Hakim - Supplementary Figure S1

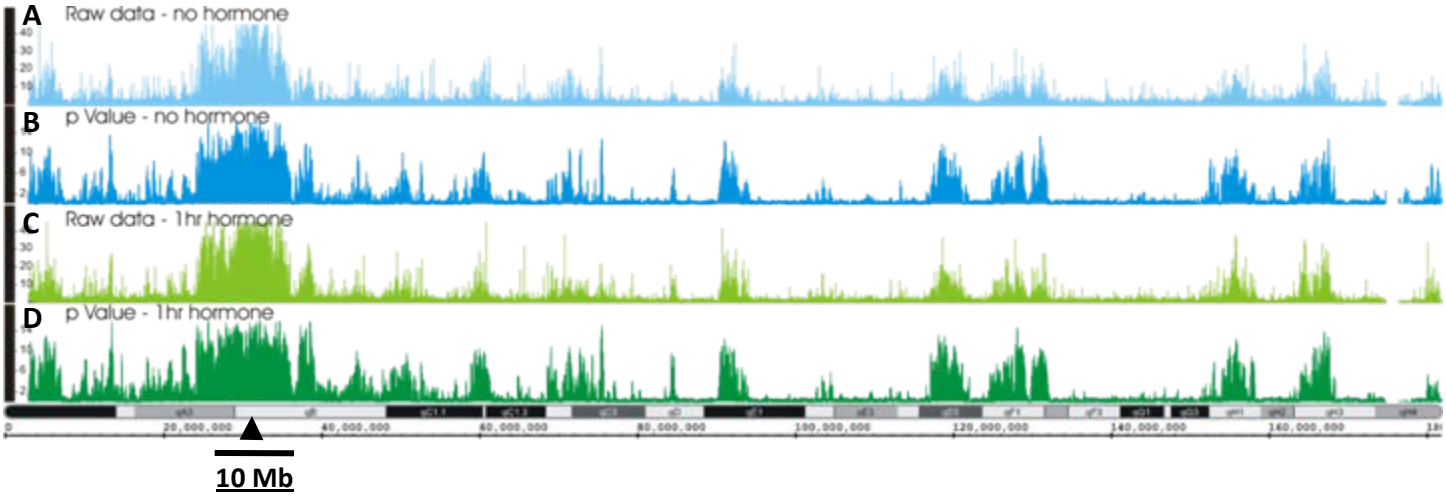


Figure S1. *Lcn2* long- range contacts on chromosome 2. Unprocessed log2 (4C/genomic control) hybridization signals (**A,C**, raw data), together with statistical analysis (**B,C**, p-value). Peaks represent interactions of *Lcn2* (*chr 2: 32.2 Mb,* black arrowhead) with loci on chromosome 2, before and one hour after hormone induction. Note the distinctively strong contact frequency of *Lcn2* with the ~10 Mb surrounding region. This 10 Mb region was excluded from all the genome-wide correlation analysis. Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S2

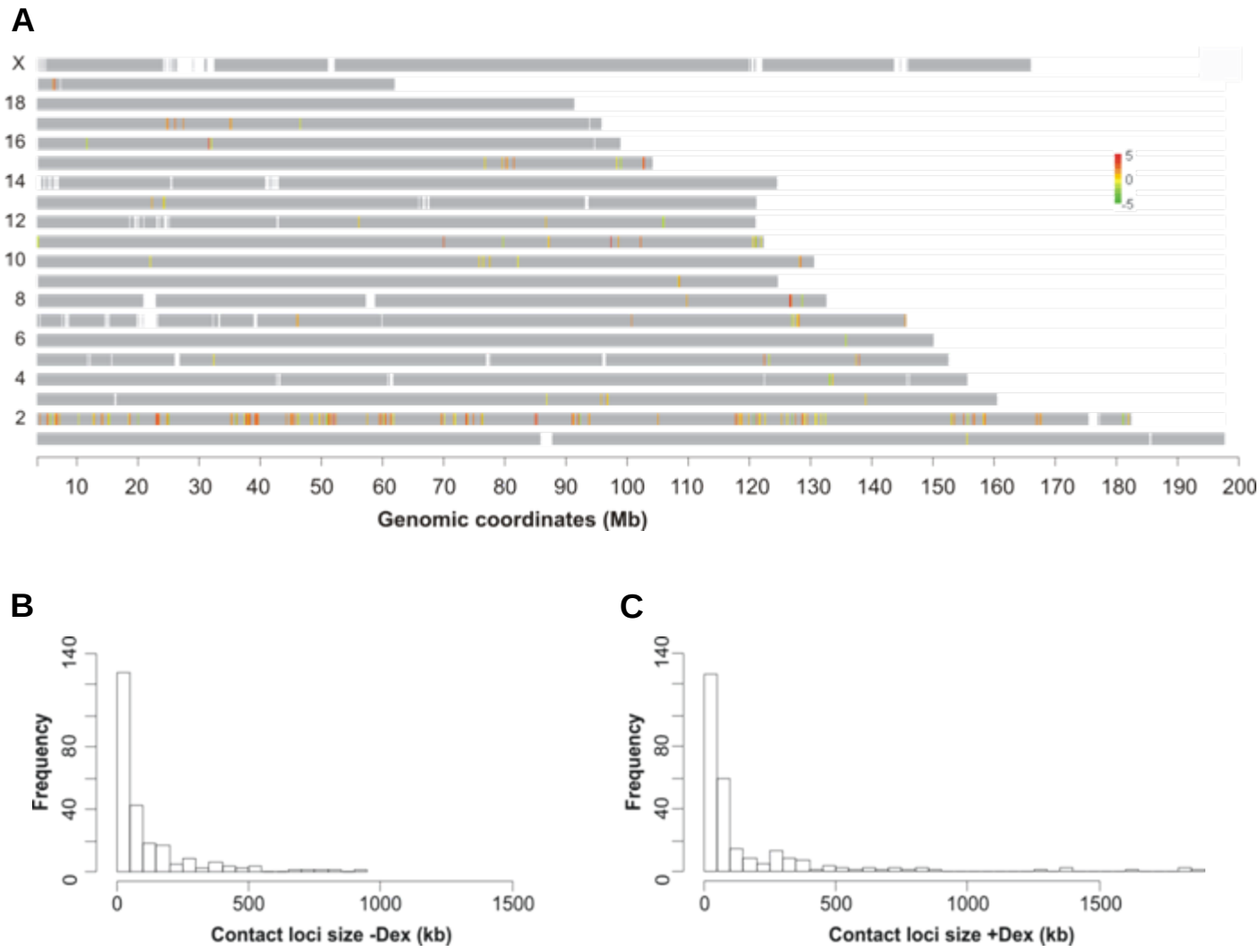


Figure S2. A. Genomic map of *Lcn2* differential contacts between the none-induced and the one hour Dex induced cells. Probes that show p-score change more than 4.5 between the two conditions were plotted. Probes with increased value are plotted in yellow-red scale, probes that show decrease in their p-score are plotted in green scale according to the Log2 (+Dex/-Dex) ratios. Probes that did not show change or a change below threshold, were plotted in gray. Genomic position in mm8 coordinates is indicated on the horizontal axis. **B.C. *Lcn2* 4C interacts with genomic loci with various sizes.** Contact loci were grouped into 50 kb bins and the number of loci in each bin is presented. B and C represent the contact size distribution before and after hormone induction respectively.

Hakim - Supplementary Figure S3

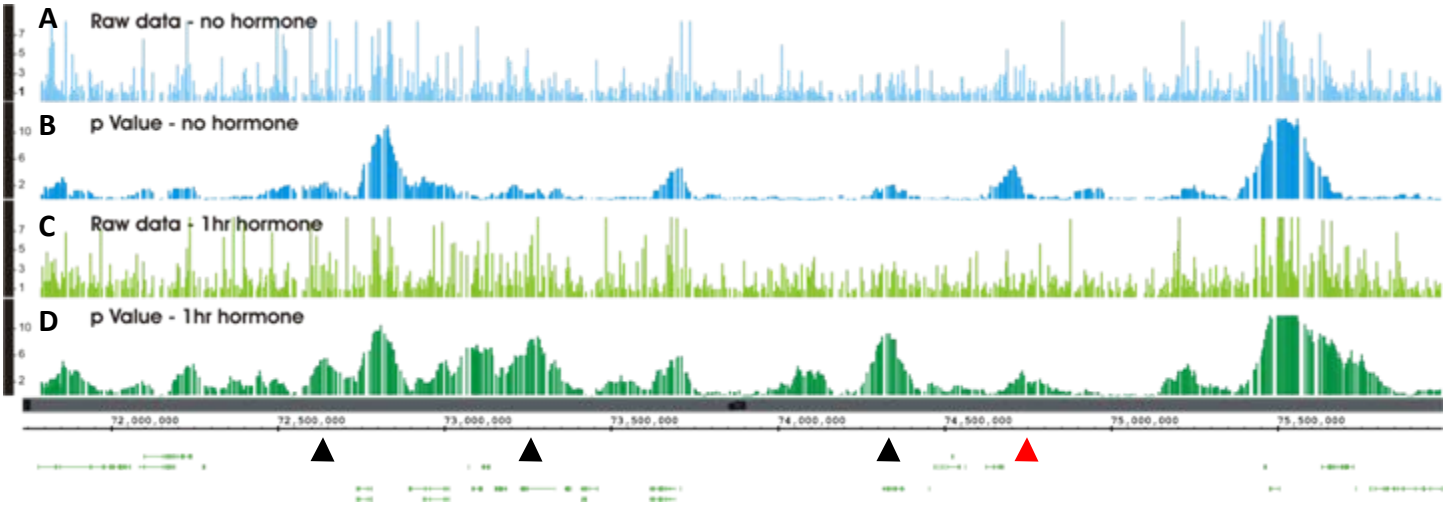


Figure S3. Long range contacts with *Lcn2* on chromosome 2:71.8Mb-75.9Mb. Unprocessed log2 (4C/genomic control) hybridization signals (**A,C**, raw data) together with statistical analysis (**B,C,** p-value) showing interactions of *Lcn2* (chr 2: 32.2 Mb) with loci on chromosome 2, before and one hour after hormone induction. Probes with p-value greater than 4 were scored as positive. Note that in general, the contacts are more frequent in response to GR activation by Dex (wider and taller peaks). Some contacts increase above statistical threshold (P-value=4) in response to GR activation (black arrowhead) and some contacts show decrease frequency (red arrowhead). Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S4

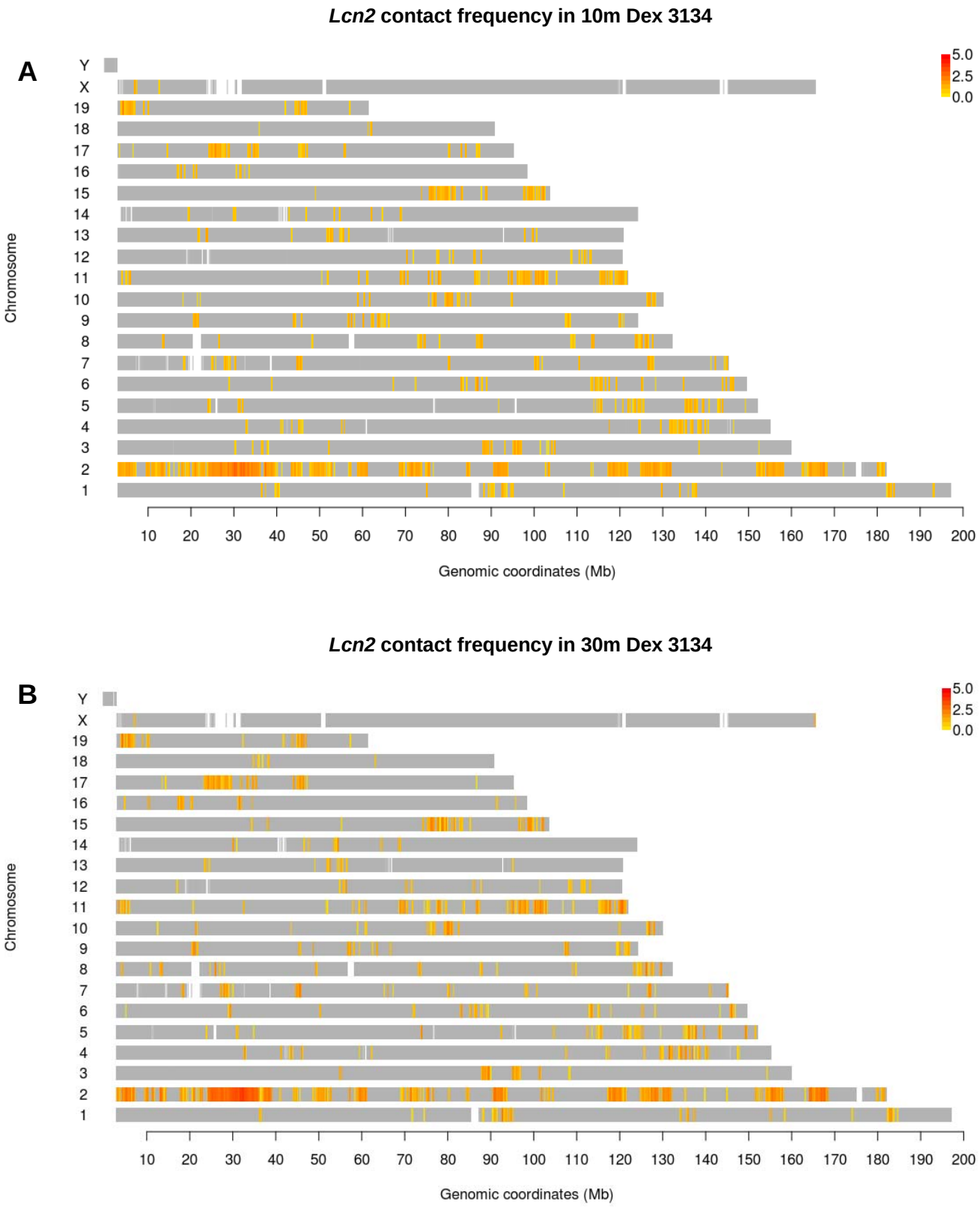
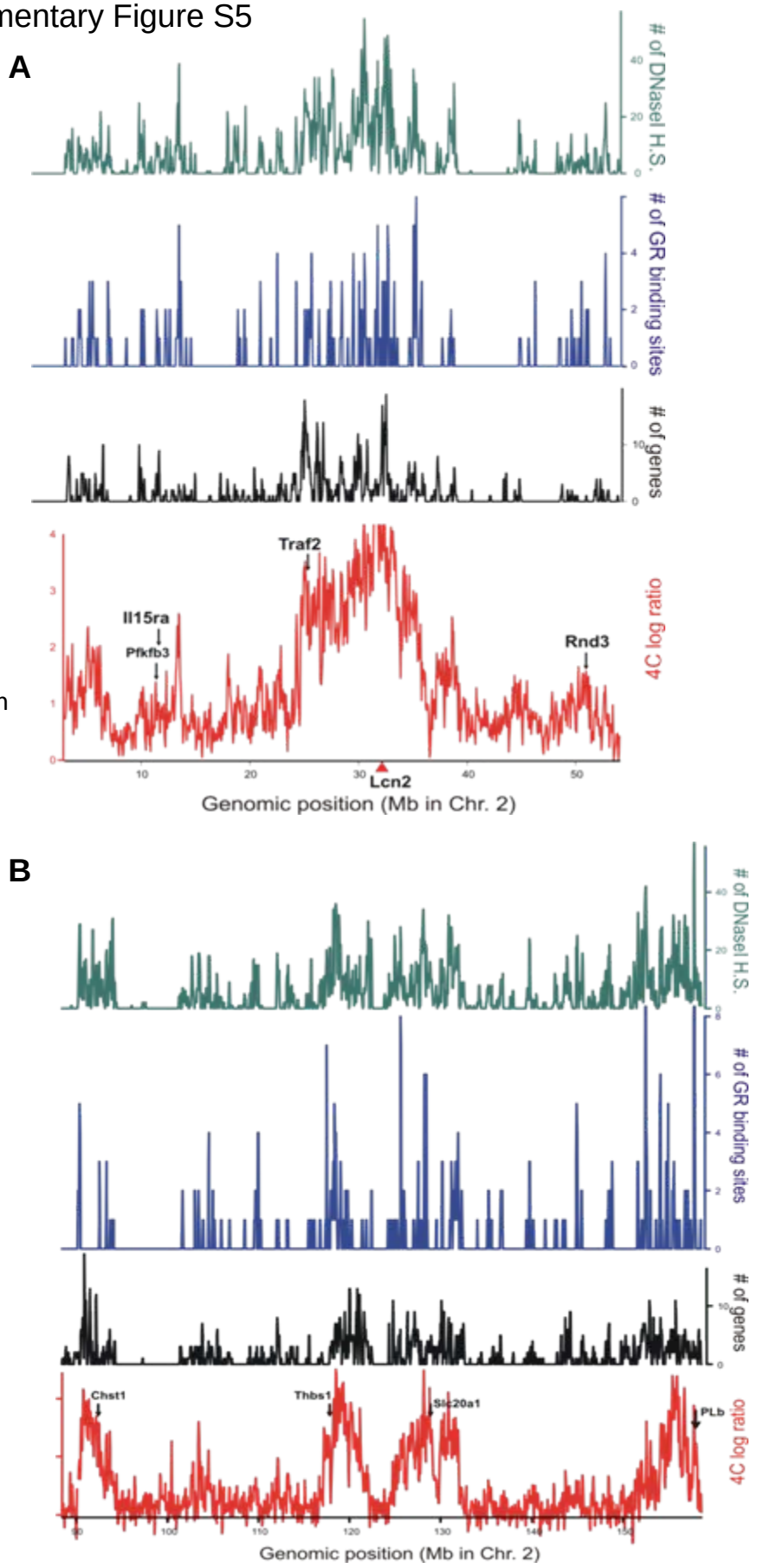


Figure S4. High temporal resolution of *Lcn2* interactions across the mouse genome in mammary cell line. Genomic map of *Lcn2* contacts ten minutes (A) and thirty minutes (B) after induction by Dex. Probes with p value above the threshold (p score = -log10 p > 4: 0.3 % FDR) are marked in a yellow-to-red color scale according to the intensity of the probe signal (log2 4C/genomic DNA). Probes with p value below the threshold are marked in gray. Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S5



Chr2 *Lcn2* region

Figure S5. Examples of smoothed data profiles from cells induced with dex for one hour, using *Lcn2* as the bait. A,B. Examples on chromosome 2 (cis chromosome). 4C profiles (average log2 ratios/100kb) are presented in red, gene density (TSS /100kb) in black, GR binding density (binding sites/100kb) in blue and DHS density (DHS /100kb) in green. Genomic position is indicated on the horizontal axis. The location of GR regulated genes is marked with black arrows. Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S5

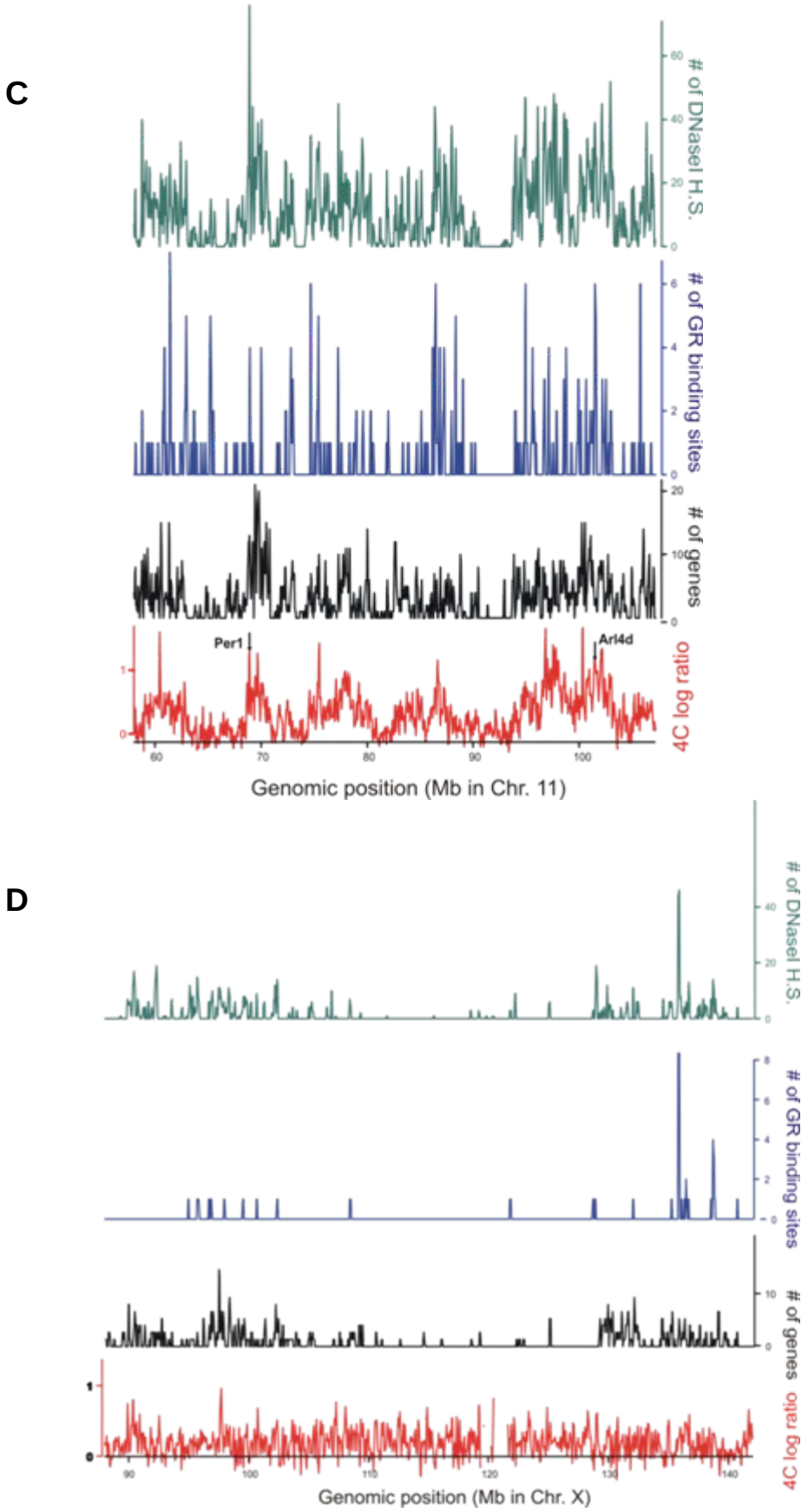


Figure S5. C. Example for positive contact region on chromosome 11. **D.** Example for negative contact region on chromosome X

Hakim - Supplementary Figure S5

E

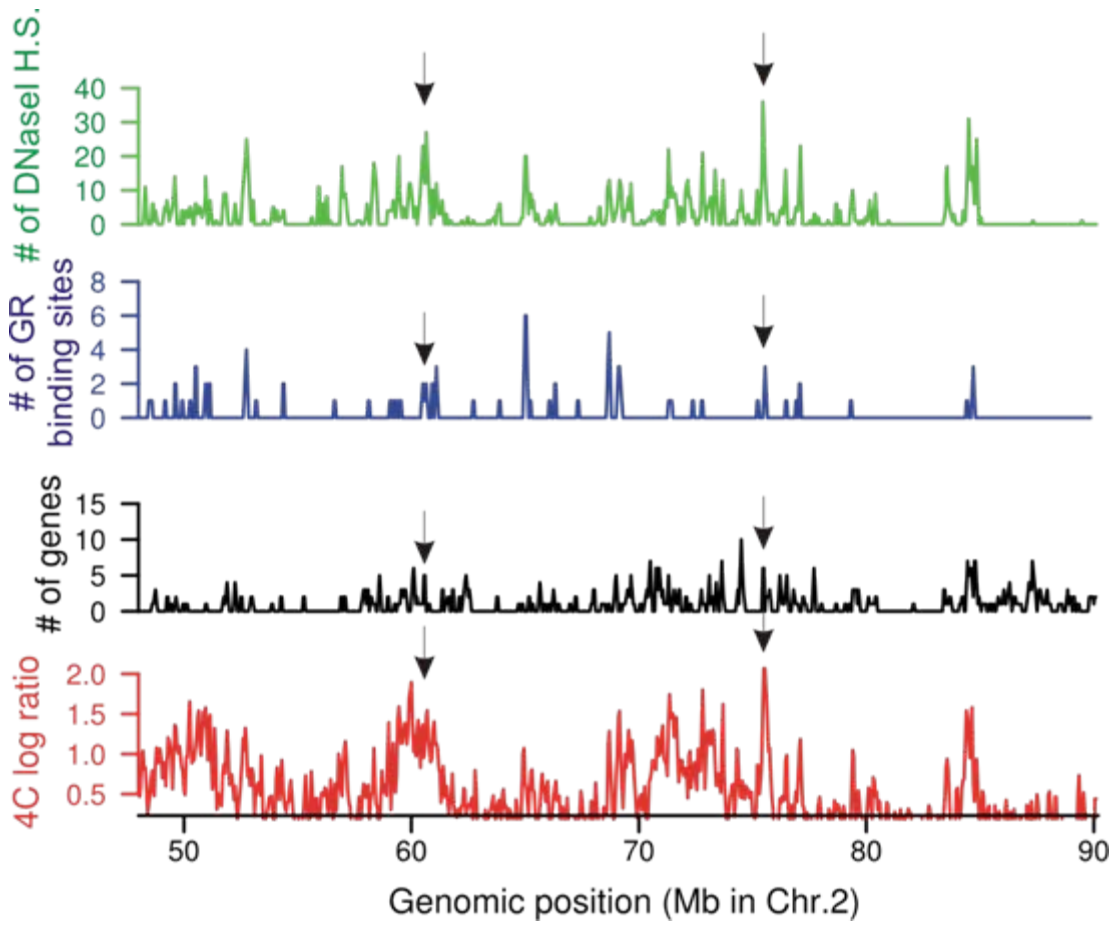


Figure S5. E. Example for contact region on chromosome 2 demonstrating the prevalence of GR binding and DHS sites over gene density in the contact loci. Arrows point to contact regions in gene-poor regions that have numerous clustered GR binding sites and DHS.

Hakim - Supplementary Figure S6

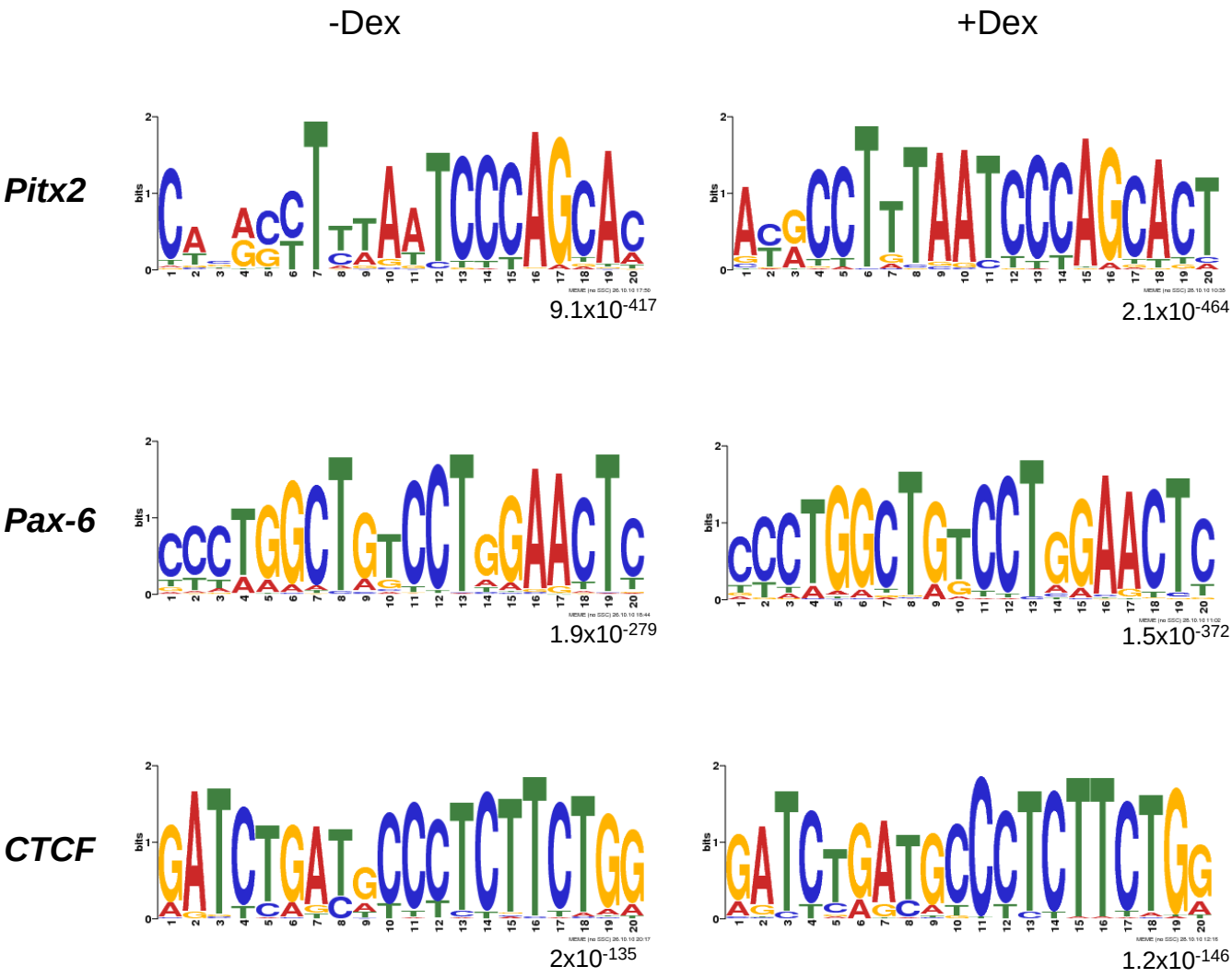


Figure S6. Enriched motifs discovered by MEME analysis on DHS sites near *Lcn2* contact regions. The DHS sites within 10 kb of positive probes from *Lcn2* 4C data were sorted by their DNaseI hypersensitivity (tag density of DHS-seq). Top 1,500 sites were obtained separately for Dex treated and untreated conditions and used as input to the MEME program. Enriched motifs from MEME were queried against the TRANSFAC database using the Tomtom program to identify matches to known transcription factor binding motifs. The number below each logo is the e-value from the MEME algorithm.

Hakim Supplementary Figure S7

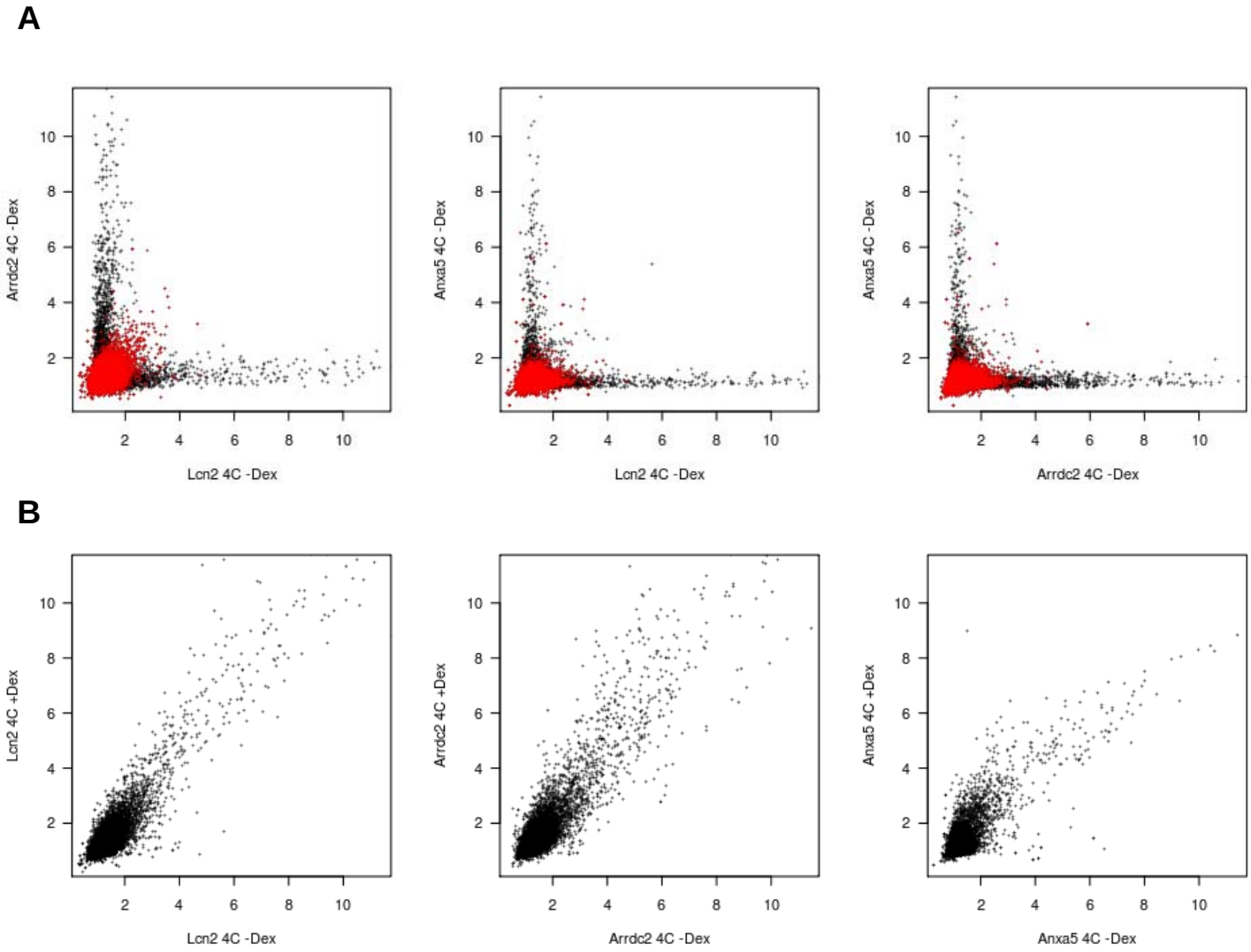


Figure S7. Comparison of 4C signal from different baits and different conditions. Each profile was obtained by averaging the 4C logratios over a 100 kb window sliding along the genome in 50 kb increments. **A.** Pairwise comparisons of the 4C profiles from the baits *Lcn2, Arrdc2, Anxa5* in untreated cells. The inter-chromosomal contacts (trans) are indicated in red color. These plots indicate that the subnuclear environments at the three bait loci have few mutual interactions. **B.** Each plot shows the 4C profiles after Dex versus before Dex for a given bait, showing a global correlation between contact frequency patterns before/after Dex.

Hakim - Supplementary Figure S8

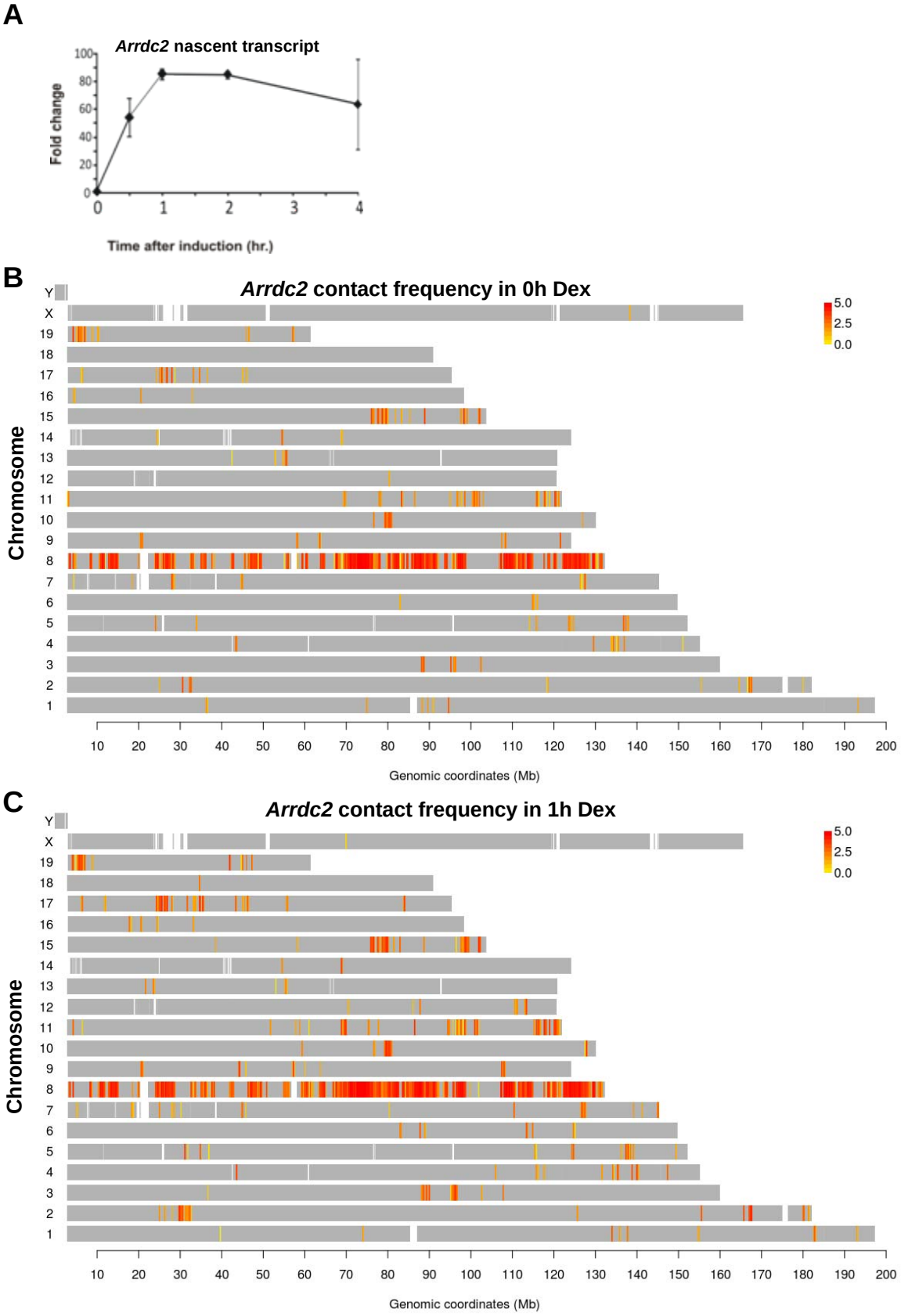


Figure S8. *Arrdc2*, GR induced gene, interactions across the mouse genome in mammary cell line. A Time course analysis by qRT-PCR of nascent transcript levels of *Arrdc2*. Samples were collected before Dex treatment (0) and 0.5,1,2,4 hours after Dex induction. Results shown are the average of three independent experiments, SD is presented. Genomic map of *Arrdc2* (chr8:73,764,127-73,768,709) contacts before (**B**) and one hour after (**C**) induction by Dex. Probes with p value above the threshold (p score = -log10 p > 4: 0.3 % FDR) are marked in a yellow-to-red color scale according to the intensity of the probe signal (log2 4C/genomic DNA). Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S9

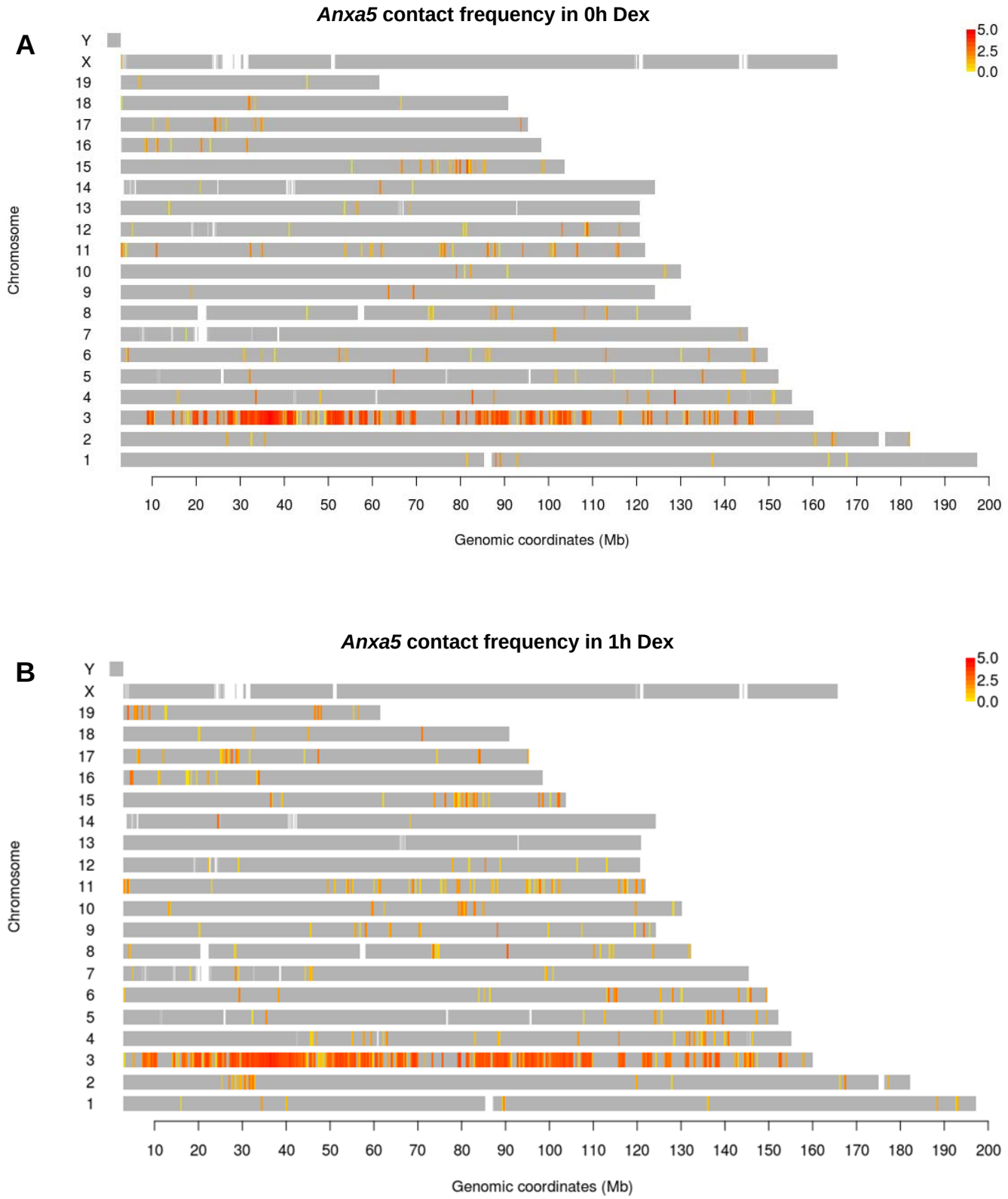


Figure S9. *Anxa5* interactions across the mouse genome in mammary cell line. Genomic map of *Anxa5* (chr3:36,640,475-36,667,247) contacts before (**A**) and one hour after (**B**) induction by Dex. Probes with p value above the threshold (p score = -log10 p > 4: 0.3 % FDR) are marked in a yellow-to-red color scale according to the intensity of the probe signal (log2 4C/genomic DNA). Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary Figure S10

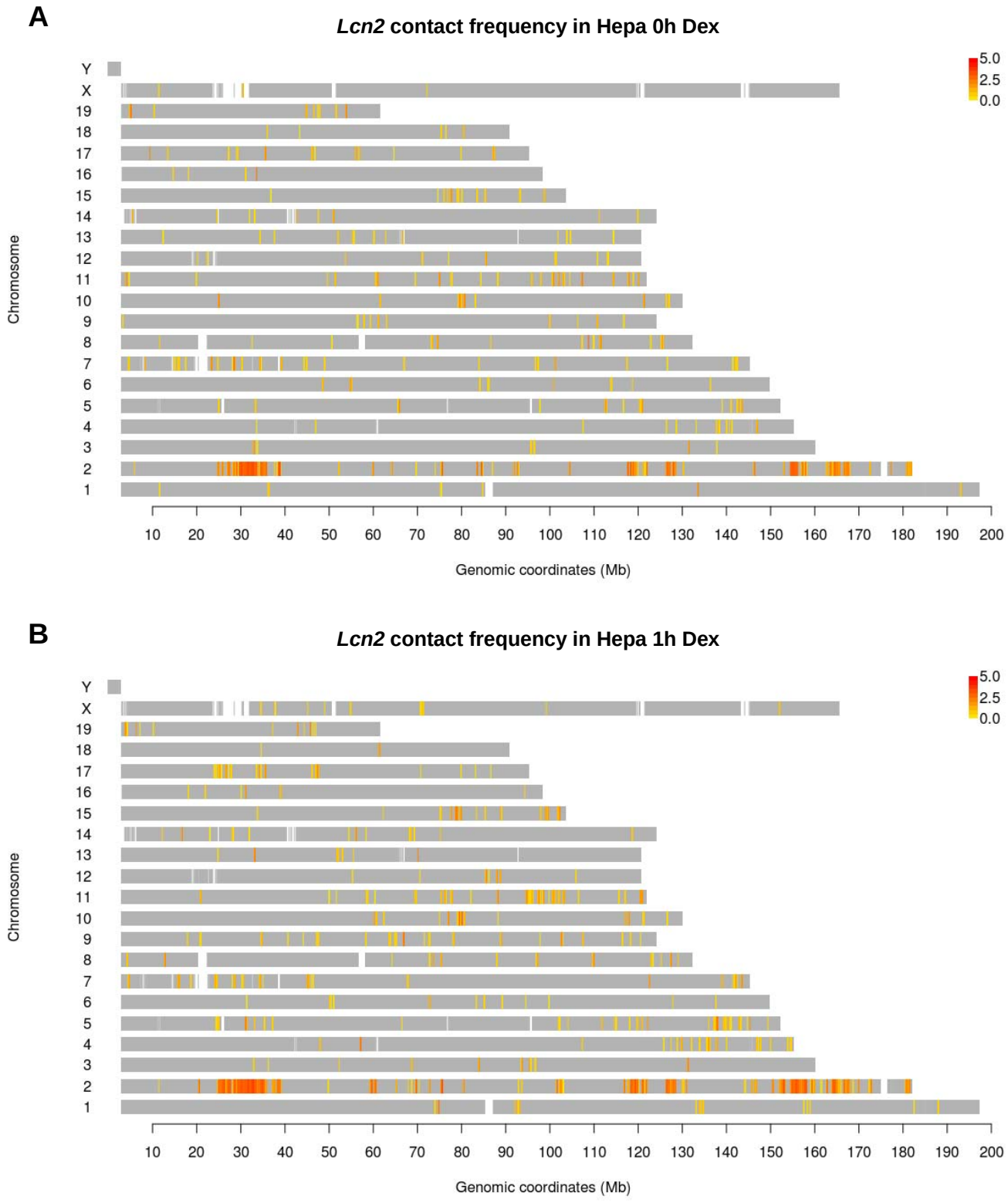


Figure S10. *Lcn2* interactions across the mouse genome in Hepa1C1C7 cell line. Genomic map of *Lcn2* contacts before (**A**) and one hour (**B**) after induction by Dex. Probes with p value above the threshold (p score = -log10 p > 4: 0.3 % FDR) are marked in a yellow-to-red color scale according to the intensity of the probe signal (log2 4C/genomic DNA). Probes with p value below the threshold are marked in gray. Genomic position in mm8 coordinates is indicated on the horizontal axis.

Hakim - Supplementary tables legends

Table S1
Gene content, expression and Dex response in the robust 101 *Lcn2* contact regions before Dex induction.

Table S2
Gene content, expression and Dex response in the robust 121 *Lcn2* contact regions one hour after Dex induction.

Hakim - Supplementary Table 3

Bac	Position chromosome (Mb)	FISH % -Dex	FISH % +Dex	4C -Dex	4C +Dex	# cells -Dex	# cells +Dex
A	2 (164.5)	24.05	19.93	61.56	55.85	237	311
B	2 (157.8)	10.56	17.64	22.87	42.90	161	204
C	2 (141.2)	2.88	2.91	-6.15	-1.11	416	378
D	8 (126.1)	7.35	11.43	16.89	39.04	381	376
E	9 (107.9)	4.46	8.86	11.08	22.85	964	959
F	12 (86.1)	5.09	5.49	8.64	18.87	491	601
G	12 (105.4)	6.73	2.30	17.02	10.99	282	261
H	15 (102.1)	6.54	8.55	25.00	28.94	688	222
I	15 (20.3)	0.43	0.00	5.91	2.37	232	247

Table S3. Interaction frequencies between *Lcn2* and selected loci are presented as the percentage of cells with two signals closer than 0.8 micron (FISH%)without (-dex) or one hour after dex induction (+dex). 4C interaction probability is the sum of 4C probes value (log2 4C/genomic) over the BAC region.

Hakim - Supplementary Table S4

Primer name	Gene	Primer sequence
Unc13d_nc_F	*Unc13d*	GTGCCACCTTCAGTTCCAGT
Unc13d_nc_R	*Unc13d*	CCATGCCAGGTATAGCCAGT
Aqp5_nc_F	*Aqp5*	TGGAGCAGGCATCCTGTACT
Aqp5_nc_R	*Aqp5*	AGCATGGAAGGTCTGGTCTG
Rpp38_nc_F	*Rpp38*	AGACATGCATTGCTGACAGG
Rpp38_nc_R	*Rpp38*	TCCGAATAGATCCCCTCTTTG
Bcl2l_nc_F	*Bcl2l*	GGTGAGTCGGATTGCAAGTT
Bcl2l_nc_R	*Bcl2l*	ACAAGGGGCGTGGTTCTTAC
Tmed1_nc_F	*Tmed1*	TTAACCCAGGCTTTCTGTGG
Tmed1_nc_R	*Tmed1*	AAGGTGAAGTCCACGTCCAG
Traf2_nc_2F	*Traf2*	AAGAAGATCCCTCGGGAGAC
Traf2_nc_2R	*Traf2*	AAGAACATGCCCATCGTAGC
Chst1_nc_F	*Chst1*	TGGCTGTGTGAAGCACCTAC
Chst1_nc_R	*Chst1*	GCCTTCCAAGAACATTGCAT
Slc20a1_nc_F	*Slc20a1*	TGTATTGTCGGTGCAACCAT
Slc20a1_nc_R	*Slc20a1*	CAGCAGCACACAACGAAAAT
Snta1_nc_F	*Snta1*	CCTCAAGAAGACAGGCAAGG
Snta1_nc_R	*Snta1*	TTGGGGAAGGTTGAAAGAAA
Csf1_nc_F	*Csf1*	GCAGGAGTATTGCCAAGGAG
Csf1_nc_R	*Csf1*	CAGTGAGGAGAAGGCATGGT
Per1_nc_F	*Per1*	AGCGCATCCACTCTGGTTAT
Per1_nc_R	*Per1*	TGCCTCCCAAACTCTCATCT
Arl4d_nc_F	*Arl4d*	GTTTAGGGGAAGGACCCAAA
Arl4d_nc_R	*Arl4d*	CCTTAAAACGGCAGGTAGCA
Ier3_nc_F	*Ier3*	TCGATCTGACGTTTCCCTCT
Ier3_nc_R	*Ier3*	AAGATGATGGCGAACAGGAG
Il15ra_nc_F	*Il15ra*	ACAACTCCCAGCCTCAAGTG
Il15ra_nc_R	*Il15ra*	AGATGTCTCTGGCTCCCACA
Pfkfb3_nc_F	*Pfkfb3*	CAACCGTGATTGTGATGGTG
Pfkfb3_nc_R	*Pfkfb3*	CAGACCTGGCTTACCTTTCG
Rnd3_nc_F	*Rnd3*	GTTGAGCCTGTGGGACACTT
Rnd3_nc_R	*Rnd3*	CCTCAAGGAGCCACATTAGC
Thbs1_nc_F	*Thbs1*	AGGTGTCCTGTTCCTGTTGC
Thbs1_nc_R	*Thbs1*	AGGAGAAGGGGGAGGAAAAT
Lbp_nc_F	*Lbp*	GTCGTGGGCAGTACGAGTTT
Lbp_nc_R	*Lbp*	CTGACCCAAGAGGTTTCCAG

Table S4. Primers for nascent transcript amplification by q-PCR.

Hakim - Supplementary Table S5

		Bait (fixed point)			
Genome-wide correlation		***Lcn2***	***Arrdc2***	***Anxa5***	***Lcn2* in Hepa**
A	Gene density: 4C -Dex	0.288	0.350	0.169	0.254
B	Gene density: 4C +Dex	0.328	0.362	0.264	0.305
C	Expression: 4C -Dex	0.225	0.236	0.182	0.147
D	Expression: 4C +Dex	0.240	0.230	0.225	0.201
E	GR binding: 4C +Dex	0.226	0.275	0.214	0.171
F	DHS: 4C -Dex	0.391	0.474	0.286	0.302
G	DHS: 4C +Dex	**0.436**	**0.502**	**0.385**	**0.370**

Table S5. Genome wide correlations of 4C contact profiles to gene density, expression, GR binding, and DHS profiles.
Genome-wide Pearson correlation coefficient between 4C profiles and each of the other profiles was calculated in a window of size 100 kb, sliding along the genome at 50 kb increments. For all the baits in the different cell lines, the highest correlation is found between 4C and DHS (bold).
Correlations:
A.4C before Dex induction to gene density.
B.4C after Dex induction to gene density.
C.4C before Dex induction to expression before Dex induction.
D.4C after Dex induction to expression after Dex induction.
E.4C after Dex induction to GR binding after Dex induction.
F.4C before Dex induction to DHS before Dex induction.
G.4C After Dex induction to DHS After Dex induction.

Hakim - Supplementary Table S6

Clone ID	chromosome	from	to
RP23-61N22	2	32059424	32315976
RP24-157M4	8	126128372	126268396
RP24-345G23	9	107836316	107976312
RP23-326N15	12	105292186	105481531
RP23-398J10	2	164438367	164638709
RP23-330E15	2	157764571	157934900
RP24-338B7	2	141153253	141309830
RP23-137O23	15	20234277	20430707
RP23-298N20	15	101957990	102103632
RP24-285P5	12	85975822	86128109

Table S6. BACs that were used as DNA FISH probes. Genomic position in mm8 coordinates is indicated.