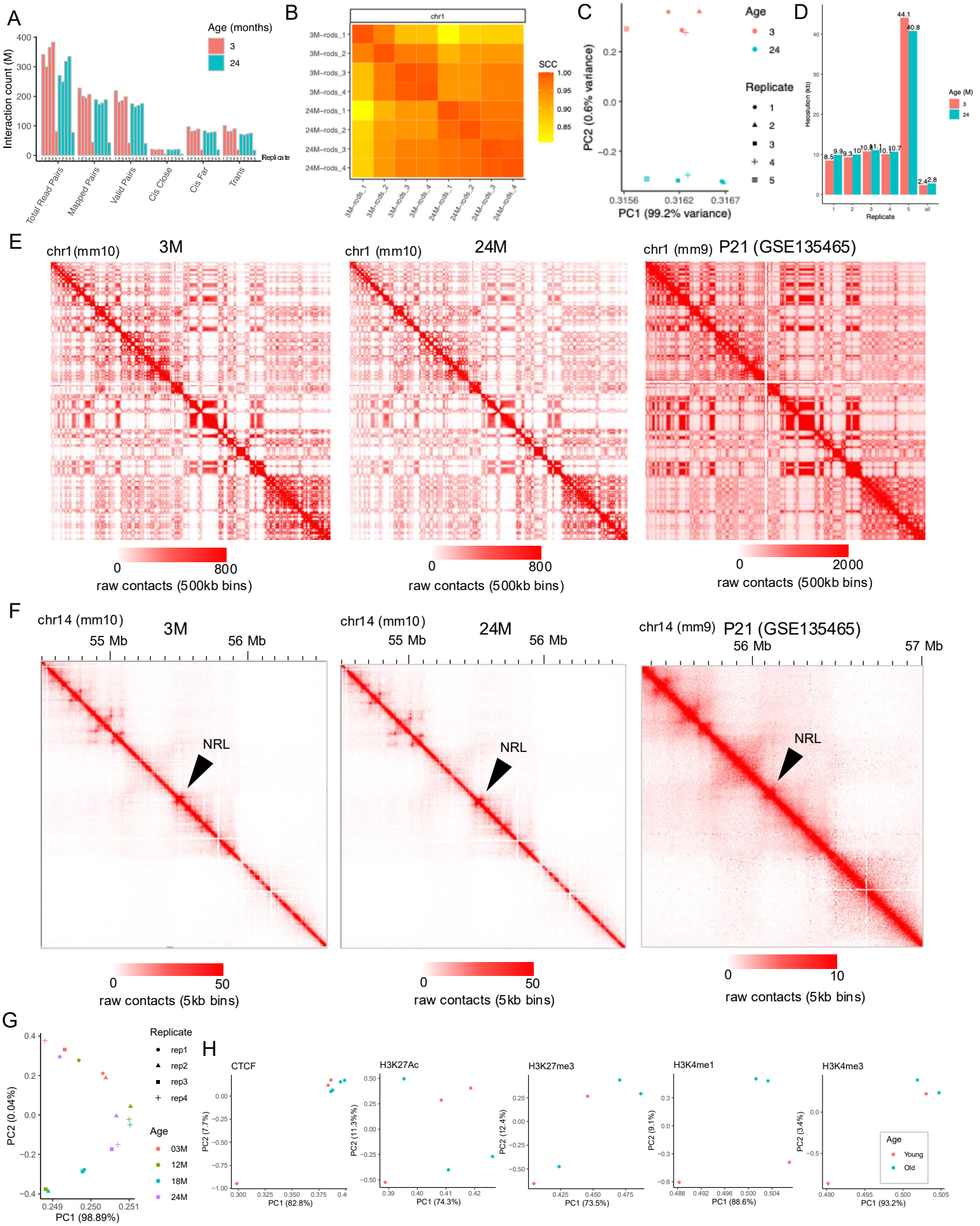
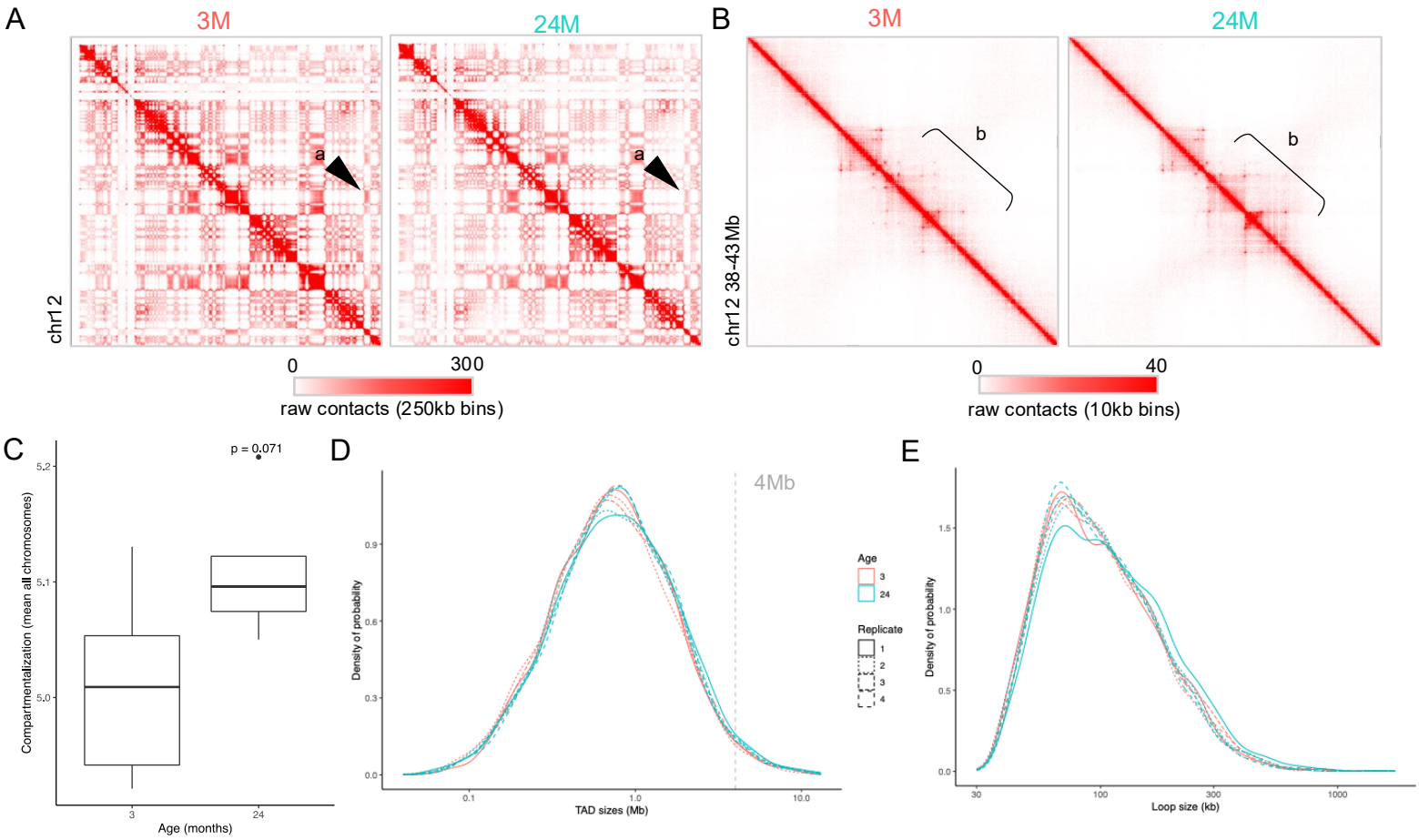
Supplementary Figure 1



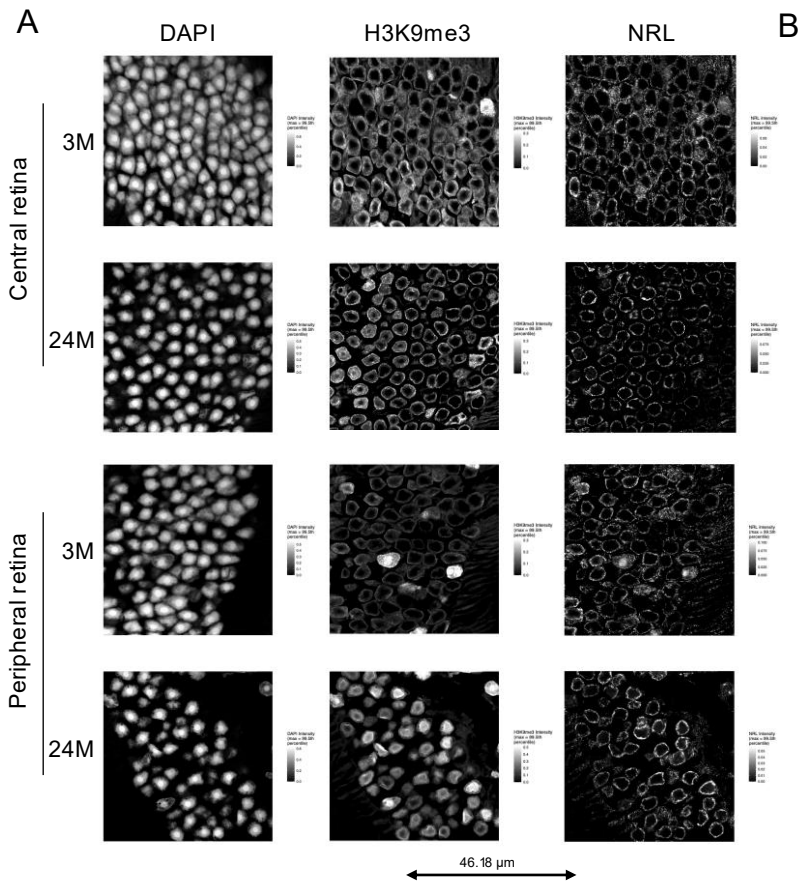
Supplementary Figure 1, associated to Figure 1. A. Statistics from mapping and filtering Hi-C interactions. Data are from 5 biological replicates of sorted rods from 3- and 24-month mice. Replicate #5 is low resolution. **B.** 3D interactions SCC across samples on chr1. **C.** PCA of compartments scores (PC1) across replicates. **D.** Theorical resolution of Hi-C for each replicate and of replicates merged togethers computed on chr1. **E-F.** Contact maps of merged replicates (left and middle) and public data (right) on chr1 (**E.**) and on a portion of chr14 centered on NRL gene (**F.**). **G.** PCA on ATAC-seq replicates using coverage in 500bp genomic bins (coverage normalized in rpm). **H.** From left to right: PCA on CTCF, H3K27ac, H3K27me3, H3K4me1 and H3K4me3 CUT&Tag replicates, using coverages in 500bp genomic bins (coverage normalized in rpm).

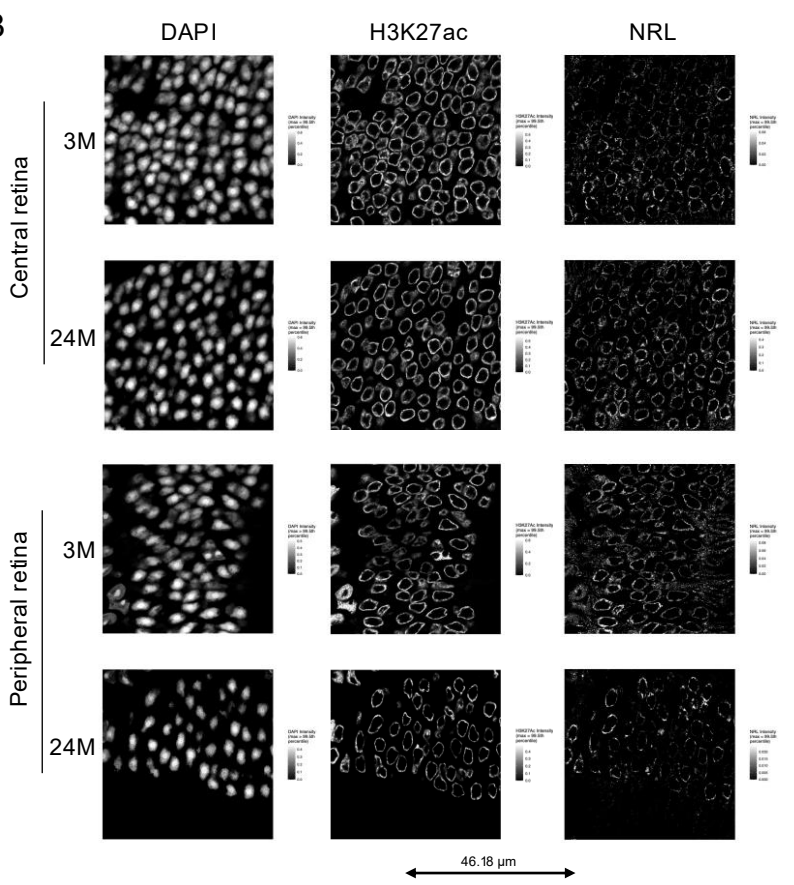
Supplementary Figure 2



Supplementary Figure 2, associated to Figure 2. A. Contact maps on chr12 of merged replicates. Region **a** highlights changing interactions during aging. **B.** Contact maps on one 5Mb locus on chr12 of merged replicate. Region **b** shows changing interactions during aging. **C.** Mean compartmentalization of all chromosomes. Each data point is one biological replicate (n=5). **D.** TAD size distribution in young vs. old mice. The vertical dashed line represent the threshold set for large TADs (4Mb, n=4). **E.** Loop size distribution in young vs. old mice (n=4)

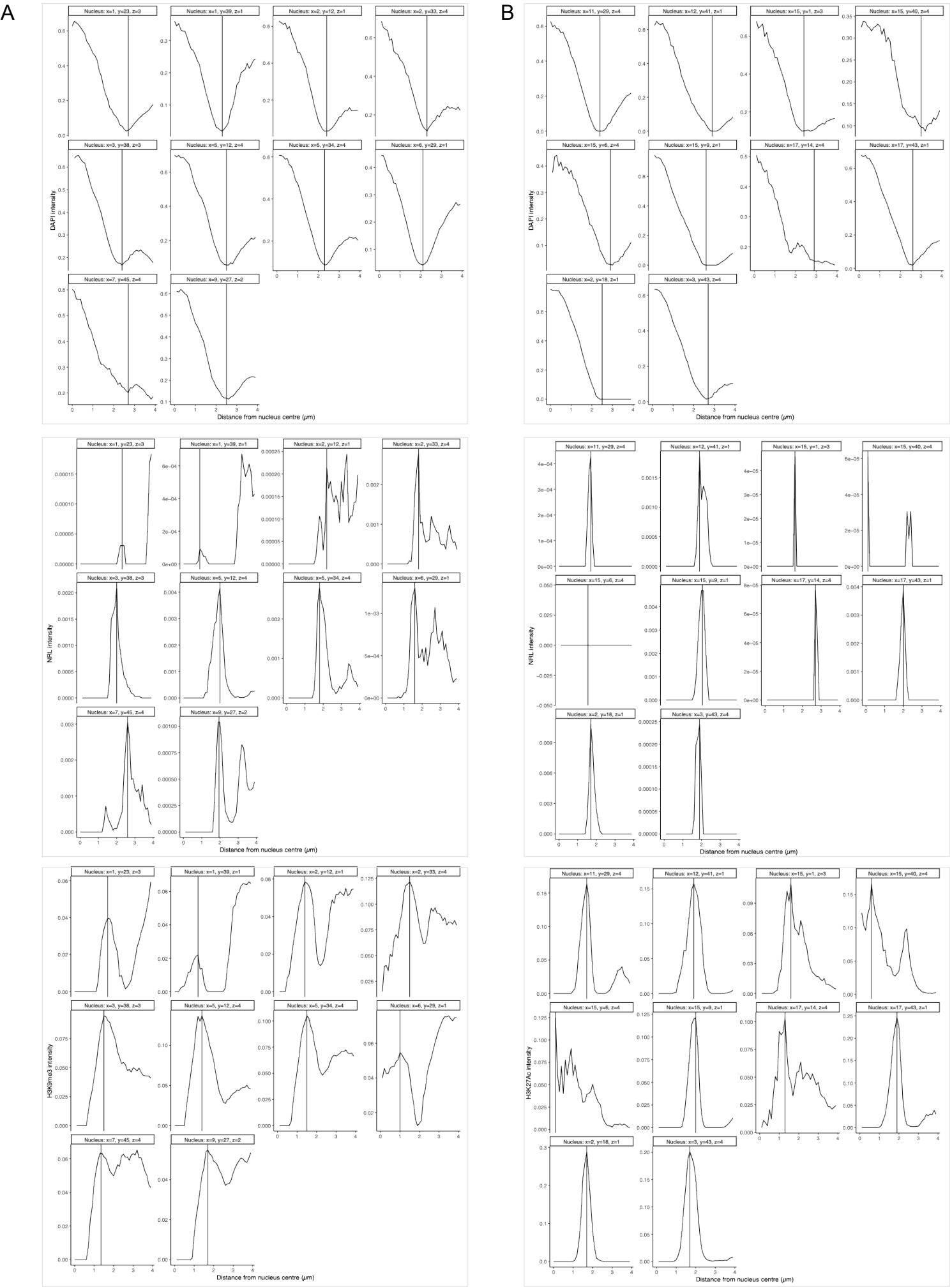
Supplementary Figure 3





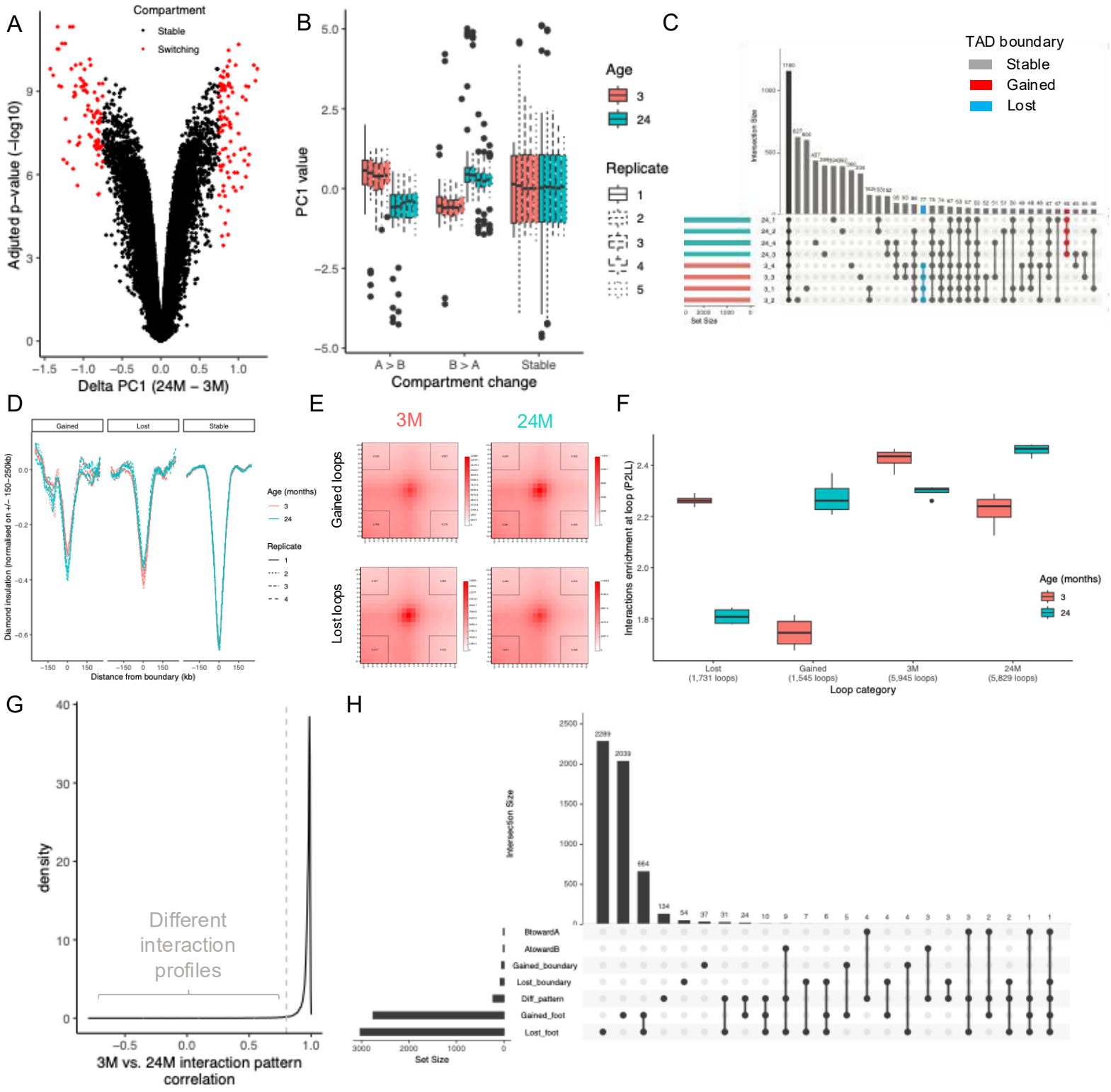
Supplementary Figure 3, associated to Figure 2. A. Microscopy image of one full z-stack with the most unfiltered nuclei for replicate A of each condition (3- vs 24-month, central vs peripheral retina). Grey scales represent the indicated signal intensity (DAPI, H3K9me3 or NRL), from 0 to 99.5th percentile of the signal on the given image. **B.** Microscopy image of the full z-stack with the most unfiltered nuclei for replicate A of each condition (3 /24 month, central / peripheral retina). Grey scales represent the indicated signal intensity (DAPI, H3K27ac or NRL), from 0 to 99.5th percentile of the signal on the given image.

Supplementary Figure 4



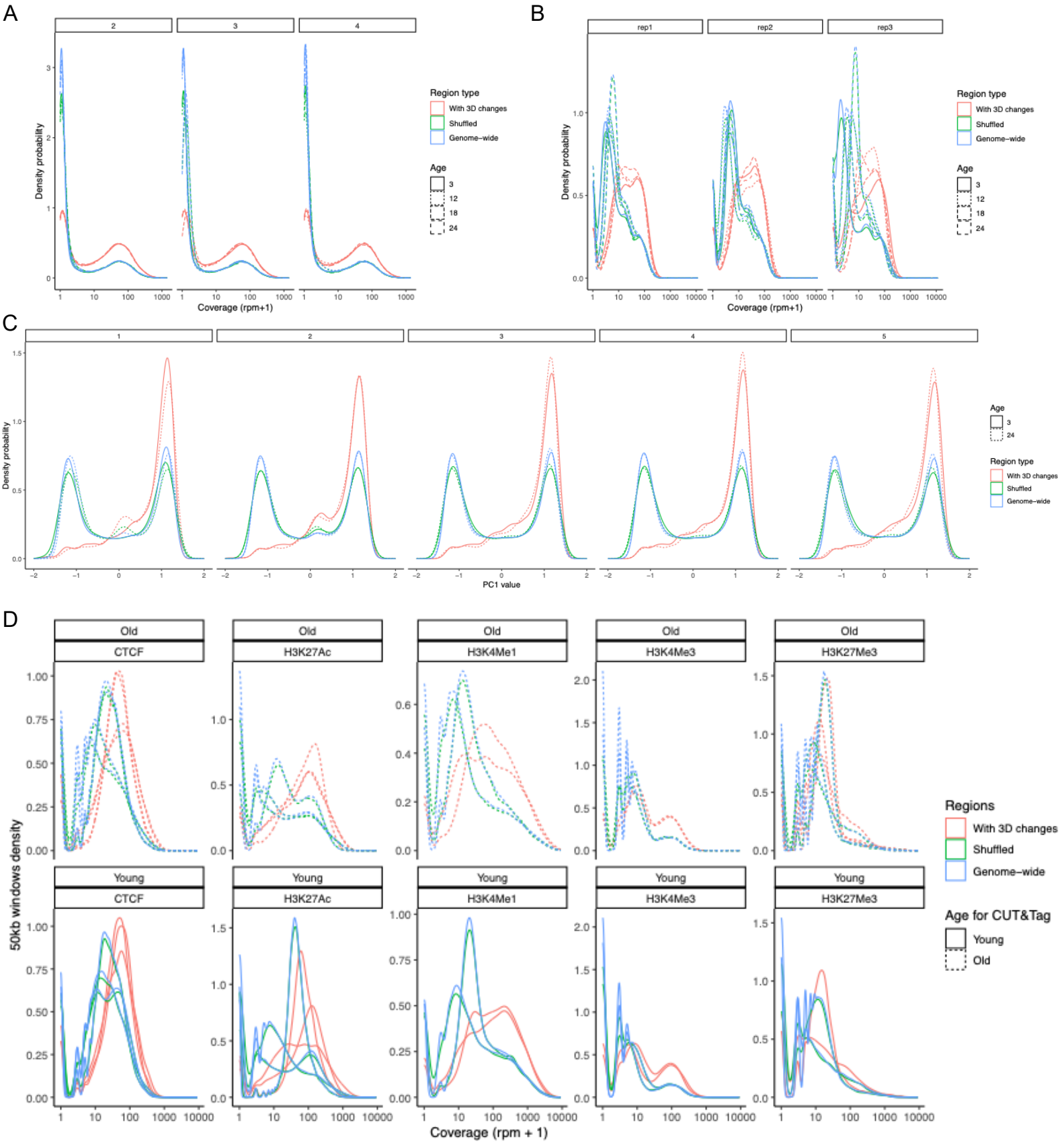
Supplementary Figure 4, associated to Figure 2. A. Computation of DAPI limit from nucleus center (top) and NRL (middle) and H3K9me3 (bottom) maximum intensity peak distance from the nucleus center (vertical lines) for 10 nuclei of 3 month old mice central retina, replicate A. **B.** Computation of DAPI limit from nucleus center (top) and NRL (middle) and H3K27ac (bottom) maximum intensity peak distance from the nucleus center (vertical lines) for 10 nuclei of 3 month old mice central retina, replicate A.

Supplementary Figure 5



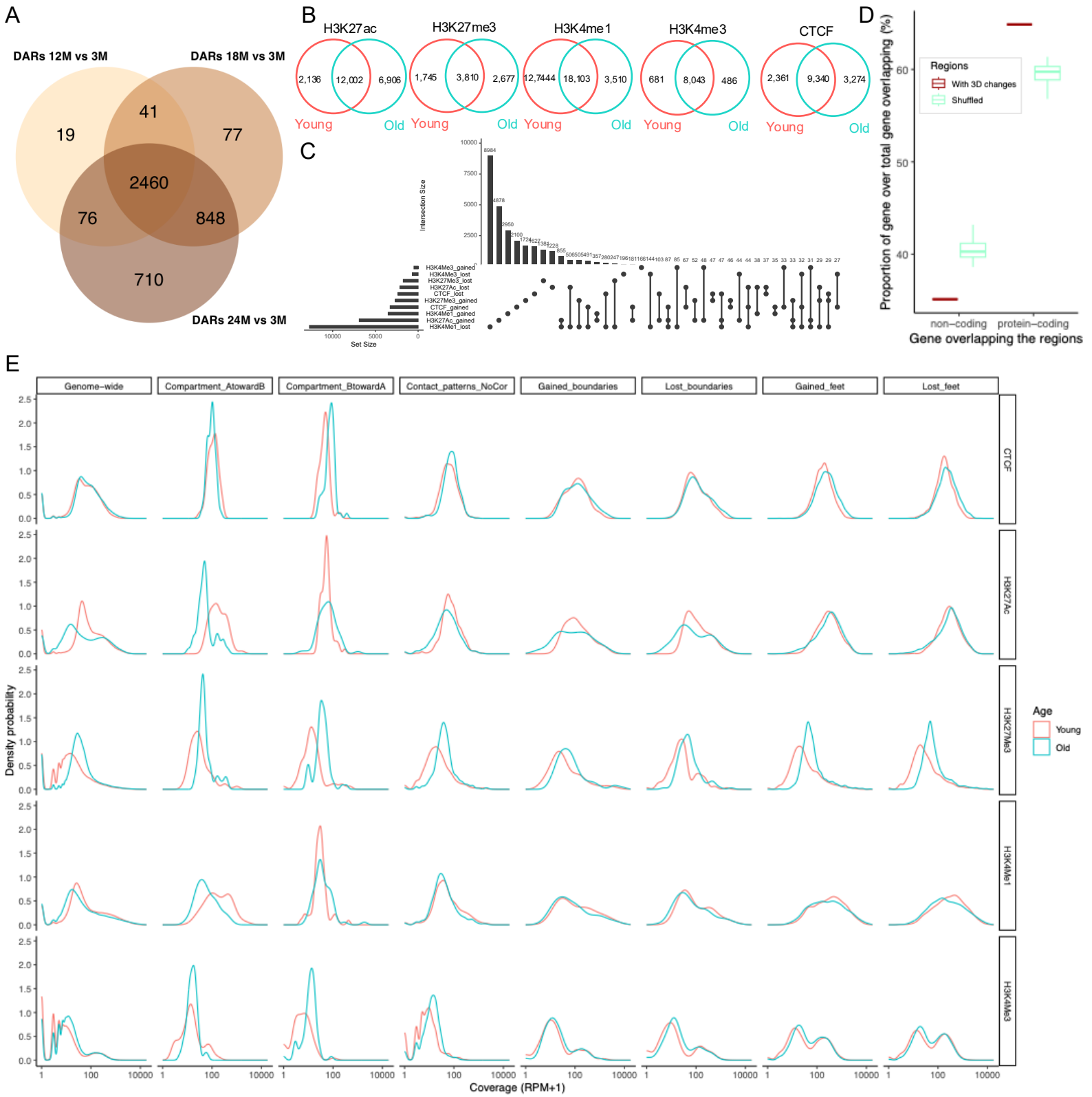
Supplementary Figure 5, associated to Figure 3. A. Identification of genomic bins with significant compartment score change. **B.** Compartment score (PC1) at A toward B (A > B) and B toward A (B > A) changing and stable regions during aging. **C.** TAD boundary overlap across samples. Stable, gained and lost boundaries are colored in black, red and blue, respectively. **D.** Normalized diamond insulation score at TAD boundaries stable, gained or lost during aging. Lower scores correspond to higher insulation. Scores are normalized on score in the 200 to 250kb regions each side of the boundaries. **E-F.** Aggregate peaks analysis (APA) of dynamic loops in merged replicates (**E**) and their corresponding P2LL scores in each replicates (n=4) (**F**). The indicated loop count represent the total loop count from each category, before selection for APA (thus, the final number of loops used for P2LL computation may be slightly lower). **G.** Distribution of correlation between interaction profiles at 3- vs. 24-months, using 50kb genomic bins. The grey dashed line represents the threshold used to select bins with different (i.e., low correlation) patterns (0.8). **H.** Overlap between regions with different types of 3D interactions changes. Boxplots represent the median and interquartile range (IQR); whiskers mark 1.5x the IQR; data beyond 1.5x the IQR are plotted as individual points.

Supplementary Figure 6



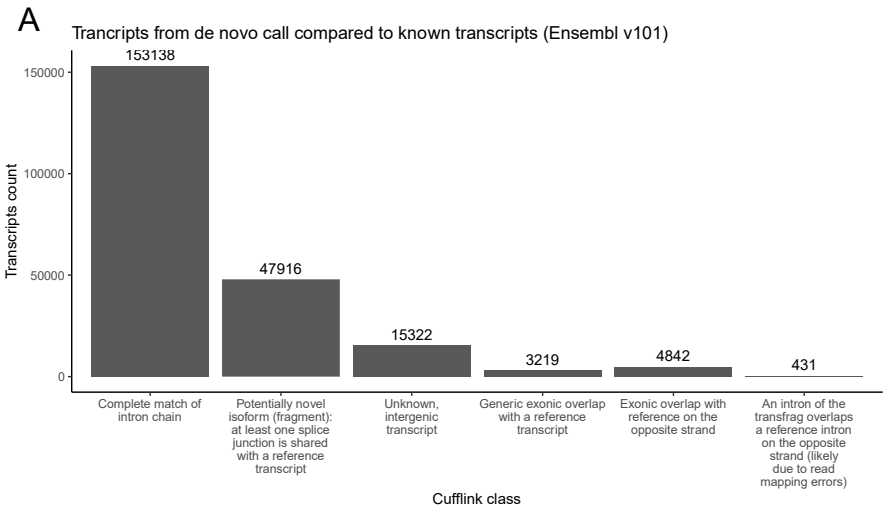
Supplementary Figure 6, associated to Figure 3. A. Transcription level (read per million, rpm, +1) distribution in 50kb windows overlapping dynamic regions, shuffled dynamic regions or genome-wide for RNA-seq replicates. **B.** Accessibility level (read per million, rpm, +1) distribution in 50kb windows overlapping dynamic regions, shuffled dynamic regions or genome-wide for ATAC-seq replicates. **C.** Compartment score (PC1) distribution in 50kb windows overlapping dynamic regions, shuffled dynamic regions or genome-wide for the 5 Hi-C replicates. **D.** CTCF, H3K27ac, H3K4me1, H3K4me3 and H3K27me3 coverages (read per million, rpm, +1) distribution in 50kb windows overlapping dynamic regions, shuffled dynamic regions or genome-wide for Cut&Tag replicates.

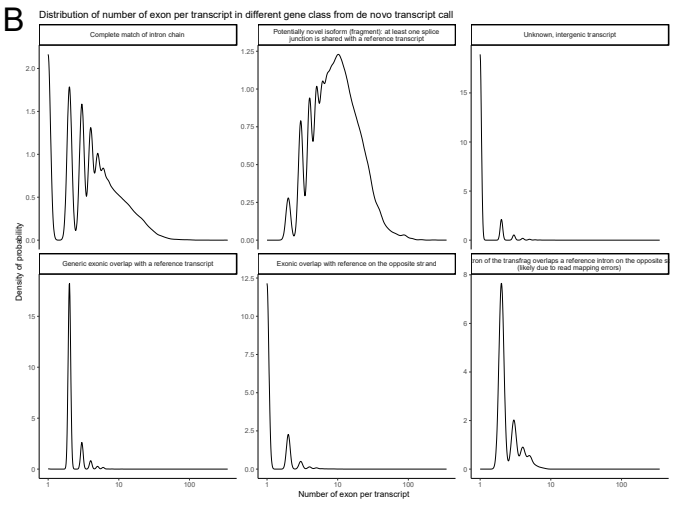
Supplementary Figure 7

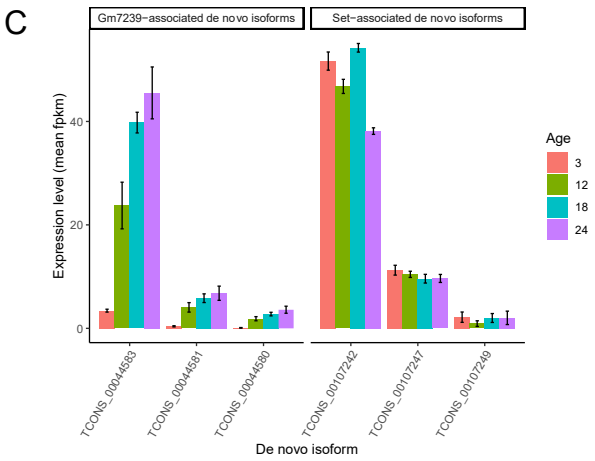


Supplementary Figure 7, associated to Figure 4. A. Differentially accessible regions (DARs) identified through aging. **B.** Chromatin mark peaks overlap between young and old mice. **C**. Upset plot showing the overlap between differential peaks for various chromatin marks. **D.** Overlap between regions with 3D interactions changes and gene types. **E.** Histone marks and CTCF coverages (read per million, rpm, +1) at different subsets of regions with 3D changes at 3- and 24-month

Supplementary Figure 8

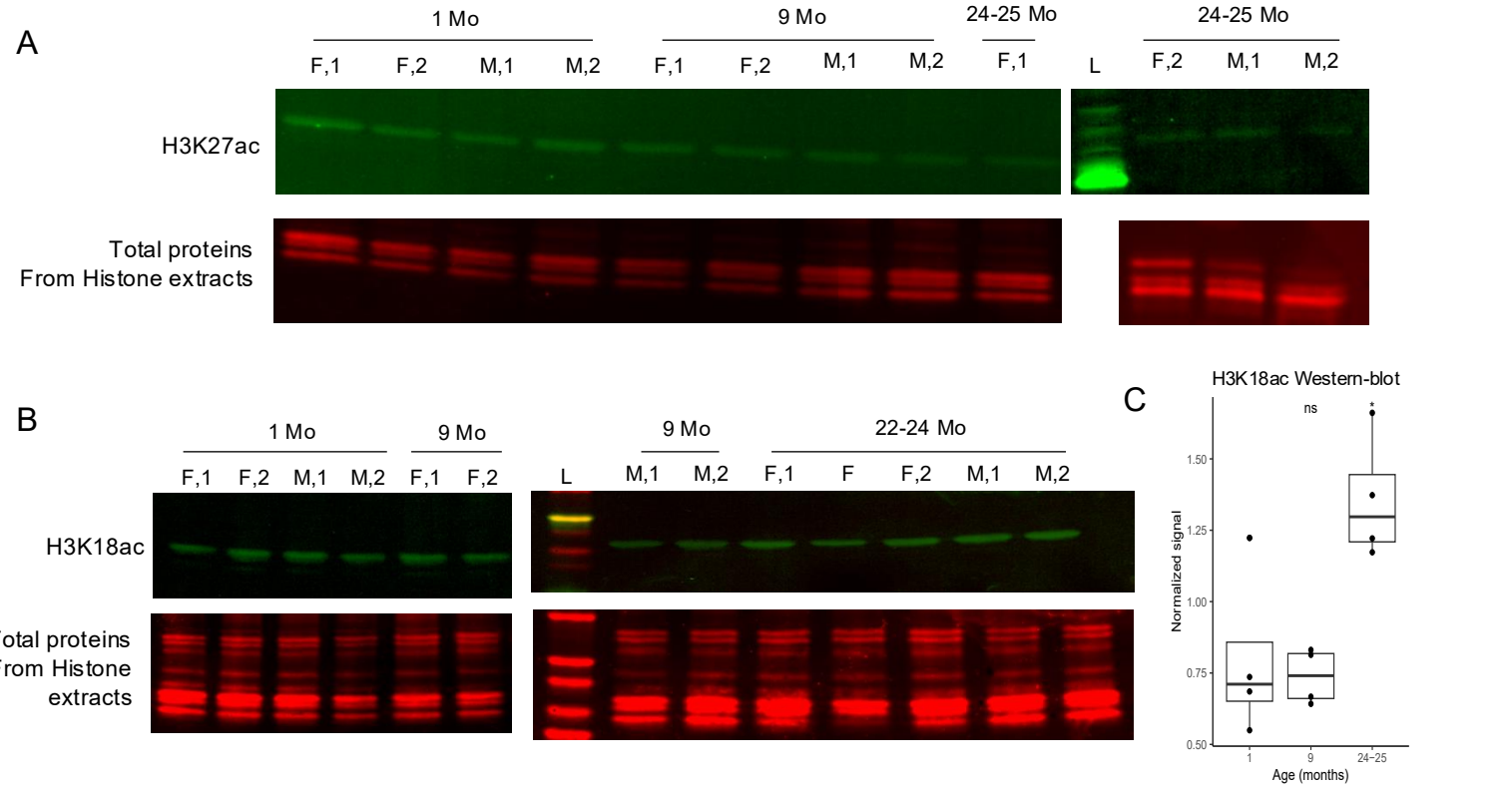




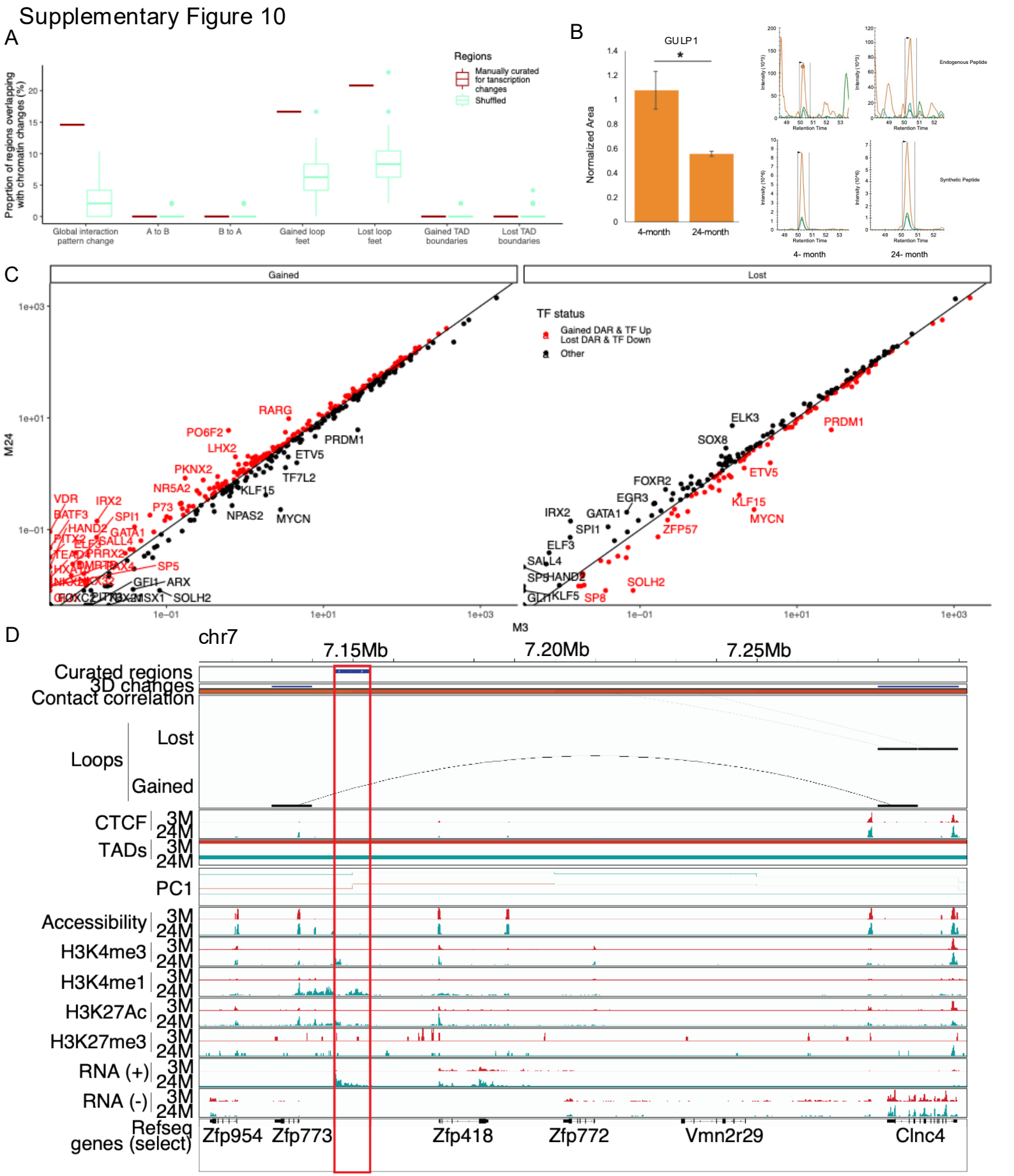


Supplementary Figure 8, associated to Figure 6. A. Overlap between transcripts identified through *de novo* transcript analysis and known transcripts from Ensembl v101. **B.** Number of exon per transcripts identified through *de novo* transcript analysis split by their overlap with known transcripts. **C.** Expression level (mean FPKM) of the de novo isoforms automatically associated by cufflink to Gm7239 or Set genes at different ages. Error bars represents the standard error of the mean from 4 replicates.

Supplementary Figure 9



Supplementary Figure 9, associated to Figure 6. A. Quantification of H3K27ac level by Western-blot during aging. **B-C**. Quantification of H3K18ac level by Western-blot during aging. Boxplot represents the median and interquartile range (IQR); whiskers mark 1.5x the IQR; data beyond 1.5x the IQR are plotted as individual points. In addition, each individual replicate is plotted has a point. **D**. Gm7239 ORF expression control by Western-blot in HEK293 cells transfected with empty vector ("- insert") or vector with Gm7239 ORF coupled with HA tag insert ("+ insert"). **E**. Quantification of pan-lysine acetylation level by Western-blot in HEK293 transfected with empty vector ("- insert") or vector with Gm7239 ORF coupled with HA tag insert ("+ insert").



Supplementary Figure 10, associated to Figure 7. A. Proportion of regions manually curated for transcription change (n=48) or 100 sets of 48 shuffled regions, overlapping with 3D chromatin features changing during aging. **B.** Left: Parallel reaction monitoring (PRM)-based targeted proteomics was used to quantify Gulp1 protein levels in the retina of C57BL/6J mice using the unique peptide FLGSTEVEQPK. Extracted ion chromatograms (XICs) and fragment-ion peak areas for the top transition ions were integrated and normalized to internal standards. Data represent mean ± SEM from three biological replicates, and statistical significance was assessed using a two-tailed test ($p < 0.05$). Right: Shown are representative XIC traces for the monitored fragment ions of the peptide FLGSTEVEQPK, unique to the GULP1 protein, obtained by PRM analysis. The chromatograms illustrate retention time alignment and relative peak intensities in samples from 4-month-old and 24-month-old mice. All chromatograms were processed using identical parameters for peak picking, integration, and normalization. The top panel displays XICs of the endogenous peptide, whereas the bottom panel shows the corresponding synthetic peptide labeled with $^{13}C/^{15}N$. **C.** Transcription factor motifs present in accessible footprints at DARs overlapping regions manually curated for transcription change. Each dot represents one motif; the expression level of the motif's corresponding transcription factor is represented on the x axis for 3-month mice and y axis for 24-months mice. Motifs with potential interest (transcription factor expression level changing in aging in the same direction as accessibility at the motif) are highlighted in red. **D.** Overview of the ZFP coding genes cluster on chr7. Tracks represent from top to bottom: genomic coordinates (mm10), manually curated regions for transcription change, regions with 3D changes, global pattern correlation between 3- and 24-month (yellow for low correlation, red for high correlation), chromatin loops, CTCF coverage, TADs, compartments (PC1), chromatin accessibility (log scale), H3K4me3, H3K4me1, H3K27ac and H3K27me3 coverages, transcription on + strand and - strand at 3- (red) or 24-month old (blue), and a selection of RefSeq genes.

Supplementary Table 1: Valid Hi-C interactions across age groups and biological replicates

Age	Replicate	Number of valid interactions
3M	1	209,069,651
24M	1	166,094,916
3M	2	171,064,763
24M	2	156,303,315
3M	3	161,646,749
24M	3	149,710,749
3M	4	174,913,777
24M	4	154,795,023
3M	5	38,833,409
24M	5	37,884,693

Supplementary Table 2: Genomic regions showing significant age-associated changes in local transcription

Chromosome	Start (bp)	End (bp)	Expression with aging	Gene(s) (manual annotation)
chr17	48,065,119	48,087,069	Down	Gm30068
chr1	44,550,774	44,797,800	Down	Gulp1
chr13	23,746,719	23,747,237	Down	H2bc3
chr4	136,622,239	136,641,954	Down	Lactbl1
chr16	34,898,891	35,003,007	Down	Mylk
chr15	25,621,466	25,814,810	Down	Myo10 (long isoform)
chr1	180,842,174	180,842,682	Down	-
chr9	47,407,269	47,475,120	Down	-
chr13	51,170,975	51,183,384	Down	Nxnl2
chr17	46,927,141	46,933,965	Down	Prph2 (3' region only)
chr6	115,940,013	115,944,670	Down	Rho (3' region only)
chr19	18,929,901	19,006,418	Down	Rorb
chr17	17,828,530	17,842,196	Down	Spaca6
chr11	114,674,998	114,757,947	Down	Ttyh2 and Dnaic2
chr4	62,448,439	62,471,093	Down	Wdr31
chr15	60,892,425	61,044,206	Up	4930402D18Rik
chr10	122,526,559	122,678,679	Up	A130077B15Rik Gm36284
chr4	53,029,915	53,160,187	Up	Abca1
chr7	48,830,416	48,841,153	Up	Csrp3
chr17	7,737,167	7,828,443	Up	Fndc1
chr8	57,829,626	57,837,599	Up	Galntl6
chr5	31,297,246	31,327,391	Up	Gckr
chr9	26,817,682	26,860,904	Up	Glb1l3
chr9	88,816,801	88,896,262	Up	Gm10634 Trim43c XR_003948453.1 Gm26611
chr11	4,620,247	4,627,776	Up	Gm11961
chr7	139,949,983	139,963,036	Up	Gm16201

Supplementary Table 2 (continued)

Chromosome	Start (bp)	End (bp)	Expression with aging	Gene(s) (manual annotation)
chr15	103,095,211	103,102,277	Up	Gm28876
chr12	7,285,895	7,566,402	Up	Gm32773 1700101O22Rik Gm32828
chr15	35,200,724	35,233,009	Up	Gm33497
chr2	126,593,618	126,619,141	Up	Hdc
chr2	60,291,906	60,383,947	Up	Ly75
chr13	83,524,890	83,525,212	Up	Mef2c (alternate promoter)
chr3	113,565,427	113,601,929	Up	-
chr6	3,671,844	3,712,498	Up	-
chr6	142,971,455	143,001,676	Up	-
chr6	147,210,353	147,233,640	Up	-
chr7	98,656,206	98,680,983	Up	-
chr12	40,813,734	40,904,436	Up	-
chr14	97,529,916	97,744,106	Up	-
chr15	73,956,789	73,994,067	Up	-
chr15	103,104,303	103,104,948	Up	-
chr18	82,711,165	82,726,289	Up	-
chr7	7,145,384	7,154,081	Up	-
chr15	12,549,736	12,742,360	Up	Pddz2 (long isoform)
chr10	127,759,317	127,793,746	Up	Rdh1 Rdh9
chr5	121,462,607	121,530,959	Up	Tmem116
chr4	129,354,446	129,404,100	Up	XR_001784447.2 XR_003955284.1
chr4	129,353,512	129,378,132	Up	C330020E22Rik Zbtb8a