# Supplementary Information

## Two independent modes of chromatin organization revealed by cohesin removal

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### Supplementary Tables.

Supplementary Table 1 – Summary statistics of read pairs for TCC (Hi-C) libraries in this study.

Supplementary Table 2 – Statistics of Hi-C libraries in Schmitt et.al, 2016[27], an example of a contemporary study on primary tissues.

Supplementary Table 3 – Statistics of Hi-C libraries in other cohesin depletion studies.

Supplementary Table 4 - The list of enriched GO terms for differentially expressed genes, with a Benjamini-Hochberg p-value < 0.05.

Supplementary Table 5 – Public data sources

### Supplementary Data 1.

Original scans of western blots. The selected regions for the different panels shown on Fig.1b are boxed in red. Additional biological replicates of the two conditions can be seen (samples 1 and 4)

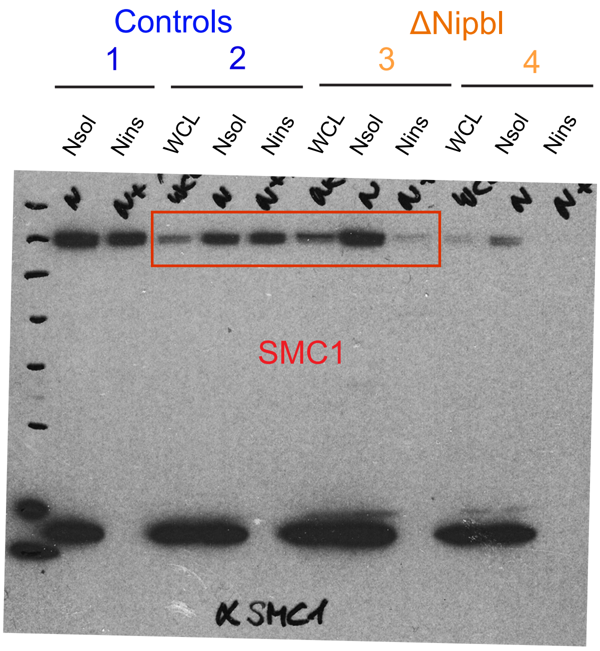
### Supplementary Data 2.

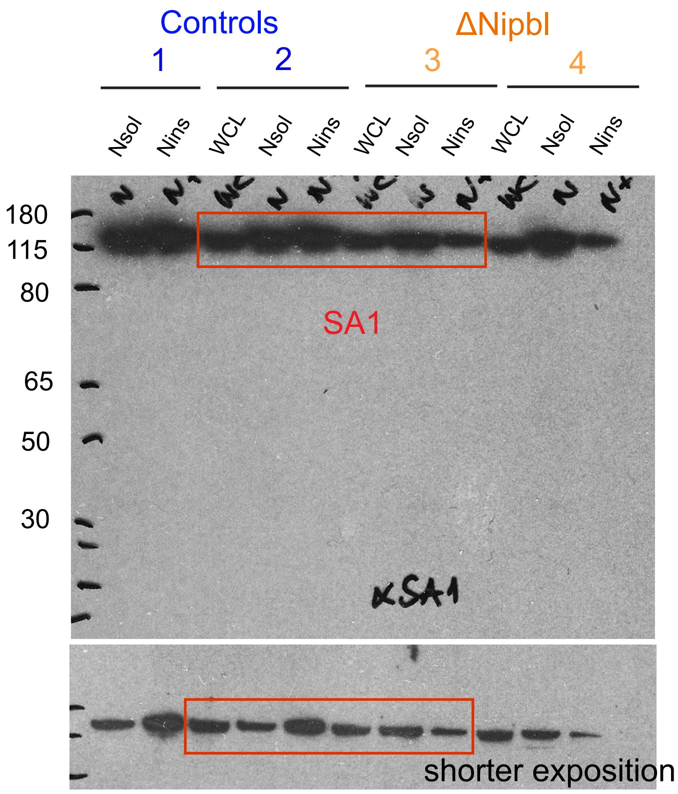
Experimental Hi-C maps show extensive similarities between replicates. (a) The curves of contact frequency P(s) vs genomic distance s. (b) Pearson correlation coefficients between *cis* eigenvectors at 100kb. (c) The average Hi-C maps around 102 500kb-600kb peaks. (d) Compartmentalization saddle plots.

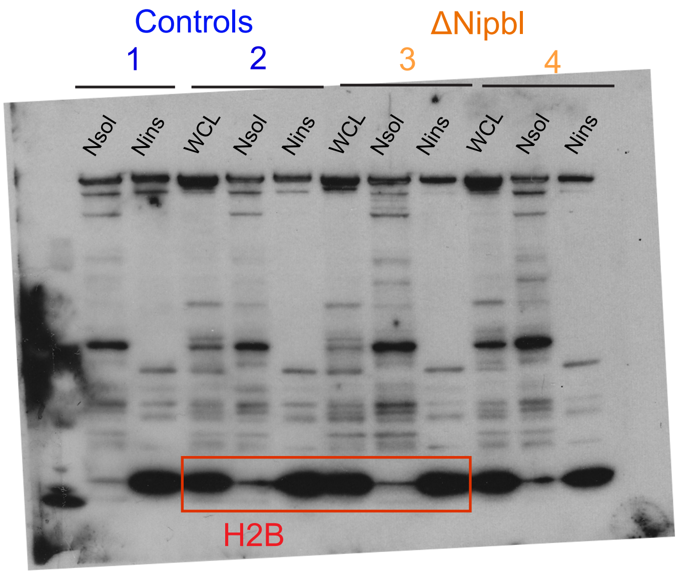
### Supplementary Data 3.

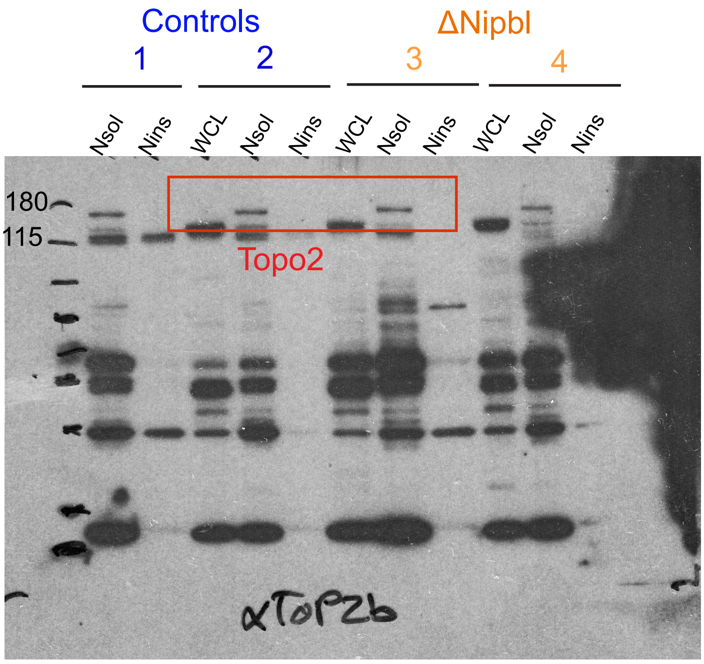
Consistent differences in compartment eigenvector upon Nipbl deletion (a) The genome-wide *cis* eigenvectors at 100kb: WT (green), TAM (blue), ΔNipbl (red) are shown. (b) Zoom-in of the region shaded in grey in (a) using 20kb eigenvectors. In (a-b), the curves are shown for each of two replicates of each condition.

# Supplementary Data 1

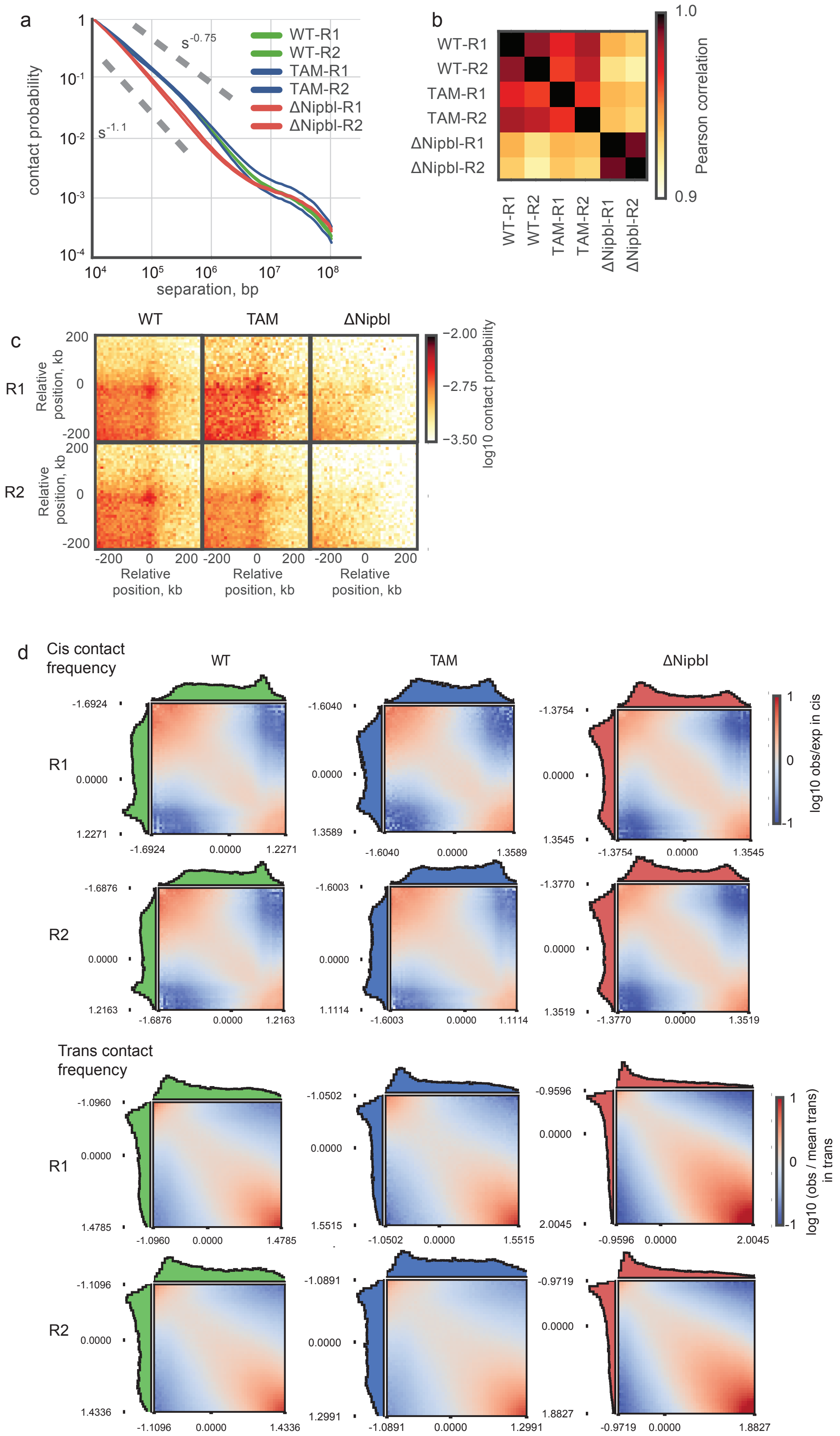




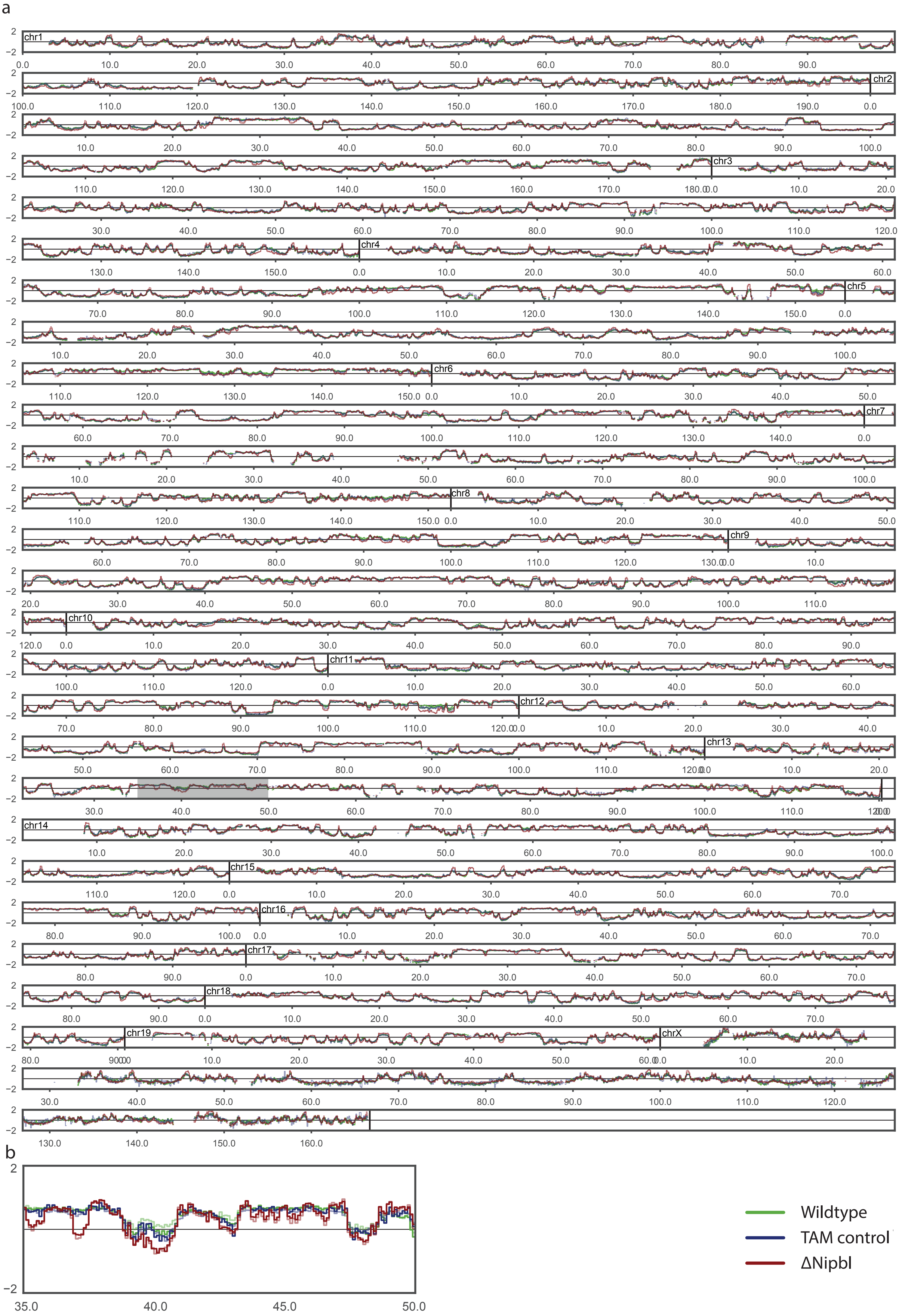




# Supplementary Data 2



## Supplementary Data 3



**Supplementary Table 1 – Summary statistics of read pairs for TCC (Hi-C) libraries in this study.**

| Replicate | codename | Raw read pairs | Mapped read pairs | Filtered read pairs | Cis read pairs, separation >10kb |
|---|---|---|---|---|---|
| WT-R1 | 014637Untr | 139,343,707 | 75,465,383 | 51,745,705 | 35,529,637 |
| WT-R2 | 019440Untr | 114,258,179 | 60,638,254 | 43,097,410 | 28,704,961 |
| TAM-R1 | 014199TAMcontr | 94,032,309 | 53,285,208 | 14,530,511 | 9,870,917 |
| TAM-R2 | 014399TAMcontr | 134,045,253 | 72,789,581 | 51,281,408 | 34,490,881 |
| ΔNipbl-R1 | 014200Nipbl | 131,409,162 | 66,635,374 | 42,405,784 | 26,633,610 |
| ΔNipbl-R2 | 016350Nipbl | 133,914,046 | 69,894,091 | 50,527,104 | 31,561,513 |

**Supplementary Table 2 – Statistics of Hi-C libraries in Schmitt et.al, 2016, an example of a contemporary study on primary tissues.**

| Study | Raw read pairs | Filtered pairs | Cis read pairs, separation >10kb |
|---|---|---|---|
| Bladder, R1 | 233,041,838 | 52,456,550 | 24,121,444 |
| Bladder, R2 | 236,250,557 | 43,395,294 | 19,659,511 |
| Adrenal Gland, R1 | 181,680,303 | 48,951,415 | 22,449,886 |
| Psoas Muscle, R1 | 196,863,028 | 36,856,215 | 13,566,008 |
| Psoas Muscle, R2 | 95,110,351 | 25,776,091 | 10,410,829 |
| Pancreas, R1 | 160,416,883 | 49,627,891 | 21,200,091 |
| Pancreas, R2 | 12,147,138 | 3,538,979 | 1,367,214 |
| Pancreas, R3 | 128,745,528 | 15,683,831 | 7,787,867 |
| Lung, R1 | 308,335,703 | 85,597,004 | 24,417,652 |
| Hippocampus, R1 | 187,658,680 | 64,151,770 | 29,220,961 |
| Right Ventricle, R1 | 672,319,838 | 179,219,920 | 63,091,486 |
| Small Bowel, R1 | 177,864,628 | 58,017,249 | 21,073,296 |
| Spleen, R1 | 378,529,216 | 107,599,392 | 33,032,593 |
| Ovary, R1 | 201,215,217 | 70,283,904 | 20,909,766 |
| Dorsolateral Prefrontal Cortex, R1 | 165,728,687 | 52,713,868 | 25,426,433 |

## Supplementary Table 3 – Statistics of Hi-C libraries in other cohesin depletion studies.

| Study | Filtered read pairs | Cis read pairs, separation >10kb |
|---|---|---|
| Seitan et al, 2013, WT, R1 | 51,337,902 | 12,676,930 |
| Seitan et al, 2013, WT, R2 | 96,784,574 | 28,679,223 |
| Seitan et al, 2013, ΔRad21, R1 | 57,060,666 | 14,219,809 |
| Seitan et al, 2013, ΔRad21, R2 | 96,784,574 | 22,594,749 |
| Zuin et.al, 2014, Control, R1 | 120,366,592 | 48,221,154 |
| Zuin et.al, 2014, Control, R2 | 134,277,024 | 46,378,835 |
| Zuin et.al, 2014, Rad 21 cleaved, R1 | 113,394,855 | 41,623,810 |
| Zuin et.al, 2014, Rad 21 cleaved, R2 | 159,090,030 | 51,870,950 |
| Sofueva et.al, 2012, Control NSC, R1 | 16,886,965 | 12,761,787 |
| Sofueva et.al, 2012, ΔRad21 NSC Lox, R1 | 69,788,779 | 52,087,400 |
| Sofueva et.al, 2012, ΔRad21 NSC Lox, R2 | 63,347,539 | 47,760,318 |
| Sofueva et.al, 2012, Control AST, R1 | 29,246,903 | 21,885,386 |
| Sofueva et.al, 2012, ΔRad21 AST Lox, R1 | 24,710,993 | 15,866,342 |
| Sofueva et.al, 2012, ΔRad21 AST Lox, R2 | 20,287,207 | 13,980,244 |

**Supplementary Table 4 - The list of enriched GO terms for differentially expressed genes, with a Benjamini-Hochberg p-value < 0.05.**

| Term | Category | Name | Regulated | Count | % |
|---|---|---|---|---|---|
| GO:0060271 | BP | cilium morphogenesis | up | 16 | 3.6 |
| GO:0070062 | CC | extracellular exosome | up | 107 | 23.8 |
| GO:0042995 | CC | cell projection | up | 36 | 8.0 |
| GO:0005929 | CC | cilium | up | 18 | 4.0 |
| GO:0005930 | CC | axoneme | up | 10 | 2.2 |
| GO:0032869 | BP | cellular response to insulin stimulus | down | 14 | 2.4 |
| GO:0006629 | BP | lipid metabolic process | down | 35 | 6.0 |
| GO:0005615 | CC | extracellular space | down | 83 | 14.0 |
| GO:0016021 | CC | integral component of membrane | down | 231 | 39.1 |
| GO:0005783 | CC | endoplasmic reticulum | down | 88 | 14.9 |
| GO:0005576 | CC | extracellular region | down | 84 | 14.2 |
| GO:0005789 | CC | endoplasmic reticulum membrane | down | 54 | 9.1 |
| GO:0043231 | CC | intracellular membrane-bounded organelle | down | 48 | 8.1 |
| GO:0016020 | CC | membrane | down | 273 | 46.2 |
| GO:0016324 | CC | apical plasma membrane | down | 25 | 4.2 |
| GO:0005887 | CC | integral component of plasma membrane | down | 51 | 8.6 |
| GO:0020037 | MF | heme binding | down | 21 | 3.6 |
| GO:0016491 | MF | oxidoreductase activity | down | 47 | 8.0 |
| GO:0052689 | MF | carboxylic ester hydrolase activity | down | 11 | 1.9 |

## Supplementary Table 5 – Public data sources

| Data type | Description | Cell-type | Ref. | URL |
|---|---|---|---|---|
| Hi-C data | Hi-C raw reads | Mouse ESC, NSC, AST | 18 | https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE49018 |
| | Hi-C raw reads | Mouse Developing Thymocytes | 19 | https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE48763 |
| | Hi-C raw reads | Human HEK293T | 17 | https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE44267 |
| Peaks | Annotations from Hi-C | Mouse CH12-LX | 8 | ftp://ftp.ncbi.nlm.nih.gov/geo/series/GSE63nnn/GSE63525/suppl/GSE63525_CH12-LX_HiCCUPS_looplist.txt.gz |
| CTCF M1 motif | PWM for mouse | | 56 | ftp://ftp.ebi.ac.uk/pub/databases/vertebrategenomics/FOG03/calls/CTCF_canonical_species |
| Lamin-B1 DamID | Normalized signal | Mouse ESCs | 37 | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/laminB1_AC.txt.gz |
| | Normalized signal | NPCs | | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/laminB1_EF.txt.gz |
| | Normalized signal | Astrocytes | | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/laminB1_ES.txt.gz |
| | Normalized signal | MEFs | | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/database/laminB1_NP.txt.gz |
| | HMM state calls | | 38 | https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE17051 |
| ChromHMM | Chromatin state segmentation trained on ENCODE mouse ChIP-seq data | Mouse Liver, Adult8wks | 55 | https://github.com/gireeshkbogu/chromatin_states_chromHMM_mm9 |
| ENCODE Histone ChIP-seq | ChIP-seq, peak and bigwig files<br>Input<br>H3K27ac<br>H3K27me3<br>H3K4me3<br>H3K4me1<br>H3K9me3<br>H3K36me3<br>H3K79me2 | Mouse Liver, Adult8wks | 45 and ENCODE | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/encodeDCC/wgEncodeLicrHistone/ |
| ENCODE TFBS ChIP-seq | ChIP-seq, Peak and bigwig files<br>Input<br>PolII<br>CTCF | Mouse Liver, Adult8wks | 45 and ENCODE | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/encodeDCC/wgEncodeLicrTfbs/ |
| ENCODE DNase-seq | DNAse I HS, bigwig | Mouse Liver, Adult8wks | 45 and ENCODE | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/encodeDCC/wgEncodeUwDnase/ |
| ENCODE RNA-seq | Poly-A RNA-seq, bigwig | Mouse Liver, Adult8wks | 45 and ENCODE | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/encodeDCC/wgEncodeUwRnaSeq/ |
| | Poly-A RNA-seq, bigwig | Mouse Liver, Adult8wks | | http://hgdownload.cse.ucsc.edu/goldenPath/mm9/encodeDCC/wgEncodeCshlLongRnaSeq/ |