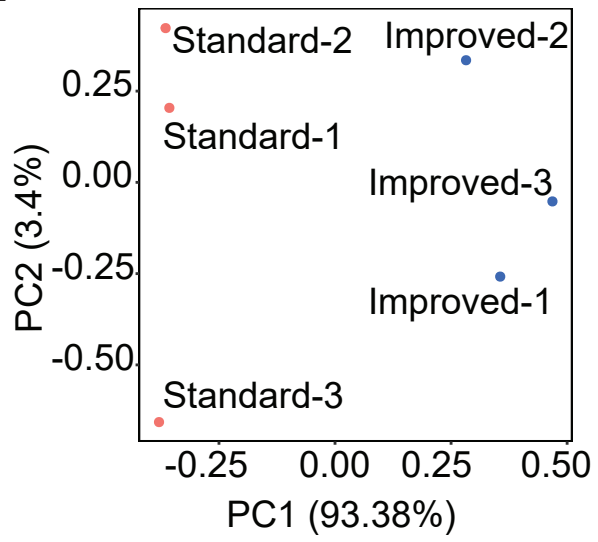
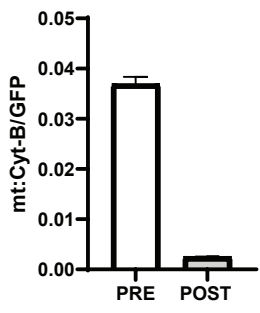
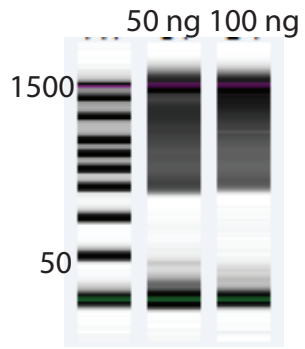


**A**

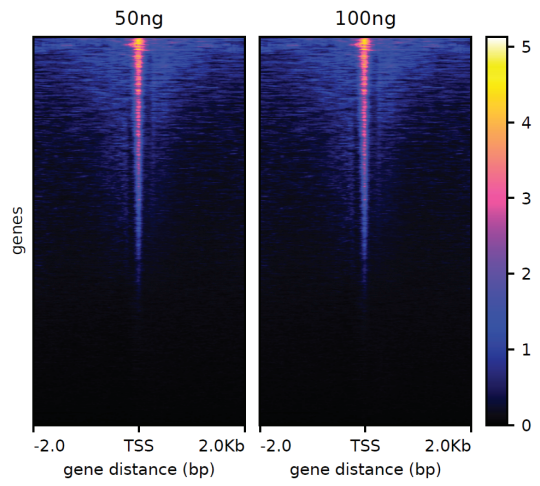
**A**



**B**



**C**

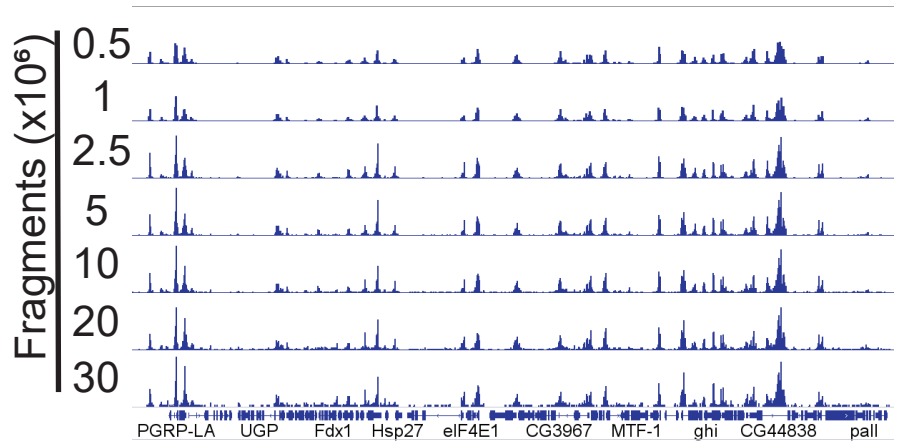


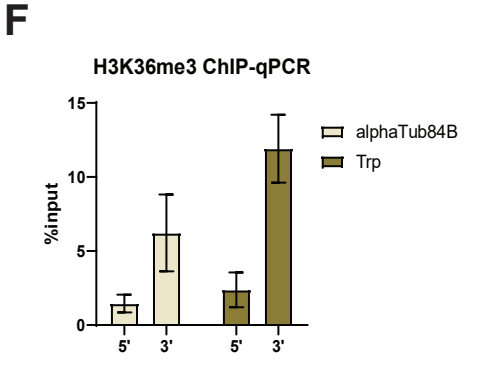
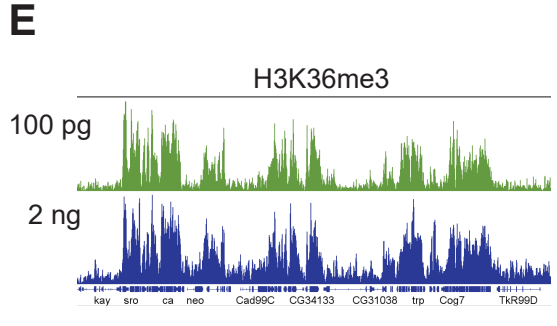
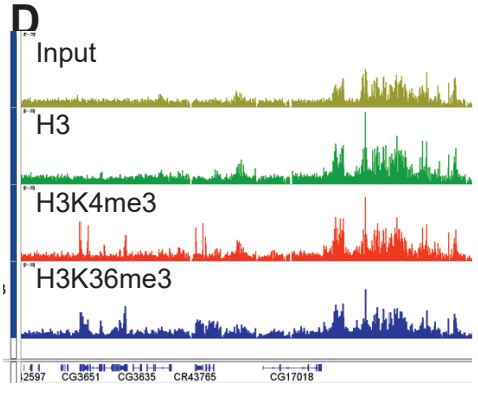
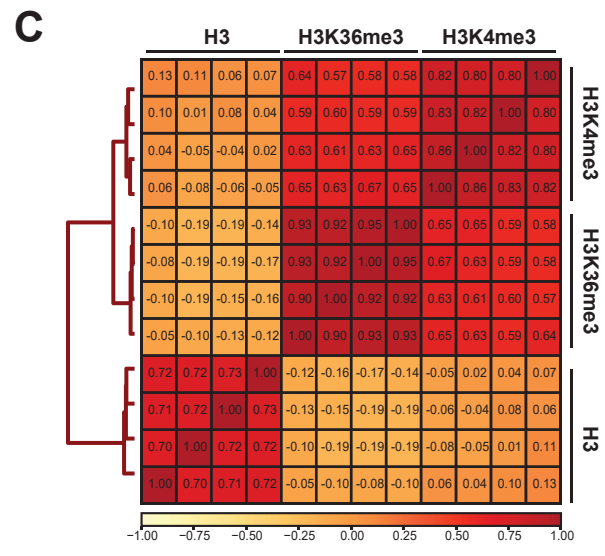
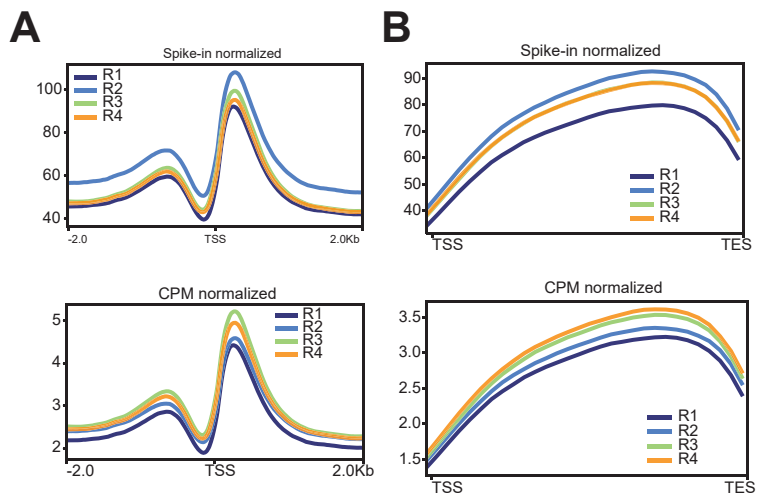
**A**

# peaks passing IDR < 0.05

R1	R2	R3	R4	
1.00	0.70	0.77	0.76	R1
	1.00	0.61	0.65	R2
		1.00	0.66	R3
			1.00	R4

**B**





## Figure Supplemental legends

### Figure Supplemental 1

Bar plot showing DNA yields when the “improved” NIE approach is used with flies heterozygous for both Rh1-Gal4 and UAS-GFP<sup>KASH</sup> transgenes (mean  $\pm$  standard deviation (SD), n=4)

### Figure Supplemental 2.

Principal Component Analysis (PCA) of gene counts for RNA-seq data comparing the ‘standard’ and ‘improved’ datasets.

### Figure Supplemental 3

A. Bar plot showing qPCR enrichment for GFP and mitochondrial DNA (mt:Cyt-B) in the PRE and POST-NIE. (Mean  $\pm$  SD; n=3). B. Tapestation profiles of Omni-ATAC libraries prepared using 50 ng and 100 ng datasets. C. Heatmaps showing CPM-normalized Omni-ATAC signal for 50 ng- and 100 ng-associated datasets.

### Figure Supplemental 4.

A. Pair-wise comparison of irreproducible discovery rate (IDR) values of peaks that pass the 0.05 threshold. B. Genome browser inspection of down-sampled CPM-normalized Omni-ATAC signal used for FRiP score analysis. Genes are shown in blue.

### Figure Supplemental 5.

A. H3K4me3 Metaplots of Spike-in (top) and CPM normalized (bottom) data. B. H3K36me3 Metaplots of Spike-in (top) and CPM normalized (bottom) data. C. Spearman correlation heatmap of input-normalized ChIP-seq data comparing samples based on used antibody for each ChIP reaction. Spearman’s rank scores are based on read distribution over binned genome. D. Genome browser inspection of CPM-

normalized Input (Dark yellow), H3 (Green), H3K4me3 (Red) and H3K36me3 (blue) signal. E. Genome browser inspection of CPM-normalized H3K36me3 signal comparing libraries made with 100 pg or 2 ng of DNA as starting material. F. Bar plot showing H3K36me3 ChIP-qPCR enrichment as percentage chromatin input at the 5' and 3' ends of the housekeeping gene  *$\alpha$ Tub84B* and the photoreceptor-specific gene *trp* (mean  $\pm$  SD, n=3).