

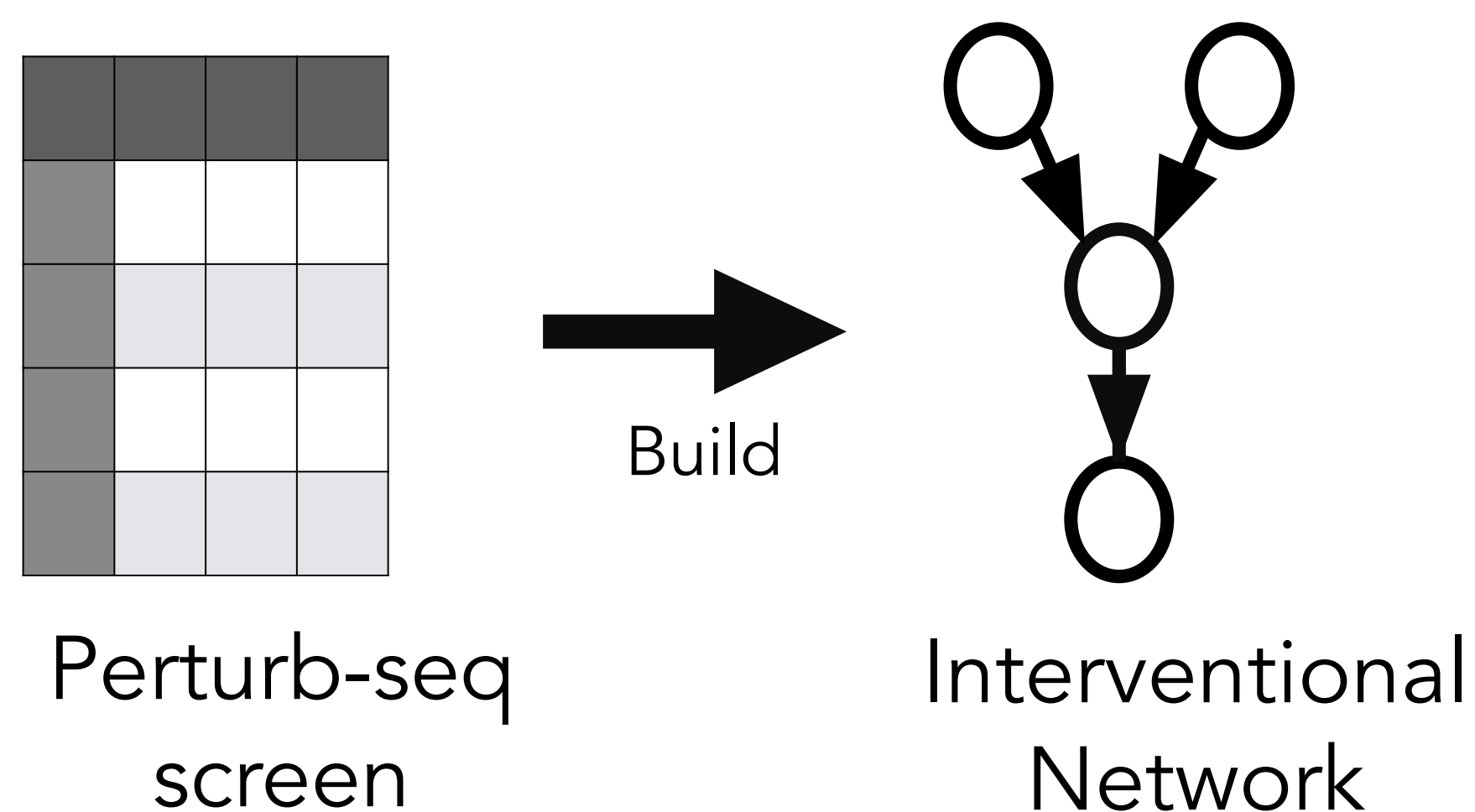
# Using dotears to build causal Gene Regulatory Networks on Genome-wide Perturb-seq

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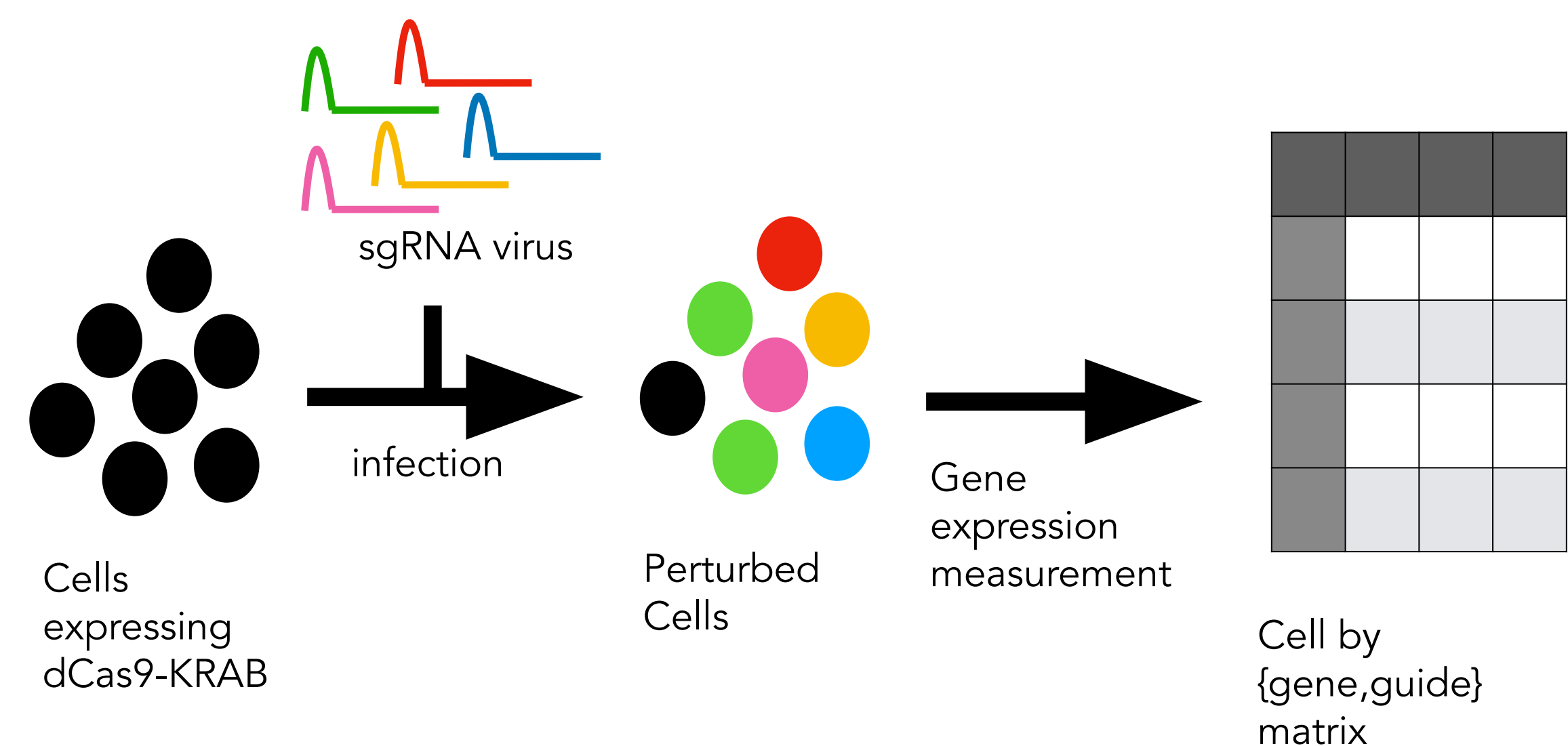
## Introduction

Gene regulatory networks describe the causal relationships between multiple different genes and their expression levels. Recent methodological advances like dotears<sup>1</sup> allow inference of causal regulatory networks from interventional data. We apply dotears to a single cell genome-wide CRISPR screen to uncover regulatory relationships in lipid pathways.



## Motivation

Perturb-seq screens use CRISPR interventions to interrogate network structure.



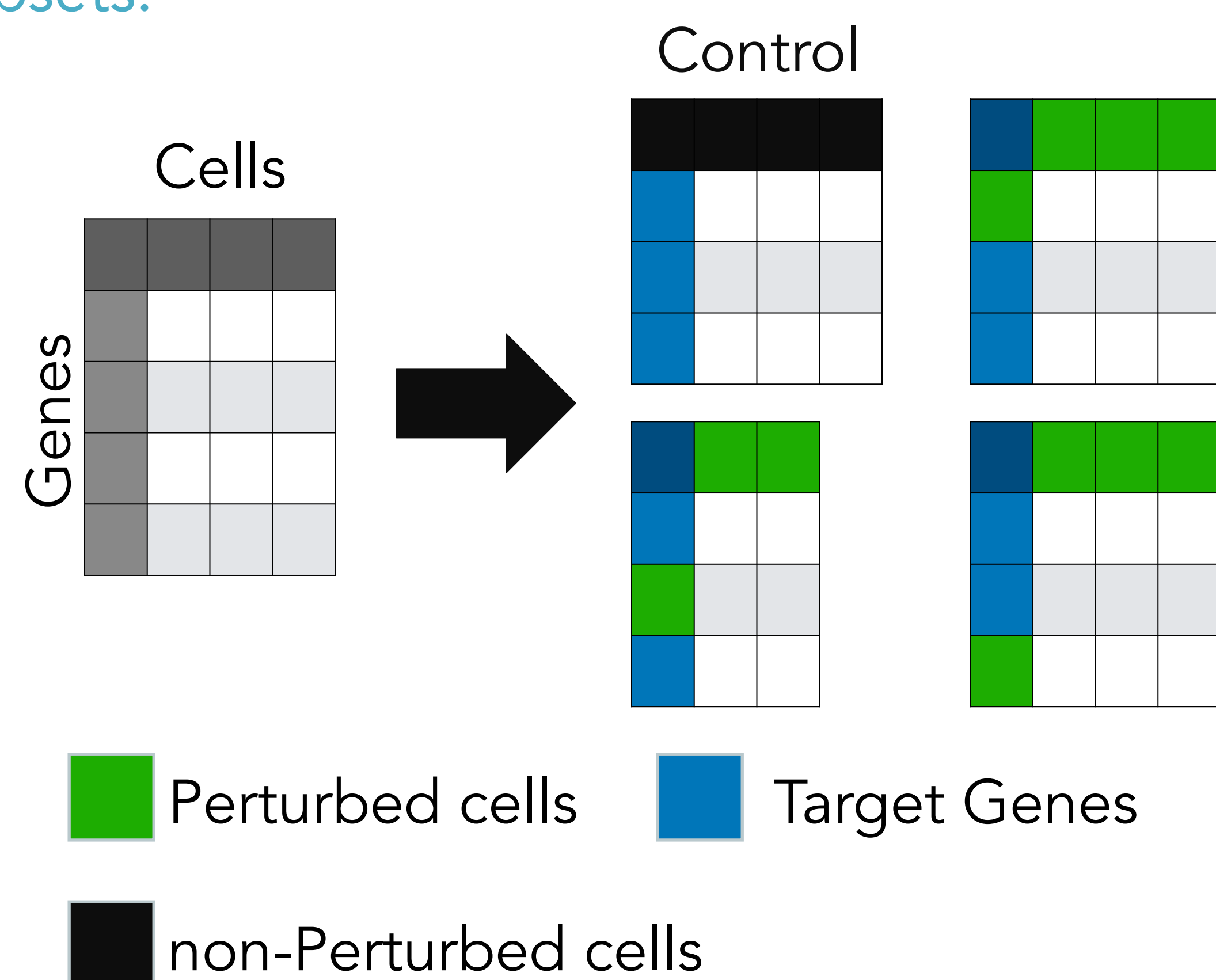
lentivirus containing sgRNA encodes a gene knockdown target.

after lentiviral uptake, expression of the target is reduced.

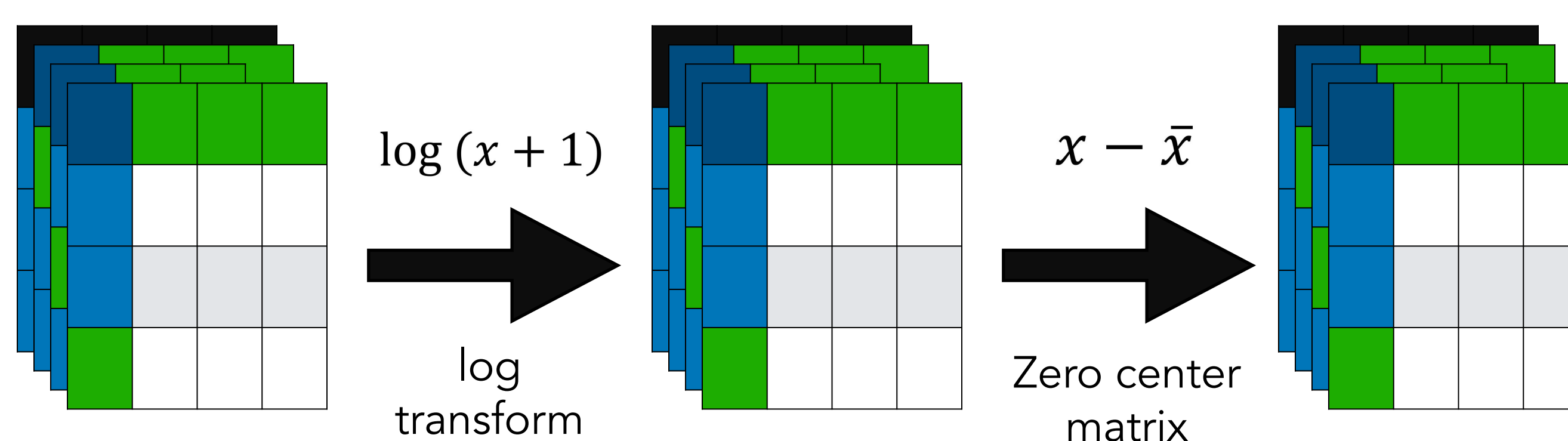
a high-dimensional transcriptomic readout reveals network changes after target knockout/suppression.

## Approach

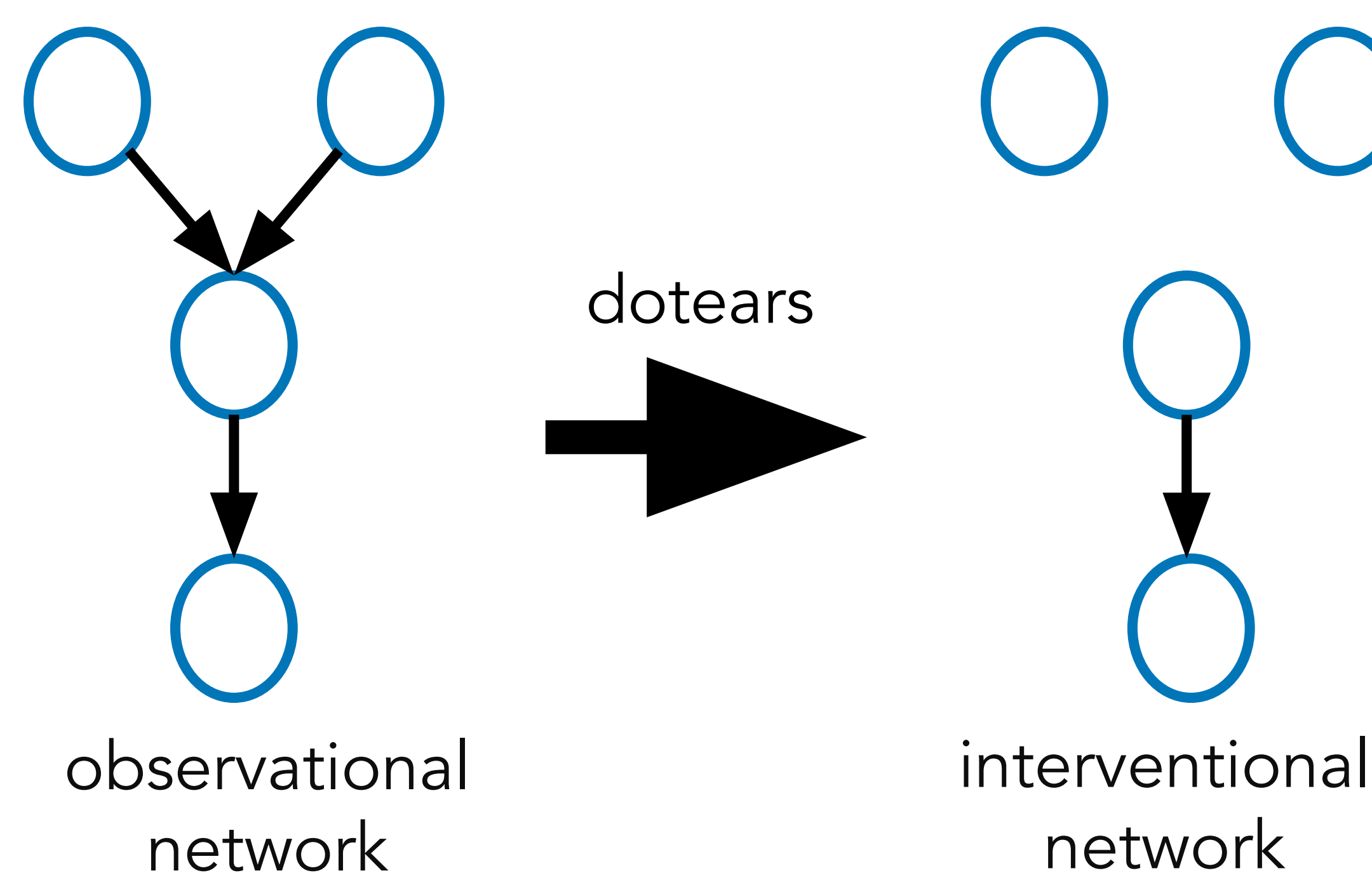
Filter Perturb-seq data<sup>2</sup> to control and target-gene subsets.



Preprocess matrix data.



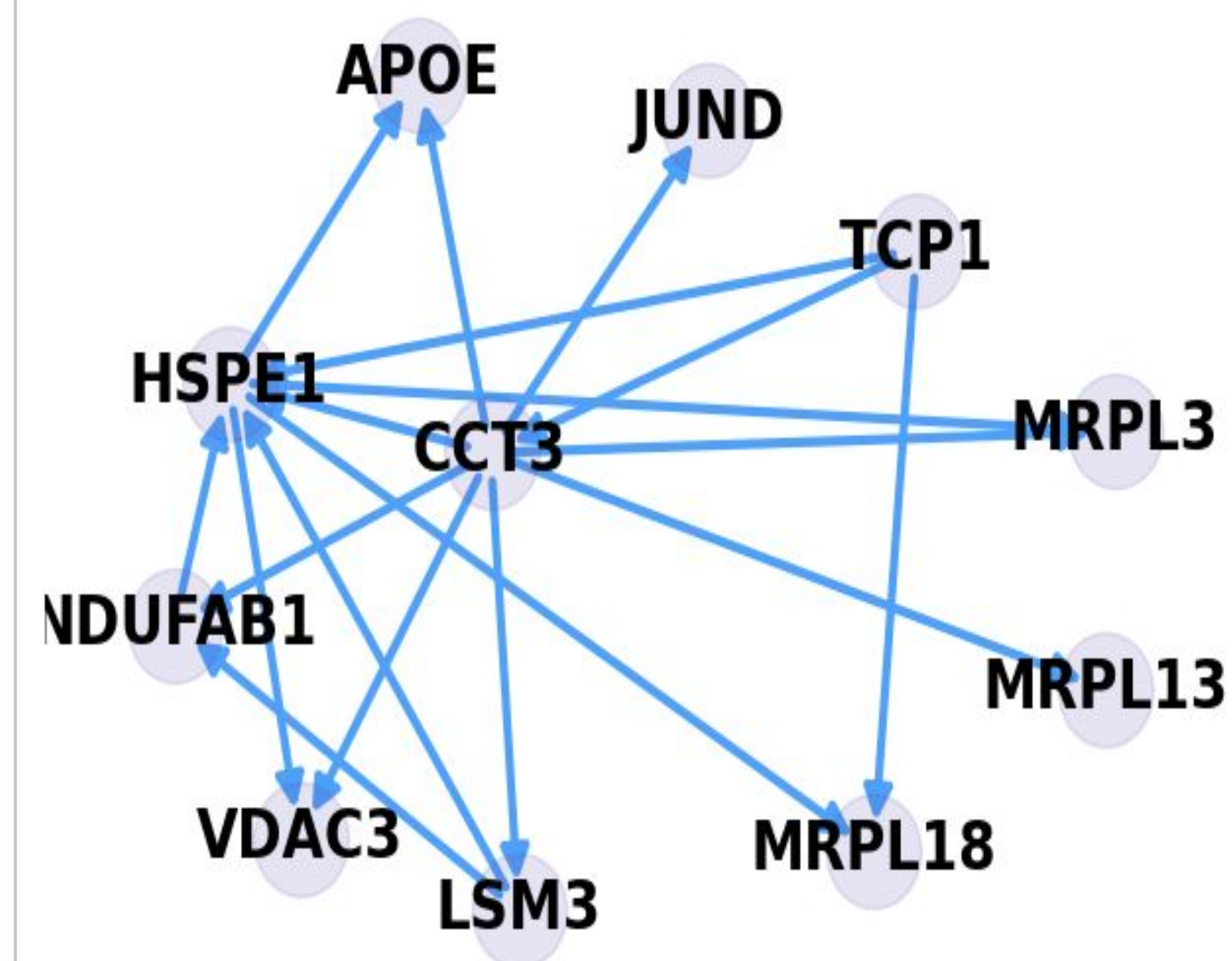
CRISPR interventions remove upstream relationships, so targets become source nodes.



comparison of network changes across targets reconstructs regulatory networks.

## Results

We applied dotears to a subset of the Perturb-seq dataset focusing on 13 genes relevant to cholesterol levels, and found 17 relationships.



## Discussion

We preprocessed single-cell RNA-seq data and ran dotears on a subset of genes. Two of the genes were shown to have a prominent influence within the networks were TCP1 and CCT3. The relative importance of these genes within the network indicates that dotears correctly identified TCP1 and CCT3 as chaperonin molecules, which is consistent with prior research<sup>3</sup>.

1. Xue, Albert., arxiv (2023). 2. Replogle, Joseph. Cell (2022). 3. Brackley KI, Grantham J. Activities of the chaperonin containing TCP-1 (CCT): implications for cell cycle progression and cytoskeletal organisation. Cell Stress Chaperones. 2009