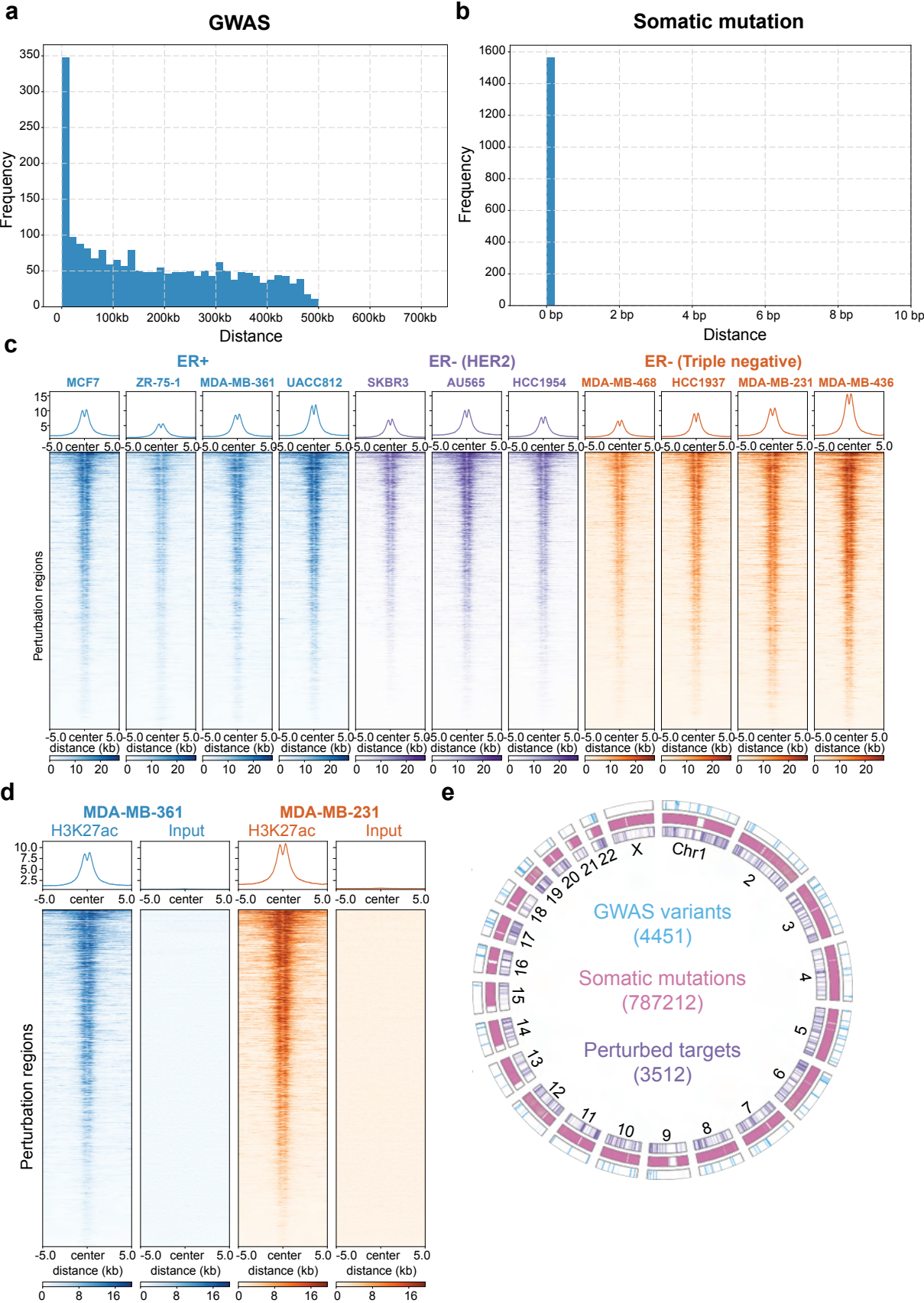
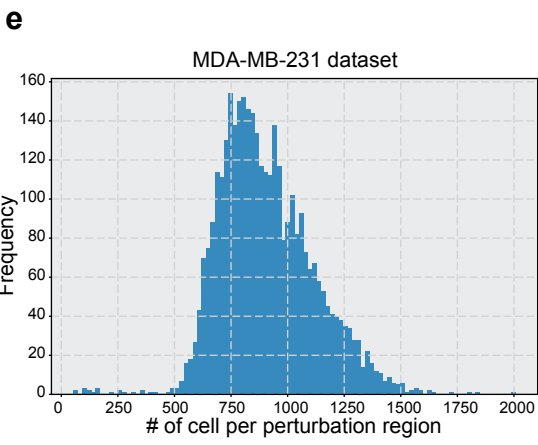
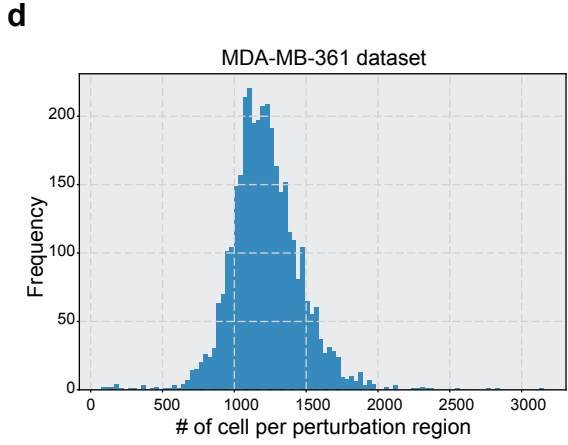
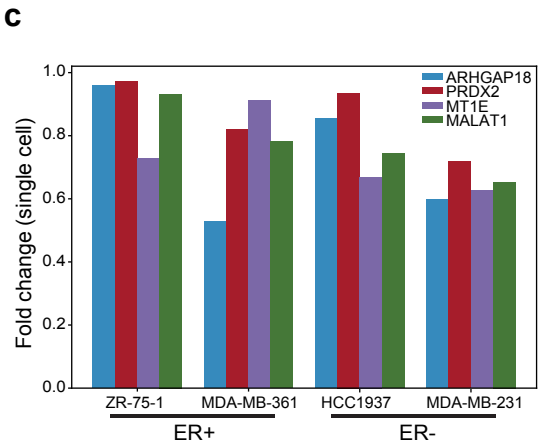
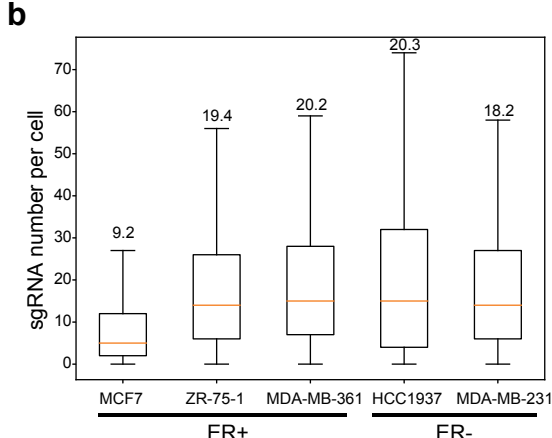
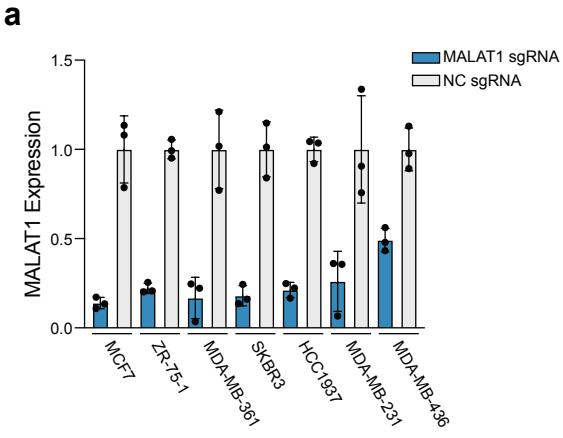


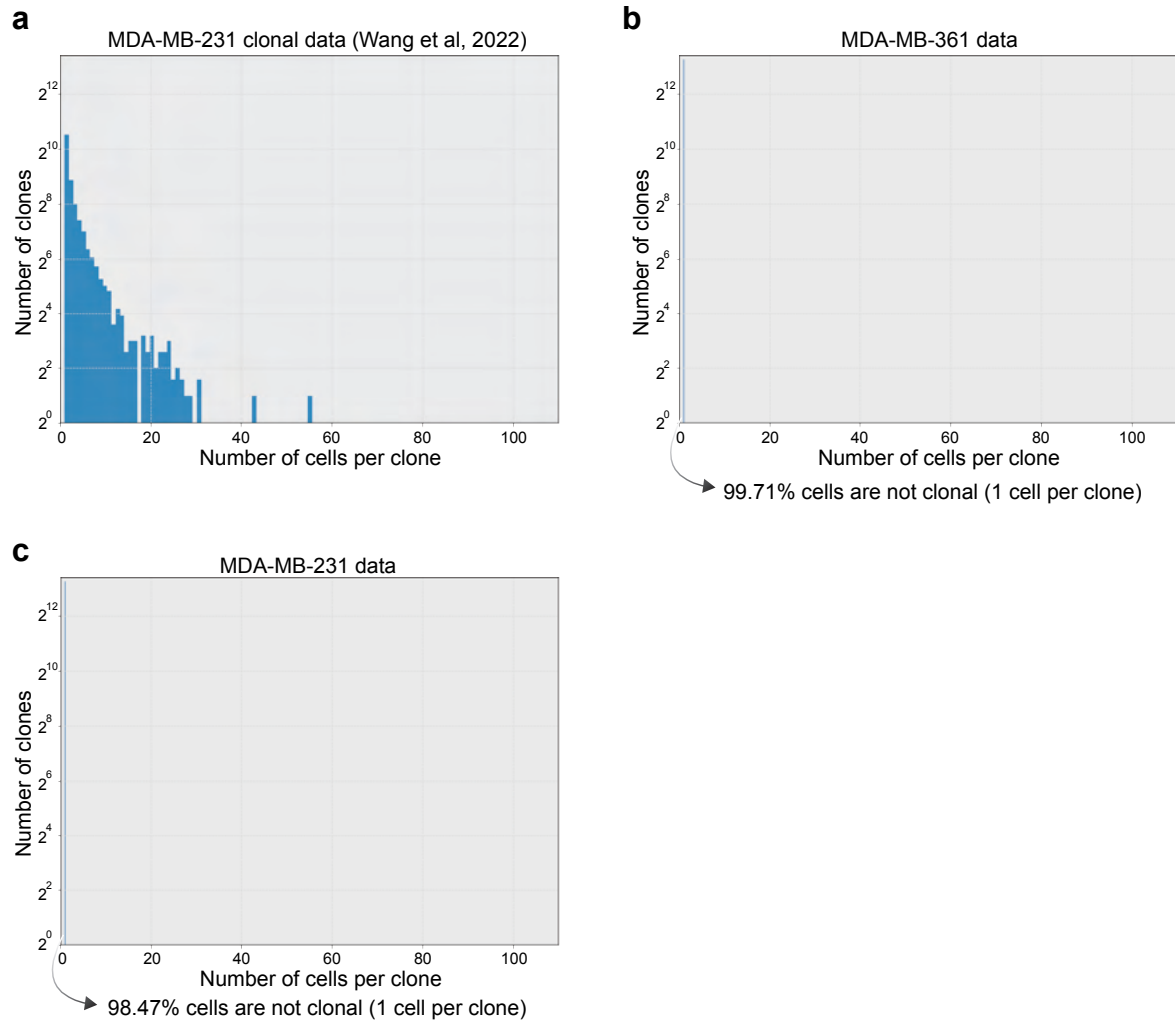
Supplementary Figure 1 - Select perturbation regions based on variants.



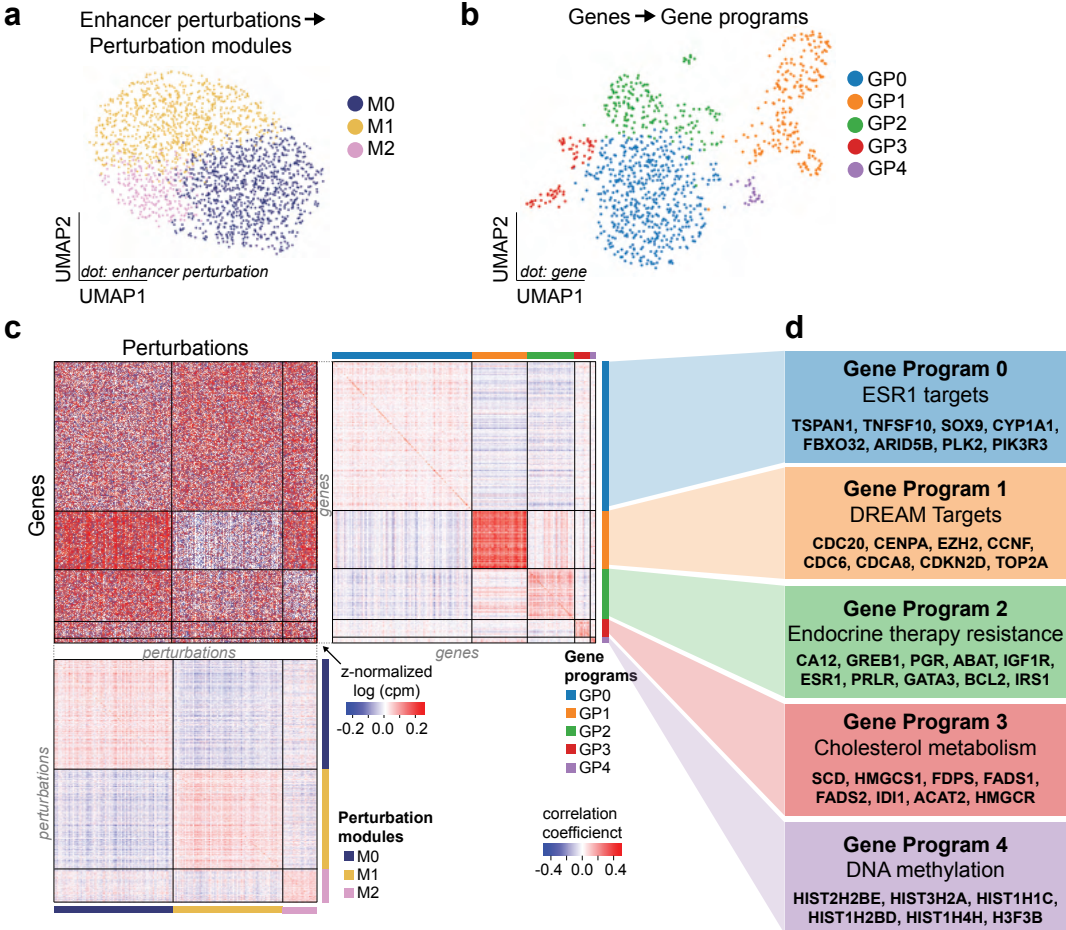
Supplementary Figure 2 - (ER+) MDA-MB-361 and (ER-) MDA-MB-231 were selected by testing different subtypes of breast cancer cell lines.



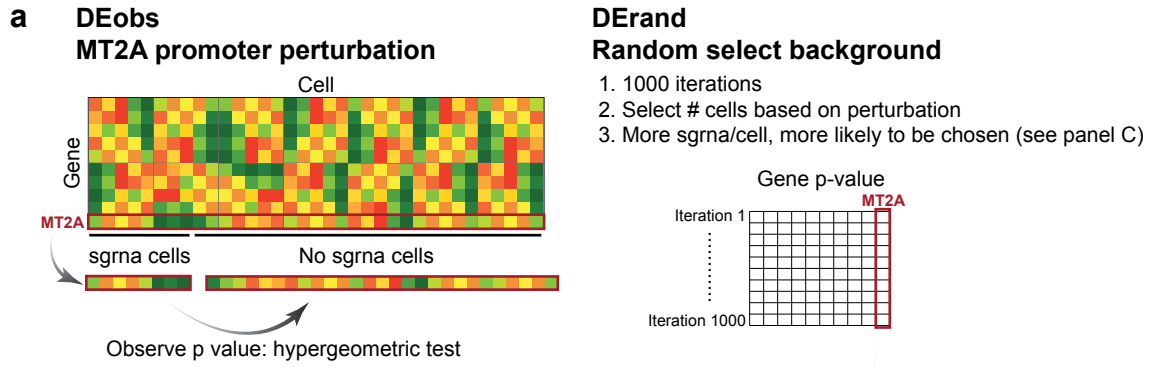
Supplementary Figure 3 - Clonality does not affect the quality of this study.



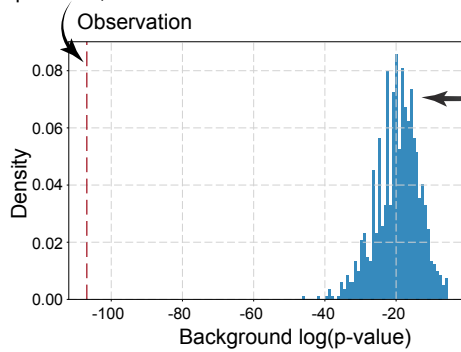
Supplementary Figure 4 - Perturbation modules and gene programs of MDA-MB-361 GWAS dataset.



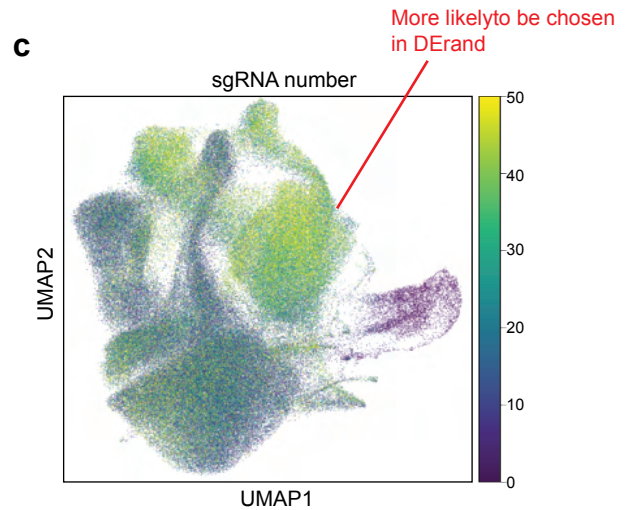
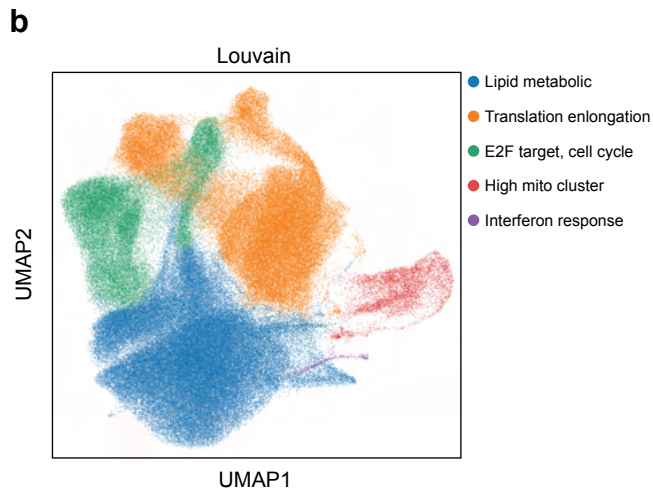
Supplementary Figure 5 - Overview of pySpade and MDA-MB-361 single cell clustering.



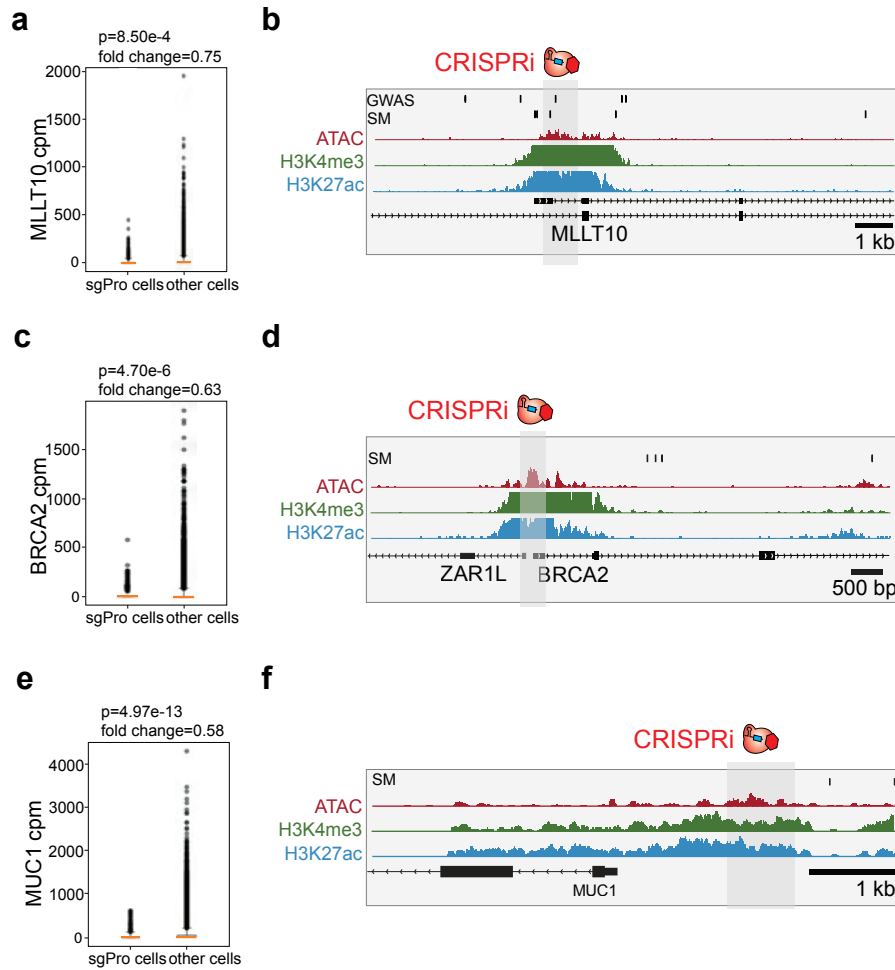
Local / Global
Calculate adjusted p-value and fold change
 MT2A promoter, MT2A



Gaussian adjustment (Significant Score):
 approximate background distribution as Gaussian distribution
 Empirical adjustment:
 $(\text{number of background p-value} < \text{observation}) / 1000$

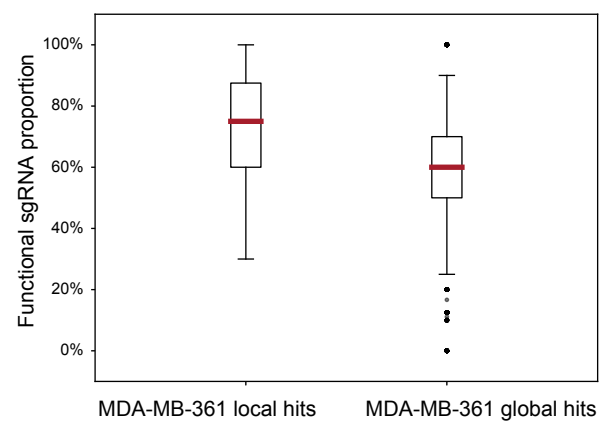


Supplementary Figure 6 - Perturb-seq identifies non-coding regulatory elements that regulate cancer genes.

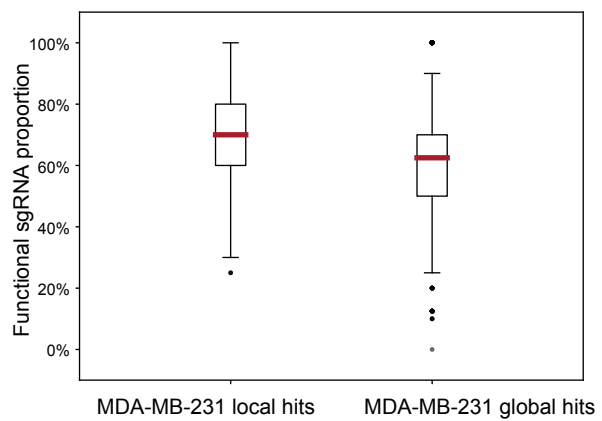


Supplementary Figure 7 - sgRNAs targeting the same region are functionally consistent with each other.

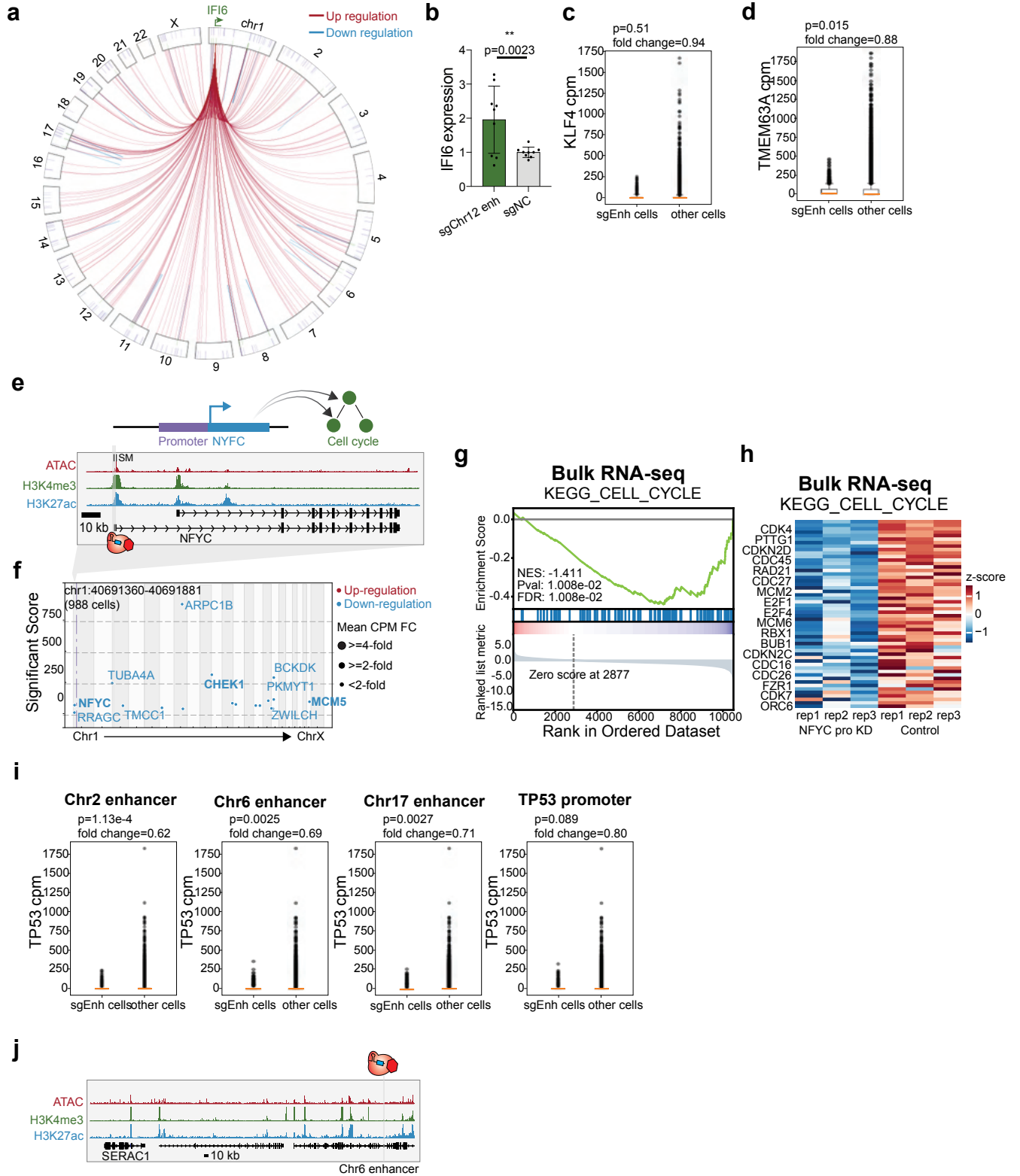
a



b



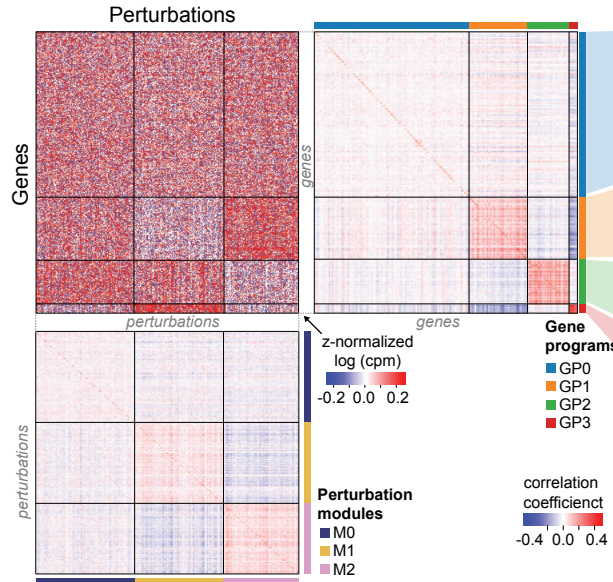
Supplementary Figure 8 - Single cell data of enhancer indirect hits.



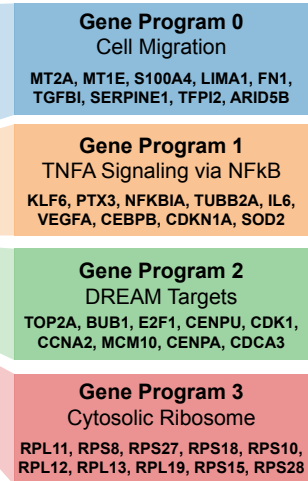
Supplementary Figure 9 - Perturbation modules and gene programs of MDA-MB-231 screens.

a

MDA-MB-231 Somatic mutations

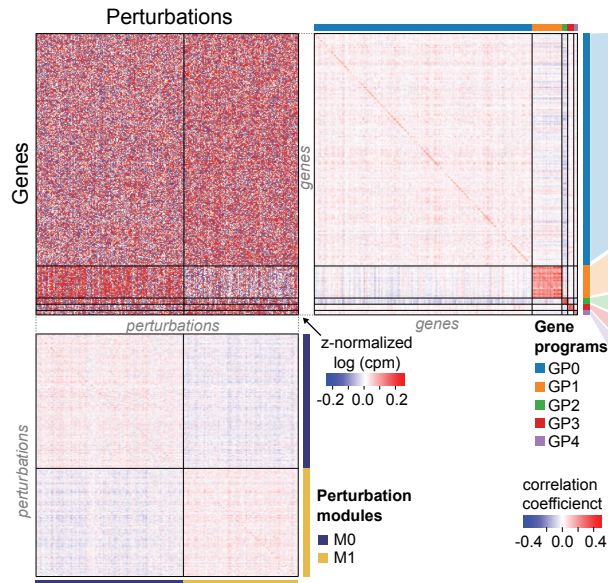


b

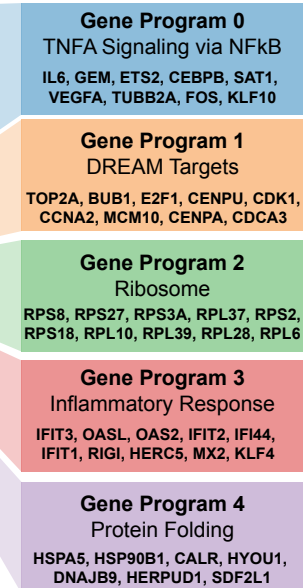


c

MDA-MB-231 GWAS

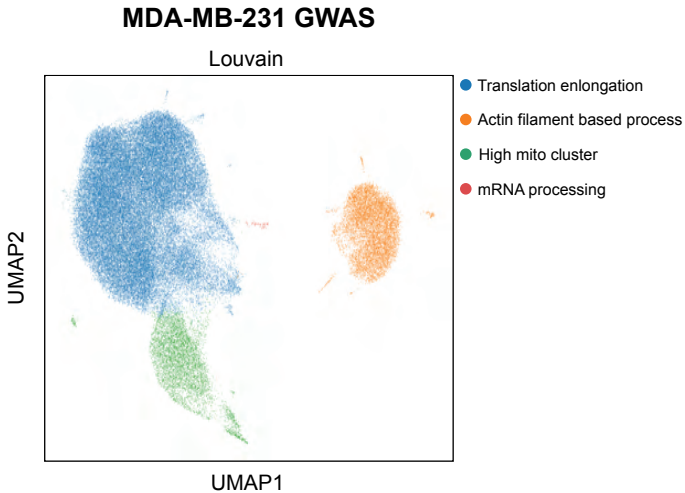


d

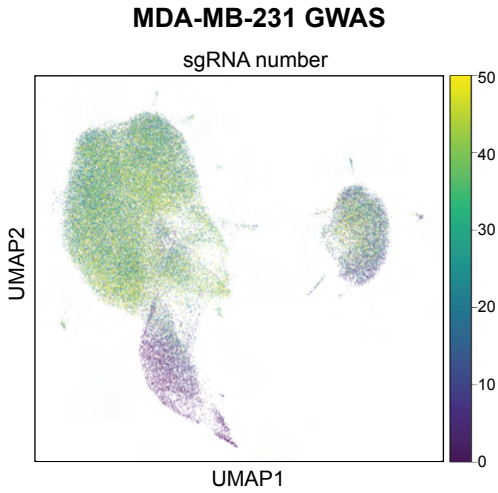


Supplementary Figure 10 - MDA-MB-231 single cell clustering.

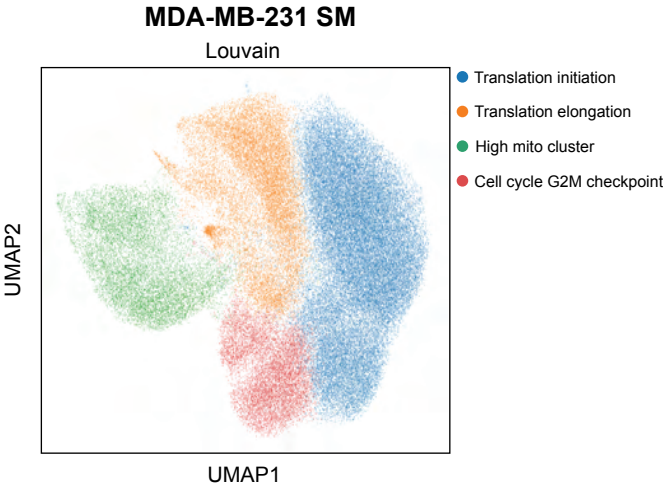
a



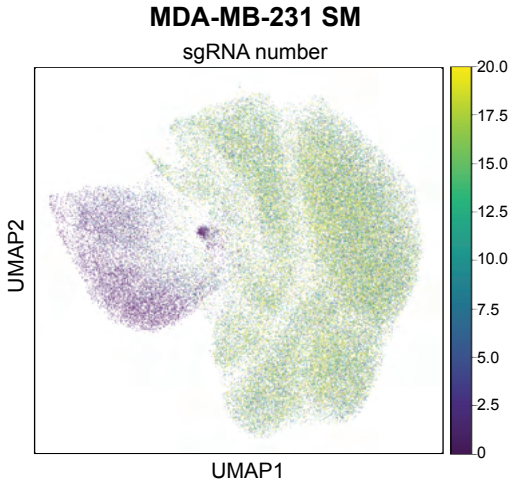
b



c

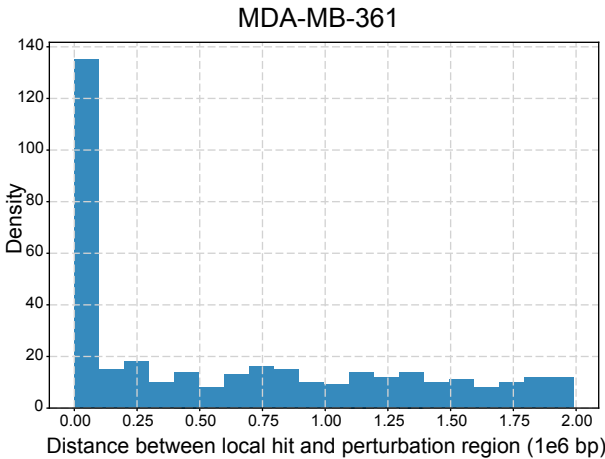


d

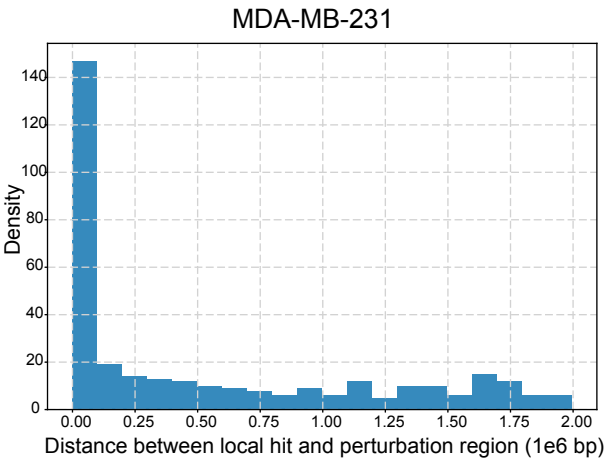


Supplementary Figure 11 - Local hit comparison in ER+ and ER- cells.

a

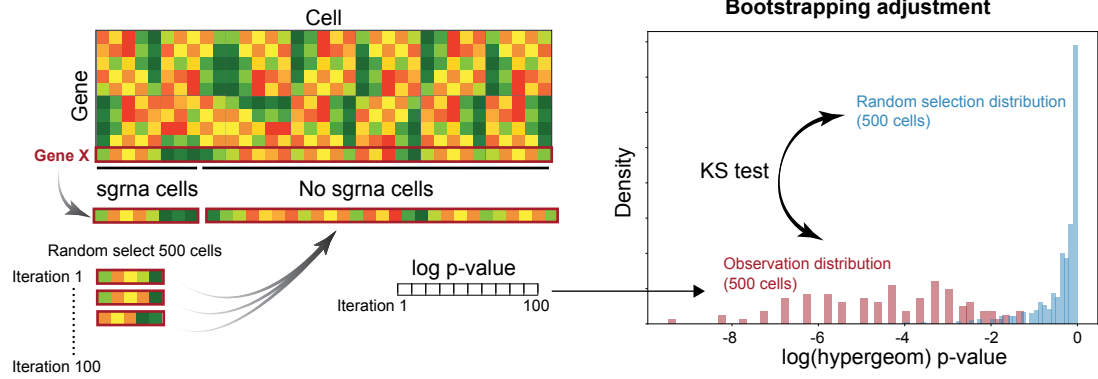


b

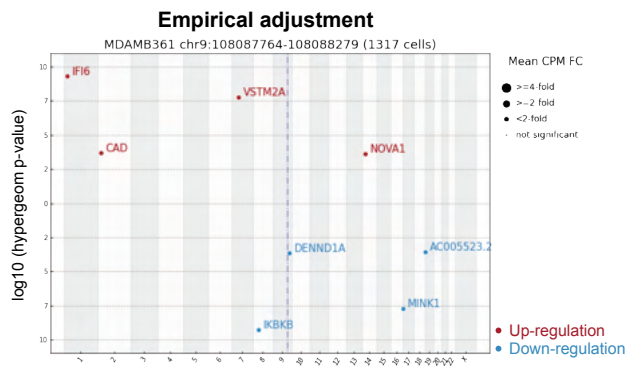


Supplementary Figure 12 - Comparison between empirical adjustment and bootstrapping adjustment.

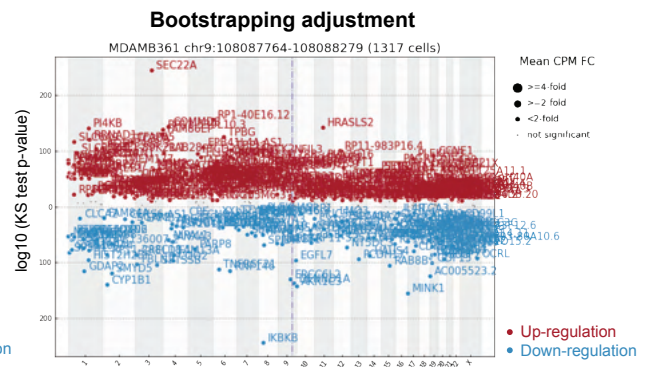
a



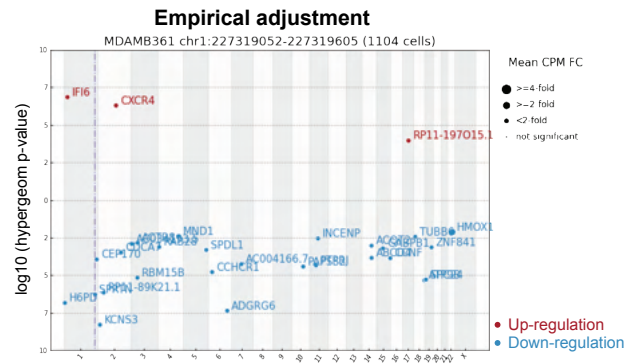
b



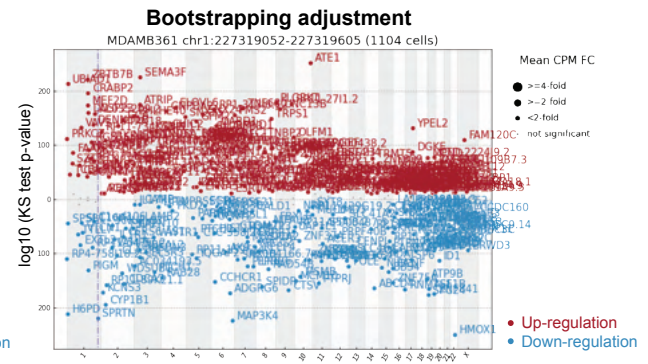
c



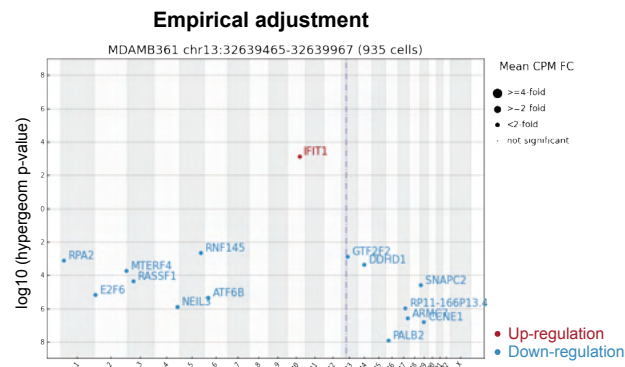
d



e



f



g

