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Supplemental Information

Cohesin-Dependent and -Independent Mechanisms Mediate Chromosomal Contacts between Promoters and Enhancers

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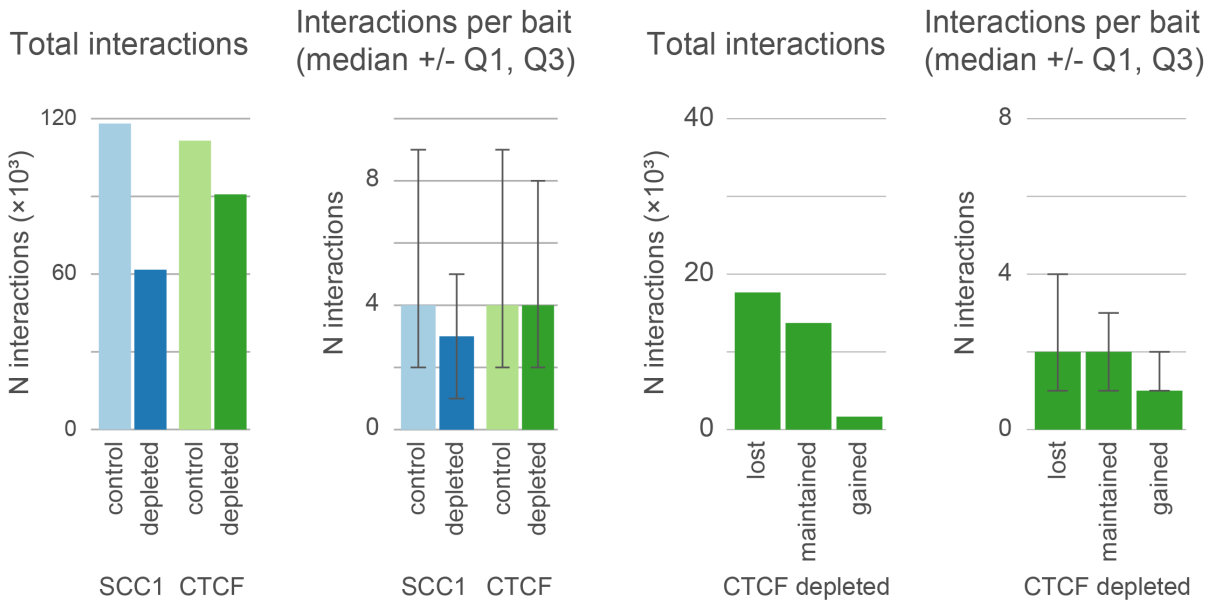


Figure S1. Summary statistics of promoter interactions in SCC1- and CTCF-depleted and control conditions, related to Figure 2

(A) The number of significant promoter interactions called using CHiCAGO.

(B) The number of significant promoter interactions per bait.

(C) The numbers of lost, maintained and gained promoter interactions upon CTCF depletion. See Figure 2A for the same statistics for SCC1 depletion.

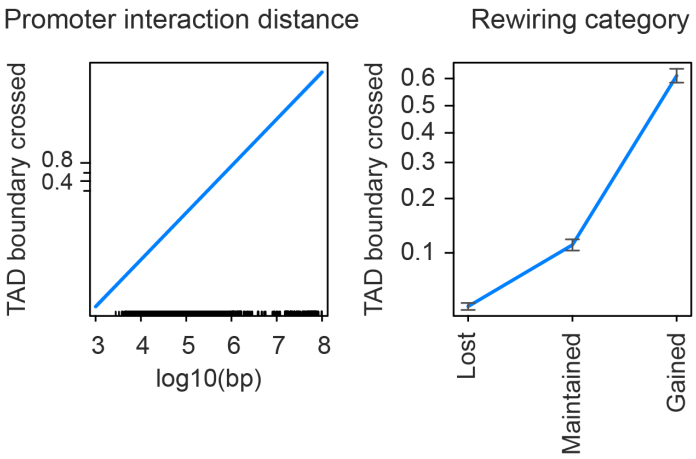


Figure S2. The linear distance and response to cohesin depletion associate with TAD boundary crossing of promoter interactions, related to Figure 3.
Effect plots summarising the results of logistic regression modelling showing using TAD boundary crossing as the response variable and $\log_{10}$ linear interaction distance (left) versus interaction rewiring in response to SCC1 depletion as predictors (right).

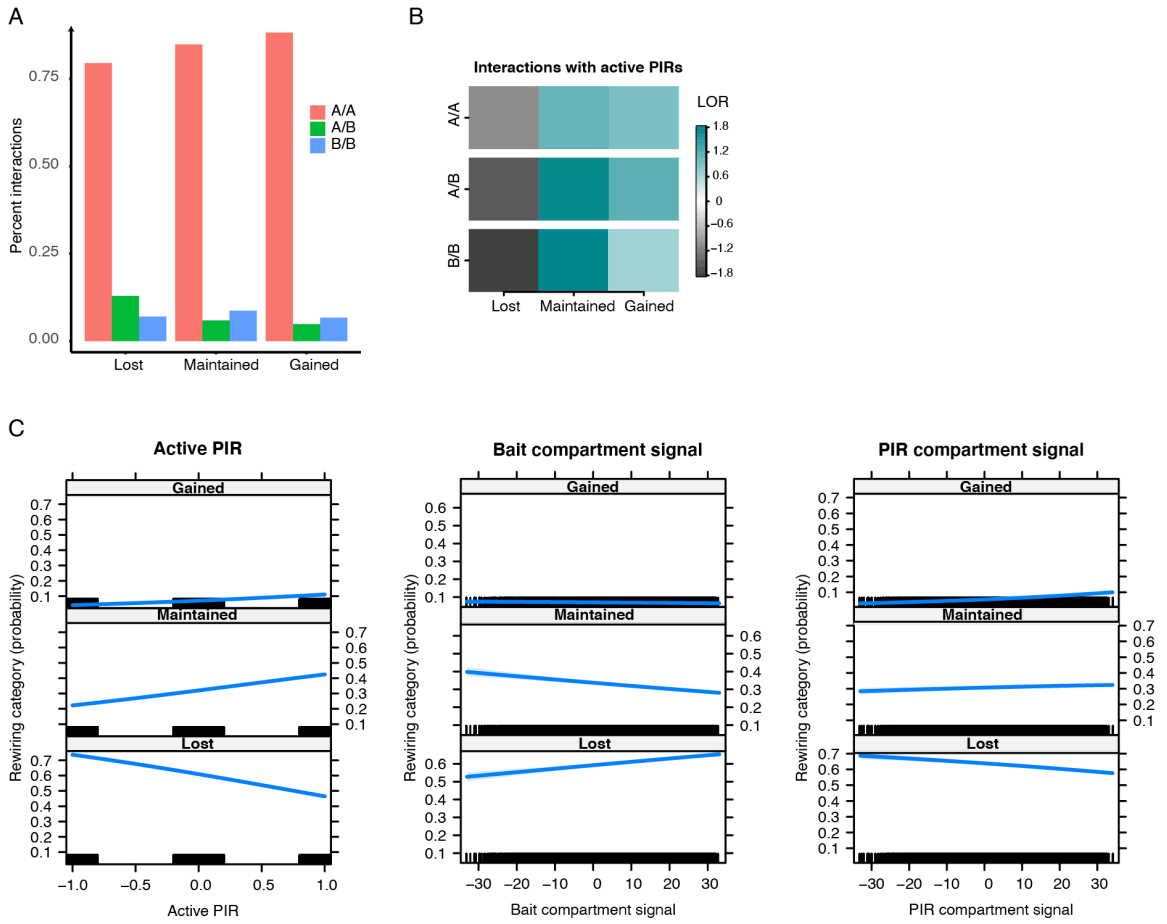
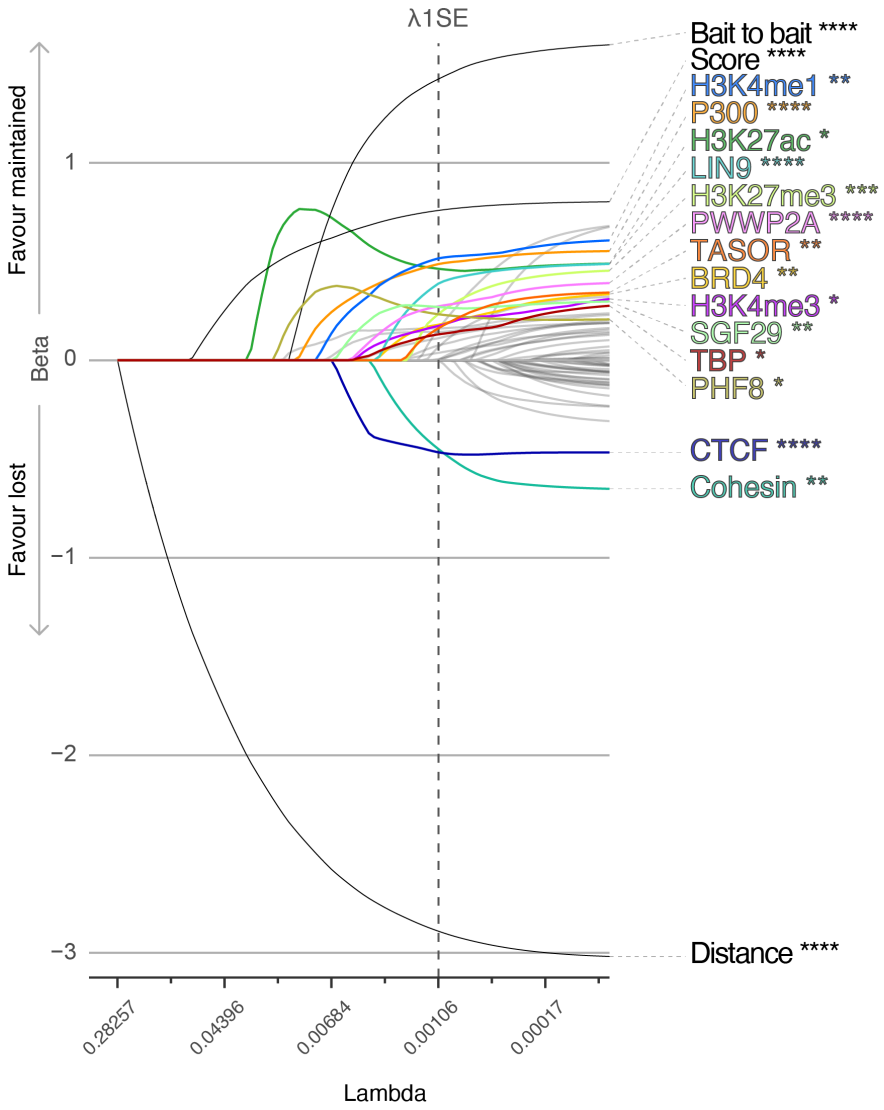


Figure S3. Relationship between compartment signals and cohesin dependence of promoter interactions, related to Figure 4.

(A) Proportions of promoter interactions that are lost, maintained and gained upon cohesin depletion that map solely to the A (red) or B (blue) compartment, or link two compartments (green).

(B) Log-odds ratios (LOR) of promoter interactions with active PIRs among the "lost", "maintained" and "gained" interactions computed separately for different compartment localisation of interaction pairs.

(C) Effect plots summarising the results of multinomial logistic regression using interaction rewiring category as the response variable versus the presence of active enhancer features at PIRs (Active PIR) and compartment signals at baited promoters and PIRs as predictors. The regression coefficients for all terms used in the model were significantly different from zero (Wald test $p << 0.05$). See Methods for details.



Predictor	p-value at λ1SE
Bait to bait	$<2.2^{-16}$
Score	$<2.2^{-16}$
P300	1.24×10^{-12}
H3K27ac	2.58×10^{-8}
H3K4me1	$<2.2^{-16}$
LIN9	5.92×10^{-8}
SGF29	1.35×10^{-3}
PWWP2A	1.18×10^{-6}
PHF8	9.6×10^{-3}
BRD4	8.0×10^{-3}
H3K9ac	9.3×10^{-3}
H3K4me3	2.44×10^{-2}
H3K27me3	1.62×10^{-4}
TASOR	1.41×10^{-2}
H3K79me3	1.06×10^{-2}
Cohesin	$<2.2^{-16}$
CTCF	1.01×10^{-10}
Distance	$<2.2^{-16}$

Figure S4. LASSO logistic regression regularisation paths for features associated with maintained versus lost interactions upon SCC1 depletion, related to Figure 4

Plots showing LASSE logistic regression coefficients (y-axis) at different values of the shrinkage parameter λ (x-axis), ranging from stringent on the left to permissive on the right. The response binary variable represents the odds of maintained or gained promoter interactions. The independent variables reflect the enrichment scores for 62 targets (TFs, histones and histone modifications), as well as the CHiCAGO score, the promoter interaction distance ($\log_{10}$ bp) and a boolean variable that indicates whether an interaction is between two baited promoters. The y-axis shows the regression beta which is positive for maintained promoter interactions and negative for lost promoter interactions. Vertical dotted line shows the λ value (λ1SE) at which the independent variables were tested for significance. The table on the right shows the FDR values at λ_{1SE} for the significant predictors.

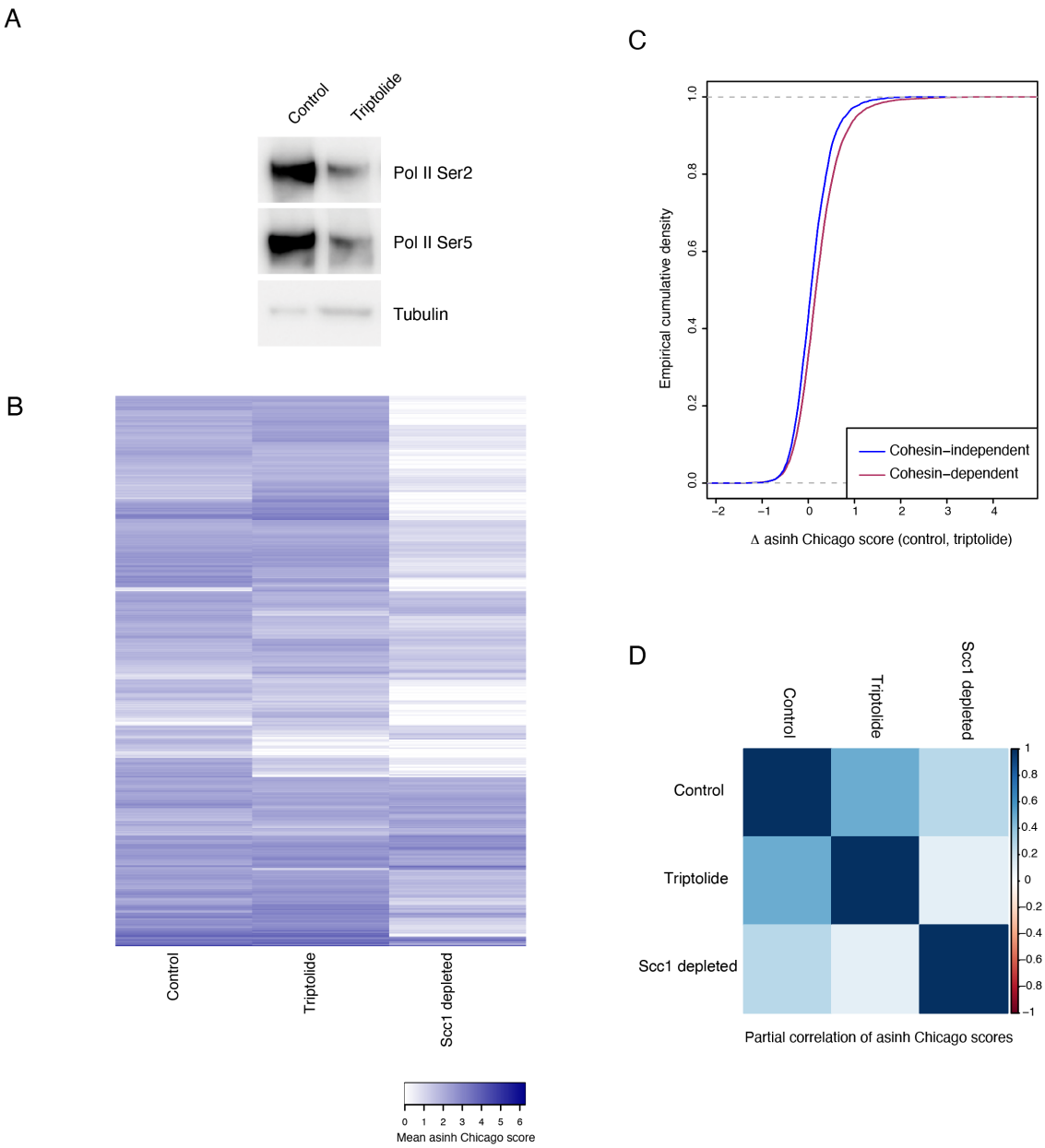


Figure S5. Triptolide treatment has a mild effect on promoter interactions, related to Figure 4
(A) Western blot analysis of control HeLa cells and those treated with 300nM triptolide for 3h using antibodies against RNA Pol II Ser2, RNA Pol II Ser5 and Tubulin as a loading control.
(B) Heatmap showing the mean asinh-transformed Chicago score for 10,000 random promoter interactions detected in control HeLa cells, those treated with triptolide and SCC1-depleted cells.
(C) Empirical cumulative density plot showing change in asinh-transformed Chicago scores upon triptolide treatment for cohesin-dependent (blue) and independent (red) interactions. Triptolide treatment has a relatively mild effect on both interaction rewiring categories, with cohesin-independent interactions showing smaller-scale changes.
(D) Heatmap showing partial correlations between asinh Chicago scores in the control, triptolide-treated and SCC1-depleted HeLa cells. Triptolide treated cells have positive partial correlations with both control cells and SCC1-depleted cells, with a much stronger effect for the former category. Jointly, these results do not favour the model of cohesin-independent interactions selectively stabilised by RNA Pol II activity or transcription.

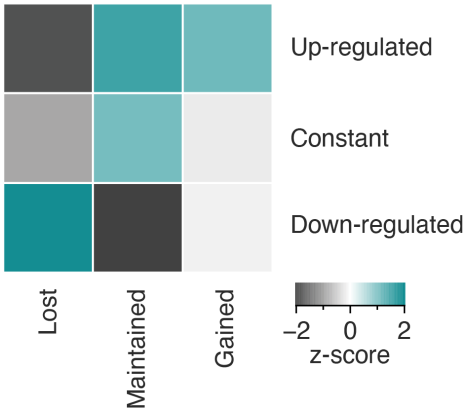


Figure S6. Association of transcriptional response upon SCC1 depletion associates with promoter interaction rewiring, related to Figure 5
Heatmap showing the z-scores of association between PIR interaction rewiring (columns) and transcriptional dynamics (rows) categories obtained from permutation analysis.