Expanded View Figures

Figure EV1. Expression levels of CRISPRa-targeted genes and neighboring genes in human RPE-1 cells.

A–H Top panels: domainograms showing changes in NL interactions around genes activated by CRISPRa. Domainograms are same as in Fig 2C. Middle panels: $\log_2$ mRNA expression (normalized read counts in 50 bp bins) as determined by mRNA-seq of CRISPRa-activated cells (red, upward *y*-axis) compared to untransfected control cells (blue, downward *y*-axis). Note that only introns give detectable reads. Data are average of two independent replicate experiments each. Bottom panels: gene annotation track. Each CRISPRa-targeted gene is highlighted in green; targeted promoters are marked by vertical green dotted line.

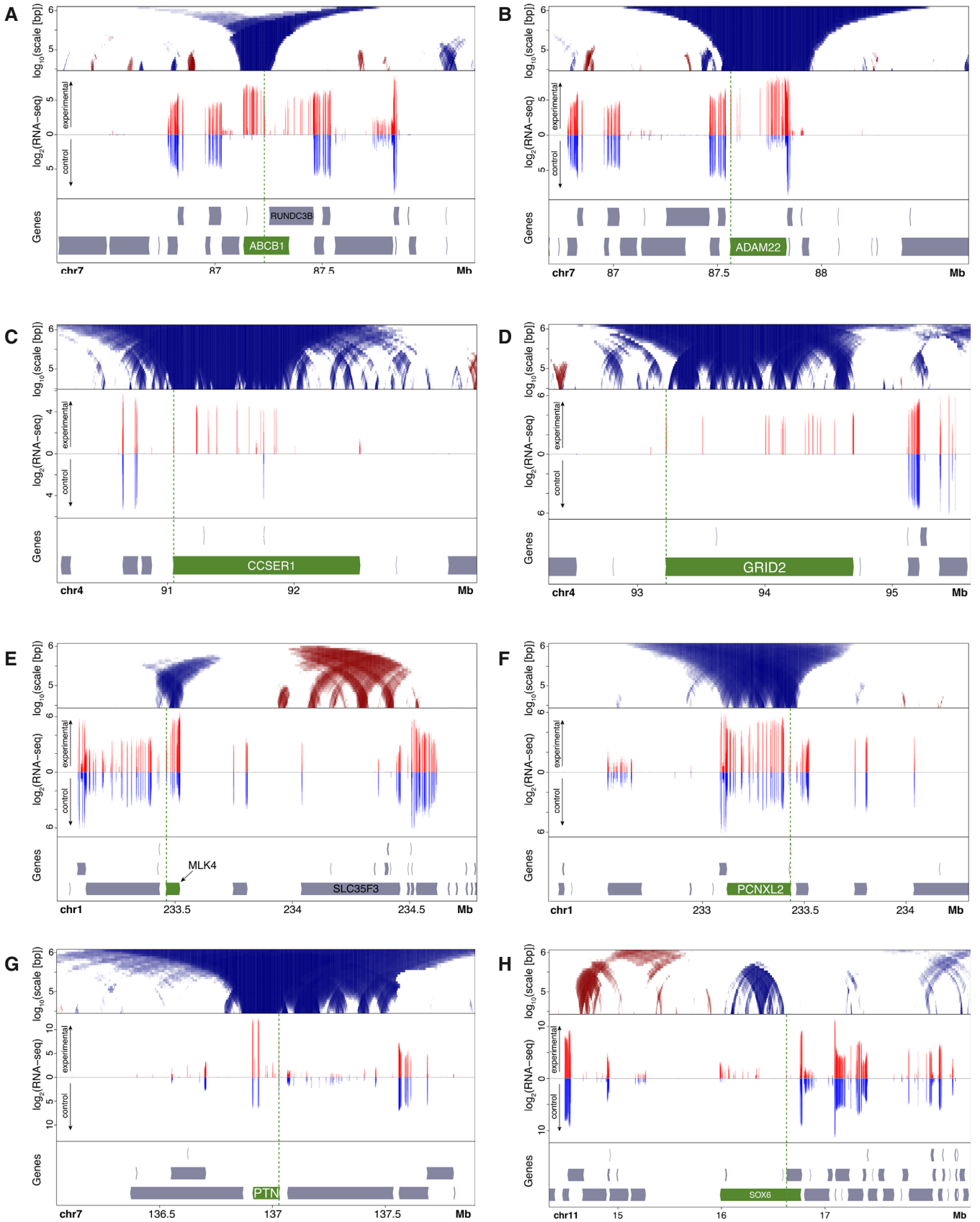
A
B
C
D
E
F
G
H
log10(scale [bp])
log2(RNA−seq)
experimental
control
Genes
RUNDC3B
ABCB1
ADAM22
CCSER1
GRID2
MLK4
SLC35F3
PCNXL2
PTN
SOX6
chr7
chr4
chr1
chr11
Mb

Figure EV1.

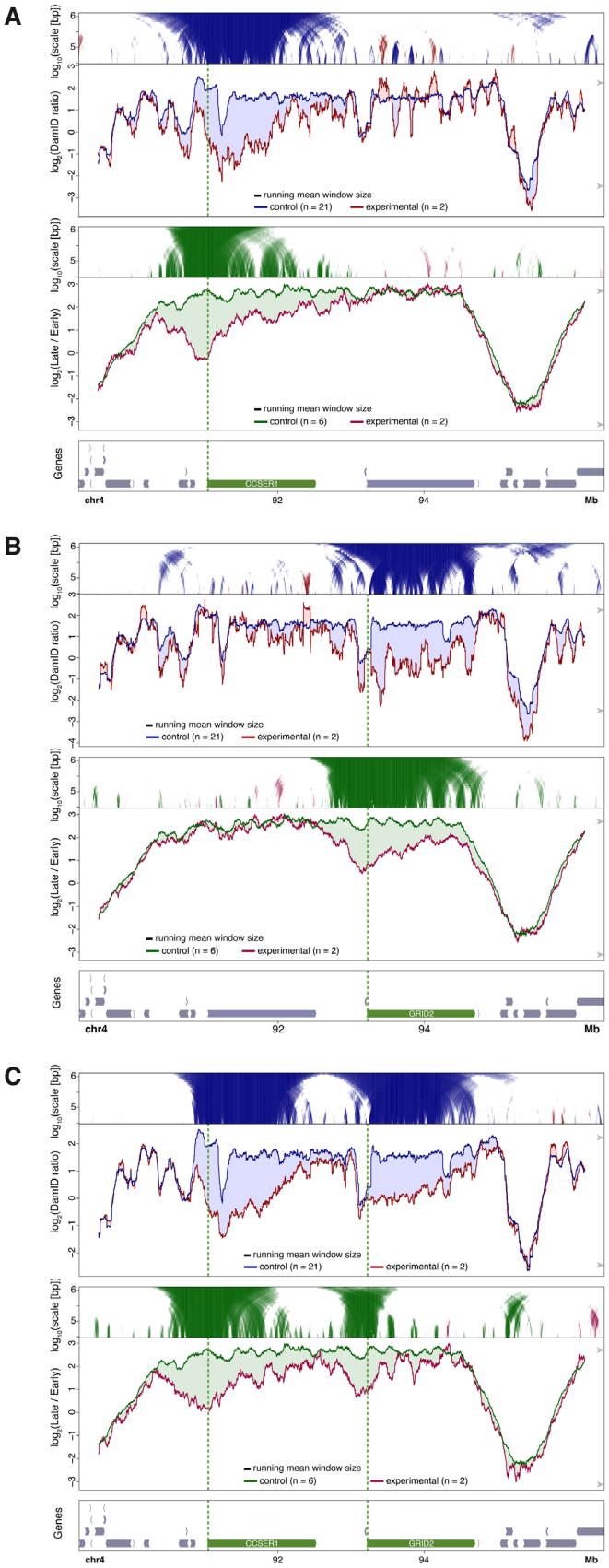

Figure EV2. Changes in NL interactions and replication timing in the CCSER1/GRID2 locus.

A–D Effects of CRISPRa activation of *CCSER1* (A), *GRID2* (B) or both genes (C) in human RPE-1 cells. Top panels show DamID data similar to Fig 2A and B. Middle panels show maps of replication timing at the same resolution and in the same plotting style as for DamID, except that different colors are used as indicated in (D). Bottom panels show gene annotation; activated gene(s) highlighted in green; targeted promoters are marked by vertical green dotted line. DamID data are the same as in Figs 2C and 6A.

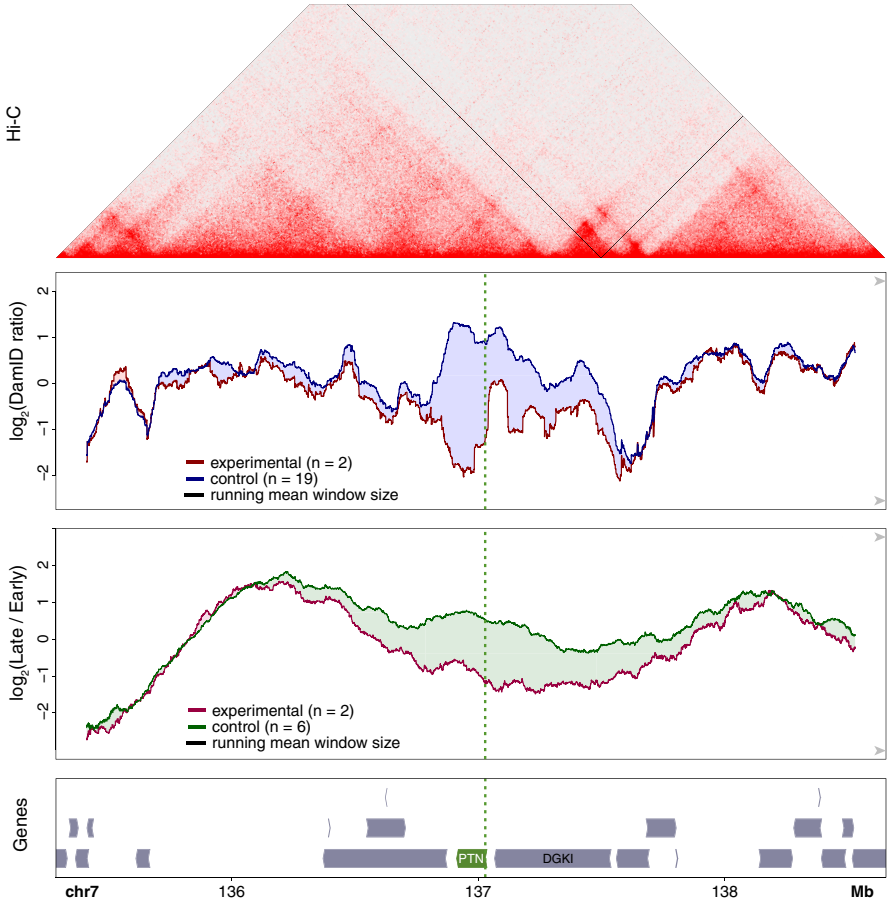

Figure EV3. Comparison of DamID and replication timing patterns around the *PTN* gene to Hi-C data.

DamID data and gene annotation track of Fig 4C (three bottom panels) aligned to Hi-C data from untreated human RPE-1 cells (top panel). Hi-C data are from (Darrow *et al*, 2016) (Data ref: Darrow *et al*, 2016).

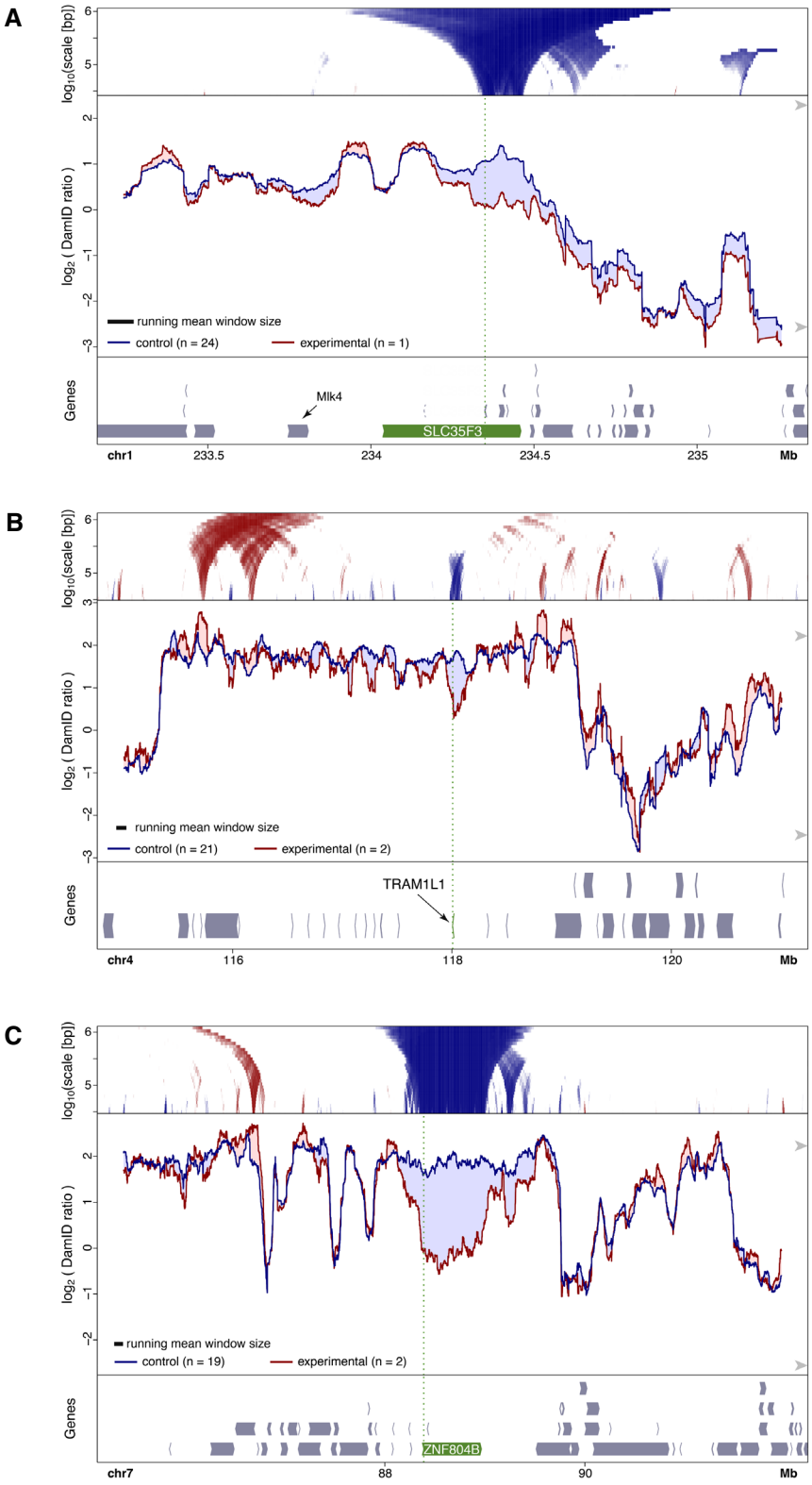

Figure EV4. Changes in NL interactions of genes upregulated by CRISPRa.

A–C DamID data obtained after CRISPRa in human RPE-1 cells of *SLC35F3* (A), *TRAM1L1* (B), *ZNF804B* (C). Domainograms are the same as in Fig 2C, but additionally show increased NL contacts in red.

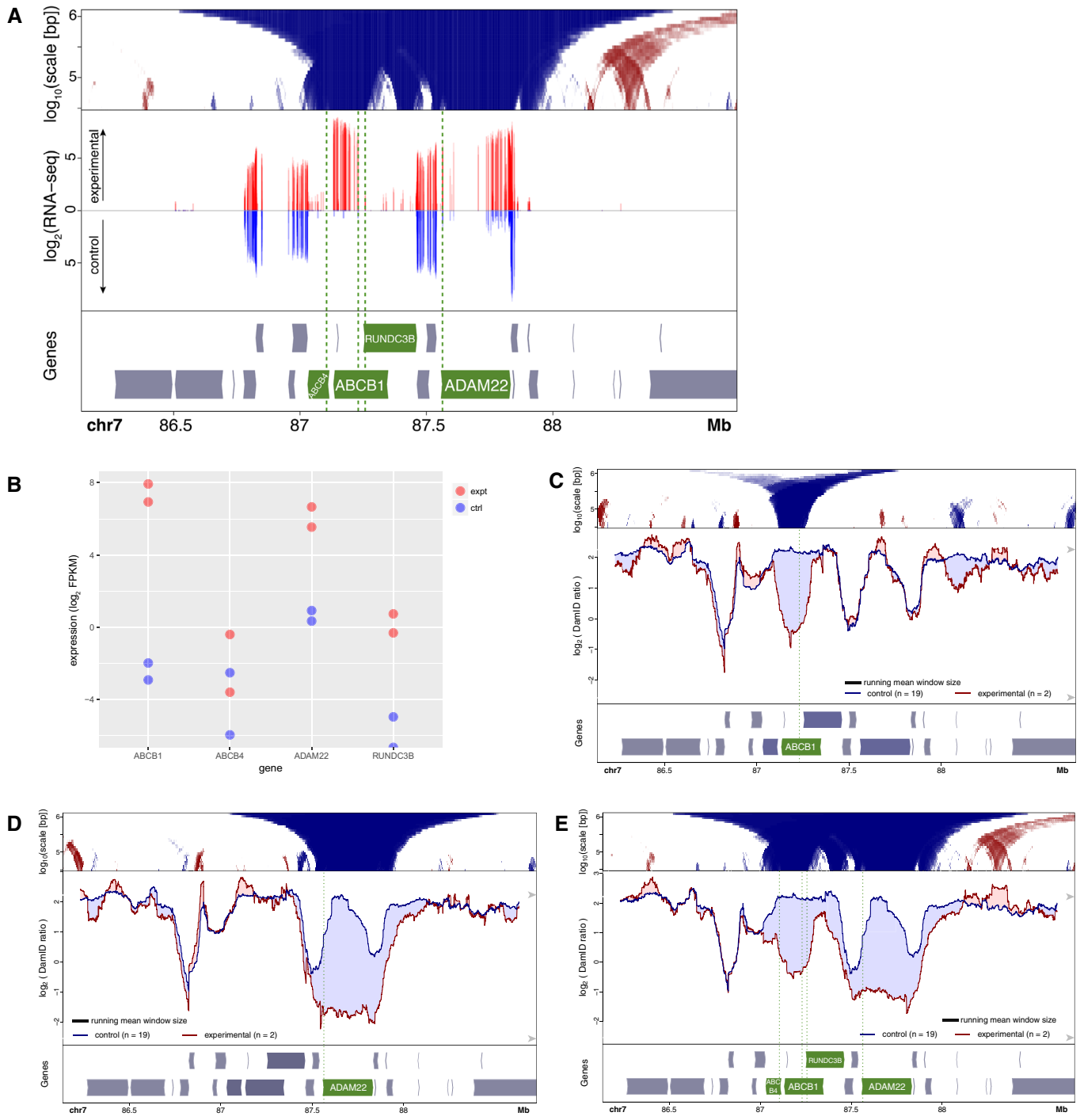

Figure EV5. Expression and NL interactions of *ABCB4*, *ABCB1*, *RUNDC3B*, and *ADAM22* after combined activation.

A Visualization of mRNA expression (middle panel), together with DamID domainogram (top panel) and gene annotation track (bottom panel) in human RPE-1 cells. CRISPRa was done using four sgRNAs simultaneously, one for each promoter. Middle panel shows $\log_2$ mRNA expression (normalized read counts in 50 bp bins) as determined by mRNA-seq of CRISPRa-activated cells (red, upward *y*-axis) compared to untransfected control cells (blue, downward *y*-axis). Note that only introns give detectable reads. Data are average of two independent replicate experiments each.

B Quantification of mRNA expression of the four genes, same mRNA-seq data as in (A).

C–E DamID profiles after activation of *ABCB1* (C), *ADAM22* (D), or *ABCB4*, *ABCB1*, ADAM22, and *RUNDC3B* simultaneously (E). Data visualization as in Fig 2A and B.

Data information: In (A, C–E), the CRISPRa-targeted genes are highlighted in green, and the sgRNA target locations are marked by vertical green dotted lines.