

# EP03: Genome-wide CRISPR screens with single-cell transcriptome readout

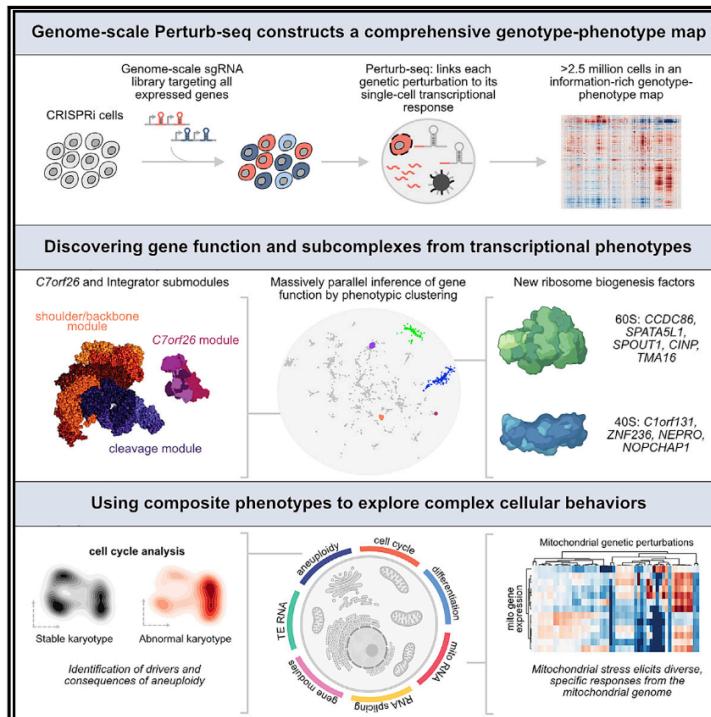
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Cell

Article

## Mapping information-rich genotype-phenotype landscapes with genome-scale Perturb-seq

### Graphical abstract



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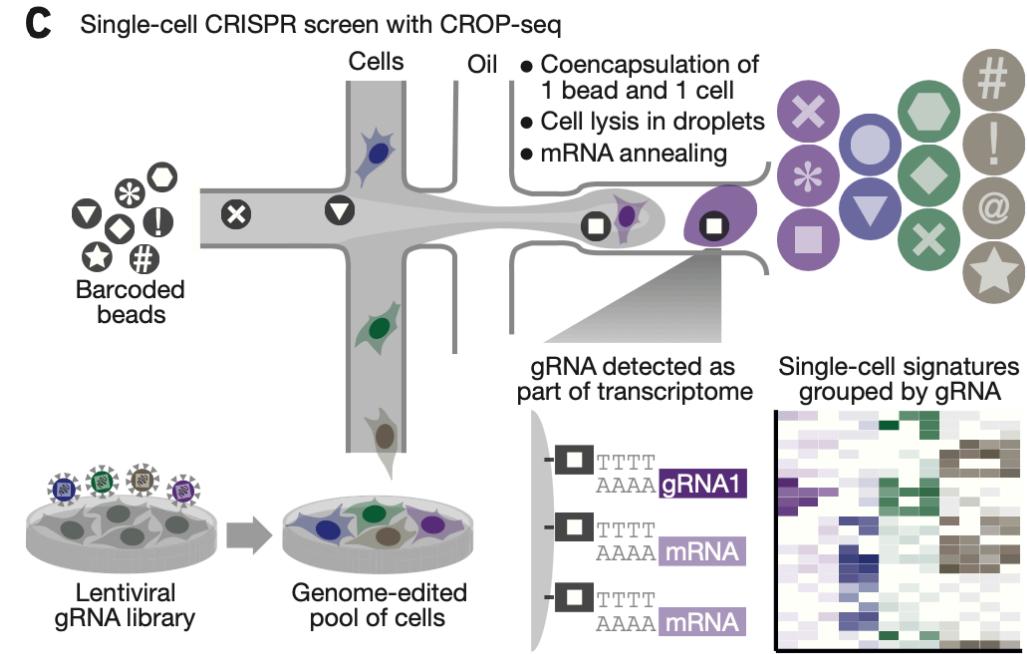
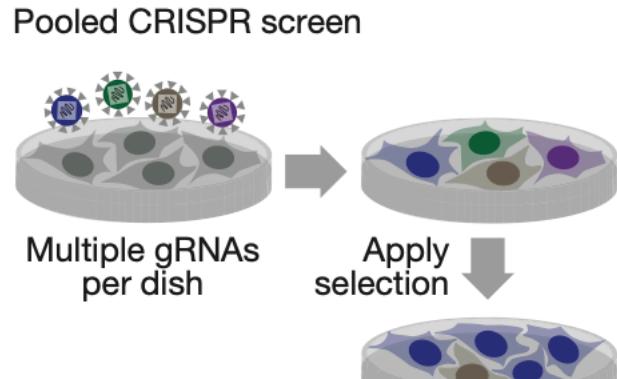
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### In brief

Unbiased, genome-scaling profiling of genetic perturbations via single-cell RNA sequencing enables systematic assignment of function to genes and in-depth study of complex cellular phenotypes such as aneuploidy and stress-specific regulation of the mitochondrial genome.

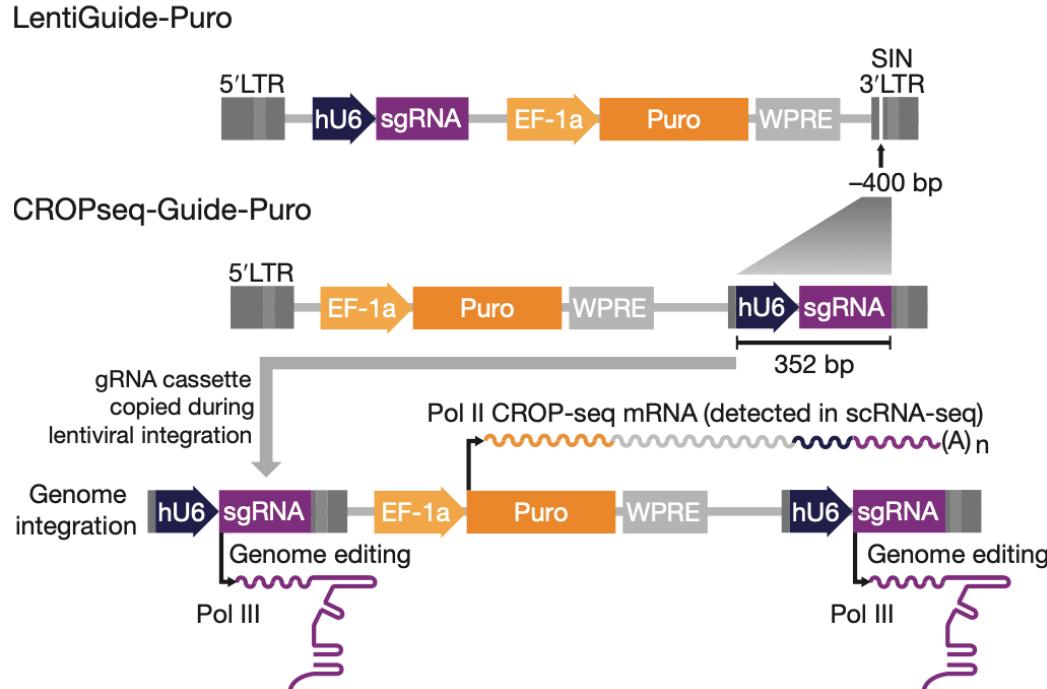
# Why single-cell CRISPR screen is necessary?



Datlinger et al., Nature Methods, 2017

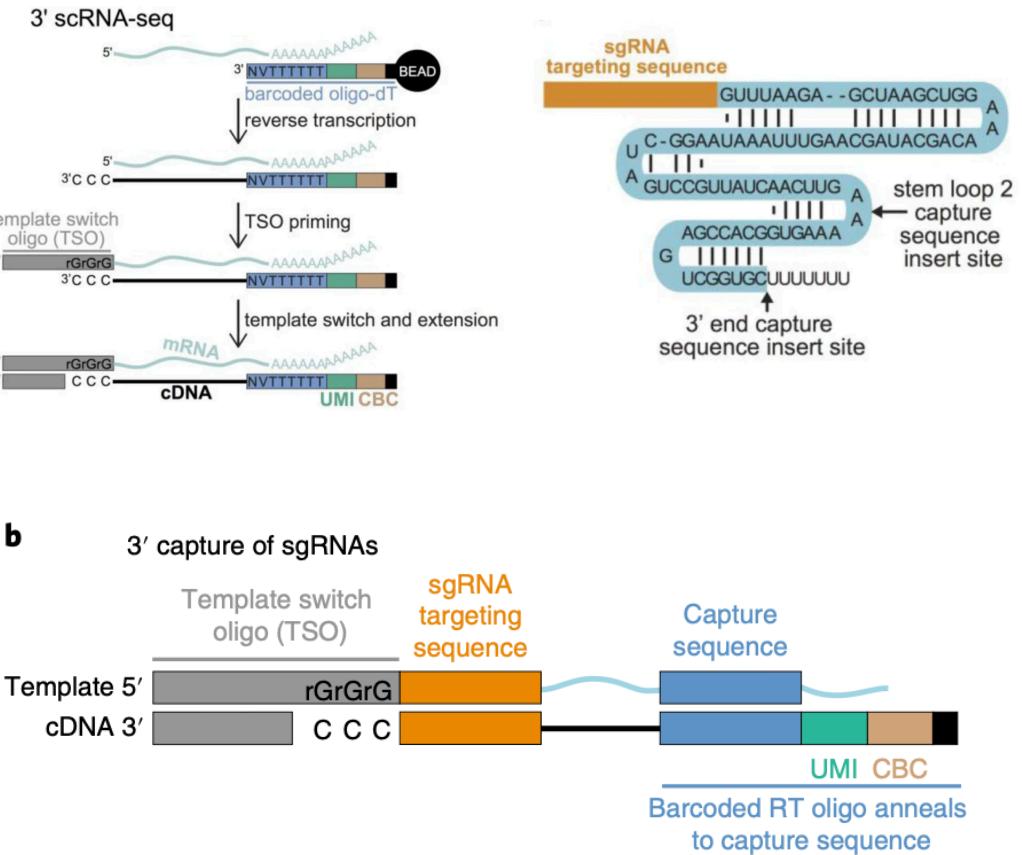
# Two different approaches to perform single-cell CRISPR screen

## CROP-seq



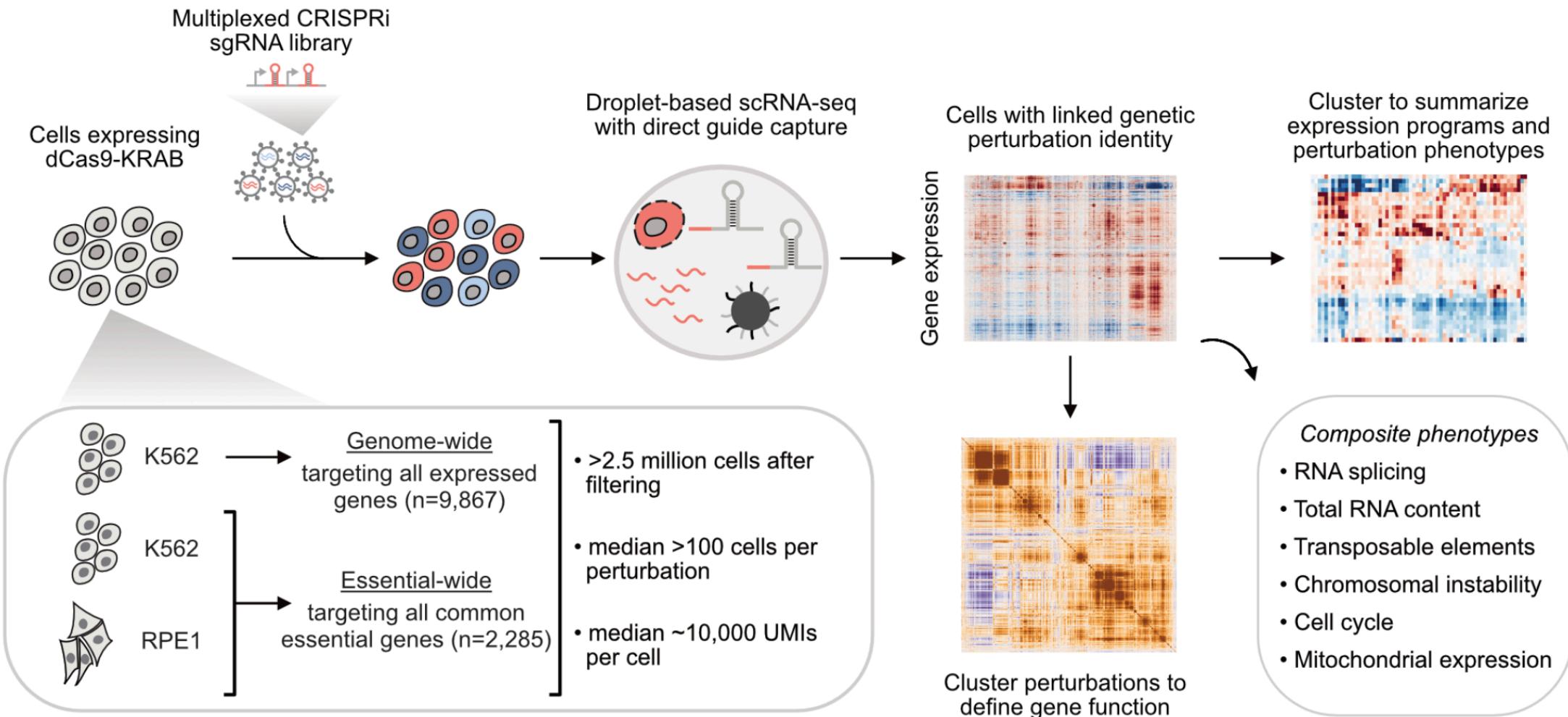
Datlinger et al., Nature Methods, 2017

## Perturb-seq

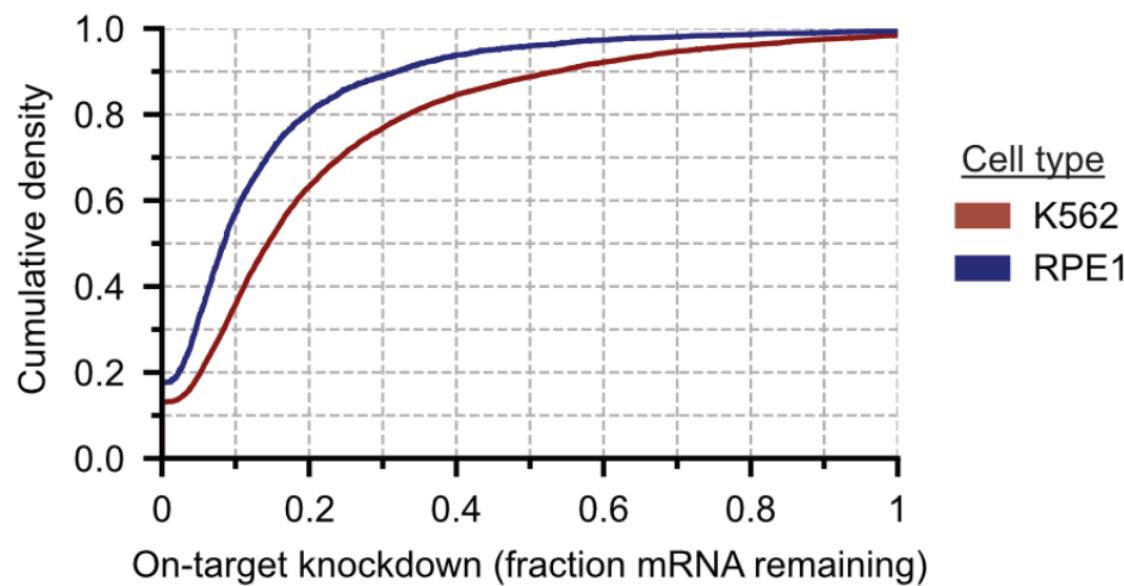


Reprogle et al., Nature Biotechnology, 2020

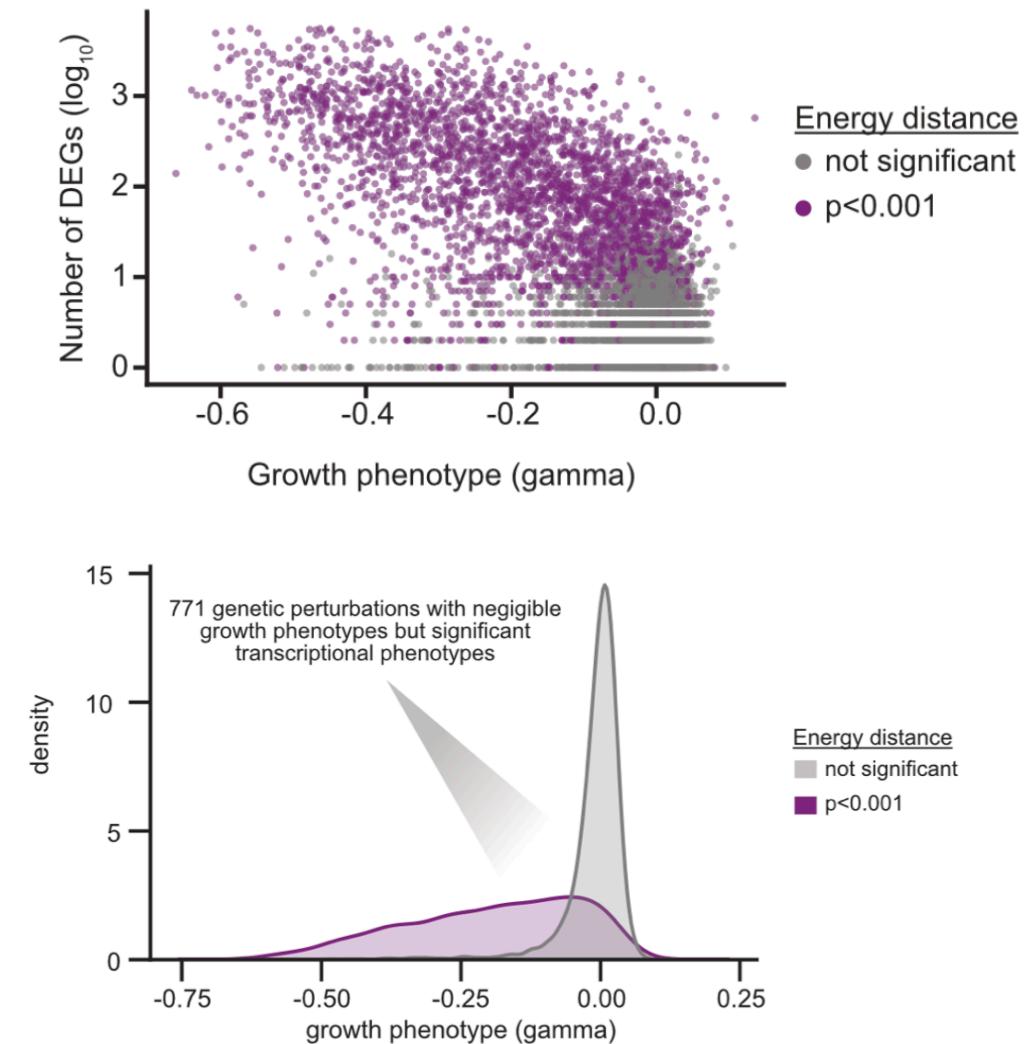
# Experimental procedure of genome-wide perturb-seq screen

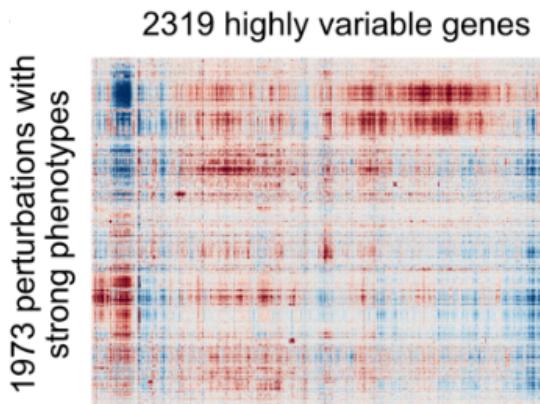


## The global efficacy of CRISPRi knockdown



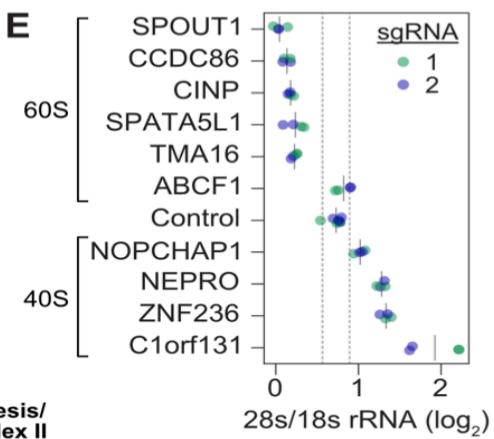
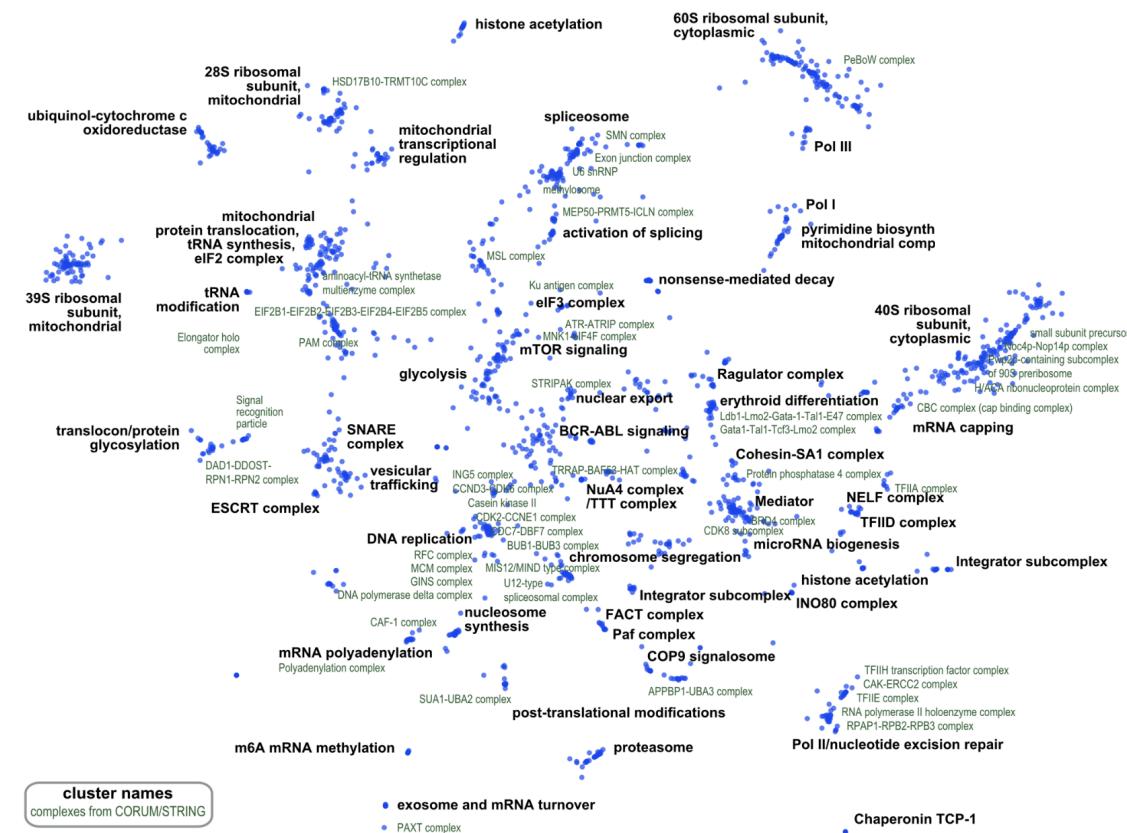
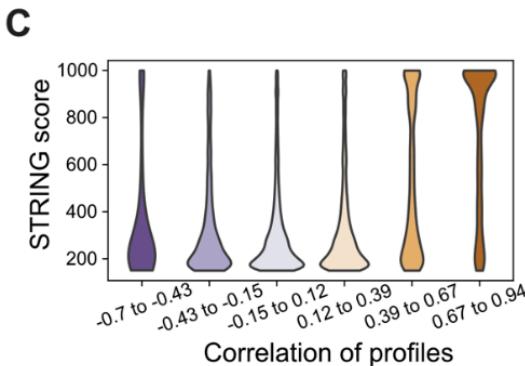
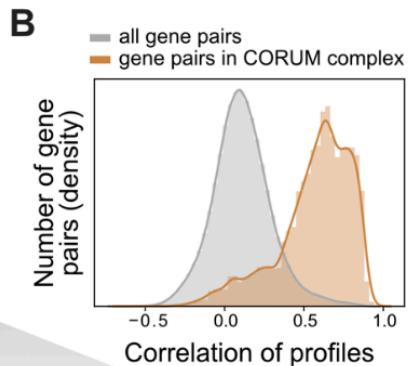
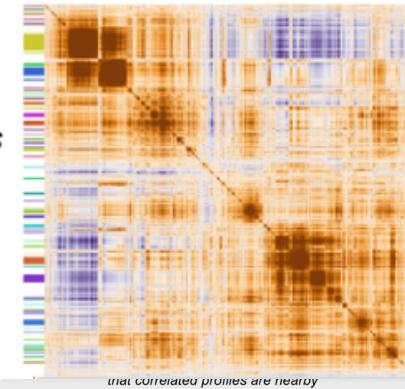
To detect individual differentially expressed genes, we applied the Anderson-Darling (AD) test to compare the distribution of expression levels for each gene in cells bearing each genetic perturbation against control cells.



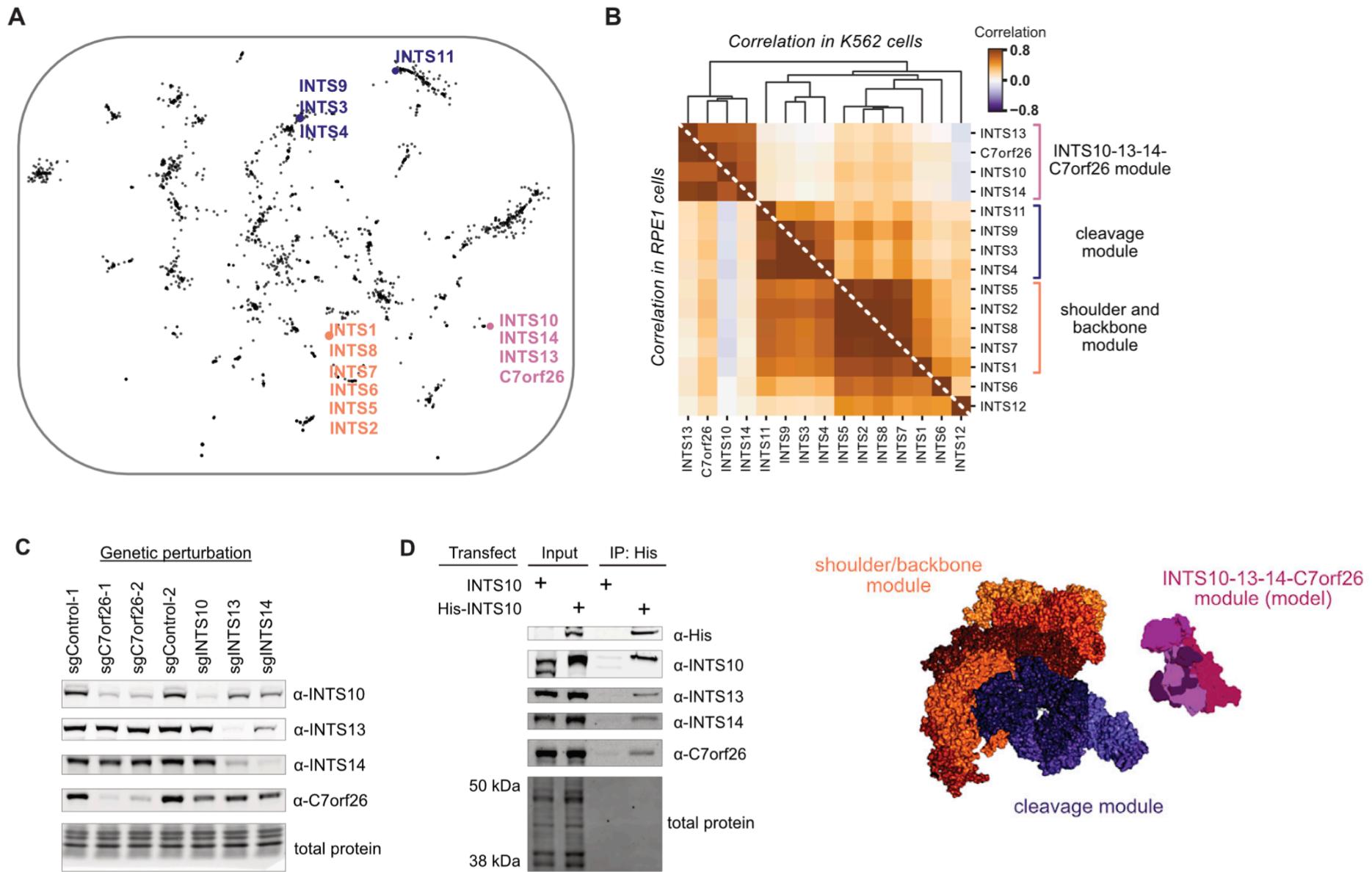


*Compare perturbations using correlation of expression profiles*

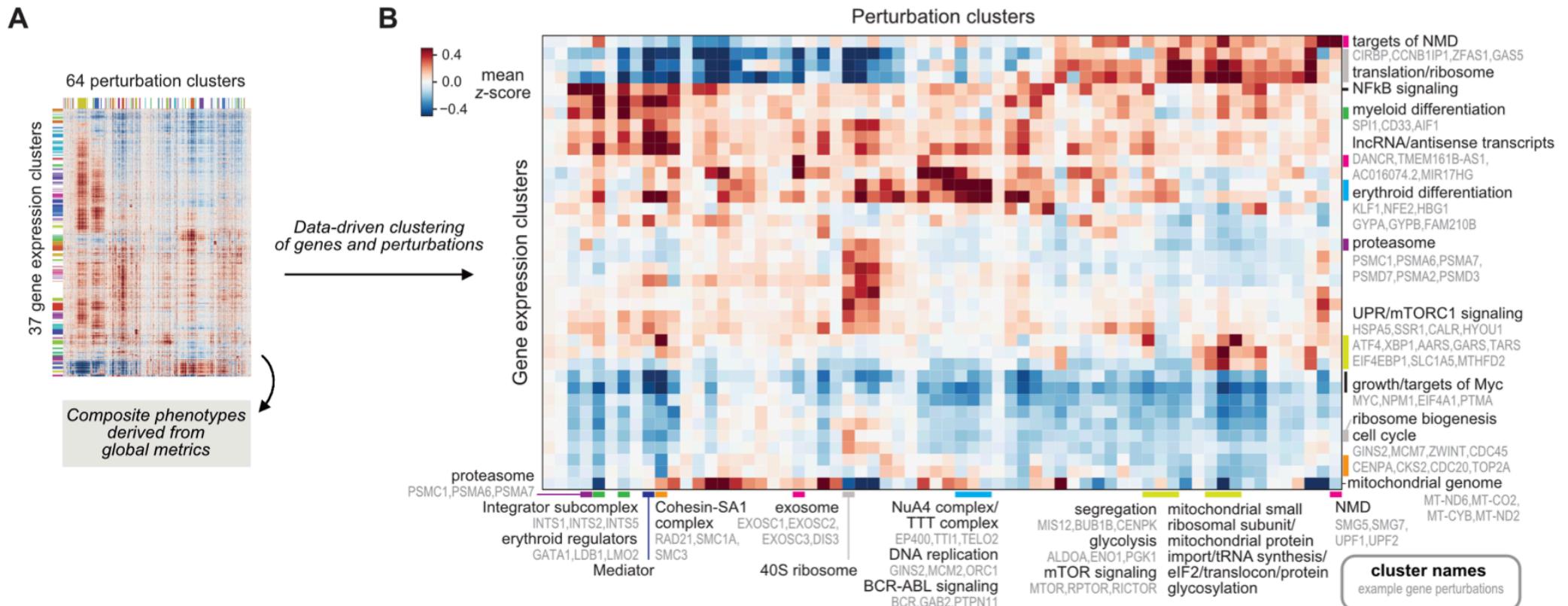
### perturbation-perturbation correlation matrix



# Identification of novel component in Integer complex

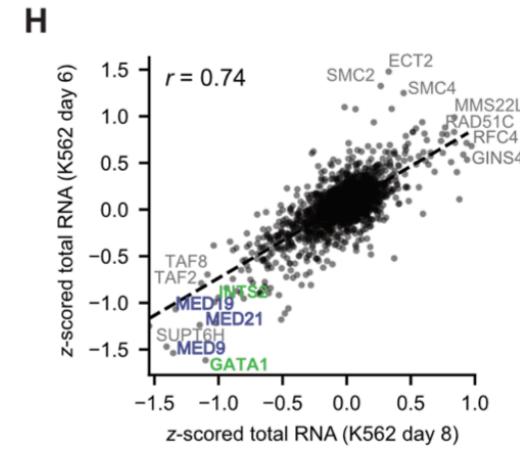
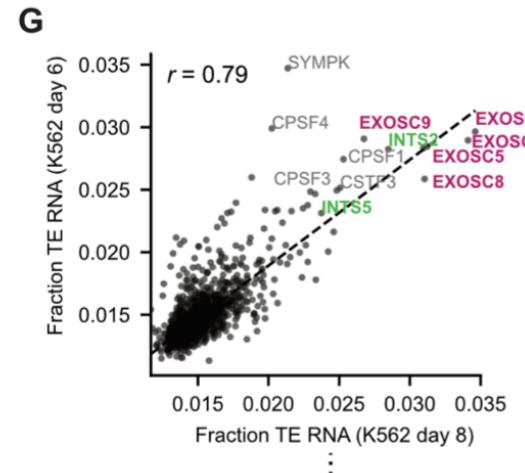
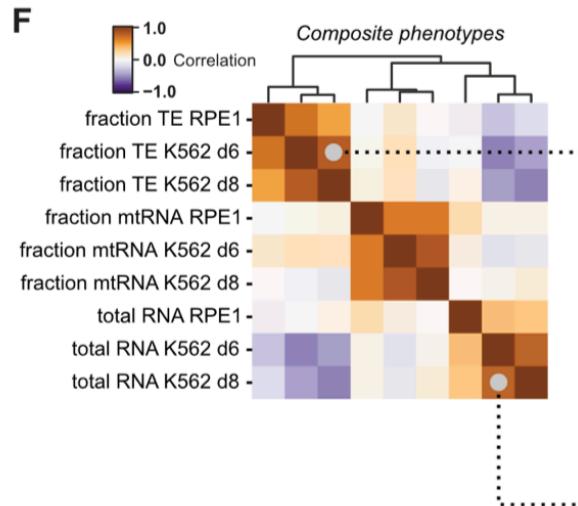
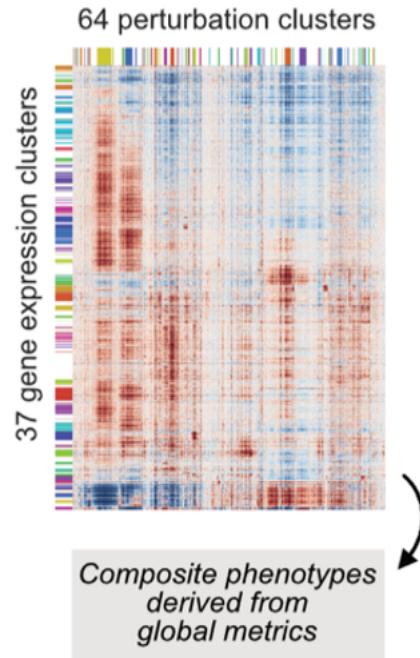


# Summarizing genotype-phenotype relationships with Perturb-seq



Unfolded protein response (UPR), activated by the loss of ER-resident chaperones and translocation machinery, and integrated stress response (ISR), activated by loss of mitochondrial proteins, aminoacyl-tRNA synthetases, and translation initiation factors

# Hypothesis-driven study of composite phenotypes



# Exploring genetic drivers and consequences of aneuploidy in single cells

