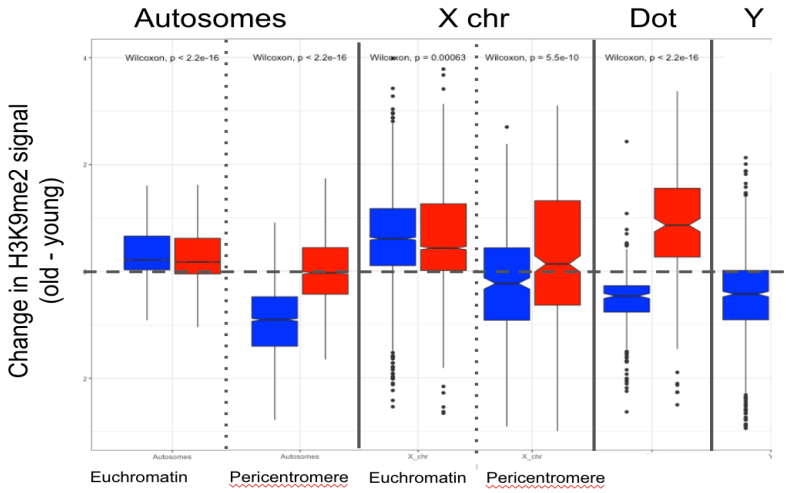
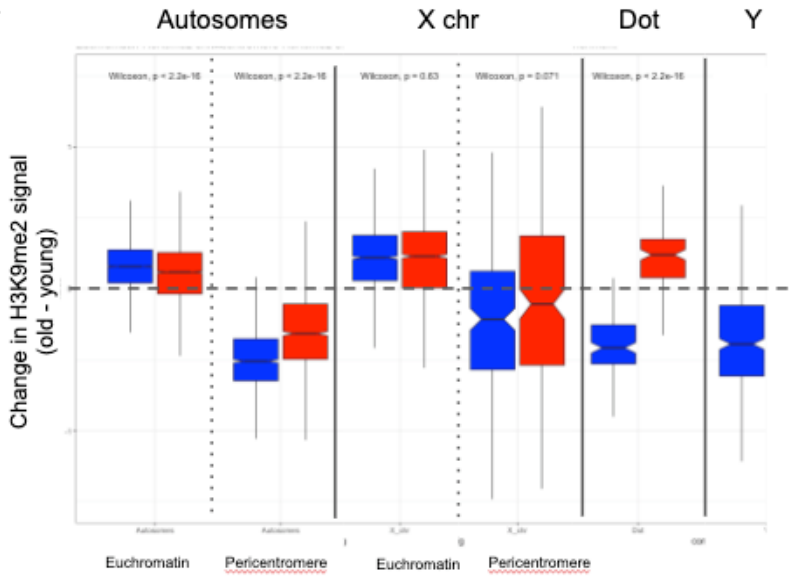
A.

normalization following Bonhoure et al. 2014

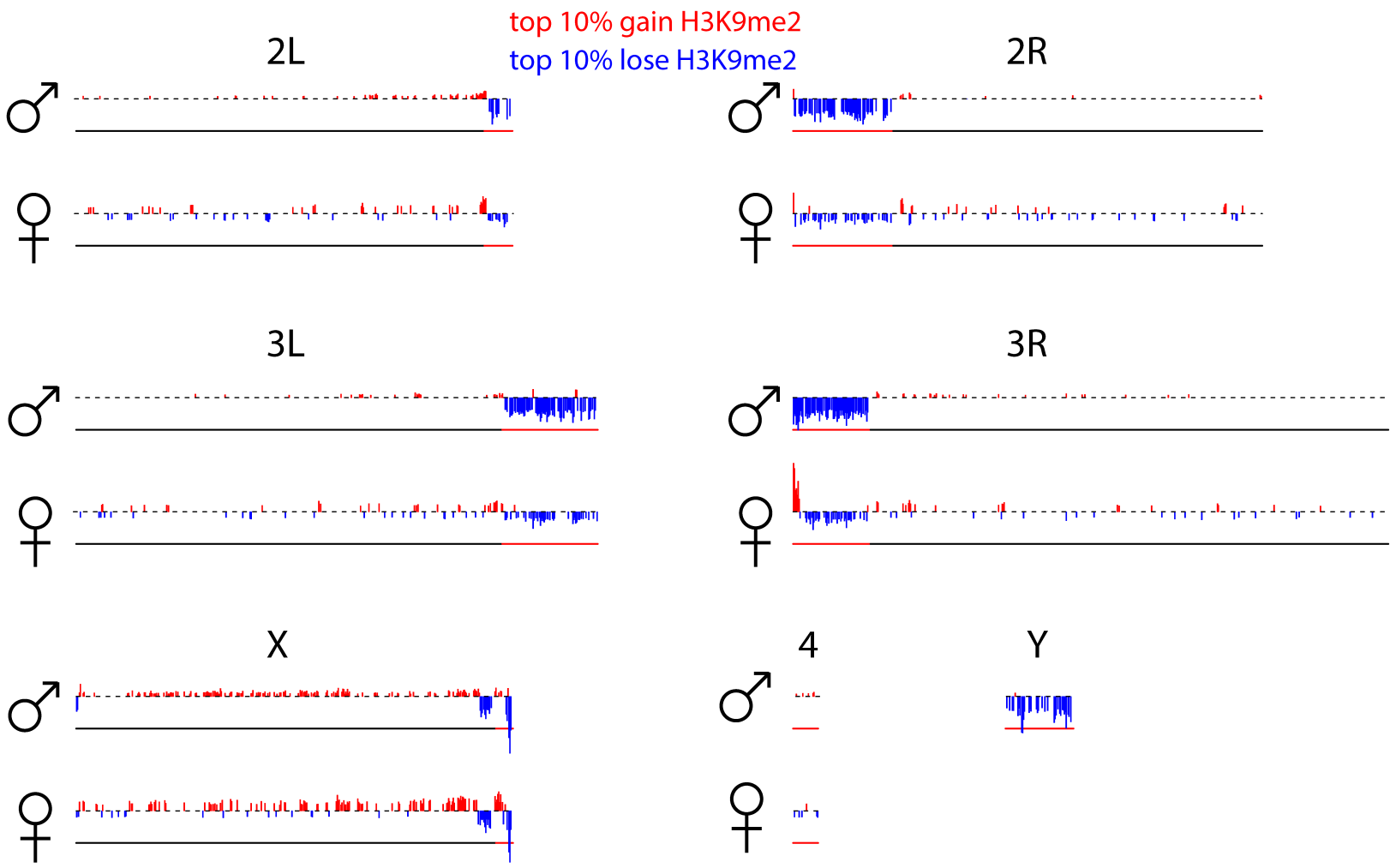


using only unique reads for mapping

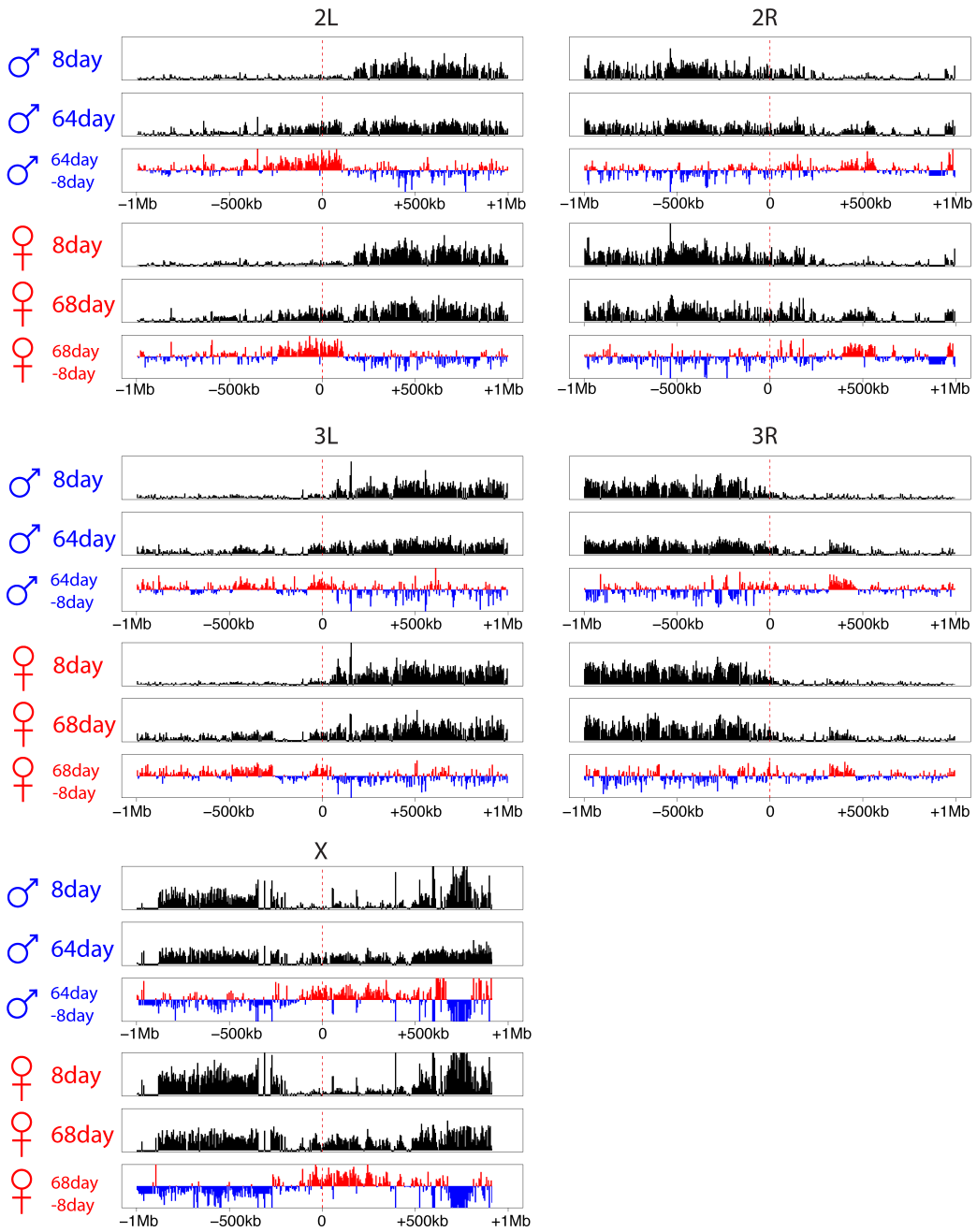
B.



Supplementary Figure 1. Same plot as Fig. 1C, but using a different normalization procedure (Bonhoure et al. 2014) (A), or using only uniquely mapping reads (B).

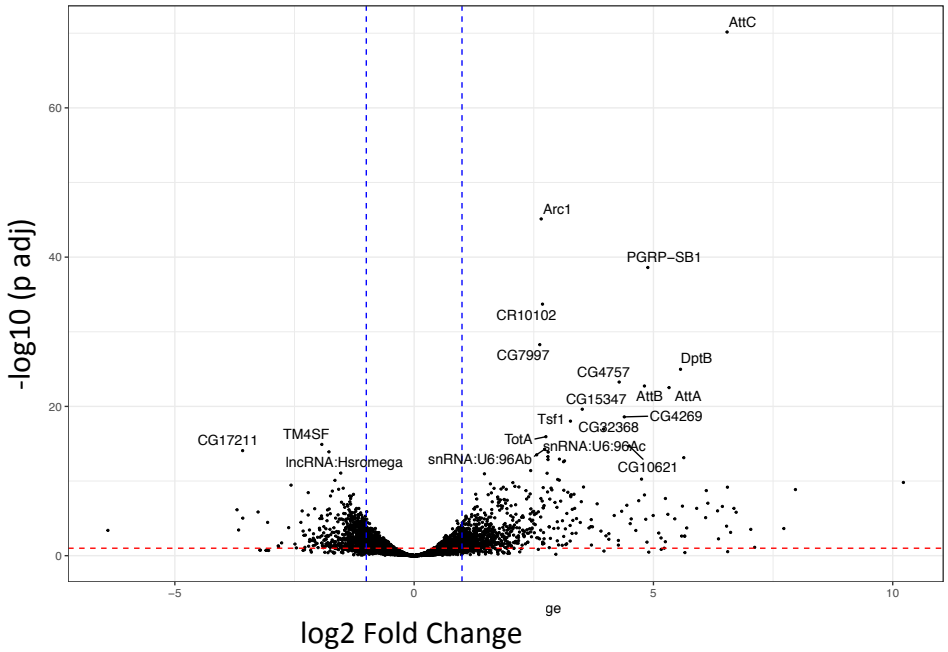


Supplementary Figure 2. Chromosomal locations of the top 10% of 50kb windows that gain (red) or lose (blue) H3K9me2 enrichment during aging for males and females. Pericentromeric regions are indicated by the red portion of the line beneath each chromosome.

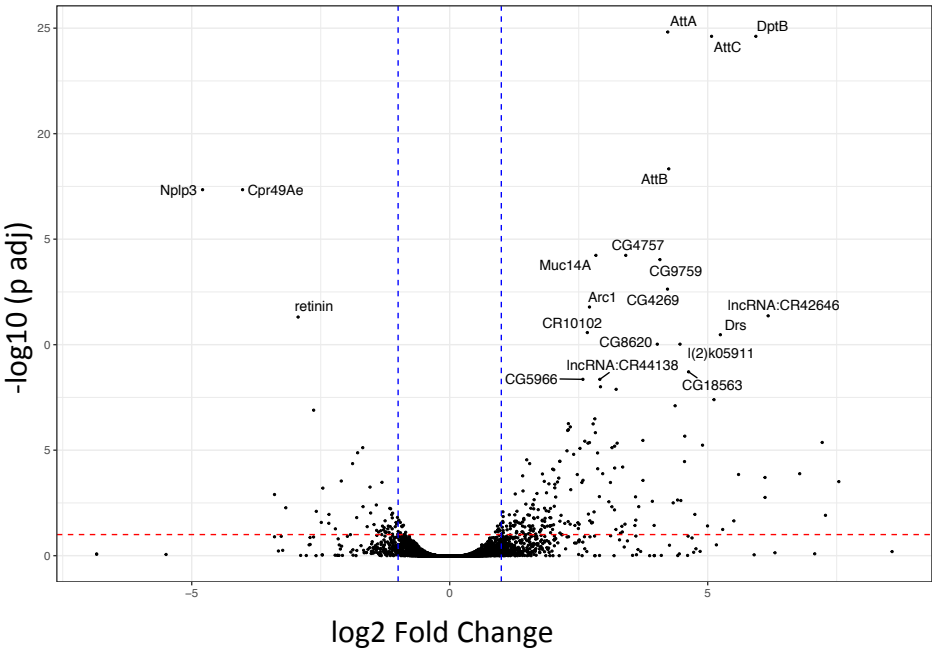


Supplementary Figure 3. Enrichment of H3K9me2 (in 5kb windows) for 1Mb upstream and downstream of the euchromatin/ pericentromere boundary, indicated by the dotted red line, on the 5 major chromosome arms. Subtraction plots show higher H3K9me2 signal in young (blue) or old (red) flies.

A. XX female old vs. young

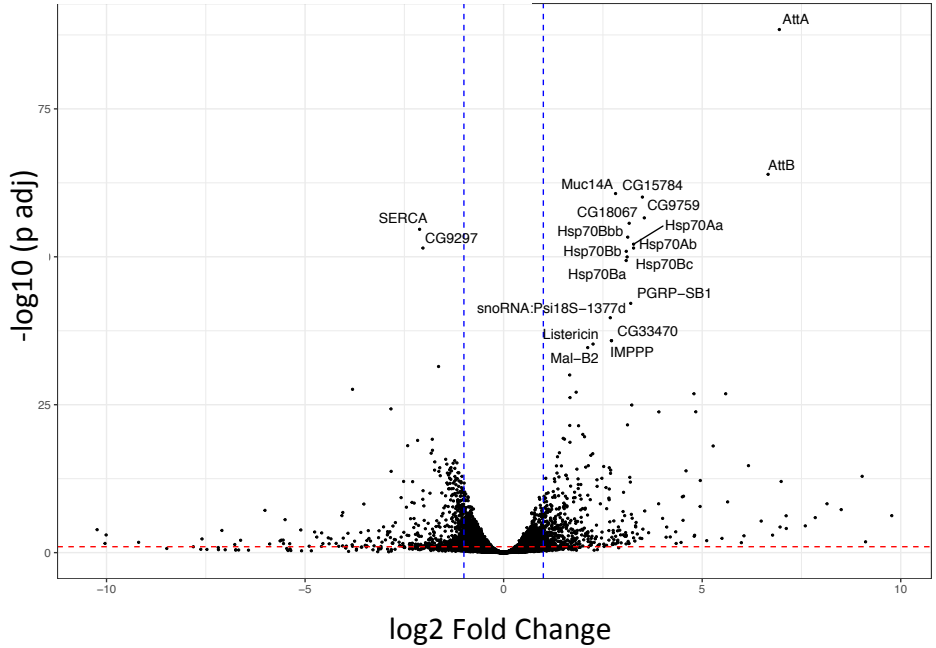


B. XY male old vs. young

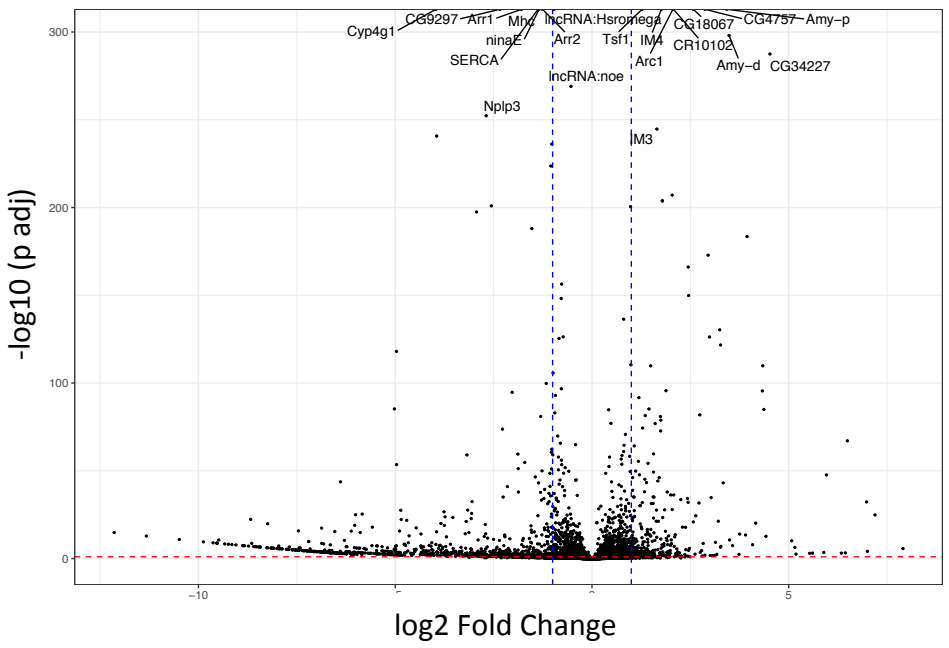


Supplementary Figure 4.

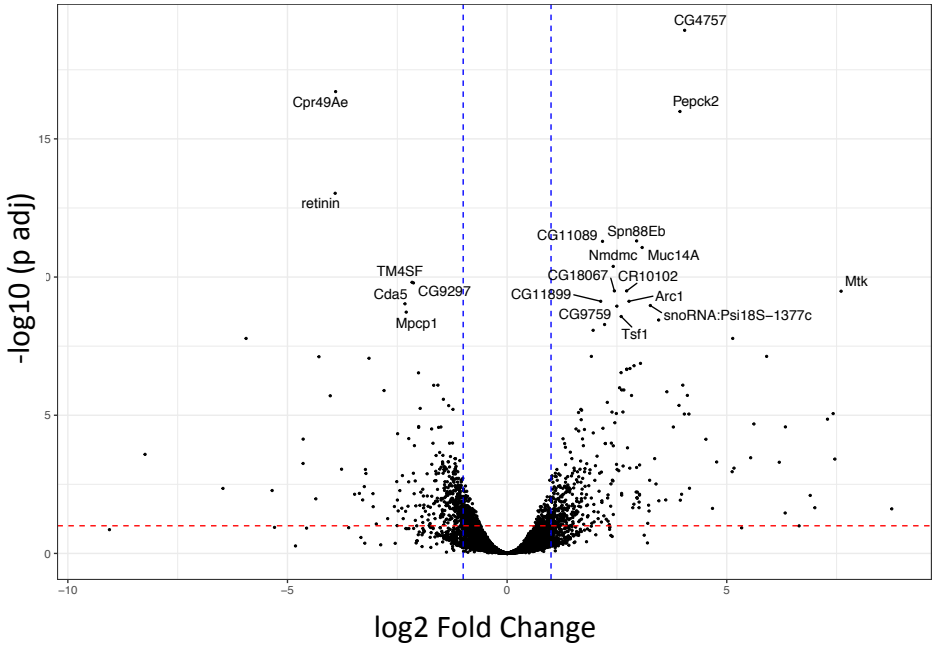
C. X0 male old vs. young



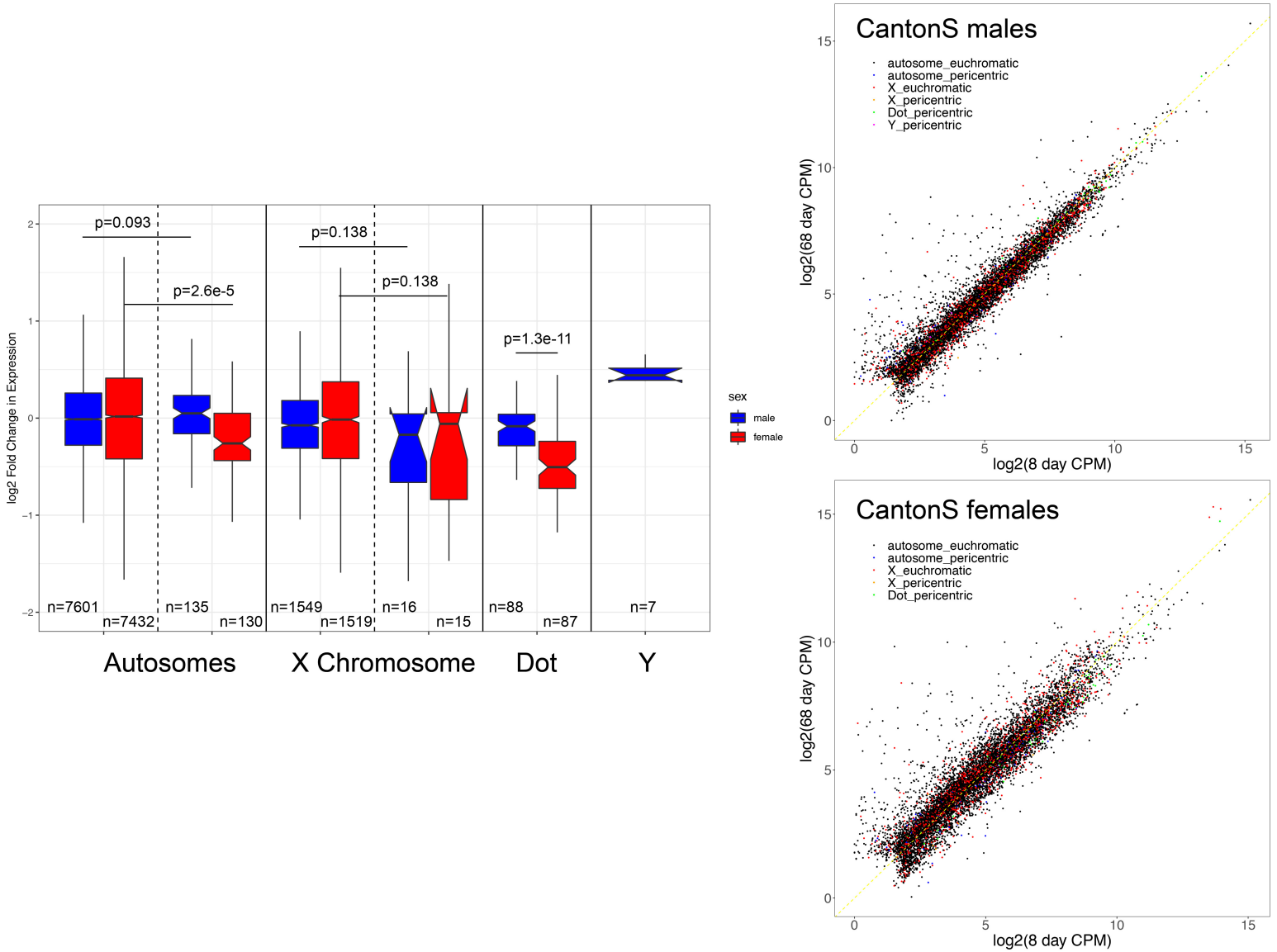
E. XYY male old vs. young



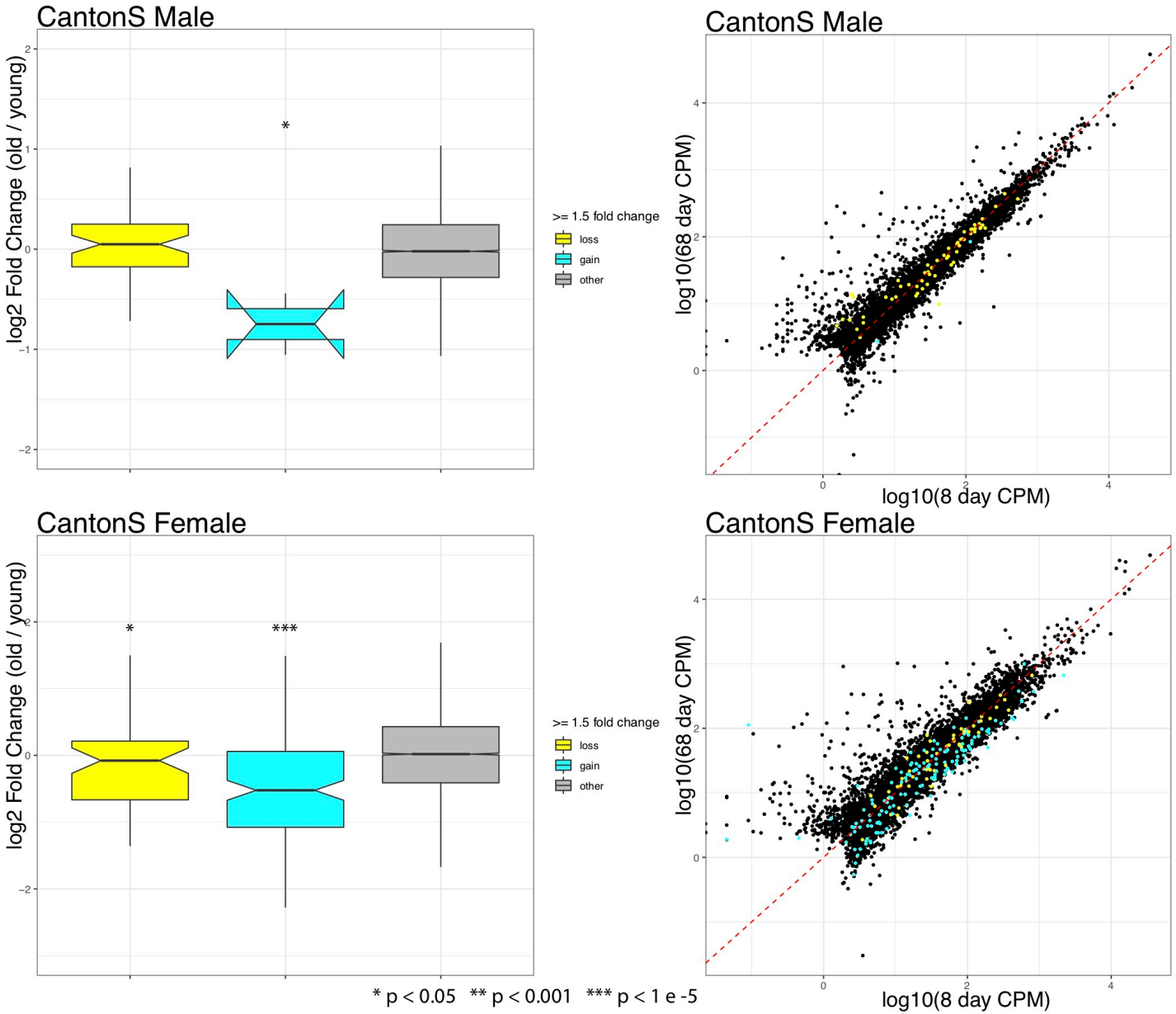
D. XXY female old vs. young



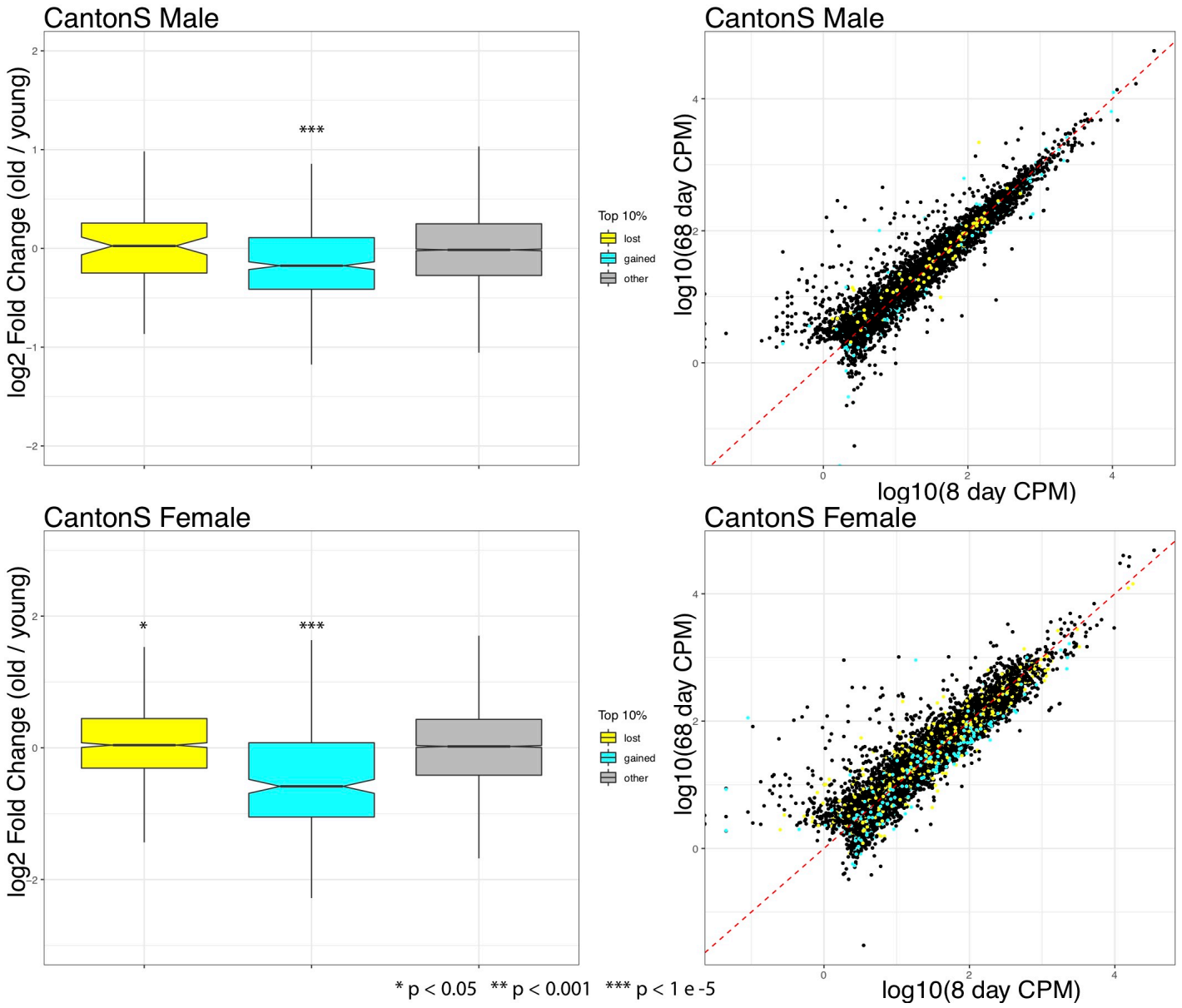
Supplementary Figure 4. Volcano plots marking the top 20 significantly differently expressed genes during aging for A. XX females; B. XY males; C. X0 males; D. XXY females; E. XYY males.



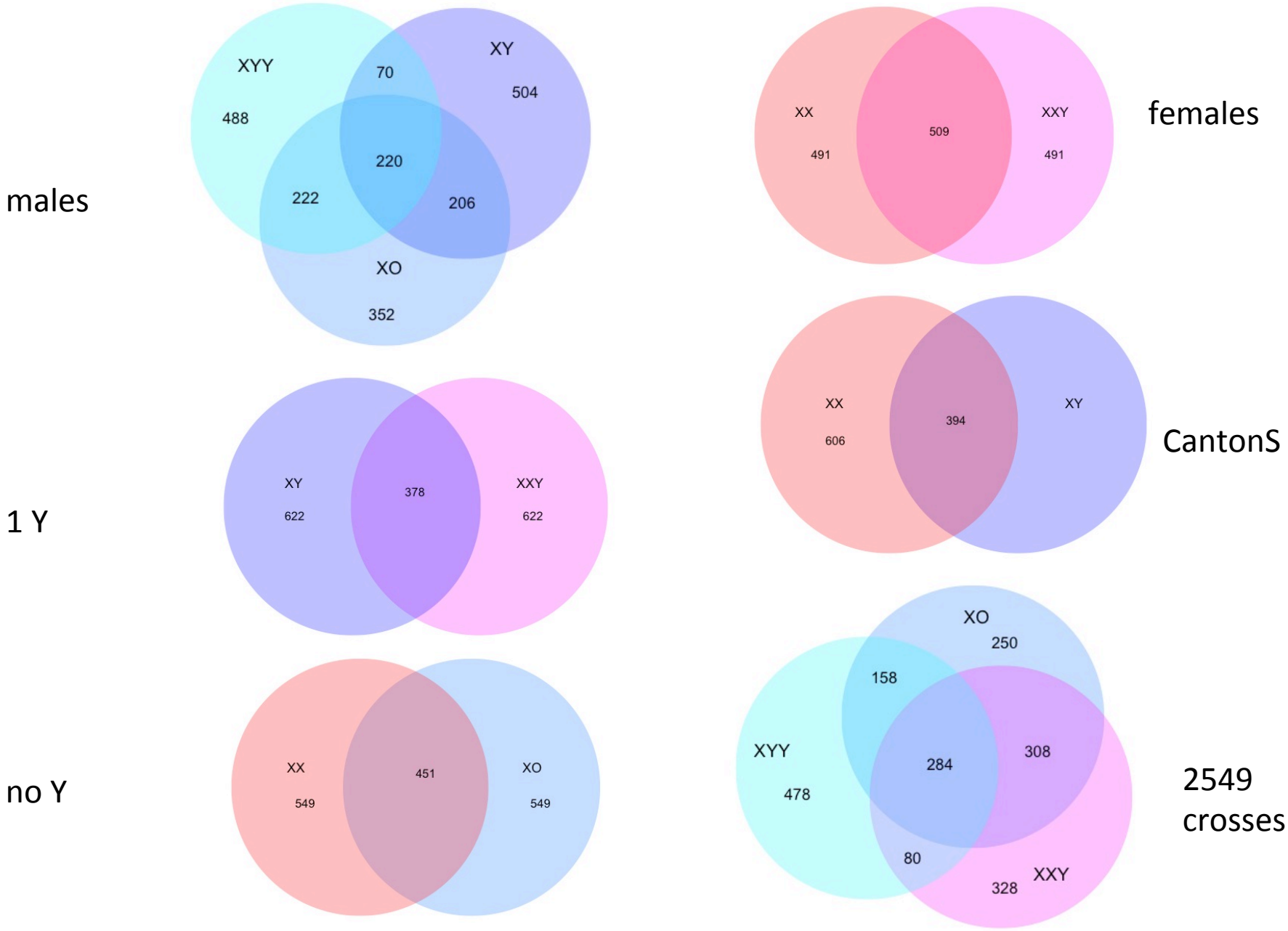
Supplementary Figure 5. Expression values of all genes, averaged across replicates, of young and old males and females by chromosome location, as annotated in the Release 6 of the *D. melanogaster* genome. We only consider genes with at least 3 reads mapped in at least 2 replicates. Significance values are calculated using the Wilcoxon test.



Supplementary Figure 6. Expression values of genes located in 50kb windows that show either a 1.5-fold loss or 1.5-fold gain of H3K9me2 during aging in males and females. Significance values are calculated using the Wilcoxon test.

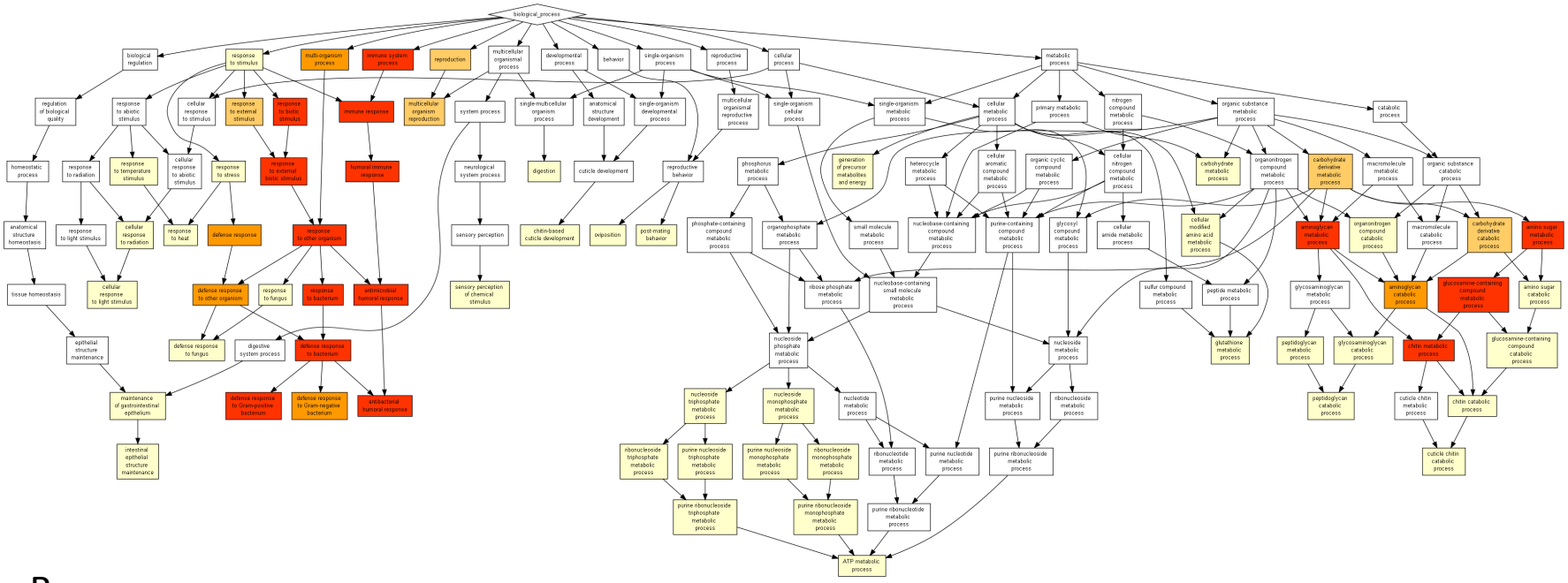


Supplementary Figure 7. Expression values of genes located in the top 10% of 50kb windows that either gain or lose H3K9me2 during aging in males and females. Significance values are calculated using the Wilcoxon test.

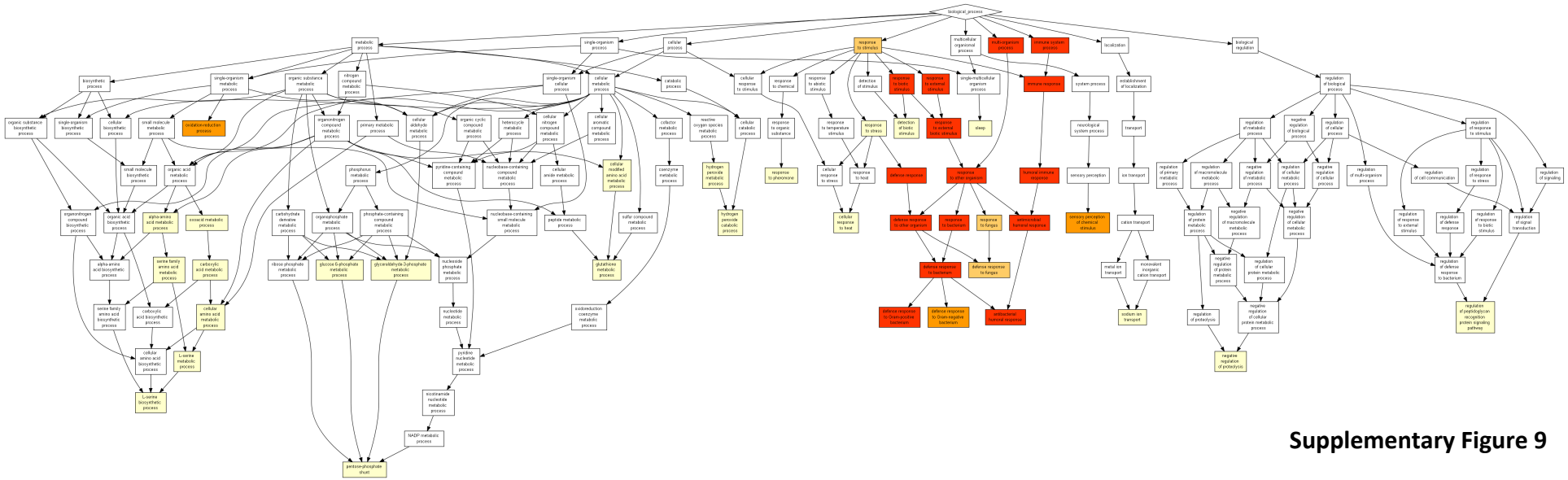


Supplementary Figure 8. Overlap of the top 1000 differentially expressed genes during aging, normalized across replicates, for various combinations of the 5 sex chromosome karyotypes examined.

A. CanS Male GO enrichment during aging

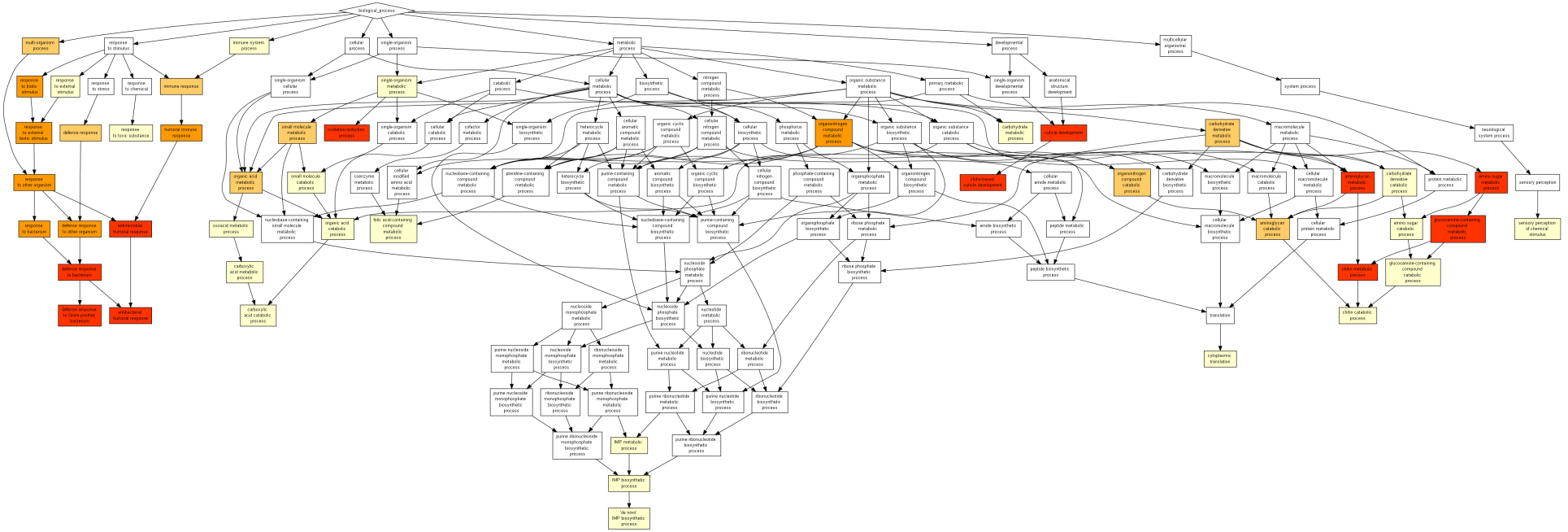


B. CanS Female GO enrichment during aging

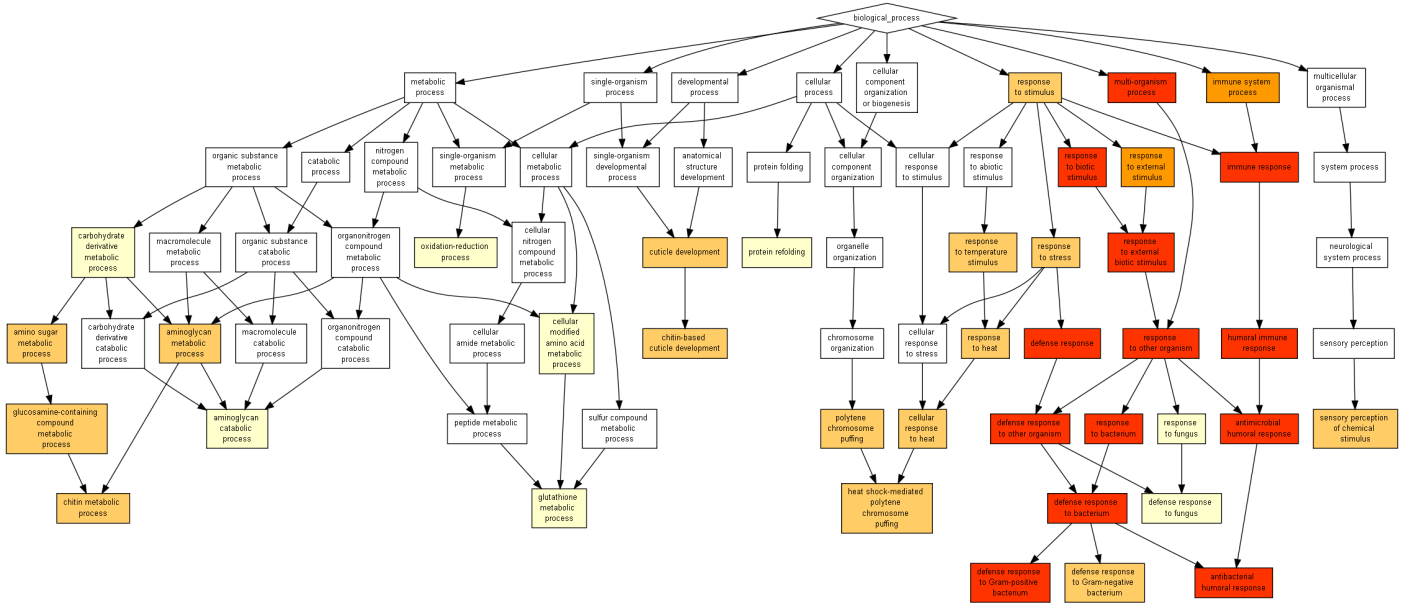


Supplementary Figure 9

C. XO male GO enrichment during aging

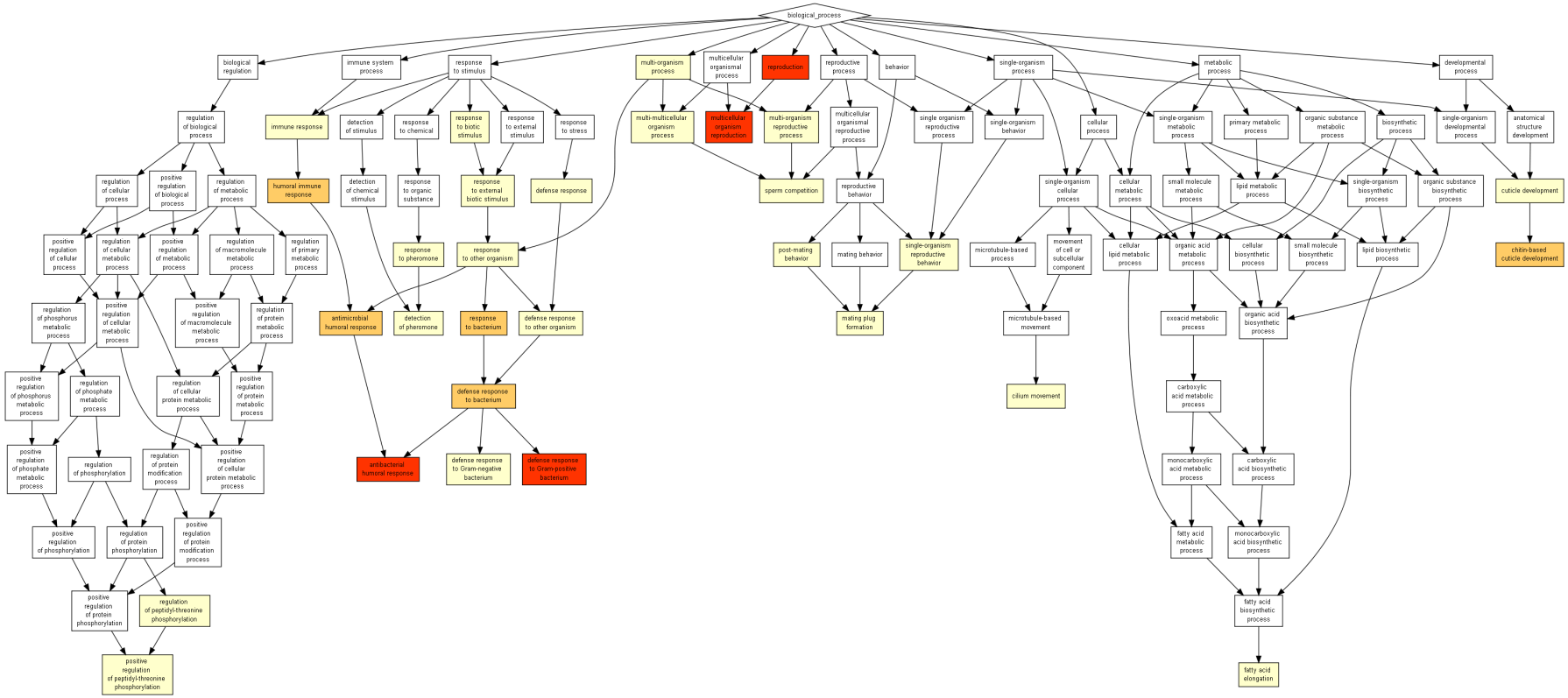


D. XXY female GO enrichment during aging



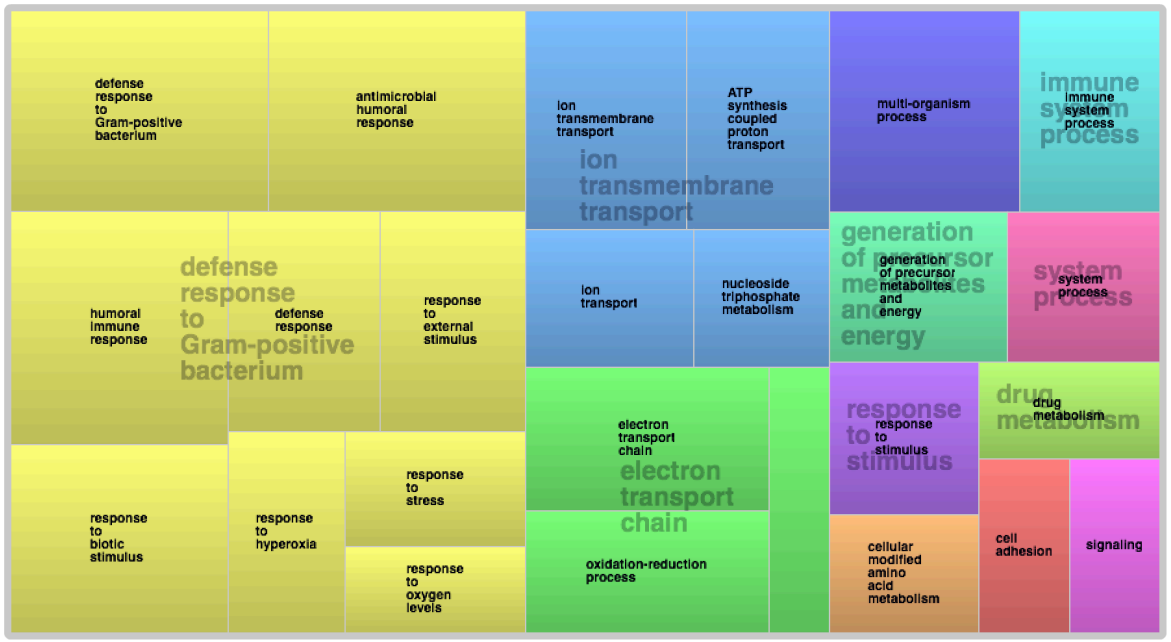
Supplementary Figure 9

E. XYY male GO enrichment during aging

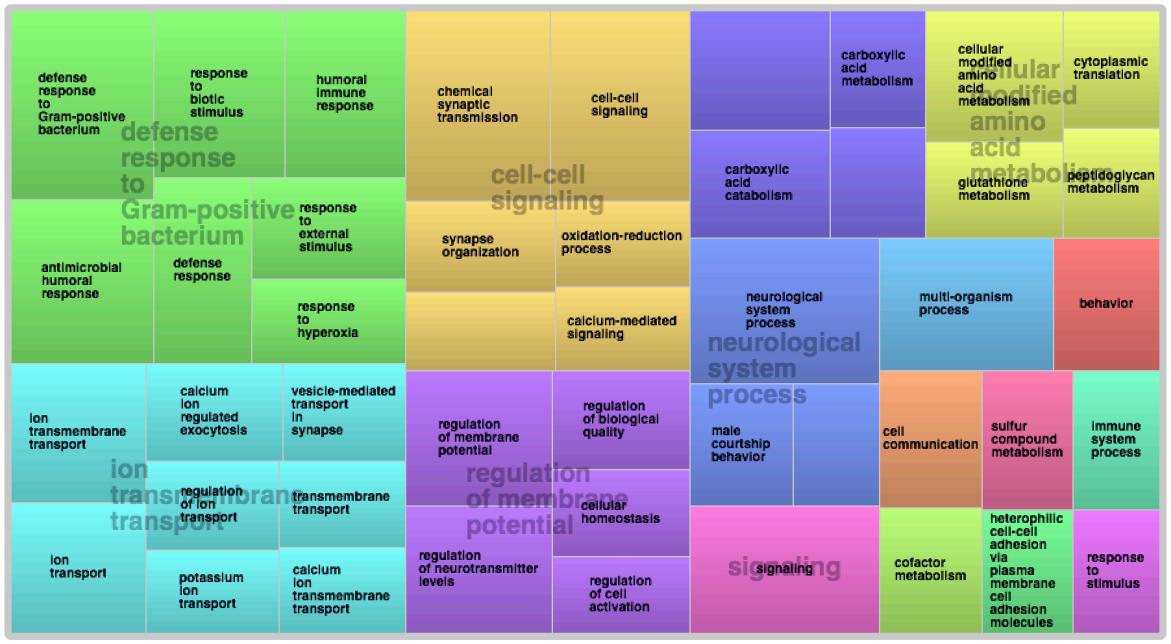


Supplementary Figure 9. GO category enrichment of genes differentially expressed during aging in wild-type Canton-S males (**A**.) and Canton-S females (**B**.), and XO males (**C**.), XXY females (**D**.), and XYY males (**E**.). Genes were ranked by their fold change in expression, averaged across replicates, regardless of direction, and submitted to Gorilla (Eden et al. 2009)} for GO category enrichment analysis.

A. CanS Male GO enrichment during aging

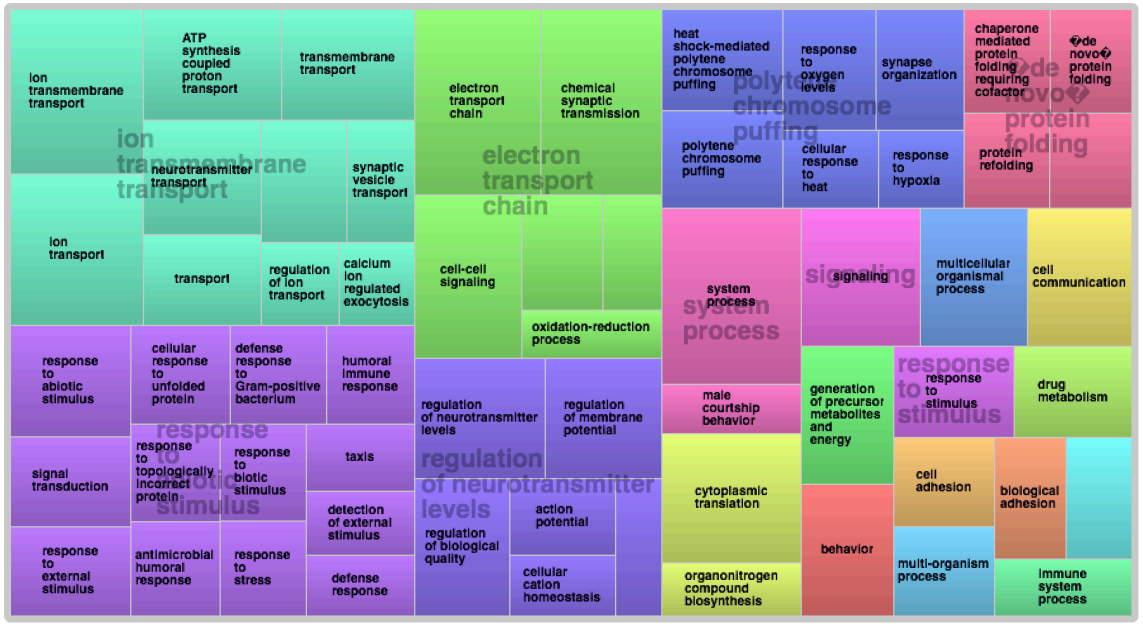


B. CanS Female GO enrichment during aging

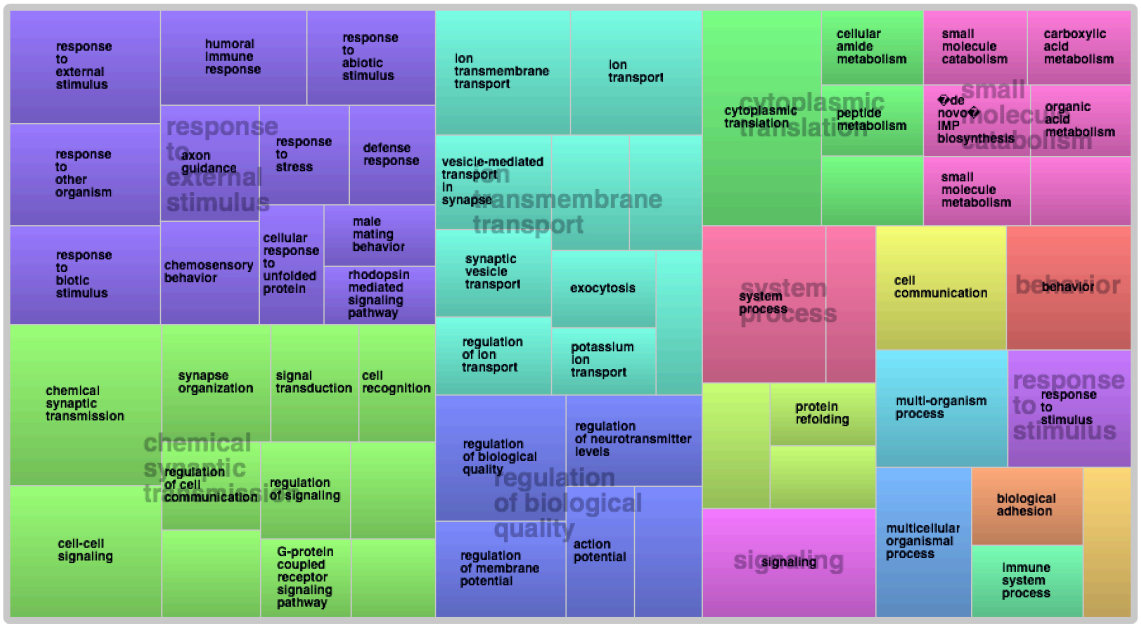


Supplementary Figure 10

C. XO male GO enrichment during aging

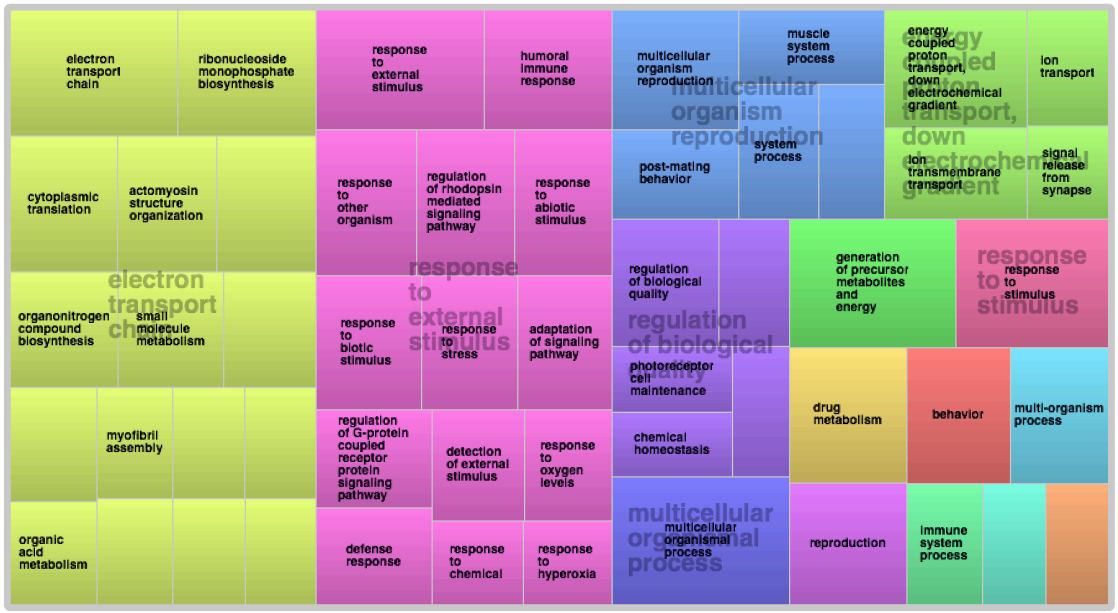


D. XXY female GO enrichment during aging

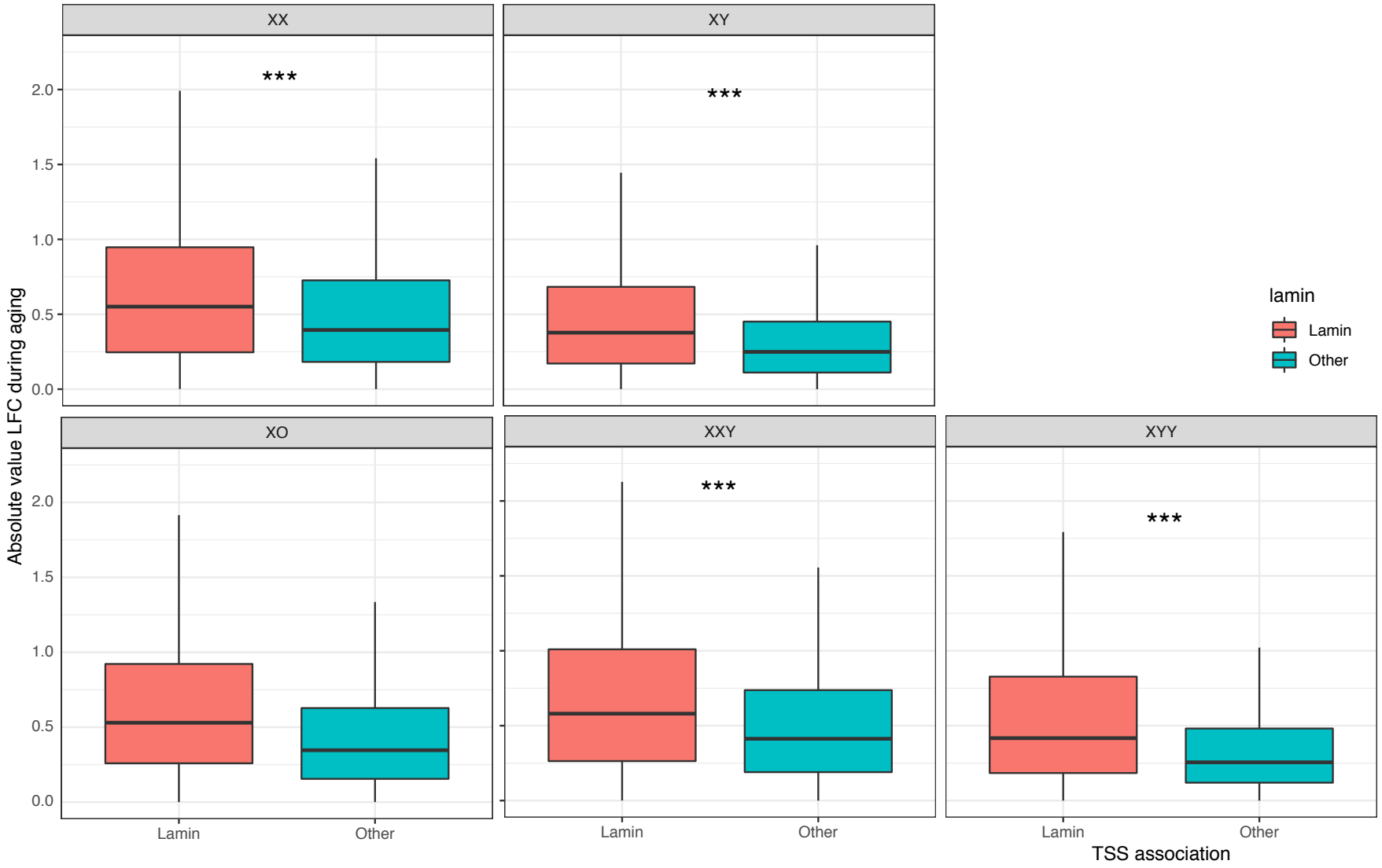


Supplementary Figure 10

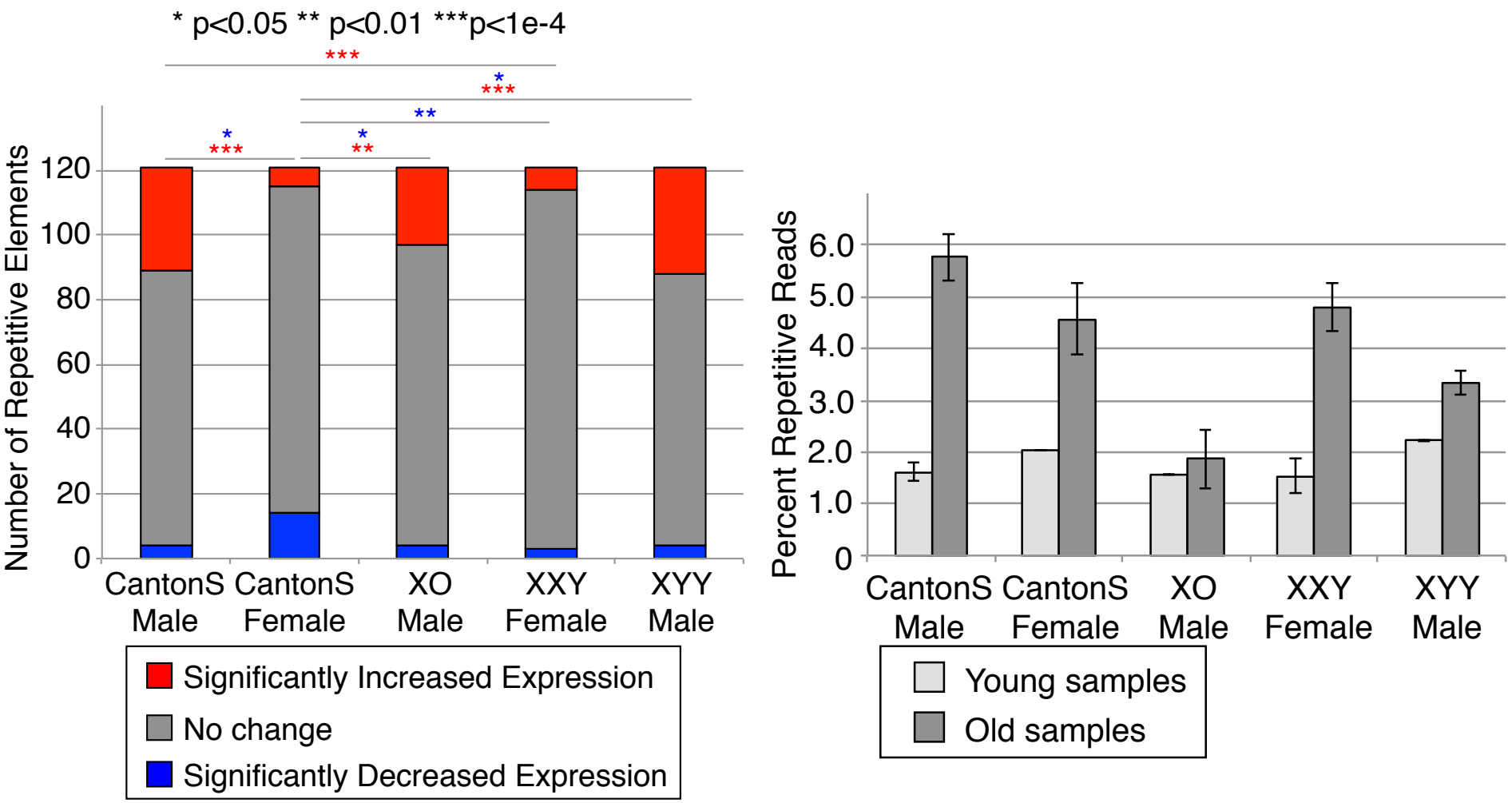
E. XYY male GO enrichment during aging



Supplementary Figure 10. TreeMap view using Revigo (Supek et al. 2011) of enriched GO terms during aging in wild-type Canton-S males (**A**.) and Canton-S females (**B**.), and XO males (**C**.), XXY females (**D**.), and XYY males (**E**.). Each rectangle is a single cluster representative. The representatives are joined into 'superclusters' of loosely related terms, visualized in different colors. Size of each rectangle reflects the P value of that GO term.



Supplementary Figure 11. Lamin-associated genes in the brain are mis-expressed during aging. Genes are classified as lamin-associated if their promoter (distal TSSs) overlaps with lamin-associated domains in central brain (from Pindyurin et al. 2018). (***$p<10^{-5}$, Wilcoxon test).



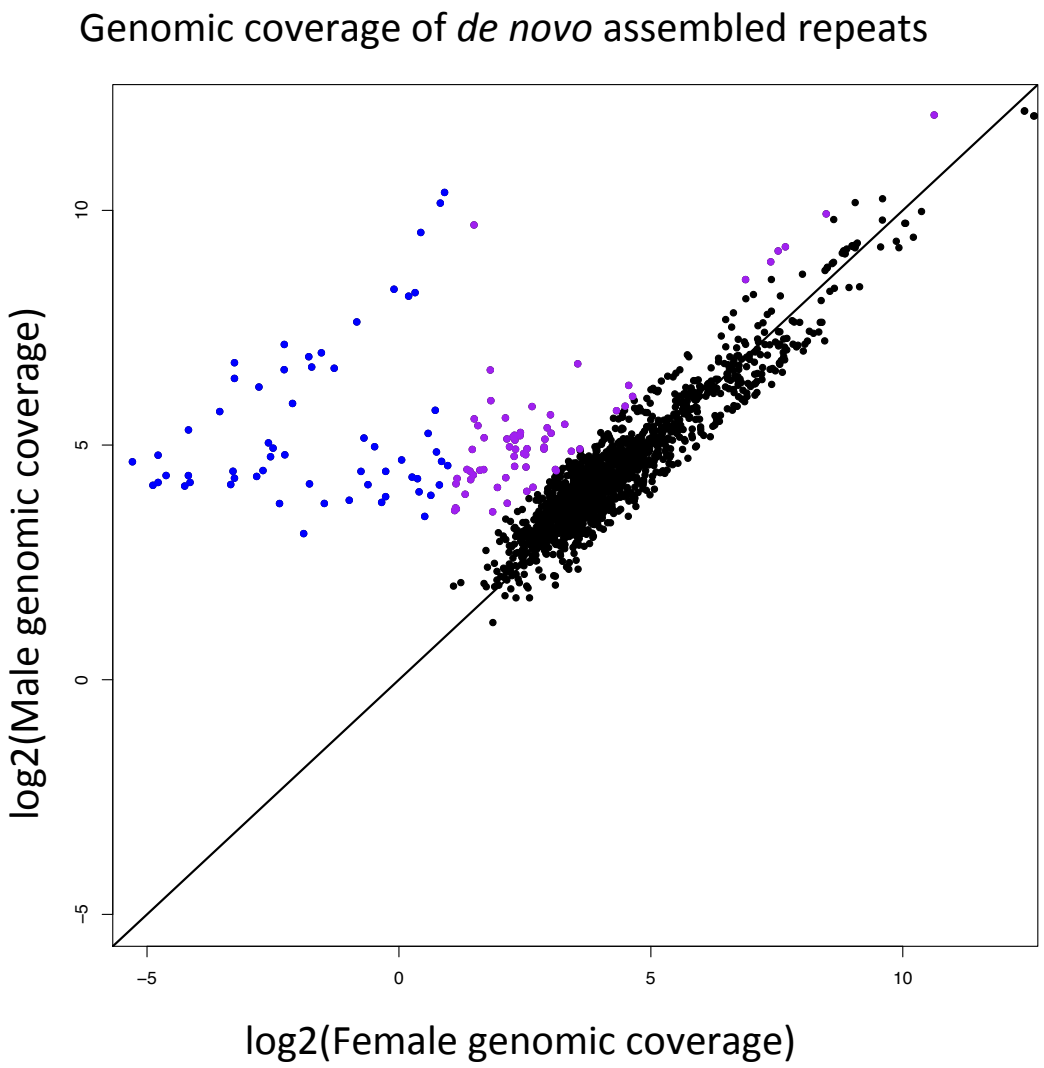
Supplementary Figure 12. Number of repeats that show a significant increase (red) or decrease (blue) in expression during aging as a fraction of all repeats from the FlyBase consensus repeat library, with significance estimated using standard errors from replicate datasets. Significance is calculated using Fisher's exact test, with red stars indicating significance for repeats that increase in expression, and blue stars indicating significance for repeats that decrease in expression during aging. We also show the estimates of the total fraction of RNA-seq reads that map to the FlyBase consensus repeat library, with error bars calculated from replicate datasets, for young and old samples from each of the 5 karyotypes.

Male specific:
Mcovg>10
Fcovg<2

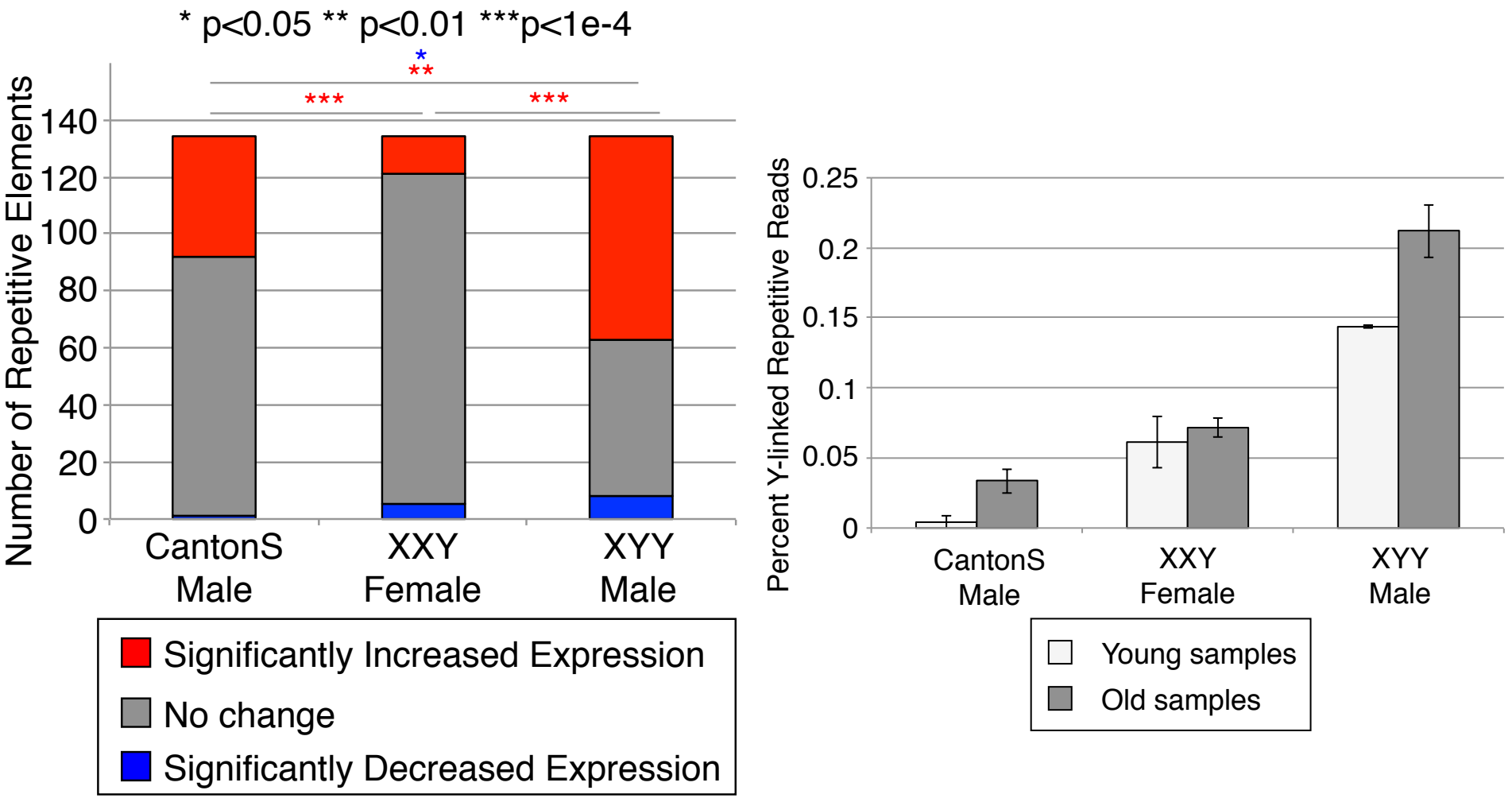
Male biased:
Mcovg>10
Fcovg>2
Mcovg>2.5xFcovg

Both Male specific and Male biased repeats are putatively Y-linked

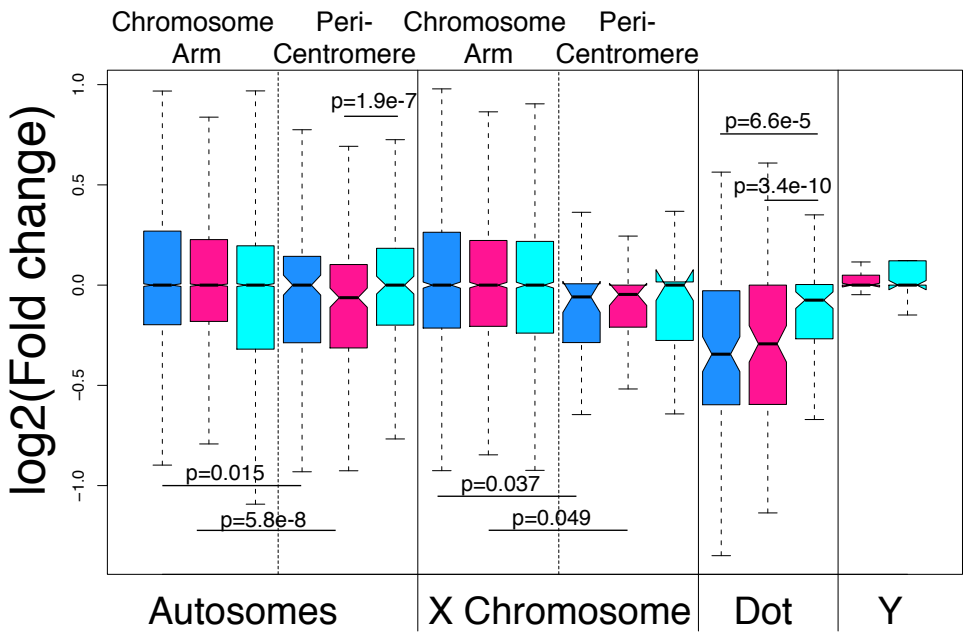
Unbiased

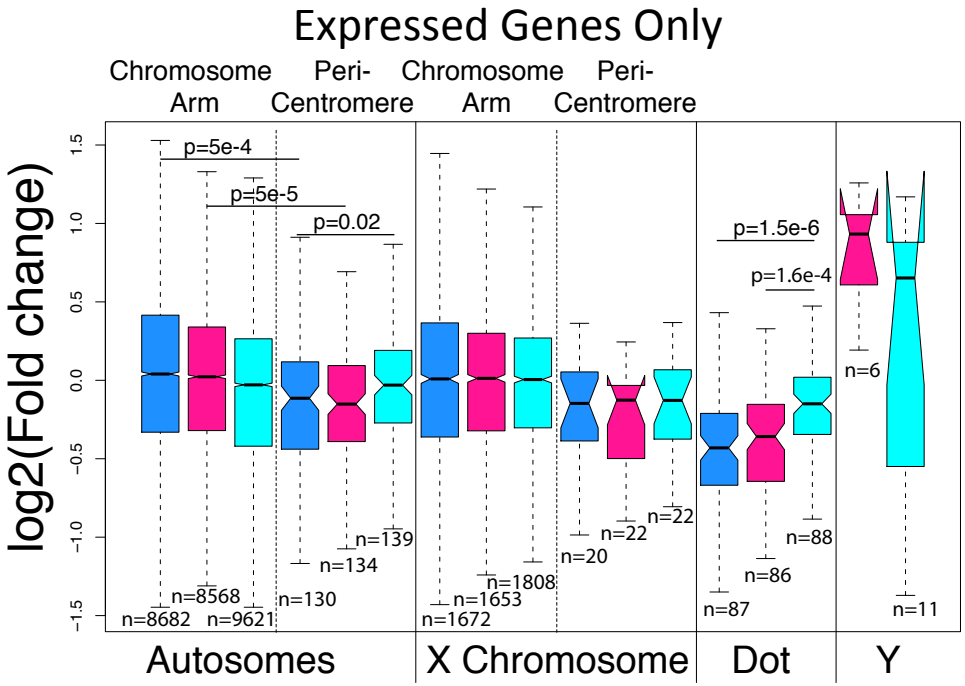


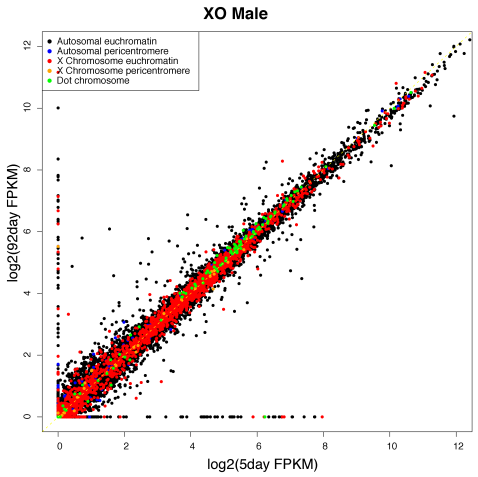
Supplementary Figure 13. Male vs. female genomic coverage of *de novo* assembled repeats, with putatively Y-linked repeats indicated in blue and purple as those with male-specific or highly male-biased genomic coverage patterns (taken from Brown et al. 2020).

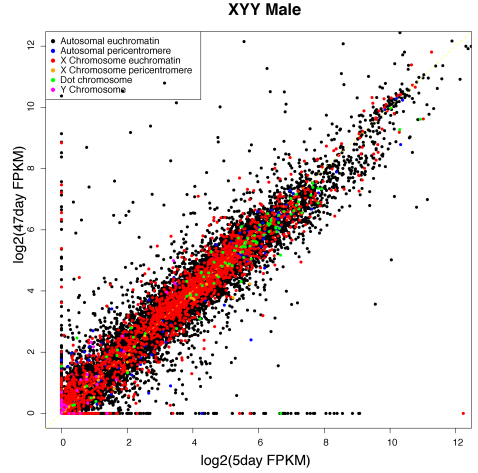


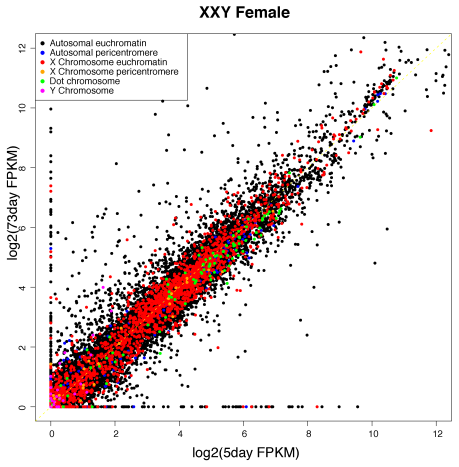
Supplementary Figure 14. Number of putative Y-linked repeats that show a significant increase (red) or decrease (blue) in expression during aging as a fraction of all repeats from a male-specific repeat library (see **Figure S12**), with significance estimated using standard errors from replicate datasets. Significance is calculated using Fisher's exact test, with red stars indicating significance for repeats that increase in expression, and blue stars indicating significance for repeats that decrease in expression during aging. We also show the estimates of the total fraction of RNA-seq reads that map to the Y-specific consensus repeat library, with error bars calculated from replicate datasets, for young and old samples from each of the 5 karyotypes.



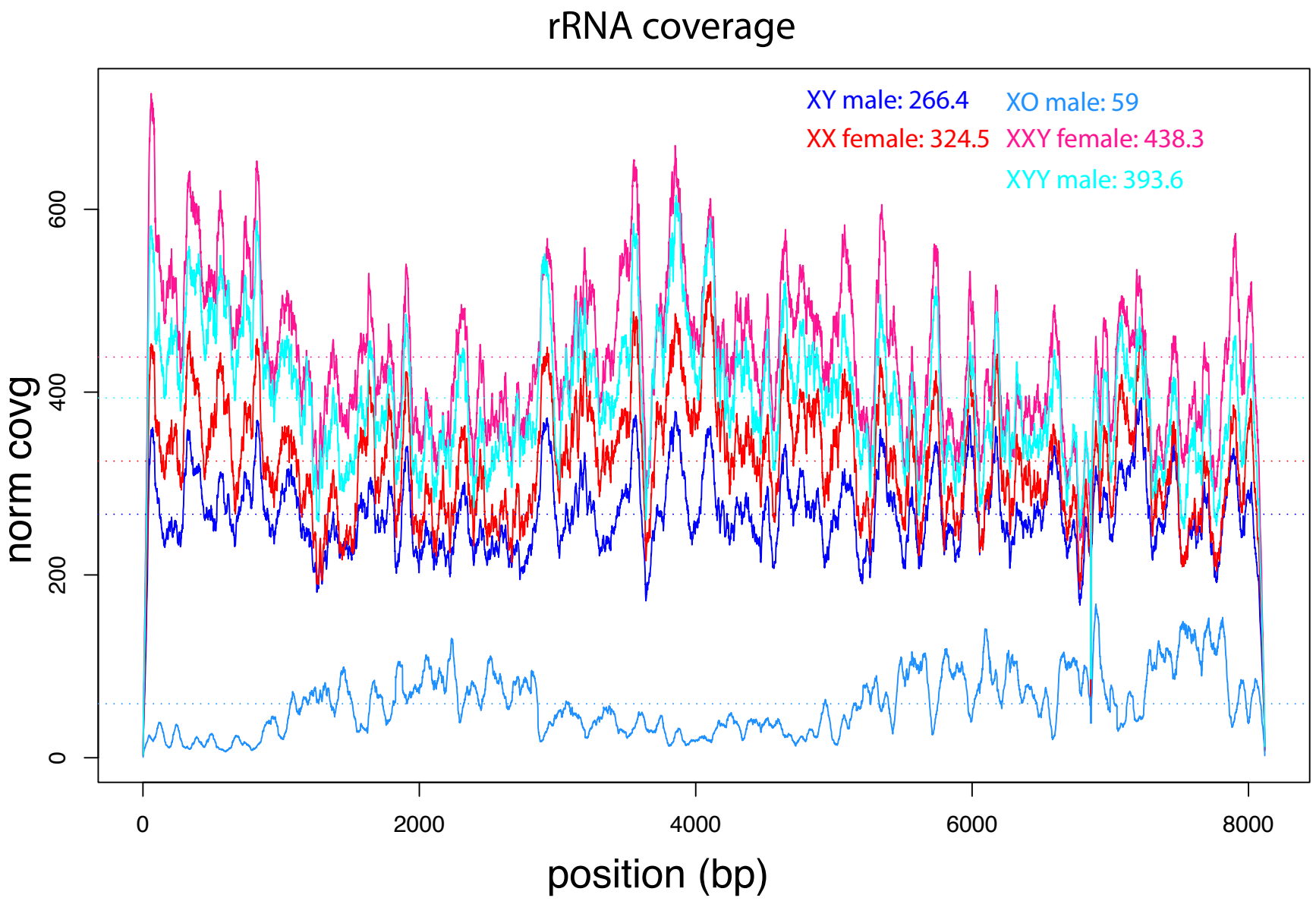




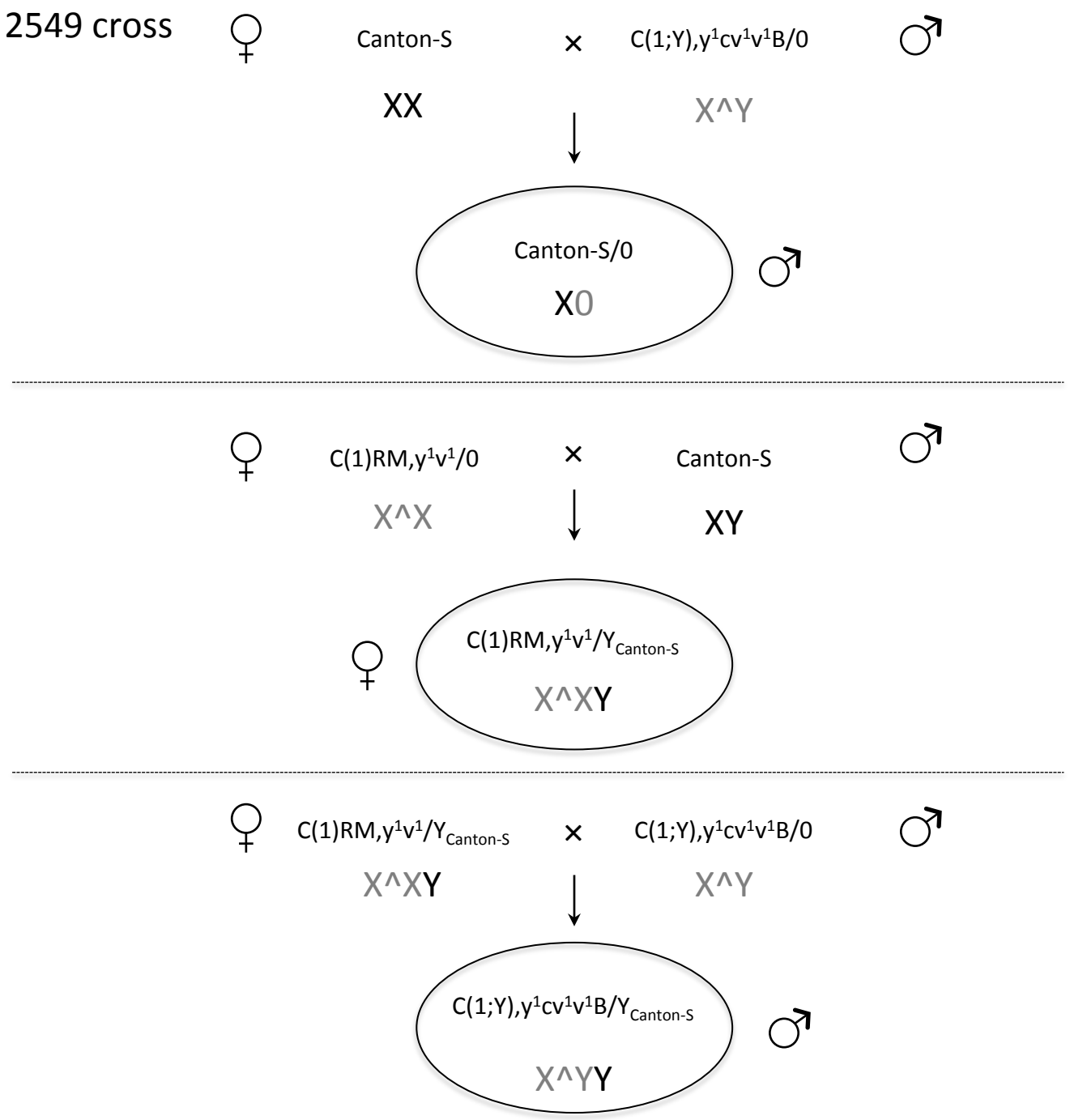




Supplementary Figure 15. Expression values of all genes, normalized across replicates, of young and old XO males, XXY females, and XYY males by chromosome location, as annotated in the Release 6 of the *D. melanogaster* genome. Significance values are calculated using the Wilcoxon test.

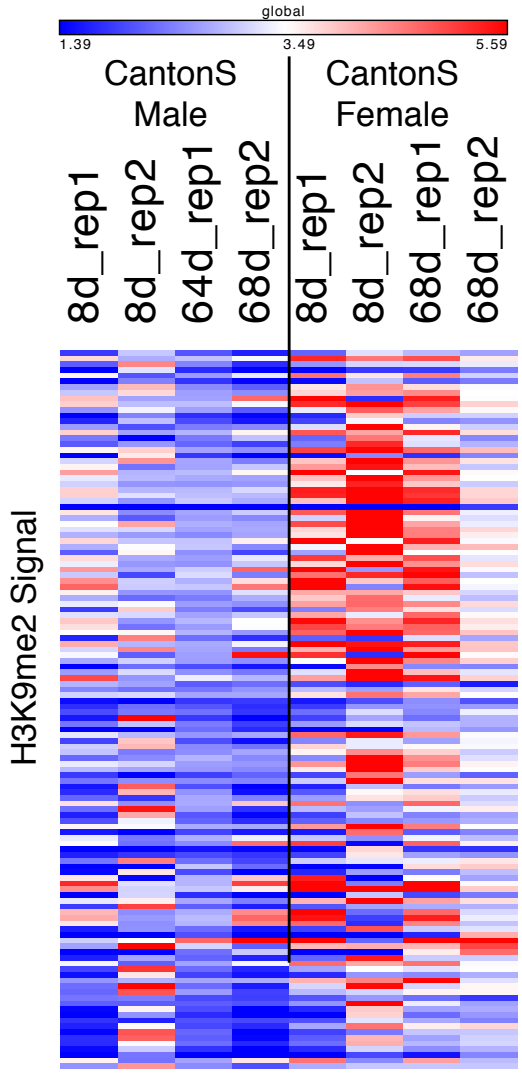


Supplementary Figure 16. Genomic coverage across the rDNA locus for flies with different sex chromosome karyotypes. Coverage is normalized to autosomes, to roughly infer rDNA copy number. The numbers show median coverage across the rDNA locus.



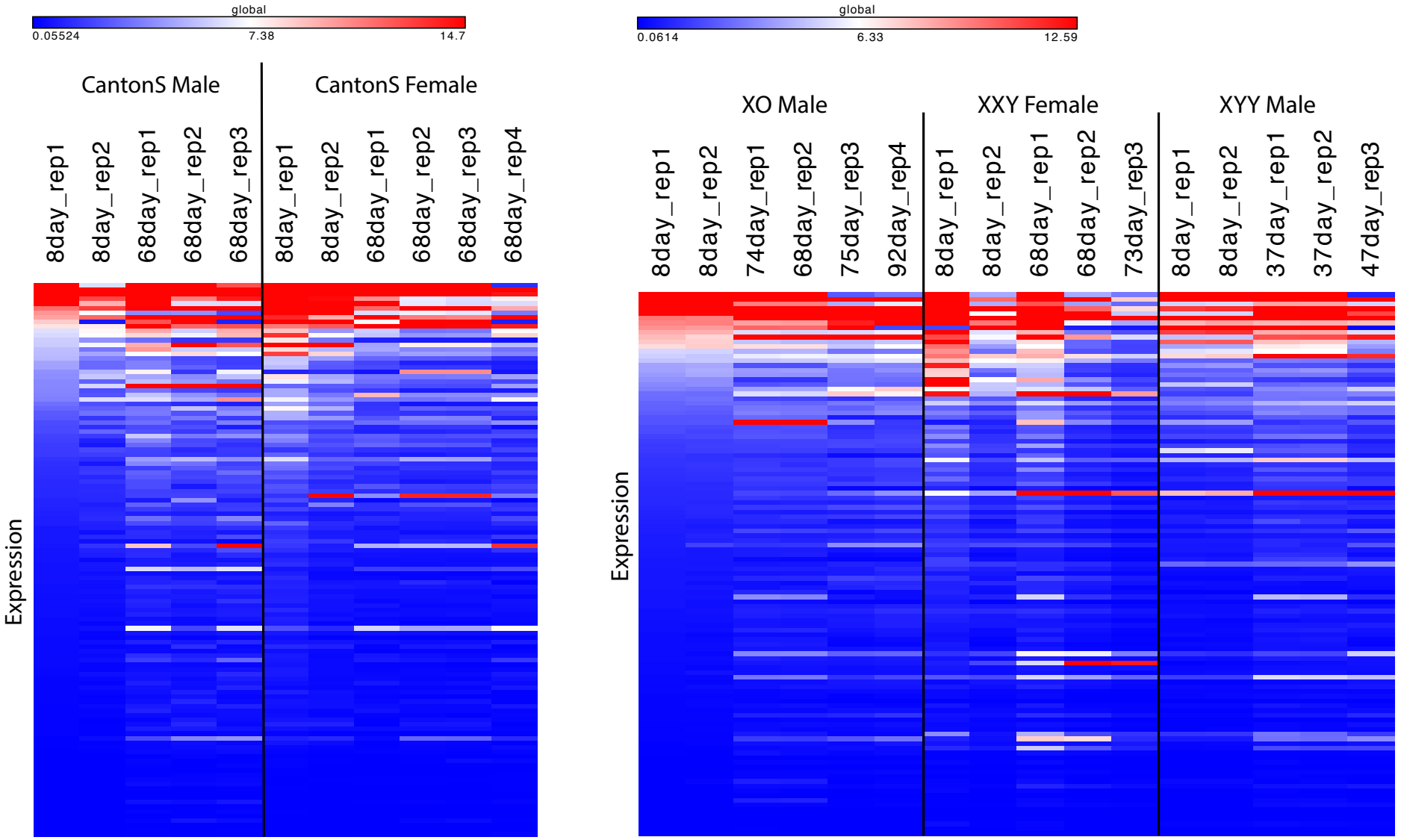
Supplementary Figure 17. Crossing scheme to generate flies with aberrant sex chromosomes.

Replicate H3K9me2 values for consensus TEs



Supplementary Figure 18. Estimates of H3K9me2 signal for the FlyBase consensus library for all replicates for all karyotypes.

Replicate expression values for consensus TEs



Supplementary Figure 19. Estimates of expression values for the FlyBase consensus library for all replicates for all karyotypes.

Supplementary Table 1. Average estimation, across all replicates, of the fraction of all RNA-seq reads that are derived from the FlyBase consensus repeat library, as well as the fold change in repetitive content during aging.

	Wild-type male	Wild-type female	XO male	XXY female	XYY male
young	1.61	2.04	1.57	1.54	2.21
old	5.76	4.56	1.87	4.80	3.33
fold change	3.57	2.23	1.19	3.12	1.51

Supplementary Table 2. Average estimation, across all replicates, of the fraction of all RNA-seq reads that are derived from the putative Y-linked consensus repeat library, as well as the fold change in repetitive content during aging.

	Wild-type male	XXY Female	XYY Male
young	0.00	0.06	0.14
old	0.03	0.07	0.21
fold change	9.12	1.17	1.48

Additional Supplementary Files (as Spreadsheet-based Tables)

Supplementary Table 3. Gene expression changes during aging. A. Expression changes during aging in XX females. B. Expression changes during aging in XY males. C. Expression changes during aging in X0 males. D. Expression changes during aging in XXY females. F. Expression changes during aging in XYY males.

Supplementary Table 4. Enriched GO categories of genes that significantly changed expression changes during aging. A. Enriched GO categories in XX females. B. Enriched GO categories in XY males. C. Enriched GO categories in X0 males. D. Enriched GO categories in XXY females. F. Enriched GO categories in XYY males.