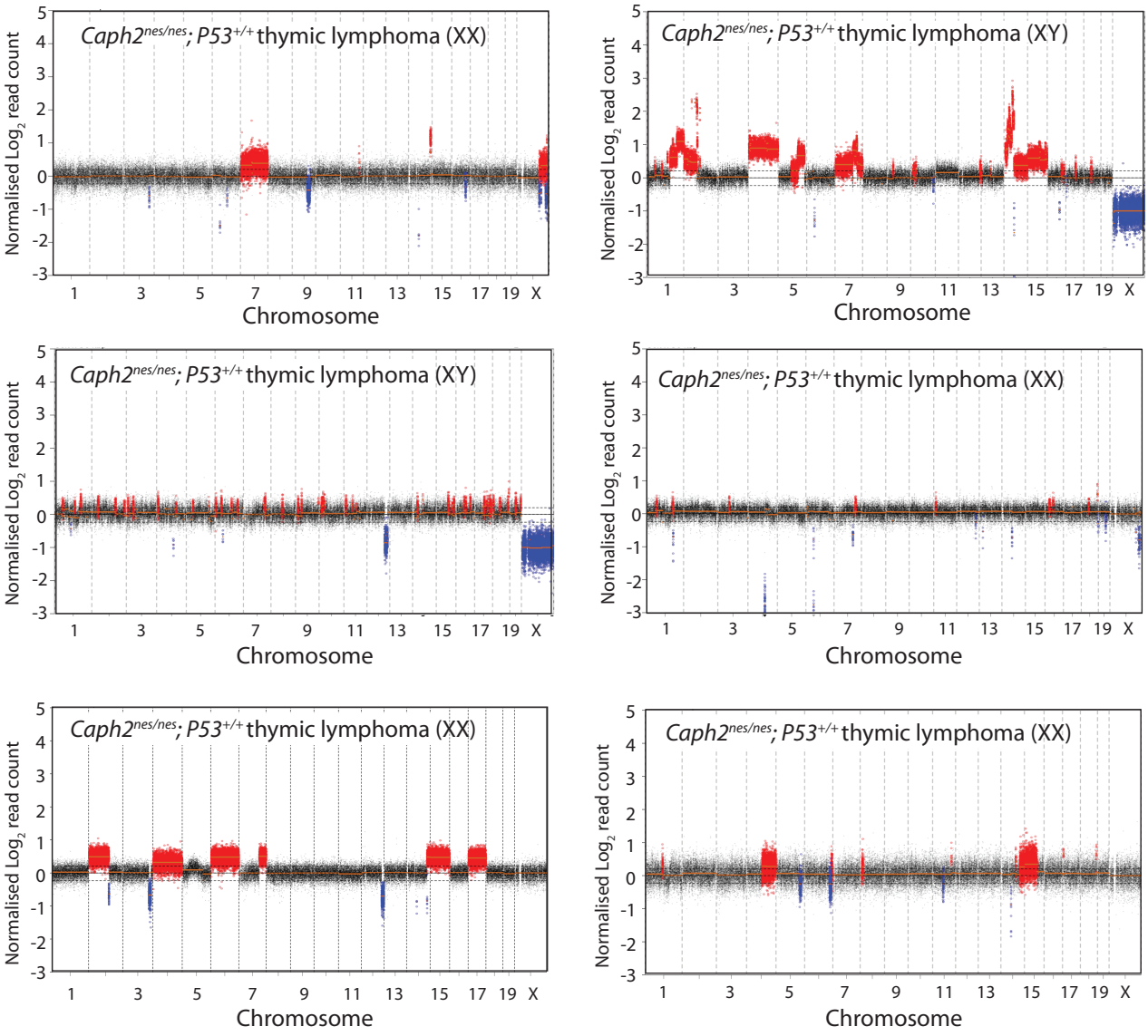
Figure S8: *Caph2* mutation induces activation of P53-responsive genes

A. Heat maps show fold change in mRNA expression for known P53 pathway genes in *Caph2*$^{nes/nes}$ and *Caph2*$^{nes/nes}$ *P53*$^{-/-}$ mutants relative to matched wildtype cells, measured by qRT-PCR array (SABioscience). RNA was purified from CD4^{+}CD8^{+} CD71^{-} thymocytes, ie. cells that have ceased proliferation after β-selection (gating shown in Figure S3A). Three genes showing robust (>2.5-fold) P53-dependent upregulation in *Caph2*$^{nes/nes}$ cells are indicated, and a full list of fold change values is detailed in Table S3. Data are from two independent samples, each with two technical replicates. **B.** qRT-PCR analysis of the P53 target genes *CDKN1A* and *NOXA* in CD4^{+}CD8^{+} thymocytes that were FACS-purified based on DNA content (Hoechst). Data were normalised to β-actin, and are represented as fold change relative to *Caph2*$^{+/+}$ 2N. Cells with >4N ploidy were rare in wildtype animals, and were therefore assessed only in *Caph2*$^{nes/nes}$. Error bars represent SEM from two independent experiments, each comprising two technical replicates.

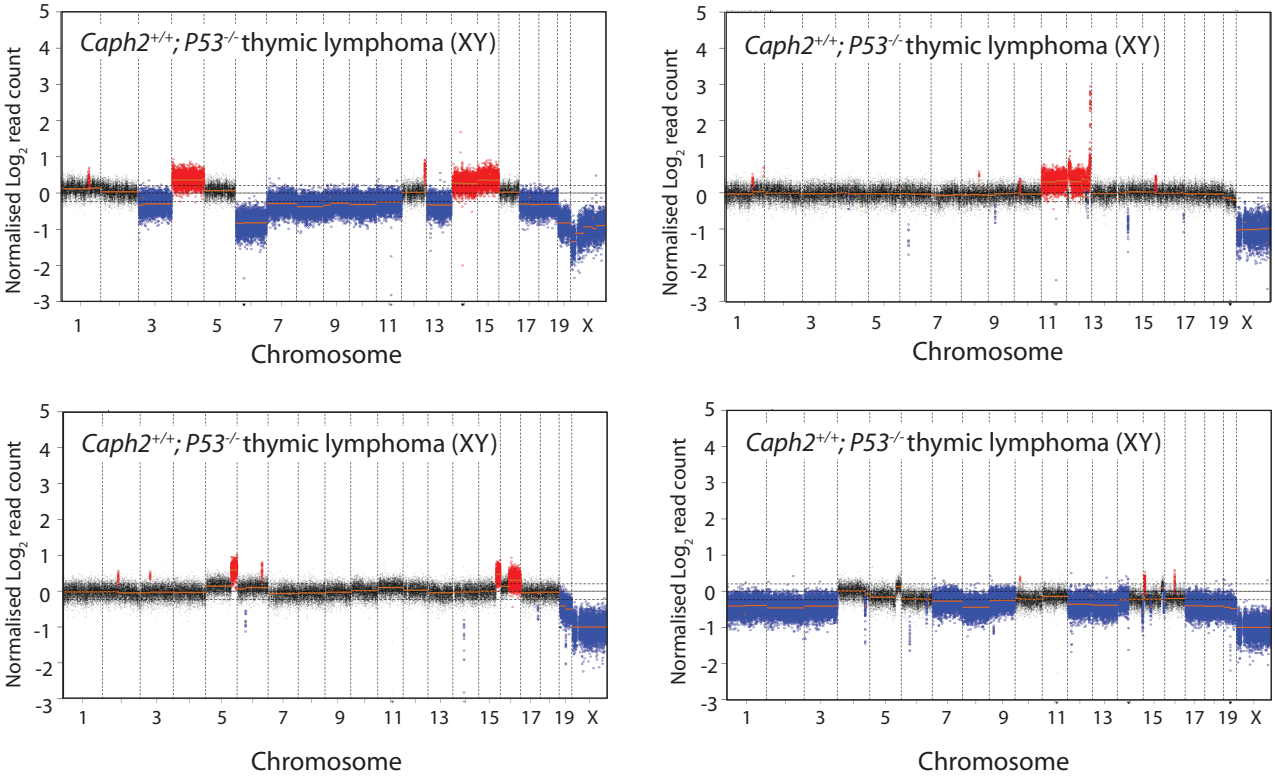
A


Caph2nes/nes; P53+/+ tail (XX)
Caph2nes/nes; P53+/+ tail (XX)
Caph2nes/nes; P53+/+ tail (XY)
Normalised Log2 read count
Chromosome

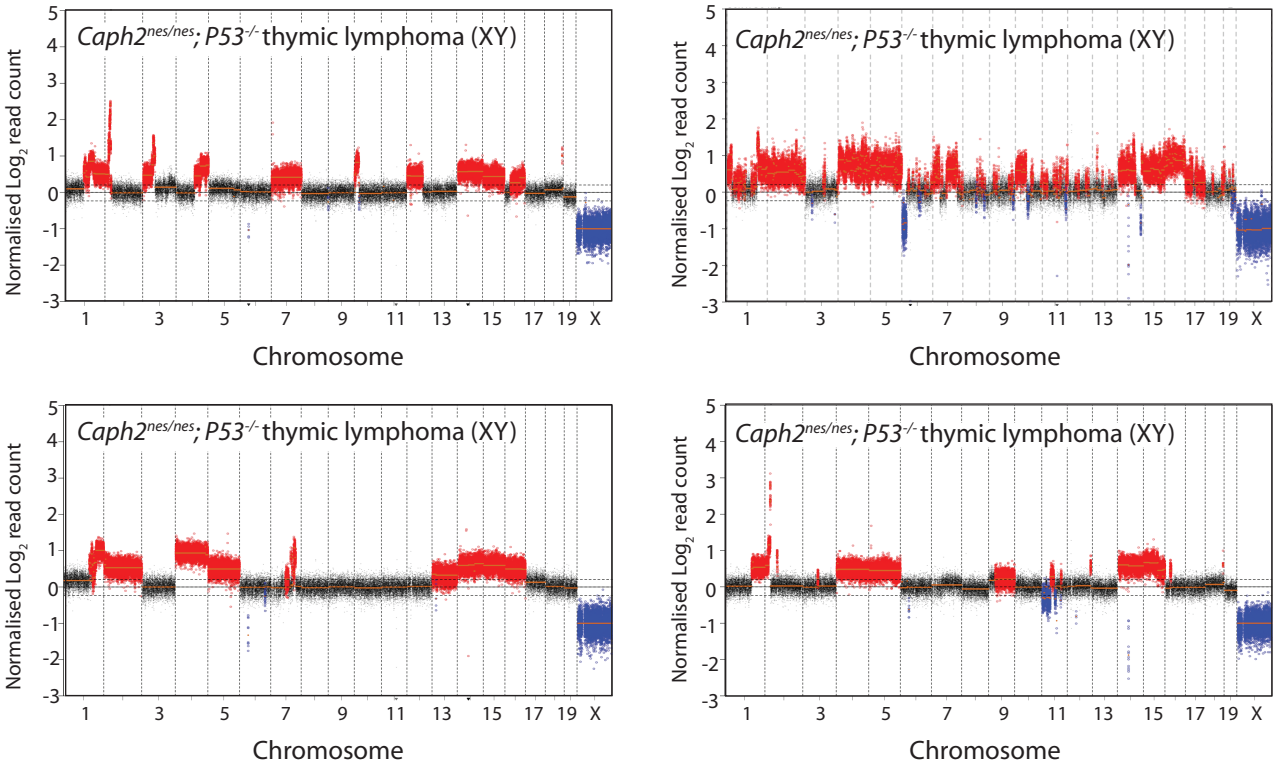
B


Caph2nes/nes; P53+/+ thymic lymphoma (XX)
Caph2nes/nes; P53+/+ thymic lymphoma (XY)
Caph2nes/nes; P53+/+ thymic lymphoma (XY)
Caph2nes/nes; P53+/+ thymic lymphoma (XX)
Caph2nes/nes; P53+/+ thymic lymphoma (XX)
Caph2nes/nes; P53+/+ thymic lymphoma (XX)
Normalised Log2 read count
Chromosome

C


Caph2+/+; P53-/- thymic lymphoma (XY)
Normalised Log2 read count
Chromosome
1 3 5 7 9 11 13 15 17 19 X
-3 -2 -1 0 1 2 3 4 5

D


Caph2nes/nes; P53-/- thymic lymphoma (XY)
Normalised Log2 read count
Chromosome
1 3 5 7 9 11 13 15 17 19 X
-3 -2 -1 0 1 2 3 4 5

D (continued)

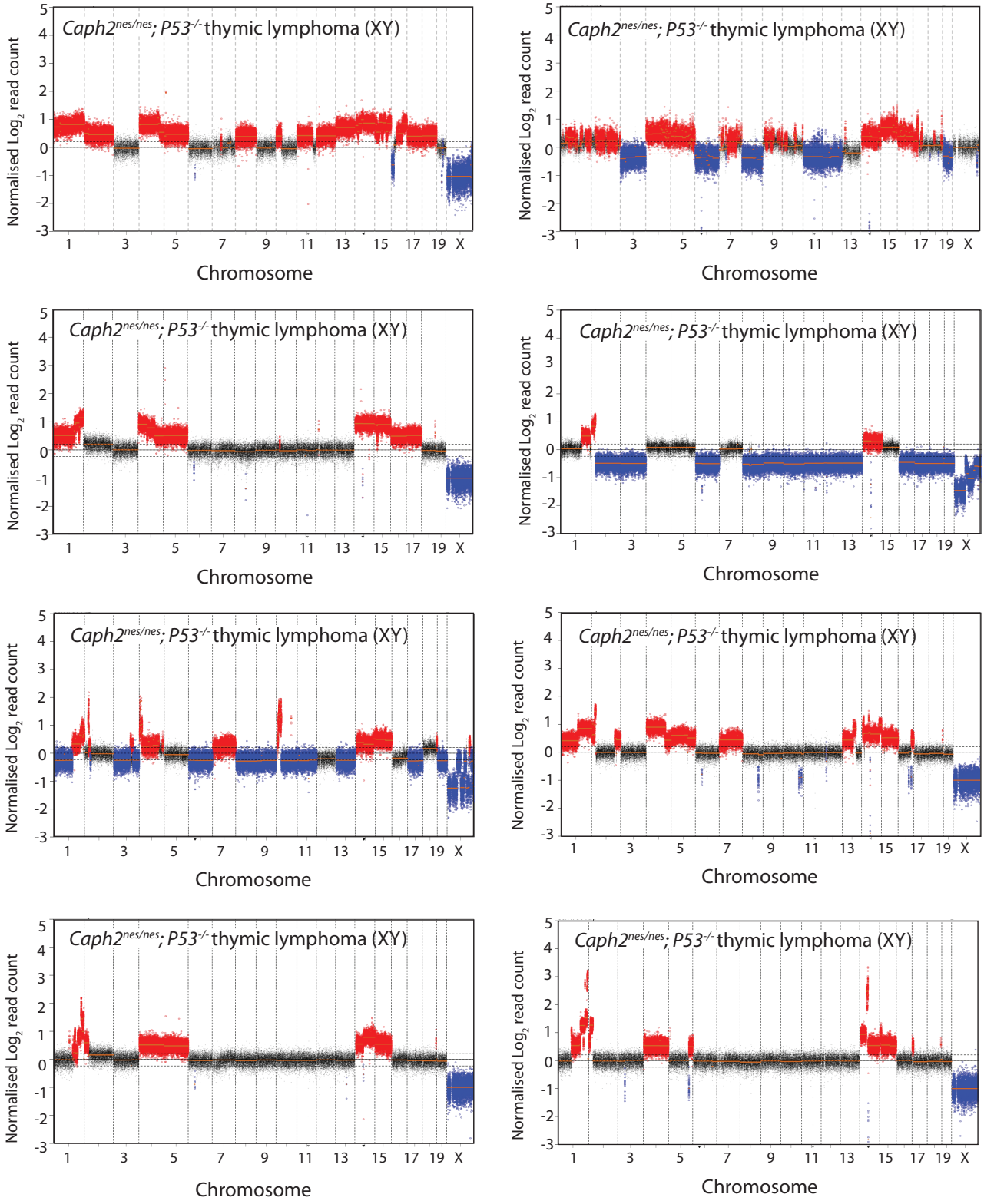
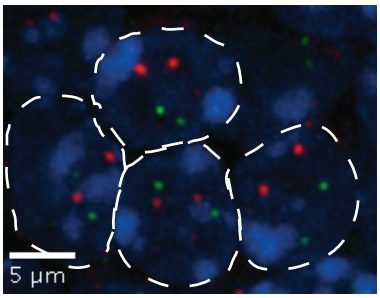
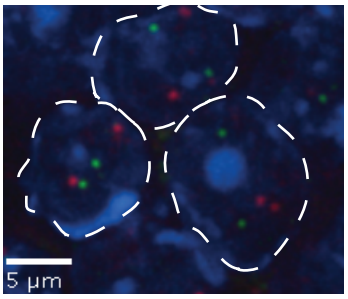

Caph2nes/nes; P53-/- thymic lymphoma (XY)
Normalised Log2 read count
Chromosome
1 3 5 7 9 11 13 15 17 19 X
-3 -2 -1 0 1 2 3 4 5

Figure S9: Copy number profiling of tumours from *Caph2* and *P53* mutant mice.

Copy number profiles showing read depth from shallow whole genome sequencing, presented as described in Figure 7A. **A:** DNA from aged (9 – 15 month) *Caph2*$^{nes/nes}$ tails. **B:** DNA from terminal (9 – 15 month) *Caph2*$^{nes/nes}$ thymic lymphoma tissue. **C:** DNA from terminal (~4 – 6 month) *Caph*$^{+/+}$ *P53*$^{-/-}$ thymic lymphoma tissue. **D.** DNA from terminal (2 – 3 month) *Caph2*$^{nes/nes}$ *P53*$^{-/-}$ thymic lymphoma tissue.

A


5 µm


5 µm

B

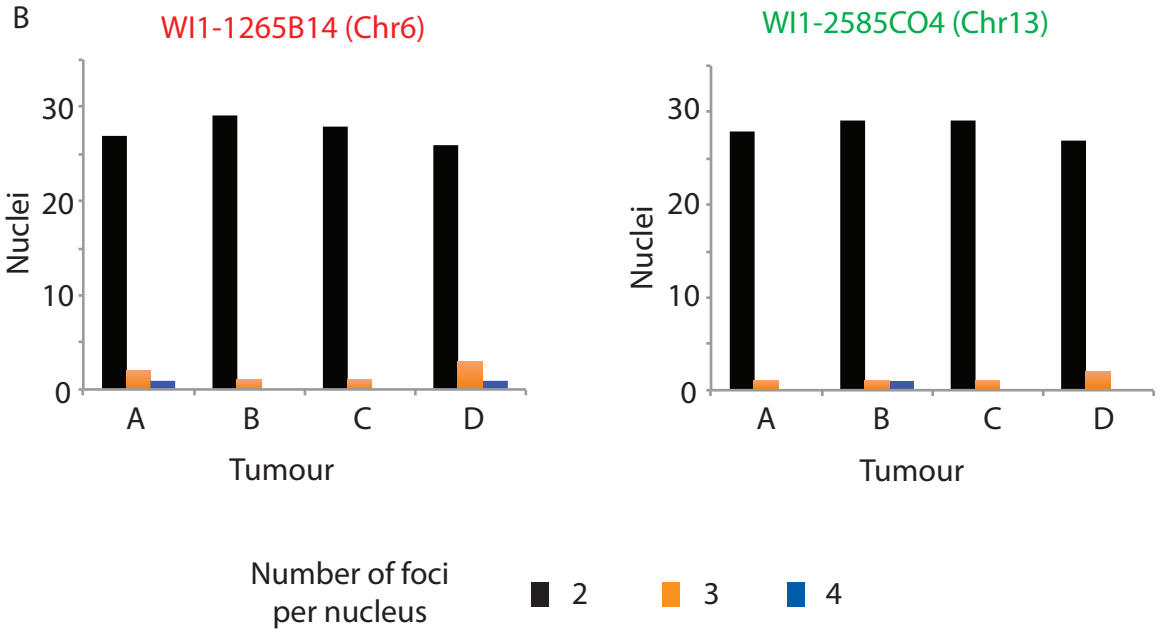

WI1-1265B14 (Chr6)
WI1-2585CO4 (Chr13)
Nuclei
30
20
10
0
A
B
C
D
Tumour
Number of foci per nucleus
2
3
4

Figure S10: *Caph2*$^{nes/nes}$ tumours are near diploid, not tetraploid

A. Representative FISH images from formalin-fixed, paraffin embedded thymic lymphoma tissue sections from *Caph2*$^{nes/nes}$ single mutant animals (n = 4). Fosmid probes were selected for loci on chromosome 6 (red) and chromosome 13 (green) which were known to be present at the "genome average" in all four tumours, based on shallow whole genome sequencing data. **B.** Quantification of fosmid foci per nucleus for four *Caph2*$^{nes/nes}$ tumour sections. 30 nuclei were counted for each tumour.

Table S1: Full list of gene ontology terms returned by the GOrilla tool for microarray transcriptome comparisons between wildtype and Caph2 mutant proliferative (CD71+) DP cells. Grey highlighting indicates terms shown in Figure S3B

GO term	Description	P-value	FDR q-value
GO:0008152	metabolic process	1.33E-47	1.65E-43
GO:0044237	cellular metabolic process	1.84E-38	1.14E-34
GO:0071704	organic substance metabolic process	2.04E-37	8.43E-34
GO:0044238	primary metabolic process	5.17E-34	1.60E-30
GO:0006412	translation	5.41E-31	1.34E-27
GO:0034641	cellular nitrogen compound metabolic process	1.14E-29	2.35E-26
GO:0046483	heterocycle metabolic process	6.20E-28	1.10E-24
GO:0034660	ncRNA metabolic process	9.12E-28	1.42E-24
GO:0006807	nitrogen compound metabolic process	3.53E-27	4.86E-24
GO:0006139	nucleobase-containing compound metabolic process	1.98E-26	2.46E-23
GO:0006725	cellular aromatic compound metabolic process	3.18E-26	3.59E-23
GO:0034470	ncRNA processing	3.27E-26	3.39E-23
GO:1901360	organic cyclic compound metabolic process	4.40E-26	4.20E-23
GO:0043170	macromolecule metabolic process	4.85E-25	4.30E-22
GO:0006396	RNA processing	2.67E-24	2.21E-21
GO:0044260	cellular macromolecule metabolic process	8.94E-24	6.93E-21
GO:0009987	cellular process	2.03E-22	1.48E-19
GO:0009058	biosynthetic process	4.36E-21	3.01E-18
GO:1901576	organic substance biosynthetic process	4.98E-21	3.25E-18
GO:0044249	cellular biosynthetic process	1.21E-20	7.53E-18
GO:0044085	cellular component biogenesis	1.56E-20	9.24E-18
GO:0006364	rRNA processing	3.54E-19	2.00E-16
GO:0016072	rRNA metabolic process	5.68E-19	3.06E-16
GO:0090304	nucleic acid metabolic process	8.50E-19	4.39E-16
GO:0022613	ribonucleoprotein complex biogenesis	1.88E-18	9.32E-16
GO:0044710	single-organism metabolic process	6.55E-18	3.13E-15
GO:0042254	ribosome biogenesis	9.32E-18	4.28E-15
GO:0006259	DNA metabolic process	2.94E-17	1.30E-14
GO:0006260	DNA replication	2.99E-16	1.28E-13
GO:0006399	tRNA metabolic process	3.63E-14	1.50E-11
GO:0034645	cellular macromolecule biosynthetic process	5.75E-14	2.30E-11
GO:0002376	immune system process	9.26E-14	3.59E-11
GO:0009059	macromolecule biosynthetic process	3.05E-13	1.15E-10
GO:0019538	protein metabolic process	9.30E-12	3.39E-09
GO:0016070	RNA metabolic process	1.84E-11	6.53E-09
GO:0006955	immune response	2.42E-11	8.34E-09
GO:0044711	single-organism biosynthetic process	6.71E-11	2.25E-08
GO:0002478	antigen processing and presentation of exogenous peptide antigen	7.45E-11	2.43E-08
GO:0034341	response to interferon-gamma	8.70E-11	2.77E-08
GO:0002504	antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	9.66E-11	3.00E-08
GO:0002495	antigen processing and presentation of peptide antigen via MHC class II	9.66E-11	2.92E-08

GO:0019886	antigen processing and presentation of exogenous peptide antigen via MHC class II	9.66E-11	2.85E-08
GO:0002252	immune effector process	2.00E-10	5.77E-08
GO:0007005	mitochondrion organization	2.01E-10	5.68E-08
GO:0006952	defense response	2.37E-10	6.54E-08
GO:1901564	organonitrogen compound metabolic process	3.78E-10	1.02E-07
GO:0019884	antigen processing and presentation of exogenous antigen	5.41E-10	1.43E-07
GO:0006281	DNA repair	9.03E-10	2.34E-07
GO:0055086	nucleobase-containing small molecule metabolic process	9.87E-10	2.50E-07
GO:0002682	regulation of immune system process	1.35E-09	3.36E-07
GO:0051716	cellular response to stimulus	1.39E-09	3.38E-07
GO:0044267	cellular protein metabolic process	1.41E-09	3.36E-07
GO:0008033	tRNA processing	1.81E-09	4.24E-07
GO:0034097	response to cytokine	1.82E-09	4.19E-07
GO:0006457	protein folding	2.33E-09	5.27E-07
GO:0019882	antigen processing and presentation	2.62E-09	5.81E-07
GO:0006974	cellular response to DNA damage stimulus	2.68E-09	5.84E-07
GO:0045071	negative regulation of viral genome replication	3.40E-09	7.27E-07
GO:0044281	small molecule metabolic process	6.21E-09	1.31E-06
GO:0002684	positive regulation of immune system process	6.41E-09	1.33E-06
GO:0048002	antigen processing and presentation of peptide antigen	6.77E-09	1.38E-06
GO:0006950	response to stress	7.46E-09	1.49E-06
GO:0065003	macromolecular complex assembly	1.29E-08	2.55E-06
GO:0043207	response to external biotic stimulus	1.31E-08	2.55E-06
GO:0009615	response to virus	1.46E-08	2.79E-06
GO:0006753	nucleoside phosphate metabolic process	1.79E-08	3.36E-06
GO:0048525	negative regulation of viral process	2.18E-08	4.03E-06
GO:0009607	response to biotic stimulus	2.36E-08	4.31E-06
GO:1901293	nucleoside phosphate biosynthetic process	4.75E-08	8.54E-06
GO:0009117	nucleotide metabolic process	7.03E-08	1.25E-05
GO:0055114	oxidation-reduction process	8.70E-08	1.52E-05
GO:0050792	regulation of viral process	9.07E-08	1.56E-05
GO:0051704	multi-organism process	9.15E-08	1.56E-05
GO:0009165	nucleotide biosynthetic process	9.46E-08	1.59E-05
GO:0045069	regulation of viral genome replication	9.89E-08	1.64E-05
GO:0090407	organophosphate biosynthetic process	1.79E-07	2.92E-05
GO:0043901	negative regulation of multi-organism process	2.66E-07	4.29E-05
GO:0043900	regulation of multi-organism process	2.69E-07	4.28E-05
GO:0033554	cellular response to stress	2.71E-07	4.25E-05
GO:0051707	response to other organism	2.73E-07	4.23E-05
GO:0009451	RNA modification	2.74E-07	4.19E-05
GO:0034622	cellular macromolecular complex assembly	2.80E-07	4.23E-05
GO:0051607	defense response to virus	4.10E-07	6.14E-05
GO:0045087	innate immune response	5.09E-07	7.52E-05
GO:0009124	nucleoside monophosphate biosynthetic process	5.79E-07	8.46E-05
GO:0019637	organophosphate metabolic process	6.57E-07	9.48E-05

GO:0043903	regulation of symbiosis, encompassing mutualism through parasitism	7.94E-07	1.13E-04
GO:0022900	electron transport chain	9.94E-07	1.40E-04
GO:0043933	macromolecular complex subunit organization	1.32E-06	1.85E-04
GO:0035455	response to interferon-alpha	1.44E-06	1.99E-04
GO:0006261	DNA-dependent DNA replication	1.60E-06	2.18E-04
GO:0022904	respiratory electron transport chain	1.88E-06	2.54E-04
GO:0006270	DNA replication initiation	2.02E-06	2.70E-04
GO:0042559	pteridine-containing compound biosynthetic process	2.05E-06	2.71E-04
GO:0008380	RNA splicing	2.20E-06	2.87E-04
GO:0050896	response to stimulus	2.30E-06	2.97E-04
GO:0051186	cofactor metabolic process	2.38E-06	3.04E-04
GO:0050776	regulation of immune response	2.52E-06	3.19E-04
GO:0006220	pyrimidine nucleotide metabolic process	2.76E-06	3.46E-04
GO:0098542	defense response to other organism	2.90E-06	3.59E-04
GO:0000387	spliceosomal snRNP assembly	3.55E-06	4.36E-04
GO:0022618	ribonucleoprotein complex assembly	3.59E-06	4.36E-04
GO:0043038	amino acid activation	5.10E-06	6.15E-04
GO:0043039	tRNA aminoacylation	5.10E-06	6.09E-04
GO:0009605	response to external stimulus	5.34E-06	6.31E-04
GO:0016071	mRNA metabolic process	6.36E-06	7.45E-04
GO:0009156	ribonucleoside monophosphate biosynthetic process	6.42E-06	7.45E-04
GO:0050778	positive regulation of immune response	7.56E-06	8.69E-04
GO:0006461	protein complex assembly	8.03E-06	9.14E-04
GO:0035456	response to interferon-beta	8.40E-06	9.47E-04

Table S2: Full list of gene ontology terms returned by the GOrilla tool for microarray transcriptome comparisons between wildtype and mutant quiescent, diploid (CD71-, FSClo) DP cells. Grey highlighting indicates terms shown in Figure S3C

GO term	Description	P-value	FDR q-value
GO:0008152	metabolic process	1.72E-20	2.13E-16
GO:0044237	cellular metabolic process	8.39E-17	5.21E-13
GO:0006412	translation	8.55E-15	3.54E-11
GO:0006259	DNA metabolic process	1.58E-14	4.90E-11
GO:0009987	cellular process	3.75E-14	9.30E-11
GO:0043170	macromolecule metabolic process	8.82E-14	1.82E-10
GO:0044238	primary metabolic process	1.12E-13	1.98E-10
GO:0071704	organic substance metabolic process	1.38E-13	2.15E-10
GO:0044260	cellular macromolecule metabolic process	4.20E-13	5.80E-10
GO:0006974	cellular response to DNA damage stimulus	8.68E-11	1.08E-07
GO:0006260	DNA replication	2.08E-10	2.35E-07
GO:0019538	protein metabolic process	2.19E-10	2.26E-07
GO:0044710	single-organism metabolic process	2.55E-10	2.43E-07
GO:0033554	cellular response to stress	8.54E-10	7.57E-07
GO:0034641	cellular nitrogen compound metabolic process	1.16E-09	9.56E-07
GO:0006139	nucleobase-containing compound metabolic process	2.57E-09	2.00E-06
GO:0006725	cellular aromatic compound metabolic process	3.66E-09	2.68E-06
GO:0046483	heterocycle metabolic process	5.09E-09	3.51E-06
GO:0044267	cellular protein metabolic process	6.83E-09	4.46E-06
GO:0006996	organelle organization	7.37E-09	4.57E-06
GO:0009058	biosynthetic process	1.01E-08	6.00E-06
GO:1901360	organic cyclic compound metabolic process	1.05E-08	5.90E-06
GO:0044249	cellular biosynthetic process	3.12E-08	1.69E-05
GO:1901576	organic substance biosynthetic process	4.90E-08	2.53E-05
GO:0006281	DNA repair	5.05E-08	2.51E-05
GO:0048525	negative regulation of viral process	7.61E-08	3.63E-05
GO:0006807	nitrogen compound metabolic process	1.03E-07	4.74E-05
GO:0050792	regulation of viral process	1.32E-07	5.84E-05
GO:0006950	response to stress	1.62E-07	6.92E-05
GO:1902589	single-organism organelle organization	1.72E-07	7.13E-05
GO:0045069	regulation of viral genome replication	3.16E-07	1.26E-04
GO:0045071	negative regulation of viral genome replication	3.49E-07	1.36E-04
GO:0034110	regulation of homotypic cell-cell adhesion	3.76E-07	1.41E-04
GO:0019884	antigen processing and presentation of exogenous	3.90E-07	1.42E-04
GO:1903037	regulation of leukocyte cell-cell adhesion	4.00E-07	1.42E-04
GO:0022402	cell cycle process	4.53E-07	1.56E-04
GO:0007067	mitotic nuclear division	5.39E-07	1.81E-04
GO:0002376	immune system process	6.03E-07	1.97E-04
GO:0050863	regulation of T cell activation	7.35E-07	2.34E-04
GO:0034341	response to interferon-gamma	7.49E-07	2.32E-04
GO:0009124	nucleoside monophosphate biosynthetic process	8.06E-07	2.44E-04
GO:0007049	cell cycle	8.28E-07	2.45E-04
GO:0034645	cellular macromolecule biosynthetic process	8.85E-07	2.55E-04
GO:0051301	cell division	9.29E-07	2.62E-04
GO:1903047	mitotic cell cycle process	9.77E-07	2.69E-04
GO:0043901	negative regulation of multi-organism process	1.05E-06	2.83E-04
GO:0006461	protein complex assembly	1.11E-06	2.92E-04
GO:0002428	antigen processing and presentation of peptide	1.25E-06	3.24E-04

GO:0009059	macromolecule biosynthetic process	1.36E-06	3.46E-04
GO:0065003	macromolecular complex assembly	1.37E-06	3.41E-04
GO:0019882	antigen processing and presentation	1.47E-06	3.57E-04
GO:0009123	nucleoside monophosphate metabolic process	1.48E-06	3.54E-04
GO:0090304	nucleic acid metabolic process	1.66E-06	3.88E-04
GO:0055114	oxidation-reduction process	1.71E-06	3.92E-04
GO:0006753	nucleoside phosphate metabolic process	1.83E-06	4.14E-04
GO:0043903	regulation of symbiosis, encompassing mutualism	1.86E-06	4.13E-04
GO:0048285	organelle fission	2.27E-06	4.93E-04
GO:0034655	nucleobase-containing compound catabolic process	2.39E-06	5.12E-04
GO:0055086	nucleobase-containing small molecule metabolic process	2.42E-06	5.10E-04
GO:0048002	antigen processing and presentation of peptide	2.59E-06	5.37E-04
GO:0045184	establishment of protein localization	2.72E-06	5.53E-04
GO:0009117	nucleotide metabolic process	3.64E-06	7.30E-04
GO:0051179	localization	3.88E-06	7.65E-04
GO:0043900	regulation of multi-organism process	3.89E-06	7.54E-04
GO:0044085	cellular component biogenesis	4.18E-06	7.97E-04
GO:0002478	antigen processing and presentation of exogenous	4.34E-06	8.17E-04
GO:0043623	cellular protein complex assembly	4.52E-06	8.37E-04
GO:0022900	electron transport chain	5.56E-06	9.99E-04
GO:0034622	cellular macromolecular complex assembly	5.56E-06	9.86E-04

Table S3: Log2 fold change values for known P53 pathway genes, determined by RT-qPCR. Data are presented as fold change relative to wildtype for Caph2 single mutants (Nes) and P53 Caph2 double homozygous mutants (DHM). Experiments were performed in total CD71- (quiescent) DP cells, and are derived from two independent experiments, each with two technical replicates. Functional annotations are based on SABiosciences product literature: "A" = apoptosis, "C" = cell cycle arrest, "N/A" = other

Symbol	Function	Fold Regulation Nes vs WT CD71+	Fold Regulation DHM vs WT CD71+	Fold Regulation in Nes vs WT CD71-	Fold Regulation in DHM vs WT CD71-
Bbc3	A	1.9	-2.1332	1.7029	-1.2852
Apaf1	A	-1.1479	-2.2008	1.2684	-1.4917
Bag1	A	1.0762	1.426	1.1274	1.6335
Bax	A	1.5168	-1.3361	1.3454	-1.3918
Bcl2	A	-1.5411	-3.8317	-1.456	-2.6153
Bid	A	-1.1559	-1.5032	-1.0224	1.5084
Birc5	A	-1.1843	-1.8764	1.5241	-1.2117
Bnip3	A	-2.2486	-2.2784	-1.4409	1.1392
Btg2	A	-1.3938	-1.8125	1.1712	1.041
Casp2	A	-1.2959	-1.498	-1.0622	1.0056
Casp9	A	-1.9507	-1.2294	-1.1463	-1.0295
Cradd	A	-1.3095	-3.2784	1.1591	-1.3168
Dapk1	A	-1.7219	-1.3315	-1.0733	-1.0733
Fadd	A	-1.1559	-1.5347	-1.1867	-1.115
Fas	A	-1.5465	-2.2784	-1.2457	-1.3918
Fasl	A	9.6532	-4.0925	3.0589	-1.2763
Foxo3	A	-1.3841	-1.4469	-1.1583	-1.0189
Mcl1	A	-1.5955	-1.6506	-1.0295	1.0446
Myc	A	1.5867	3.1976	-1.5178	1.567
Nf1	A	-1.4231	-1.6563	1.238	1.2906
Nfkb1	A	-1.5735	-1.6563	-1.3077	-1.5933
Noxa	A	2.7435	-9.6331	5.4566	-1.0996
Prkca	A	-1.5305	-1.3784	-1.2719	-1.5551
Sirt1	A	-1.168	-1.5889	-1.0882	-1.092
Tnf	A	-1.5735	1.2243	-1.0845	-1.5988
Tnfrsf10b	A	-1.0454	1.3213	-1.2286	1.0091
Traf1	A	-3.1689	-4.2516	-1.6044	-3.0568
Zmat3	A	1.4959	-5.4377	1.295	-2.0028
Atm	A + C	1.3296	1.2286	1.0196	1.0777
E2f1	A + C	1.4651	-1.1672	2.1038	2.3343
Pten	A + C	-1.629	-1.87	-1.3918	-1.1704
Trp53	A + C	-1.1559	-3.0589	-1.3679	-3.078
Trp53bp2	A + C	-1.669	-1.5779	-1.1266	-1.1266
Brca1	C	-1.2518	-2.1856	1.4876	-1.1623
Brca2	C	-1.4479	-3.3242	1.6563	-1.2117
Ccnb1	C	-1.0747	-1.3832	1.8188	-1.1384
Ccne1	C	-1.086	-1.7752	1.0966	-1.69
Ccng1	C	1.325	-2.5019	1.2252	-1.6495
Ccnh	C	-1.0133	-1.2209	-1.3775	-1.1463
Cdc25a	C	-1.1127	-1.3361	1.264	1.295

Cdc25c	C	-1.3794	-1.9697	1.5189	-1.2201
Cdk1	C	-1.1843	-1.4621	2.0181	-1.1663
Cdk4	C	1.0007	-1.2995	1.0126	1.2423
Cdkn1a	C	3.9477	-1.7508	8.6219	1.7938
Chek1	C	1.4907	1.1188	2.4674	1.1235
Chek2	C	-1.2008	-2.2784	-1.0119	1.0091
Cul9	C	2.8699	2.6889	1.3223	4.7999
E2f3	C	-1.0526	-1.1917	-1.0224	1.089
Esr1	C	-1.7159	-11.0655	-1.8366	-4.1325
Gadd45a	C	-1.579	-1.4825	1.0483	1.0852
Jun	C	1.5379	-2.7473	3.4653	3.0908
Kras	C	-1.6234	-2.1111	-1.1345	-1.077
Mdm2	C	-1.2092	-1.697	-1.1384	1.0303
Mlh1	C	-1.0747	-1.7267	-1.4712	-1.3168
Msh2	C	1.6426	-1.0231	1.1119	1.2684
Pcna	C	-1.0973	-1.4074	1.4419	1.1712
Ppm1d	C	-1.3095	-1.8895	1.0056	1.0338
Prc1	C	-1.4429	-2.0605	1.4025	-1.0958
Pttg1	C	1.455	-1.0056	-1.0512	-1.2243
Rb1	C	-1.6923	-2.2784	-1.2201	-1.2501
Sesn2	C	-1.1479	1.2159	2.0605	1.9225
Sfn	C	-1.6066	-1.1958	-1.1704	1.1274
Apex1	#N/A	-19.2796	1.7496	-1.2852	1.2294
Atr	#N/A	-1.0898	-1.1471	-1.3491	1.0374
Dnmt1	#N/A	-1.0274	-1.7938	1.2	-1.195
Egr1	#N/A	-2.4606	-2.3751	-1.6725	-1.7315
Ep300	#N/A	-1.5094	-1.0483	-1.2986	1.0592
Ercc1	#N/A	-1.3095	-1.457	-1.1463	-1.2763
Hif1a	#N/A	-1.601	-1.8895	-1.1345	-1.1111
Lig4	#N/A	-1.2825	-1.5834	1.0483	1.0852
Mdm4	#N/A	-1.7826	-2.0605	-1.4064	-1.3122
Rela	#N/A	-1.1639	-1.388	-1.0189	1.0126
Stat1	#N/A	-1.0822	-1.7569	1.2995	-1.2201
Xrcc4	#N/A	-1.8013	-1.9561	-1.426	-1.6552
Xrcc5	#N/A	-1.205	-1.6449	-1.5551	-1.5497

Table S4: The top 10 deleted regions in terminal Caph2 single mutant tumour genomes, ranked by normalised Log2 read count. Genes with characterised roles in oncogenesis are highlighted in red

Tumour ID	Chr	bpstart	bpend	Normalised Log2 read count	Genes within deletion
CNA3	19	31,980,001	33,330,000	-2.808848769	Pten
CNA11	4	89,280,001	91,020,000	-2.72312506	CDKN2A
CNA2	10	64,290,001	66,960,000	-1.326395714	Ctnna3
CNA2	4	88,950,001	93,390,000	-1.249318996	CDKN2A, CDKN2B
CNA9	16	64,830,001	65,370,000	-0.959156134	htr1f, Cggbp1
CNA8	4	89,040,001	89,280,000	-0.917241212	CDKN2A, CDKN2B
CNA8	12	93,270,001	99,210,000	-0.860903904	Many
CNA8	12	101,070,001	106,800,000	-0.860445412	Many
CNA2	4	121,260,001	122,820,000	-0.839961576	Many
CNA8	12	108,000,001	108,810,000	-0.788263764	Bcl11b, Setd3, Ccnk, Ccdc85c, Hhipl1, Eml1, Evl, Degs2, Yy1

Table S5: Cell surface markers used for immunophenotyping in this study

Cell Subset	Immunophenotype
Stem Cells and Progenitors	
LSK	(CD4-, CD5-, CD8-, CD11b-, Gr1-, B220-, Ter119-) Sca-1+, c-Kit+
Myeloid progenitors (LK)	(CD4-, CD5-, CD8-, CD11b-, Gr1-, B220-, Ter119-) Sca-1+, c-Kit-
Common Lymphoid progenitors (CLP)	(CD4-, CD5-, CD8-, CD11b-, Gr1-, B220-, Ter119-) Flt-3+, CD127+, c-Kitlo, Sca-1lo
Thymic T lymphocytes	
DN1	CD90+, CD4-, CD8-, CD44hi, CD25-
DN2	CD90+, CD4-, CD8-, CD44hi, CD25+
DN3	CD90+, CD4-, CD8-, CD44lo, CD25+
DN4	CD90+, CD4-, CD8-, CD44lo, CD25-, TCRγδ-
DP CD71+	CD4+, CD8+, CD71+
DP CD71-	CD4+, CD8+, CD71-
CD4SP	CD4+, CD8-
Bone Marrow B lymphocytes	
Fraction A	B220+, CD43+, CD24-, BP1-
Fraction B	B220+, CD43+, CD24+, BP1-
Fraction C	B220+, CD43+, CD24+, BP1+
Fraction D	B220+, CD43-, IgM-
Fraction E	B220+, CD43-, IgM+
Fraction F	B220++, CD43-, IgM+

Table S6: Antibody details

Antibody	Application	Dilution	Clone ID or Cat #	Supplier
B220	FACS	1/200	RA3-6B2	eBioScience
BP-1	FACS	1/50	6C3	eBioScience
BrdU	FACS	1/50	with kit #557892	BD Pharmingen
CD4	FACS	1/400	RM4-5	eBioScience
CD8	FACS	1/1000	53-6.7	eBioScience
CD24	FACS	1/500	30F1	eBioScience
CD25	FACS	1/100	PC61.5	eBioScience
CD43	FACS	1/200	eBio R2/60	eBioScience
CD44	FACS	1/100	IM7	eBioScience
CD71	FACS	1/100	RI7217	Biolegend
CD90	FACS	1/500	53.2.1	eBioScience
CD127	FACS	1/200	135023	Biolegend
c-kit	FACS	1/200	105826	Biolegend
Flt-3	FACS	1/100	135310	Biolegend
IgM	FACS	1/200	II/41	eBioScience
Sca-1	FACS	1/200	122506	Biolegend
alpha Tubulin	Western/IF	1/250	YOL1/34	BioRad
H3S10P	IF	1/500	6G3	CST
BM Lineage cocktail 10X:				
CD3	FACS	1/100	559971	BD
CD4	FACS	1/1600	553649	BD
CD5	FACS	1/800	553019	BD
CD8a	FACS	1/800	553029	BD
Mac-1/CD11b	FACS	1/200	553309	BD
B220	FACS	1/200	553086	BD
Ter119	FACS	1/50	553672	BD
Gr-1	FACS	1/100	553125	BD
Streptavidin	FACS	1/200	405229	Biolegend

Table S7: FISH probe details

Probe ID	Probe Type	Experiment	Chr	Coordinates (GRCm38)
Chr2 point probe	Sequence capture	Tetraploidy (Figure 6D & E)	2	74,636,100-74,767,381
Chr2 paint	Sequence Capture	Tetraploidy (Figure 6D & E)	2	Whole exome of Mmu 2
WI1-2585C04	Fosmid	Tumour ploidy (Figure S10)	13	51, 917,709 - 51,959,777
WI1 - 1265B14	Fosmid	Tumour ploidy (Figure S10)	6	30,756,571 - 30,789,822
WI1-1141E16	Fosmid	CD8 locus compaction (Figure S2)	6	71,395,924 - 71,439,942
WI1-1250E20	Fosmid	CD8 locus compaction (Figure S2)	6	71,24,174 - 71,271,897
G135P68104F	Fosmid	CD8 to Igkv compaction (Figure	6	70,041,587 - 70,083,551
G135P600867C1	Fosmid	CD8 to Mad2L1 compaction (Figure	6	66,449,639 - 66,484,514

Table S8: Full list of gene ontology terms returned by the GOrilla tool for microarray transcriptome comparisons between non-cycling diploid (CD71-, FSClo) and non-cycling tetraploid (CD71-FSChi) DP cells purified from Caph2 mutant thymus. Grey highlighting indicates terms shown in Figure S3D

GO term	Description	P-value	FDR q-value
GO:0044260	cellular macromolecule metabolic process	2.78E-53	3.91E-49
GO:0009987	cellular process	2.54E-52	1.78E-48
GO:0044237	cellular metabolic process	7.45E-50	3.49E-46
GO:0034641	cellular nitrogen compound metabolic process	1.03E-45	3.63E-42
GO:0046483	heterocycle metabolic process	2.06E-44	5.79E-41
GO:0006139	nucleobase-containing compound metabolic process	2.71E-44	6.34E-41
GO:0043170	macromolecule metabolic process	3.52E-44	7.06E-41
GO:0006725	cellular aromatic compound metabolic process	4.60E-43	8.09E-40
GO:0006807	nitrogen compound metabolic process	2.85E-41	4.45E-38
GO:0044238	primary metabolic process	2.91E-41	4.09E-38
GO:0071704	organic substance metabolic process	2.17E-39	2.77E-36
GO:0090304	nucleic acid metabolic process	2.46E-39	2.88E-36
GO:0008152	metabolic process	5.15E-39	5.56E-36
GO:1901360	organic cyclic compound metabolic process	6.14E-39	6.16E-36
GO:0071840	cellular component organization or biogenesis	2.20E-35	2.06E-32
GO:0016043	cellular component organization	3.39E-34	2.97E-31
GO:0022402	cell cycle process	4.00E-34	3.31E-31
GO:1903047	mitotic cell cycle process	2.05E-32	1.60E-29
GO:0007049	cell cycle	1.57E-31	1.16E-28
GO:0043933	macromolecular complex subunit organization	3.92E-31	2.76E-28
GO:0006259	DNA metabolic process	8.48E-31	5.68E-28
GO:0007067	mitotic nuclear division	1.12E-27	7.16E-25
GO:0000280	nuclear division	3.85E-26	2.35E-23
GO:0006325	chromatin organization	5.40E-26	3.16E-23
GO:0048285	organelle fission	3.20E-24	1.80E-21
GO:0006396	RNA processing	9.36E-24	5.06E-21
GO:0051276	chromosome organization	2.26E-23	1.18E-20
GO:0051301	cell division	2.34E-23	1.17E-20
GO:0006260	DNA replication	2.83E-23	1.37E-20
GO:0006974	cellular response to DNA damage stimulus	1.06E-21	4.97E-19
GO:0006996	organelle organization	1.08E-20	4.89E-18
GO:0016071	mRNA metabolic process	4.48E-20	1.97E-17
GO:0006281	DNA repair	5.45E-20	2.32E-17
GO:0034622	cellular macromolecular complex assembly	9.47E-20	3.91E-17
GO:0033554	cellular response to stress	4.48E-19	1.80E-16
GO:0065003	macromolecular complex assembly	4.59E-19	1.79E-16
GO:0016070	RNA metabolic process	1.76E-18	6.70E-16
GO:0044249	cellular biosynthetic process	3.16E-18	1.17E-15
GO:0022607	cellular component assembly	4.84E-18	1.74E-15
GO:0007059	chromosome segregation	1.56E-17	5.47E-15
GO:0044267	cellular protein metabolic process	2.59E-17	8.88E-15

GO:0006397	mRNA processing	3.58E-17	1.20E-14
GO:1901576	organic substance biosynthetic process	5.06E-17	1.65E-14
GO:0009058	biosynthetic process	1.30E-16	4.14E-14
GO:0043412	macromolecule modification	2.58E-15	8.06E-13
GO:0033044	regulation of chromosome organization	2.84E-15	8.67E-13
GO:0071824	protein-DNA complex subunit organization	6.99E-15	2.09E-12
GO:0051171	regulation of nitrogen compound metabolic process	1.83E-14	5.36E-12
GO:0051052	regulation of DNA metabolic process	2.58E-14	7.39E-12
GO:0006334	nucleosome assembly	3.20E-14	8.99E-12
GO:0034728	nucleosome organization	3.31E-14	9.12E-12
GO:0006333	chromatin assembly or disassembly	3.50E-14	9.45E-12
GO:0022618	ribonucleoprotein complex assembly	4.23E-14	1.12E-11
GO:0051726	regulation of cell cycle	4.56E-14	1.19E-11
GO:0010564	regulation of cell cycle process	6.03E-14	1.54E-11
GO:0065004	protein-DNA complex assembly	6.19E-14	1.55E-11
GO:0071826	ribonucleoprotein complex subunit organization	6.91E-14	1.70E-11
GO:0019538	protein metabolic process	7.93E-14	1.92E-11
GO:0007346	regulation of mitotic cell cycle	8.47E-14	2.02E-11
GO:0019222	regulation of metabolic process	1.04E-13	2.43E-11
GO:0034645	cellular macromolecule biosynthetic process	1.56E-13	3.59E-11
GO:0008380	RNA splicing	1.64E-13	3.71E-11
GO:0044271	cellular nitrogen compound biosynthetic process	1.82E-13	4.07E-11
GO:0006464	cellular protein modification process	1.88E-13	4.13E-11
GO:0036211	protein modification process	1.88E-13	4.07E-11
GO:0033043	regulation of organelle organization	2.51E-13	5.34E-11
GO:0060255	regulation of macromolecule metabolic process	2.82E-13	5.92E-11
GO:0080090	regulation of primary metabolic process	3.88E-13	8.02E-11
GO:0019219	regulation of nucleobase-containing compound metabolic process	4.11E-13	8.37E-11
GO:2001252	positive regulation of chromosome organization	4.33E-13	8.70E-11
GO:0010556	regulation of macromolecule biosynthetic process	4.49E-13	8.88E-11
GO:0051716	cellular response to stimulus	5.98E-13	1.17E-10
GO:0031323	regulation of cellular metabolic process	6.07E-13	1.17E-10
GO:2000112	regulation of cellular macromolecule biosynthetic process	6.23E-13	1.18E-10
GO:0045814	negative regulation of gene expression, epigenetic	6.74E-13	1.26E-10
GO:0050658	RNA transport	6.84E-13	1.27E-10
GO:0050657	nucleic acid transport	6.84E-13	1.25E-10
GO:0009059	macromolecule biosynthetic process	7.62E-13	1.37E-10
GO:0051236	establishment of RNA localization	9.58E-13	1.70E-10
GO:0051028	mRNA transport	1.08E-12	1.89E-10
GO:0015931	nucleobase-containing compound transport	2.05E-12	3.55E-10
GO:0040029	regulation of gene expression, epigenetic	2.83E-12	4.85E-10
GO:0044763	single-organism cellular process	3.32E-12	5.63E-10
GO:0006342	chromatin silencing	3.35E-12	5.61E-10
GO:0071103	DNA conformation change	3.37E-12	5.57E-10

GO:0010468	regulation of gene expression	6.35E-12	1.04E-09
GO:0034723	DNA replication-dependent nucleosome organization	7.01E-12	1.13E-09
GO:0006335	DNA replication-dependent nucleosome assembly	7.01E-12	1.12E-09
GO:0010638	positive regulation of organelle organization	8.95E-12	1.41E-09
GO:0009889	regulation of biosynthetic process	1.73E-11	2.70E-09
GO:0007017	microtubule-based process	1.80E-11	2.78E-09
GO:0071822	protein complex subunit organization	2.07E-11	3.16E-09
GO:0000075	cell cycle checkpoint	2.31E-11	3.49E-09
GO:0000226	microtubule cytoskeleton organization	2.41E-11	3.60E-09
GO:0006310	DNA recombination	2.77E-11	4.10E-09
GO:0042278	purine nucleoside metabolic process	3.01E-11	4.41E-09
GO:0016458	gene silencing	3.68E-11	5.33E-09
GO:0006302	double-strand break repair	3.81E-11	5.46E-09
GO:0009116	nucleoside metabolic process	5.06E-11	7.18E-09
GO:0031326	regulation of cellular biosynthetic process	6.52E-11	9.16E-09
GO:0051252	regulation of RNA metabolic process	6.52E-11	9.08E-09
GO:0006270	DNA replication initiation	9.02E-11	1.24E-08
GO:0033365	protein localization to organelle	1.02E-10	1.40E-08
GO:0046128	purine ribonucleoside metabolic process	1.05E-10	1.42E-08
GO:0042451	purine nucleoside biosynthetic process	1.51E-10	2.02E-08
GO:0046129	purine ribonucleoside biosynthetic process	1.51E-10	2.00E-08
GO:0044265	cellular macromolecule catabolic process	1.64E-10	2.16E-08
GO:0000819	sister chromatid segregation	2.07E-10	2.69E-08
GO:0009119	ribonucleoside metabolic process	2.08E-10	2.69E-08
GO:0006461	protein complex assembly	2.24E-10	2.87E-08
GO:0009165	nucleotide biosynthetic process	3.16E-10	4.00E-08
GO:0051641	cellular localization	3.16E-10	3.97E-08
GO:1901657	glycosyl compound metabolic process	3.39E-10	4.22E-08
GO:0000724	double-strand break repair via homologous recombination	3.79E-10	4.68E-08
GO:0000725	recombinational repair	3.79E-10	4.63E-08
GO:0034660	ncRNA metabolic process	6.17E-10	7.47E-08
GO:0042455	ribonucleoside biosynthetic process	6.97E-10	8.37E-08
GO:0044699	single-organism process	7.02E-10	8.36E-08
GO:1901293	nucleoside phosphate biosynthetic process	7.22E-10	8.52E-08
GO:1901990	regulation of mitotic cell cycle phase transition	7.41E-10	8.68E-08
GO:0009163	nucleoside biosynthetic process	1.14E-09	1.32E-07
GO:0006163	purine nucleotide metabolic process	1.36E-09	1.57E-07
GO:0009057	macromolecule catabolic process	1.46E-09	1.67E-07
GO:0016569	covalent chromatin modification	1.46E-09	1.66E-07
GO:1901659	glycosyl compound biosynthetic process	1.49E-09	1.67E-07
GO:0034724	DNA replication-independent nucleosome organization	1.58E-09	1.76E-07
GO:0006336	DNA replication-independent nucleosome assembly	1.58E-09	1.75E-07
GO:0034470	ncRNA processing	1.69E-09	1.85E-07

GO:0006401	RNA catabolic process	2.04E-09	2.23E-07
GO:0007093	mitotic cell cycle checkpoint	2.34E-09	2.53E-07
GO:0072521	purine-containing compound metabolic process	2.74E-09	2.94E-07
GO:0006753	nucleoside phosphate metabolic process	2.77E-09	2.95E-07
GO:0018130	heterocycle biosynthetic process	2.81E-09	2.97E-07
GO:0055086	nucleobase-containing small molecule metabolic process	2.97E-09	3.12E-07
GO:0098813	nuclear chromosome segregation	3.01E-09	3.13E-07
GO:0009117	nucleotide metabolic process	3.03E-09	3.13E-07
GO:1901566	organonitrogen compound biosynthetic process	3.19E-09	3.27E-07
GO:0006913	nucleocytoplasmic transport	3.29E-09	3.35E-07
GO:1901987	regulation of cell cycle phase transition	3.64E-09	3.69E-07
GO:0034654	nucleobase-containing compound biosynthetic process	3.69E-09	3.71E-07
GO:0000070	mitotic sister chromatid segregation	5.94E-09	5.92E-07
GO:0051169	nuclear transport	6.01E-09	5.95E-07
GO:0019438	aromatic compound biosynthetic process	6.58E-09	6.46E-07
GO:0006796	phosphate-containing compound metabolic process	7.23E-09	7.06E-07
GO:0006275	regulation of DNA replication	7.39E-09	7.16E-07
GO:2000113	negative regulation of cellular macromolecule biosynthetic process	7.83E-09	7.54E-07
GO:0016072	rRNA metabolic process	8.09E-09	7.74E-07
GO:0045934	negative regulation of nucleobase-containing compound metabolic process	8.79E-09	8.35E-07
GO:0006793	phosphorus metabolic process	9.84E-09	9.28E-07
GO:0072522	purine-containing compound biosynthetic process	1.01E-08	9.42E-07
GO:0051290	protein heterotetramerization	1.04E-08	9.68E-07
GO:0006164	purine nucleotide biosynthetic process	1.08E-08	1.00E-06
GO:0051262	protein tetramerization	1.08E-08	9.96E-07
GO:0051783	regulation of nuclear division	1.25E-08	1.14E-06
GO:2001141	regulation of RNA biosynthetic process	1.35E-08	1.22E-06
GO:0009259	ribonucleotide metabolic process	1.56E-08	1.41E-06
GO:0018193	peptidyl-amino acid modification	1.62E-08	1.45E-06
GO:0045930	negative regulation of mitotic cell cycle	1.86E-08	1.66E-06
GO:0010558	negative regulation of macromolecule biosynthetic process	2.15E-08	1.90E-06
GO:2001251	negative regulation of chromosome organization	2.39E-08	2.10E-06
GO:0006402	mRNA catabolic process	2.41E-08	2.10E-06
GO:0030261	chromosome condensation	2.86E-08	2.48E-06
GO:0006355	regulation of transcription, DNA-templated	2.89E-08	2.49E-06
GO:0009150	purine ribonucleotide metabolic process	2.93E-08	2.51E-06
GO:1902275	regulation of chromatin organization	3.05E-08	2.60E-06
GO:1903506	regulation of nucleic acid-templated transcription	3.11E-08	2.64E-06
GO:1901362	organic cyclic compound biosynthetic process	3.35E-08	2.82E-06
GO:0006950	response to stress	3.57E-08	2.98E-06
GO:0006364	rRNA processing	4.12E-08	3.42E-06

GO:0051172	negative regulation of nitrogen compound metabolic process	4.21E-08	3.48E-06
GO:0090329	regulation of DNA-dependent DNA replication	4.90E-08	4.03E-06
GO:0019693	ribose phosphate metabolic process	4.99E-08	4.07E-06
GO:0007088	regulation of mitotic nuclear division	5.39E-08	4.38E-06
GO:0010629	negative regulation of gene expression	6.12E-08	4.94E-06
GO:0051649	establishment of localization in cell	6.34E-08	5.09E-06
GO:0051130	positive regulation of cellular component organization	6.41E-08	5.12E-06
GO:0034502	protein localization to chromosome	7.31E-08	5.80E-06
GO:0010948	negative regulation of cell cycle process	7.75E-08	6.12E-06
GO:0044770	cell cycle phase transition	8.35E-08	6.56E-06
GO:0007076	mitotic chromosome condensation	8.57E-08	6.69E-06
GO:0009890	negative regulation of biosynthetic process	8.66E-08	6.73E-06
GO:0051168	nuclear export	8.75E-08	6.76E-06
GO:1903827	regulation of cellular protein localization	1.03E-07	7.88E-06
GO:0033036	macromolecule localization	1.06E-07	8.12E-06
GO:0051128	regulation of cellular component organization	1.34E-07	1.02E-05
GO:0000387	spliceosomal snRNP assembly	1.42E-07	1.07E-05
GO:0006412	translation	1.44E-07	1.08E-05
GO:0000956	nuclear-transcribed mRNA catabolic process	1.47E-07	1.10E-05
GO:1904666	regulation of ubiquitin protein ligase activity	1.57E-07	1.17E-05
GO:0009123	nucleoside monophosphate metabolic process	1.67E-07	1.24E-05
GO:0090407	organophosphate biosynthetic process	1.68E-07	1.24E-05
GO:0045786	negative regulation of cell cycle	1.90E-07	1.39E-05
GO:0031327	negative regulation of cellular biosynthetic process	1.96E-07	1.43E-05
GO:0007051	spindle organization	2.03E-07	1.47E-05
GO:1901991	negative regulation of mitotic cell cycle phase transition	2.13E-07	1.54E-05
GO:0070646	protein modification by small protein removal	2.16E-07	1.55E-05
GO:0017038	protein import	2.26E-07	1.61E-05
GO:0009126	purine nucleoside monophosphate metabolic process	2.32E-07	1.65E-05
GO:0009167	purine ribonucleoside monophosphate metabolic process	2.32E-07	1.64E-05
GO:0034655	nucleobase-containing compound catabolic process	2.41E-07	1.69E-05
GO:0008104	protein localization	2.49E-07	1.74E-05
GO:0009260	ribonucleotide biosynthetic process	2.53E-07	1.76E-05
GO:0046907	intracellular transport	3.16E-07	2.19E-05
GO:0034504	protein localization to nucleus	3.46E-07	2.38E-05
GO:0009892	negative regulation of metabolic process	3.46E-07	2.37E-05
GO:0009161	ribonucleoside monophosphate metabolic process	3.58E-07	2.44E-05
GO:0009141	nucleoside triphosphate metabolic process	3.59E-07	2.44E-05
GO:0032200	telomere organization	3.72E-07	2.51E-05
GO:0006323	DNA packaging	3.78E-07	2.54E-05

GO:0010605	negative regulation of macromolecule metabolic process	3.88E-07	2.60E-05
GO:0045184	establishment of protein localization	3.98E-07	2.65E-05
GO:0051253	negative regulation of RNA metabolic process	4.24E-07	2.81E-05
GO:0009152	purine ribonucleotide biosynthetic process	4.31E-07	2.84E-05
GO:0046390	ribose phosphate biosynthetic process	4.35E-07	2.86E-05
GO:0070727	cellular macromolecule localization	4.46E-07	2.91E-05
GO:0070647	protein modification by small protein conjugation or removal	4.79E-07	3.11E-05
GO:0048523	negative regulation of cellular process	4.80E-07	3.11E-05
GO:0032392	DNA geometric change	5.22E-07	3.36E-05
GO:0006457	protein folding	5.96E-07	3.83E-05
GO:0044270	cellular nitrogen compound catabolic process	6.03E-07	3.85E-05
GO:0051983	regulation of chromosome segregation	6.85E-07	4.36E-05
GO:0034613	cellular protein localization	7.18E-07	4.55E-05
GO:0051054	positive regulation of DNA metabolic process	7.27E-07	4.58E-05
GO:0046700	heterocycle catabolic process	7.68E-07	4.82E-05
GO:1901988	negative regulation of cell cycle phase transition	8.82E-07	5.51E-05
GO:0006268	DNA unwinding involved in DNA replication	8.85E-07	5.51E-05
GO:1905269	positive regulation of chromatin organization	9.52E-07	5.89E-05
GO:0019637	organophosphate metabolic process	9.53E-07	5.88E-05
GO:1902589	single-organism organelle organization	1.00E-06	6.14E-05
GO:0043043	peptide biosynthetic process	1.10E-06	6.71E-05
GO:0033157	regulation of intracellular protein transport	1.11E-06	6.77E-05
GO:1901564	organonitrogen compound metabolic process	1.13E-06	6.83E-05
GO:0048519	negative regulation of biological process	1.21E-06	7.32E-05
GO:0019439	aromatic compound catabolic process	1.22E-06	7.34E-05
GO:0007010	cytoskeleton organization	1.27E-06	7.60E-05
GO:0006261	DNA-dependent DNA replication	1.32E-06	7.88E-05
GO:0000723	telomere maintenance	1.36E-06	8.09E-05
GO:0007080	mitotic metaphase plate congression	1.44E-06	8.51E-05
GO:0032508	DNA duplex unwinding	1.49E-06	8.78E-05
GO:0009144	purine nucleoside triphosphate metabolic process	1.53E-06	8.97E-05
GO:0072594	establishment of protein localization to organelle	1.58E-06	9.23E-05
GO:0071459	protein localization to chromosome, centromeric region	1.79E-06	1.04E-04
GO:0031324	negative regulation of cellular metabolic process	1.81E-06	1.05E-04
GO:0031056	regulation of histone modification	1.92E-06	1.10E-04
GO:0000377	RNA splicing, via transesterification reactions with bulged adenosine as nucleophile	1.96E-06	1.12E-04
GO:0000398	mRNA splicing, via spliceosome	1.96E-06	1.12E-04
GO:1901137	carbohydrate derivative biosynthetic process	1.99E-06	1.13E-04
GO:0031570	DNA integrity checkpoint	2.20E-06	1.24E-04
GO:0000375	RNA splicing, via transesterification reactions	2.33E-06	1.32E-04
GO:0044772	mitotic cell cycle phase transition	2.44E-06	1.37E-04
GO:0045892	negative regulation of transcription, DNA-templated	2.53E-06	1.42E-04

GO:0051310	metaphase plate congression	2.69E-06	1.50E-04
GO:1902679	negative regulation of RNA biosynthetic process	2.76E-06	1.53E-04
GO:1901135	carbohydrate derivative metabolic process	2.80E-06	1.55E-04
GO:0048522	positive regulation of cellular process	2.97E-06	1.64E-04
GO:1904668	positive regulation of ubiquitin protein ligase activity	3.07E-06	1.68E-04
GO:0051291	protein heterooligomerization	3.38E-06	1.85E-04
GO:0007062	sister chromatid cohesion	3.76E-06	2.05E-04
GO:0006606	protein import into nucleus	3.80E-06	2.06E-04
GO:1902593	single-organism nuclear import	3.80E-06	2.05E-04
GO:1903507	negative regulation of nucleic acid-templated transcription	3.86E-06	2.08E-04
GO:0032386	regulation of intracellular transport	3.87E-06	2.08E-04
GO:0006405	RNA export from nucleus	3.95E-06	2.11E-04
GO:0009199	ribonucleoside triphosphate metabolic process	4.18E-06	2.23E-04
GO:0034248	regulation of cellular amide metabolic process	4.30E-06	2.28E-04
GO:0050684	regulation of mRNA processing	4.43E-06	2.34E-04
GO:0051170	nuclear import	4.65E-06	2.45E-04
GO:0016310	phosphorylation	4.67E-06	2.45E-04
GO:0044085	cellular component biogenesis	4.87E-06	2.55E-04
GO:0051053	negative regulation of DNA metabolic process	4.96E-06	2.58E-04
GO:0010639	negative regulation of organelle organization	5.01E-06	2.60E-04
GO:0006417	regulation of translation	5.16E-06	2.67E-04
GO:1903046	meiotic cell cycle process	5.96E-06	3.07E-04
GO:1901361	organic cyclic compound catabolic process	5.97E-06	3.06E-04
GO:0042127	regulation of cell proliferation	6.36E-06	3.25E-04
GO:1903829	positive regulation of cellular protein localization	6.85E-06	3.49E-04
GO:0006886	intracellular protein transport	8.06E-06	4.09E-04
GO:0051656	establishment of organelle localization	8.29E-06	4.19E-04
GO:0048518	positive regulation of biological process	8.30E-06	4.18E-04
GO:0000077	DNA damage checkpoint	8.74E-06	4.39E-04
GO:1901976	regulation of cell cycle checkpoint	8.94E-06	4.47E-04
GO:0006406	mRNA export from nucleus	9.25E-06	4.61E-04
GO:0010608	posttranscriptional regulation of gene expression	9.74E-06	4.84E-04
GO:0031058	positive regulation of histone modification	1.02E-05	5.03E-04
GO:0046822	regulation of nucleocytoplasmic transport	1.14E-05	5.62E-04
GO:0000910	cytokinesis	1.16E-05	5.69E-04
GO:0051246	regulation of protein metabolic process	1.17E-05	5.71E-04
GO:1903533	regulation of protein targeting	1.18E-05	5.74E-04
GO:0051640	organelle localization	1.21E-05	5.90E-04
GO:0051098	regulation of binding	1.24E-05	6.03E-04
GO:0044843	cell cycle G1/S phase transition	1.28E-05	6.20E-04
GO:0000082	G1/S transition of mitotic cell cycle	1.28E-05	6.18E-04
GO:0009205	purine ribonucleoside triphosphate metabolic process	1.32E-05	6.35E-04
GO:0071478	cellular response to radiation	1.46E-05	6.98E-04
GO:0051297	centrosome organization	1.47E-05	6.99E-04

GO:0060341	regulation of cellular localization	1.52E-05	7.23E-04
GO:0090316	positive regulation of intracellular protein transport	1.61E-05	7.60E-04
GO:0045653	negative regulation of megakaryocyte differentiation	1.91E-05	9.02E-04
GO:0051303	establishment of chromosome localization	1.98E-05	9.31E-04
GO:0031023	microtubule organizing center organization	1.99E-05	9.32E-04
GO:0033047	regulation of mitotic sister chromatid segregation	2.13E-05	9.96E-04
GO:1903311	regulation of mRNA metabolic process	2.15E-05	1.00E-03
GO:0090231	regulation of spindle checkpoint	2.22E-05	1.03E-03
GO:0002683	negative regulation of immune system process	2.24E-05	1.03E-03
GO:0050000	chromosome localization	2.25E-05	1.04E-03
GO:0006518	peptide metabolic process	2.32E-05	1.06E-03
GO:0009124	nucleoside monophosphate biosynthetic process	2.45E-05	1.12E-03
GO:0031497	chromatin assembly	2.54E-05	1.16E-03
GO:0043604	amide biosynthetic process	2.64E-05	1.20E-03
GO:0051438	regulation of ubiquitin-protein transferase activity	2.65E-05	1.20E-03
GO:0046034	ATP metabolic process	2.70E-05	1.22E-03
GO:0000727	double-strand break repair via break-induced replication	2.73E-05	1.23E-03
GO:0022613	ribonucleoprotein complex biogenesis	3.01E-05	1.35E-03
GO:0009127	purine nucleoside monophosphate biosynthetic process	3.08E-05	1.38E-03
GO:0009168	purine ribonucleoside monophosphate biosynthetic process	3.08E-05	1.37E-03
GO:0045931	positive regulation of mitotic cell cycle	3.12E-05	1.39E-03
GO:0018205	peptidyl-lysine modification	3.13E-05	1.39E-03
GO:0033045	regulation of sister chromatid segregation	3.19E-05	1.41E-03
GO:0071479	cellular response to ionizing radiation	3.22E-05	1.42E-03
GO:0006458	'de novo' protein folding	3.25E-05	1.43E-03
GO:0051084	'de novo' posttranslational protein folding	3.25E-05	1.42E-03
GO:0009263	deoxyribonucleotide biosynthetic process	3.26E-05	1.42E-03
GO:0009145	purine nucleoside triphosphate biosynthetic process	3.63E-05	1.58E-03
GO:0044248	cellular catabolic process	4.06E-05	1.76E-03
GO:0031055	chromatin remodeling at centromere	4.24E-05	1.83E-03
GO:0051259	protein oligomerization	4.35E-05	1.87E-03
GO:0002504	antigen processing and presentation of peptide or polysaccharide antigen via MHC class II	4.35E-05	1.87E-03
GO:0002495	antigen processing and presentation of peptide antigen via MHC class II	4.35E-05	1.87E-03
GO:0019886	antigen processing and presentation of exogenous peptide antigen via MHC class II	4.35E-05	1.86E-03
GO:0051603	proteolysis involved in cellular protein catabolic process	4.36E-05	1.86E-03
GO:0042493	response to drug	4.39E-05	1.86E-03
GO:0015031	protein transport	4.42E-05	1.87E-03
GO:0009201	ribonucleoside triphosphate biosynthetic process	4.51E-05	1.90E-03
GO:0000245	spliceosomal complex assembly	5.44E-05	2.29E-03

GO:0032268	regulation of cellular protein metabolic process	5.63E-05	2.36E-03
GO:0031577	spindle checkpoint	5.65E-05	2.37E-03
GO:0000184	nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	5.76E-05	2.40E-03
GO:0009142	nucleoside triphosphate biosynthetic process	5.93E-05	2.47E-03
GO:0009156	ribonucleoside monophosphate biosynthetic process	5.93E-05	2.46E-03
GO:0008284	positive regulation of cell proliferation	6.33E-05	2.62E-03
GO:0045787	positive regulation of cell cycle	6.34E-05	2.61E-03
GO:0051225	spindle assembly	6.64E-05	2.73E-03
GO:0043484	regulation of RNA splicing	6.65E-05	2.72E-03
GO:0010965	regulation of mitotic sister chromatid separation	6.94E-05	2.84E-03
GO:0006338	chromatin remodeling	7.21E-05	2.94E-03
GO:0007100	mitotic centrosome separation	7.33E-05	2.98E-03
GO:1901575	organic substance catabolic process	7.82E-05	3.17E-03
GO:2001020	regulation of response to DNA damage stimulus	7.92E-05	3.20E-03
GO:0071353	cellular response to interleukin-4	8.20E-05	3.30E-03
GO:0030951	establishment or maintenance of microtubule cytoskeleton polarity	8.38E-05	3.37E-03
GO:0009314	response to radiation	8.47E-05	3.39E-03
GO:0015937	coenzyme A biosynthetic process	8.96E-05	3.58E-03
GO:0044711	single-organism biosynthetic process	9.36E-05	3.73E-03
GO:0007064	mitotic sister chromatid cohesion	9.84E-05	3.91E-03
GO:0032388	positive regulation of intracellular transport	1.01E-04	4.01E-03
GO:0009411	response to UV	1.05E-04	4.13E-03
GO:2000104	negative regulation of DNA-dependent DNA replication	1.06E-04	4.18E-03
GO:0043632	modification-dependent macromolecule catabolic process	1.13E-04	4.45E-03
GO:0031647	regulation of protein stability	1.15E-04	4.49E-03
GO:0045870	positive regulation of single stranded viral RNA replication via double stranded DNA intermediate	1.17E-04	4.57E-03
GO:0016073	snRNA metabolic process	1.17E-04	4.56E-03
GO:0030071	regulation of mitotic metaphase/anaphase transition	1.20E-04	4.67E-03
GO:0007052	mitotic spindle organization	1.25E-04	4.83E-03
GO:0032880	regulation of protein localization	1.34E-04	5.17E-03
GO:2000278	regulation of DNA biosynthetic process	1.35E-04	5.20E-03
GO:0043414	macromolecule methylation	1.36E-04	5.24E-03
GO:0051188	cofactor biosynthetic process	1.45E-04	5.56E-03
GO:2000501	regulation of natural killer cell chemotaxis	1.51E-04	5.76E-03
GO:2000503	positive regulation of natural killer cell chemotaxis	1.51E-04	5.75E-03
GO:0043624	cellular protein complex disassembly	1.52E-04	5.79E-03
GO:0006351	transcription, DNA-templated	1.53E-04	5.79E-03
GO:0045652	regulation of megakaryocyte differentiation	1.54E-04	5.83E-03
GO:2000341	regulation of chemokine (C-X-C motif) ligand 2 production	1.57E-04	5.90E-03

GO:0050792	regulation of viral process	1.57E-04	5.89E-03
GO:0097659	nucleic acid-templated transcription	1.59E-04	5.97E-03
GO:0006998	nuclear envelope organization	1.60E-04	5.99E-03
GO:1903707	negative regulation of hemopoiesis	1.62E-04	6.04E-03
GO:0051443	positive regulation of ubiquitin-protein transferase activity	1.63E-04	6.05E-03
GO:0051984	positive regulation of chromosome segregation	1.63E-04	6.03E-03
GO:2000816	negative regulation of mitotic sister chromatid separation	1.68E-04	6.21E-03
GO:0071174	mitotic spindle checkpoint	1.68E-04	6.20E-03
GO:0045841	negative regulation of mitotic metaphase/anaphase transition	1.68E-04	6.18E-03
GO:1901992	positive regulation of mitotic cell cycle phase transition	1.75E-04	6.43E-03
GO:0090068	positive regulation of cell cycle process	1.76E-04	6.42E-03
GO:2000343	positive regulation of chemokine (C-X-C motif) ligand 2 production	1.81E-04	6.60E-03
GO:0032774	RNA biosynthetic process	1.81E-04	6.59E-03
GO:0034033	purine nucleoside bisphosphate biosynthetic process	1.83E-04	6.63E-03
GO:0034030	ribonucleoside bisphosphate biosynthetic process	1.83E-04	6.61E-03
GO:0033866	nucleoside bisphosphate biosynthetic process	1.83E-04	6.60E-03
GO:0016570	histone modification	1.86E-04	6.69E-03
GO:0009206	purine ribonucleoside triphosphate biosynthetic process	1.89E-04	6.81E-03
GO:0045005	DNA-dependent DNA replication maintenance of fidelity	1.92E-04	6.88E-03
GO:0071168	protein localization to chromatin	2.00E-04	7.13E-03
GO:0002478	antigen processing and presentation of exogenous peptide antigen	2.03E-04	7.24E-03
GO:0000028	ribosomal small subunit assembly	2.20E-04	7.84E-03
GO:0019941	modification-dependent protein catabolic process	2.27E-04	8.04E-03
GO:1902099	regulation of metaphase/anaphase transition of cell cycle	2.30E-04	8.16E-03
GO:0051299	centrosome separation	2.32E-04	8.20E-03
GO:0060968	regulation of gene silencing	2.33E-04	8.20E-03
GO:0051186	cofactor metabolic process	2.50E-04	8.77E-03
GO:0007084	mitotic nuclear envelope reassembly	2.54E-04	8.90E-03
GO:0006511	ubiquitin-dependent protein catabolic process	2.56E-04	8.95E-03
GO:0046831	regulation of RNA export from nucleus	2.61E-04	9.09E-03
GO:1902850	microtubule cytoskeleton organization involved in mitosis	2.62E-04	9.12E-03
GO:0090307	mitotic spindle assembly	2.62E-04	9.10E-03
GO:0042254	ribosome biogenesis	2.66E-04	9.20E-03
GO:0016180	snRNA processing	2.69E-04	9.29E-03
GO:0070670	response to interleukin-4	2.75E-04	9.49E-03

GO:0006241	CTP biosynthetic process	2.77E-04	9.53E-03
GO:0046036	CTP metabolic process	2.77E-04	9.51E-03
GO:0010212	response to ionizing radiation	2.92E-04	9.99E-03
GO:0051985	negative regulation of chromosome segregation	2.96E-04	1.01E-02
GO:1901989	positive regulation of cell cycle phase transition	3.00E-04	1.02E-02
GO:0015936	coenzyme A metabolic process	3.01E-04	1.02E-02
GO:0051293	establishment of spindle localization	3.10E-04	1.05E-02
GO:0007094	mitotic spindle assembly checkpoint	3.10E-04	1.05E-02
GO:0008156	negative regulation of DNA replication	3.12E-04	1.05E-02
GO:0010389	regulation of G2/M transition of mitotic cell cycle	3.18E-04	1.07E-02
GO:0007569	cell aging	3.28E-04	1.10E-02
GO:1902580	single-organism cellular localization	3.38E-04	1.13E-02
GO:0018105	peptidyl-serine phosphorylation	3.51E-04	1.17E-02
GO:0050896	response to stimulus	3.52E-04	1.17E-02
GO:0000244	spliceosomal tri-snRNP complex assembly	3.53E-04	1.17E-02
GO:0008608	attachment of spindle microtubules to kinetochore	3.53E-04	1.17E-02
GO:0000338	protein deneddylation	3.56E-04	1.18E-02
GO:0071173	spindle assembly checkpoint	3.66E-04	1.21E-02
GO:0046824	positive regulation of nucleocytoplasmic transport	3.73E-04	1.23E-02
GO:0032434	regulation of proteasomal ubiquitin-dependent protein catabolic process	3.82E-04	1.26E-02
GO:0071426	ribonucleoprotein complex export from nucleus	3.94E-04	1.29E-02
GO:1902100	negative regulation of metaphase/anaphase transition of cell cycle	3.97E-04	1.30E-02
GO:0033048	negative regulation of mitotic sister chromatid segregation	3.97E-04	1.30E-02
GO:1903320	regulation of protein modification by small protein conjugation or removal	4.11E-04	1.34E-02
GO:1903706	regulation of hemopoiesis	4.11E-04	1.33E-02
GO:0000281	mitotic cytokinesis	4.12E-04	1.33E-02
GO:0002376	immune system process	4.14E-04	1.34E-02
GO:0042110	T cell activation	4.19E-04	1.35E-02
GO:0040001	establishment of mitotic spindle localization	4.21E-04	1.35E-02
GO:0009209	pyrimidine ribonucleoside triphosphate biosynthetic process	4.32E-04	1.39E-02
GO:0071214	cellular response to abiotic stimulus	4.38E-04	1.40E-02
GO:0043922	negative regulation by host of viral transcription	4.42E-04	1.41E-02
GO:0051129	negative regulation of cellular component organization	4.46E-04	1.42E-02
GO:0070489	T cell aggregation	4.49E-04	1.43E-02
GO:0009108	coenzyme biosynthetic process	4.54E-04	1.44E-02
GO:1903050	regulation of proteolysis involved in cellular protein catabolic process	4.66E-04	1.47E-02
GO:0018209	peptidyl-serine modification	4.70E-04	1.48E-02
GO:0009056	catabolic process	4.70E-04	1.48E-02
GO:1903037	regulation of leukocyte cell-cell adhesion	4.81E-04	1.51E-02

GO:1901070	guanosine-containing compound biosynthetic process	4.91E-04	1.54E-02
GO:0031572	G2 DNA damage checkpoint	4.96E-04	1.55E-02
GO:0048024	regulation of mRNA splicing, via spliceosome	4.98E-04	1.55E-02
GO:0042306	regulation of protein import into nucleus	5.08E-04	1.58E-02
GO:0071593	lymphocyte aggregation	5.11E-04	1.59E-02
GO:0050863	regulation of T cell activation	5.21E-04	1.61E-02
GO:0010216	maintenance of DNA methylation	5.42E-04	1.68E-02
GO:0031145	anaphase-promoting complex-dependent catabolic process	5.46E-04	1.69E-02
GO:0032875	regulation of DNA endoreduplication	5.56E-04	1.71E-02
GO:0006221	pyrimidine nucleotide biosynthetic process	5.60E-04	1.72E-02
GO:2000781	positive regulation of double-strand break repair	5.70E-04	1.75E-02
GO:0033046	negative regulation of sister chromatid segregation	5.76E-04	1.76E-02
GO:0051653	spindle localization	5.78E-04	1.77E-02
GO:0019884	antigen processing and presentation of exogenous antigen	5.82E-04	1.77E-02
GO:0043393	regulation of protein binding	5.82E-04	1.77E-02
GO:0008219	cell death	5.90E-04	1.79E-02
GO:0031057	negative regulation of histone modification	6.06E-04	1.83E-02
GO:0043603	cellular amide metabolic process	6.06E-04	1.83E-02
GO:1904589	regulation of protein import	6.09E-04	1.84E-02
GO:1900264	positive regulation of DNA-directed DNA polymerase activity	6.14E-04	1.85E-02
GO:1900262	regulation of DNA-directed DNA polymerase activity	6.14E-04	1.84E-02
GO:0030952	establishment or maintenance of cytoskeleton polarity	6.17E-04	1.85E-02
GO:0009208	pyrimidine ribonucleoside triphosphate metabolic process	6.53E-04	1.95E-02
GO:0044774	mitotic DNA integrity checkpoint	6.58E-04	1.96E-02
GO:0006754	ATP biosynthetic process	6.63E-04	1.97E-02
GO:0032944	regulation of mononuclear cell proliferation	6.65E-04	1.98E-02
GO:1903362	regulation of cellular protein catabolic process	6.83E-04	2.03E-02
GO:0090233	negative regulation of spindle checkpoint	7.02E-04	2.08E-02
GO:1900182	positive regulation of protein localization to nucleus	7.05E-04	2.08E-02
GO:1900180	regulation of protein localization to nucleus	7.17E-04	2.11E-02
GO:1903504	regulation of mitotic spindle checkpoint	7.41E-04	2.18E-02
GO:0090266	regulation of mitotic cell cycle spindle assembly checkpoint	7.41E-04	2.17E-02
GO:0034501	protein localization to kinetochore	7.49E-04	2.19E-02
GO:0000706	meiotic DNA double-strand break processing	7.57E-04	2.21E-02
GO:0002682	regulation of immune system process	7.64E-04	2.23E-02
GO:1903334	positive regulation of protein folding	7.89E-04	2.30E-02
GO:0006213	pyrimidine nucleoside metabolic process	7.94E-04	2.30E-02
GO:0061136	regulation of proteasomal protein catabolic process	7.97E-04	2.31E-02
GO:1902749	regulation of cell cycle G2/M phase transition	8.07E-04	2.33E-02

GO:1902582	single-organism intracellular transport	8.13E-04	2.35E-02
GO:0043067	regulation of programmed cell death	8.20E-04	2.36E-02
GO:0015985	energy coupled proton transport, down electrochemical gradient	8.29E-04	2.38E-02
GO:0015986	ATP synthesis coupled proton transport	8.29E-04	2.38E-02
GO:0006306	DNA methylation	8.32E-04	2.38E-02
GO:0006305	DNA alkylation	8.32E-04	2.38E-02
GO:0010822	positive regulation of mitochondrion organization	8.39E-04	2.39E-02
GO:0032239	regulation of nucleobase-containing compound transport	8.42E-04	2.40E-02
GO:0007159	leukocyte cell-cell adhesion	8.58E-04	2.44E-02
GO:0010604	positive regulation of macromolecule metabolic process	8.68E-04	2.46E-02
GO:0070663	regulation of leukocyte proliferation	8.91E-04	2.52E-02
GO:0002521	leukocyte differentiation	8.92E-04	2.52E-02
GO:0009132	nucleoside diphosphate metabolic process	8.94E-04	2.52E-02
GO:0000278	mitotic cell cycle	9.00E-04	2.53E-02
GO:0070486	leukocyte aggregation	9.08E-04	2.55E-02
GO:1901970	positive regulation of mitotic sister chromatid separation	9.10E-04	2.55E-02
GO:0045069	regulation of viral genome replication	9.17E-04	2.56E-02
GO:0090311	regulation of protein deacetylation	9.33E-04	2.60E-02
GO:0042981	regulation of apoptotic process	9.33E-04	2.60E-02
GO:0061640	cytoskeleton-dependent cytokinesis	9.34E-04	2.59E-02
GO:0006611	protein export from nucleus	9.48E-04	2.63E-02
GO:0006650	glycerophospholipid metabolic process	9.51E-04	2.63E-02
GO:0043903	regulation of symbiosis, encompassing mutualism through parasitism	9.57E-04	2.64E-02
GO:0046649	lymphocyte activation	9.62E-04	2.65E-02
GO:0043241	protein complex disassembly	9.69E-04	2.67E-02
GO:0009262	deoxyribonucleotide metabolic process	9.77E-04	2.68E-02
GO:0051173	positive regulation of nitrogen compound metabolic process	9.81E-04	2.69E-02
GO:0045935	positive regulation of nucleobase-containing compound metabolic process	9.94E-04	2.72E-02
GO:0006166	purine ribonucleoside salvage	9.97E-04	2.72E-02