

Single Cell Epigenomics

scMultiomics exercises

Fides Zenk

Learning Objectives of this week

Basic principles of 10x Genomics multiome kit

Understanding of early brain organoid development

Mapping early development using multiomics

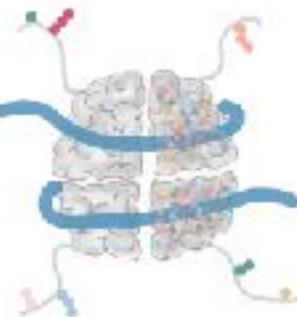
Understanding Human Brain Development



How does cellular diversity arise in the brain?

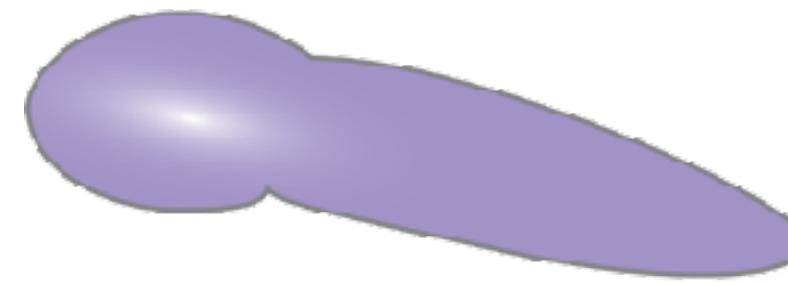


Understanding Human Brain Development



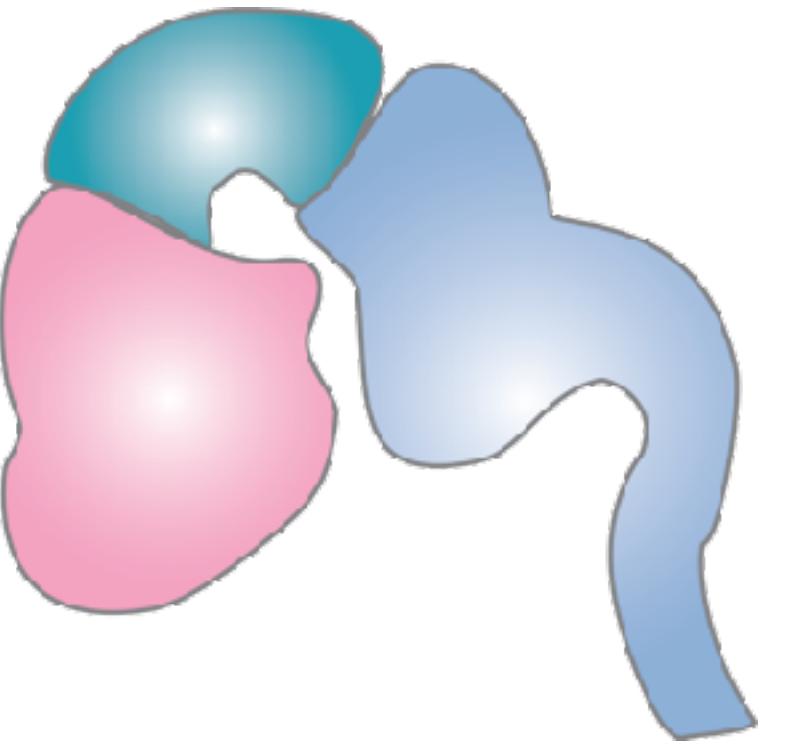
Understanding Human Brain Development

21 Days



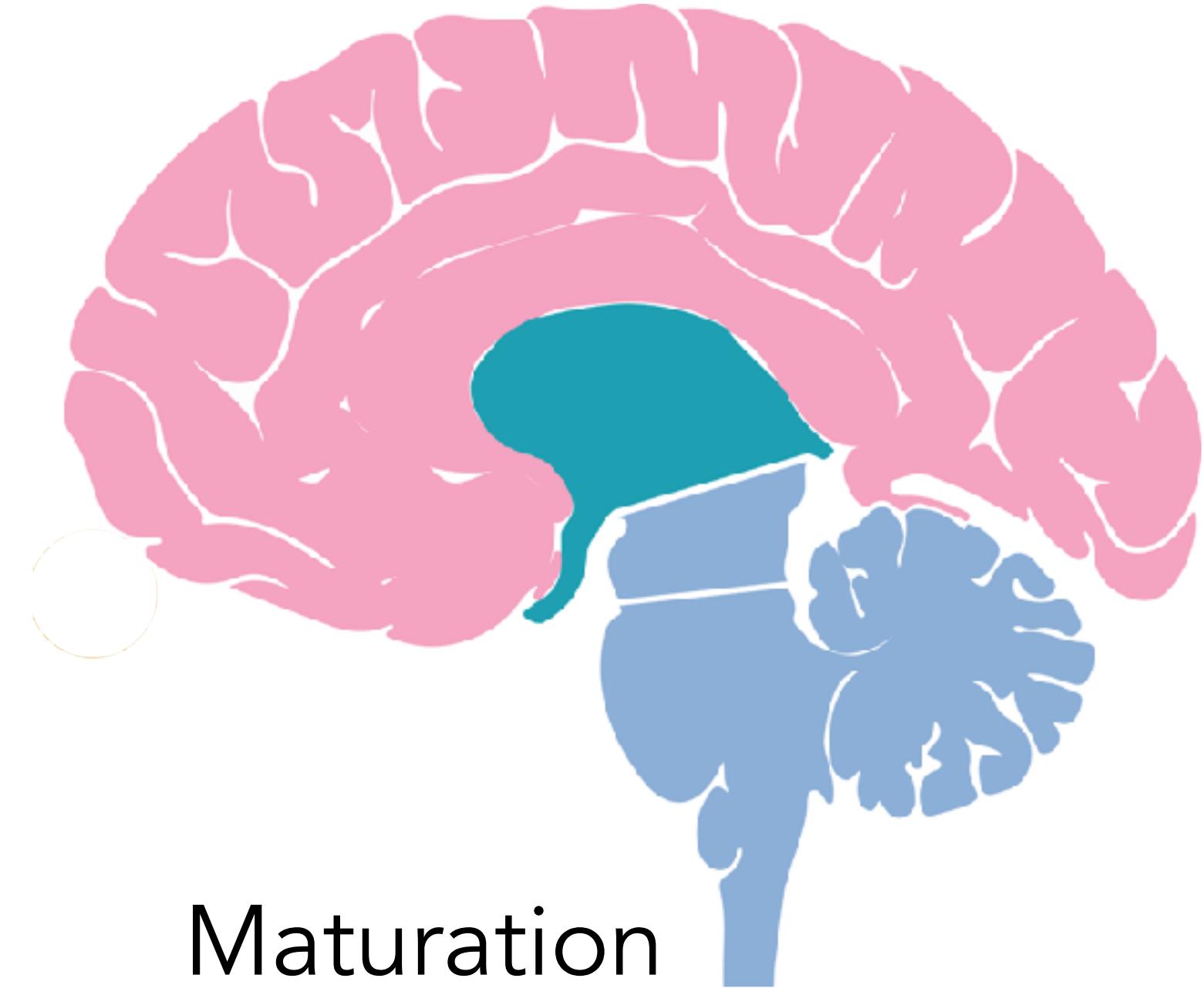
Formation of Neural Tube

35-40 Days

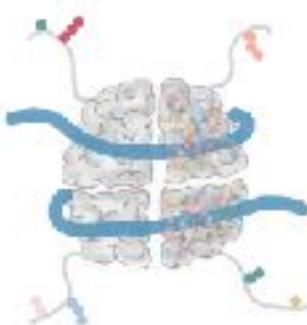


Regionalization

9 Months

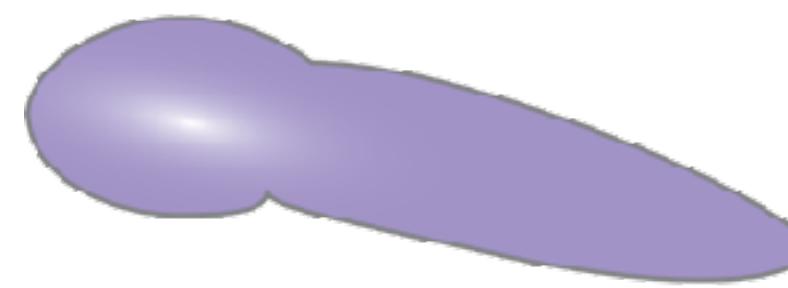


Maturation

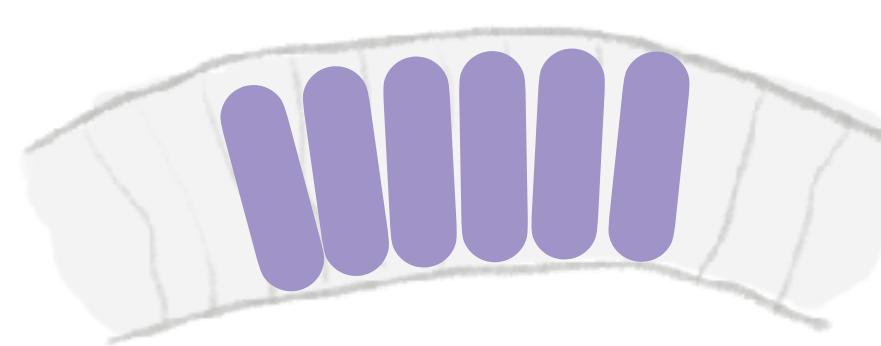


Understanding Human Brain Development

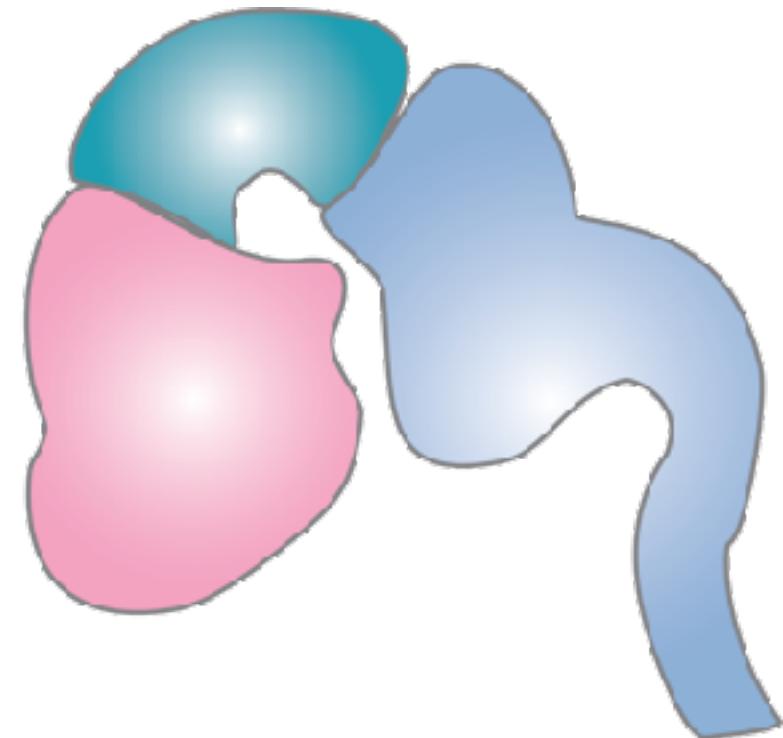
21 Days



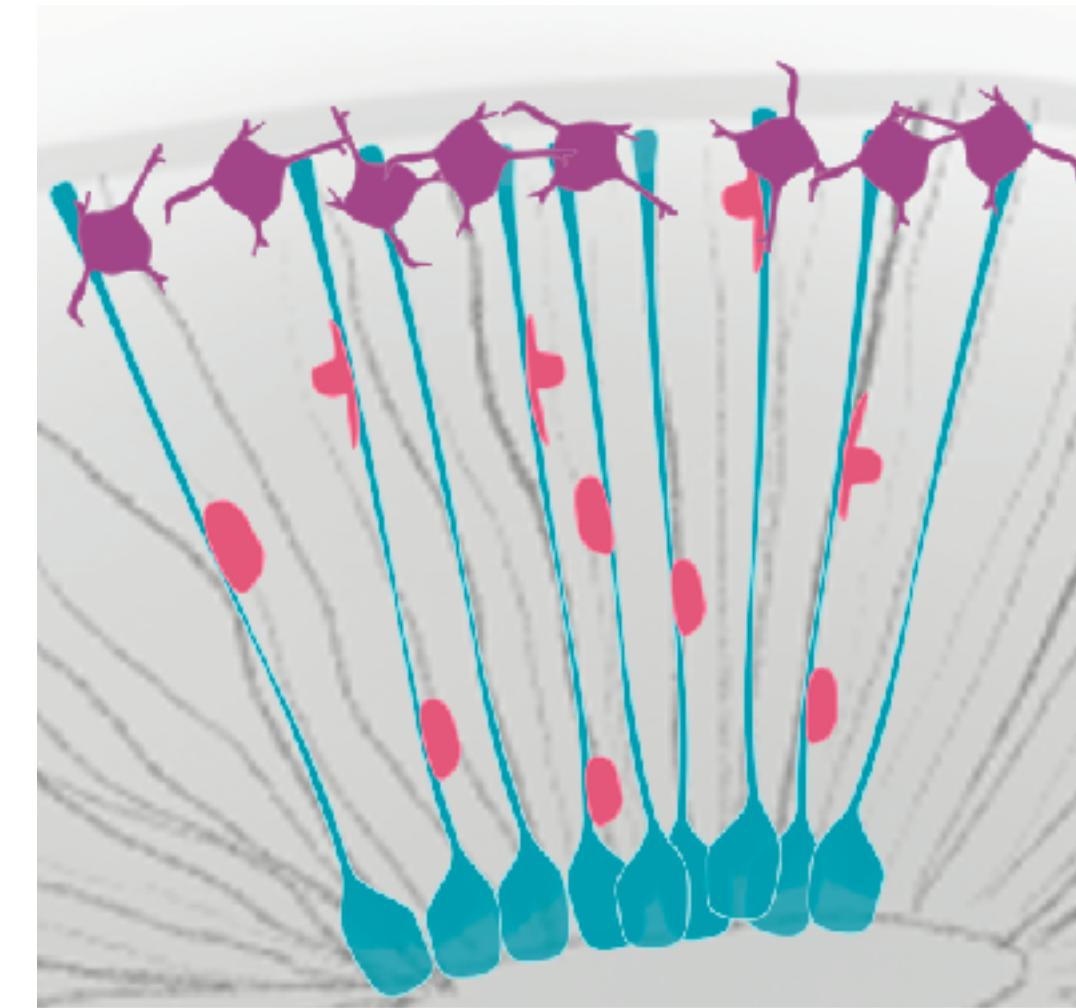
Formation of Neural Tube



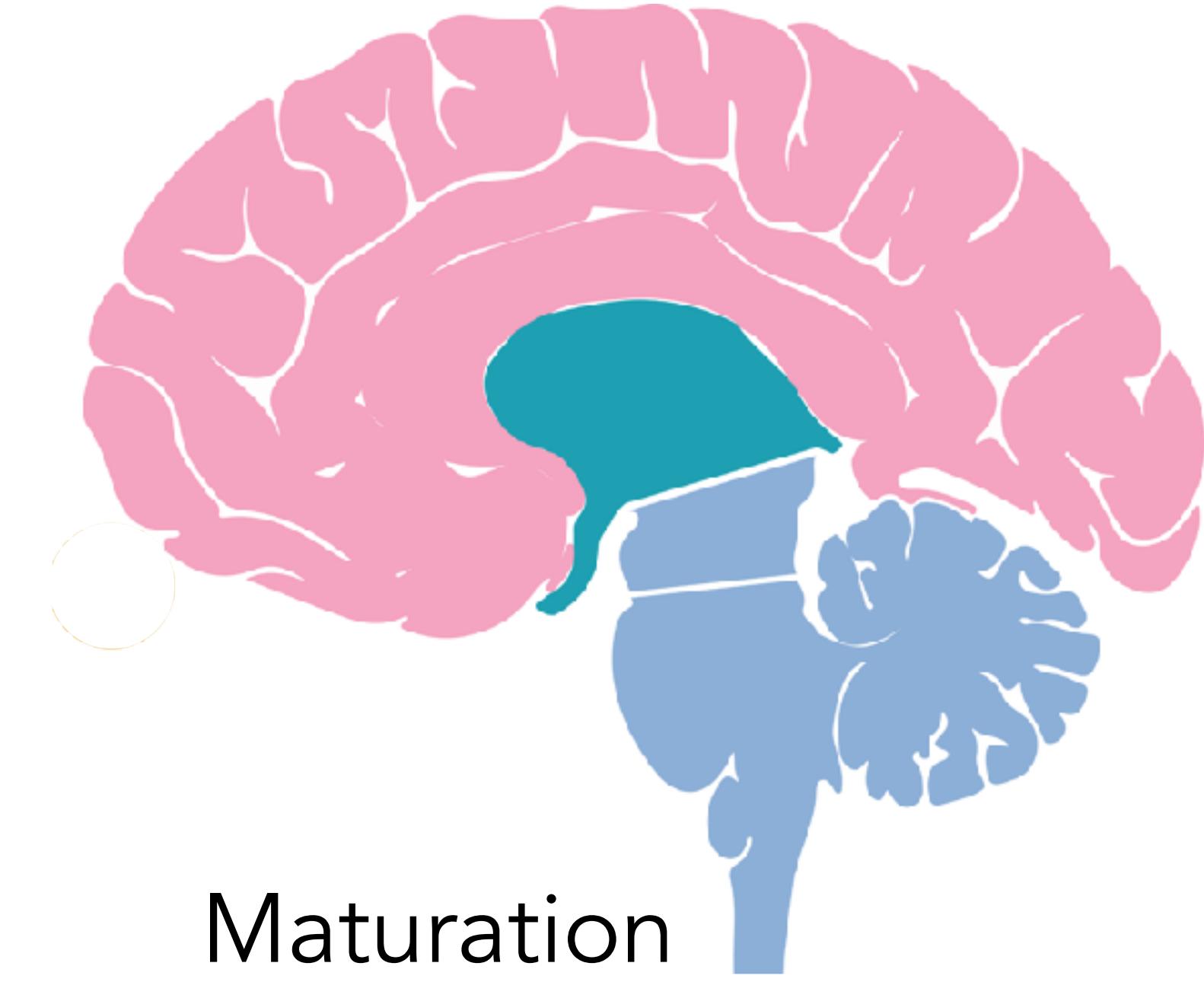
35-40 Days



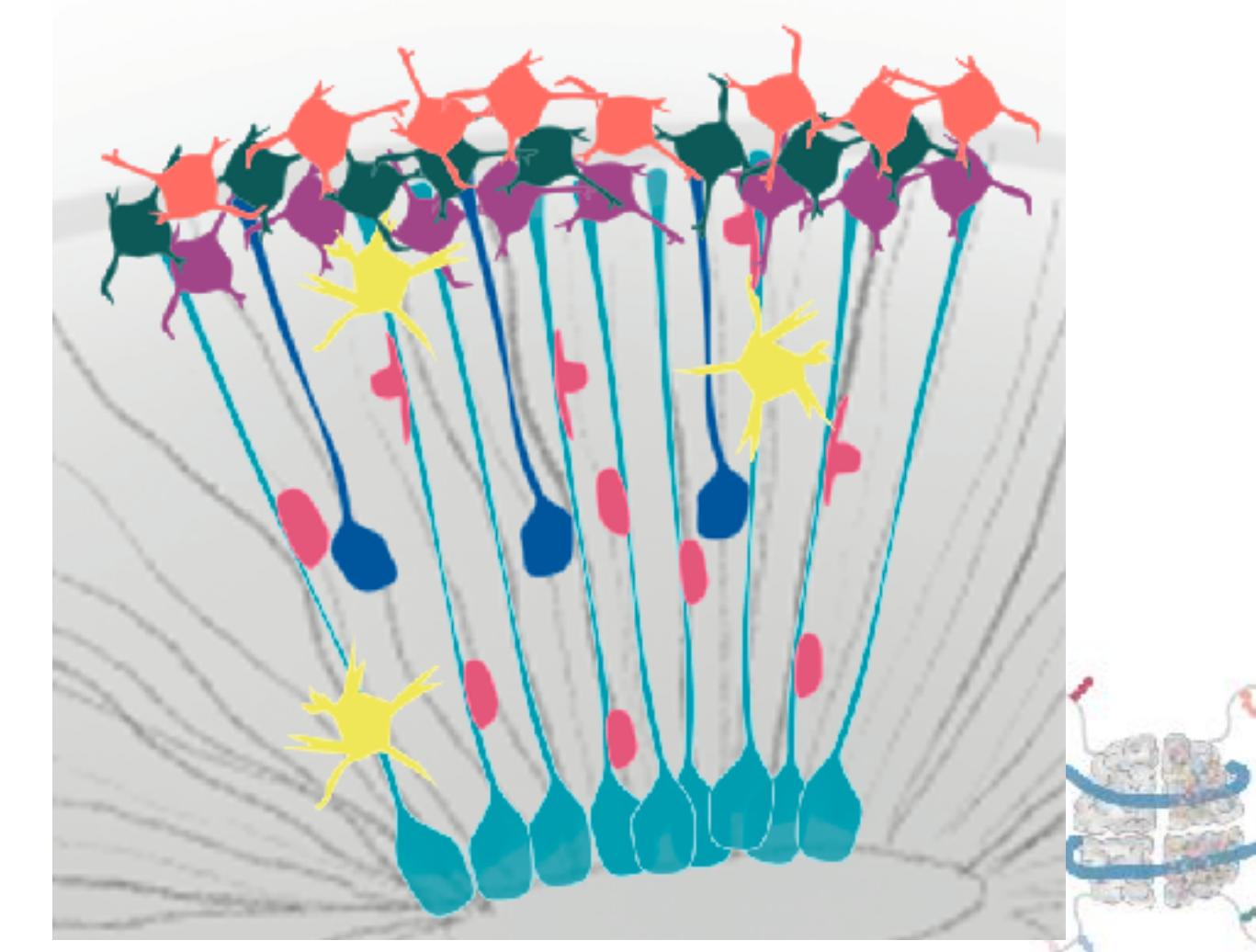
Regionalization



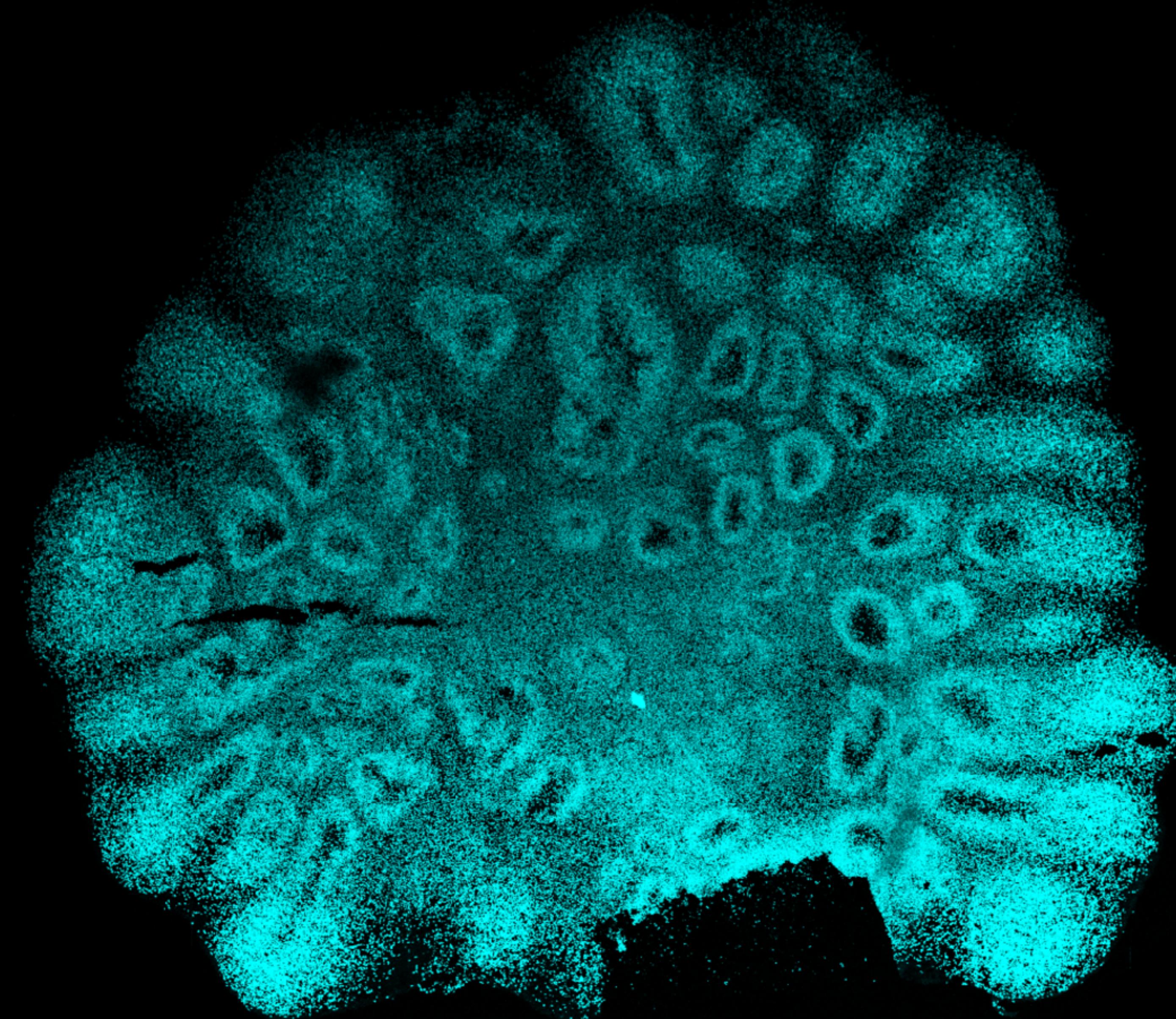
9 Months



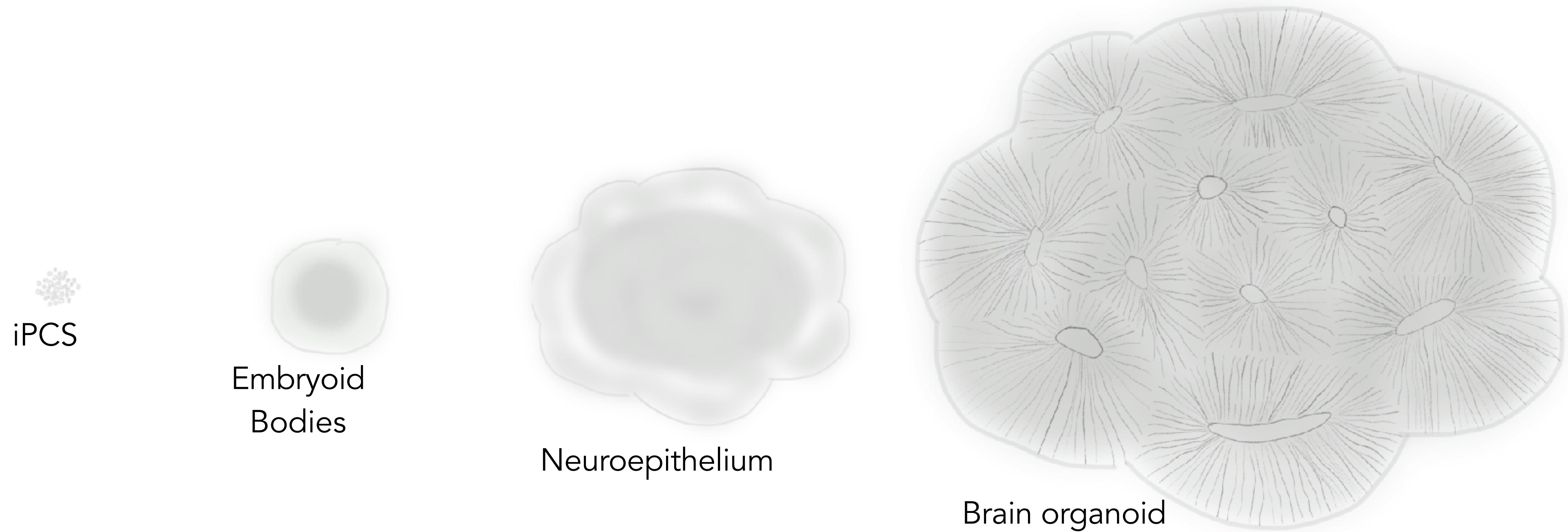
Maturation



Understanding Human Brain Development using Neural Organoids



Human Neural Organoids recapitulate embryonic Development



Human Neural Organoids recapitulate embryonic Development



How do cells acquire and maintain their developmental fate?

Human Neural Organoids recapitulate embryonic Development

Article

Inferring and perturbing cell fate regulomes in human brain organoids

<https://doi.org/10.1038/s41586-022-05279-8>

Received: 6 October 2021

Accepted: 25 August 2022

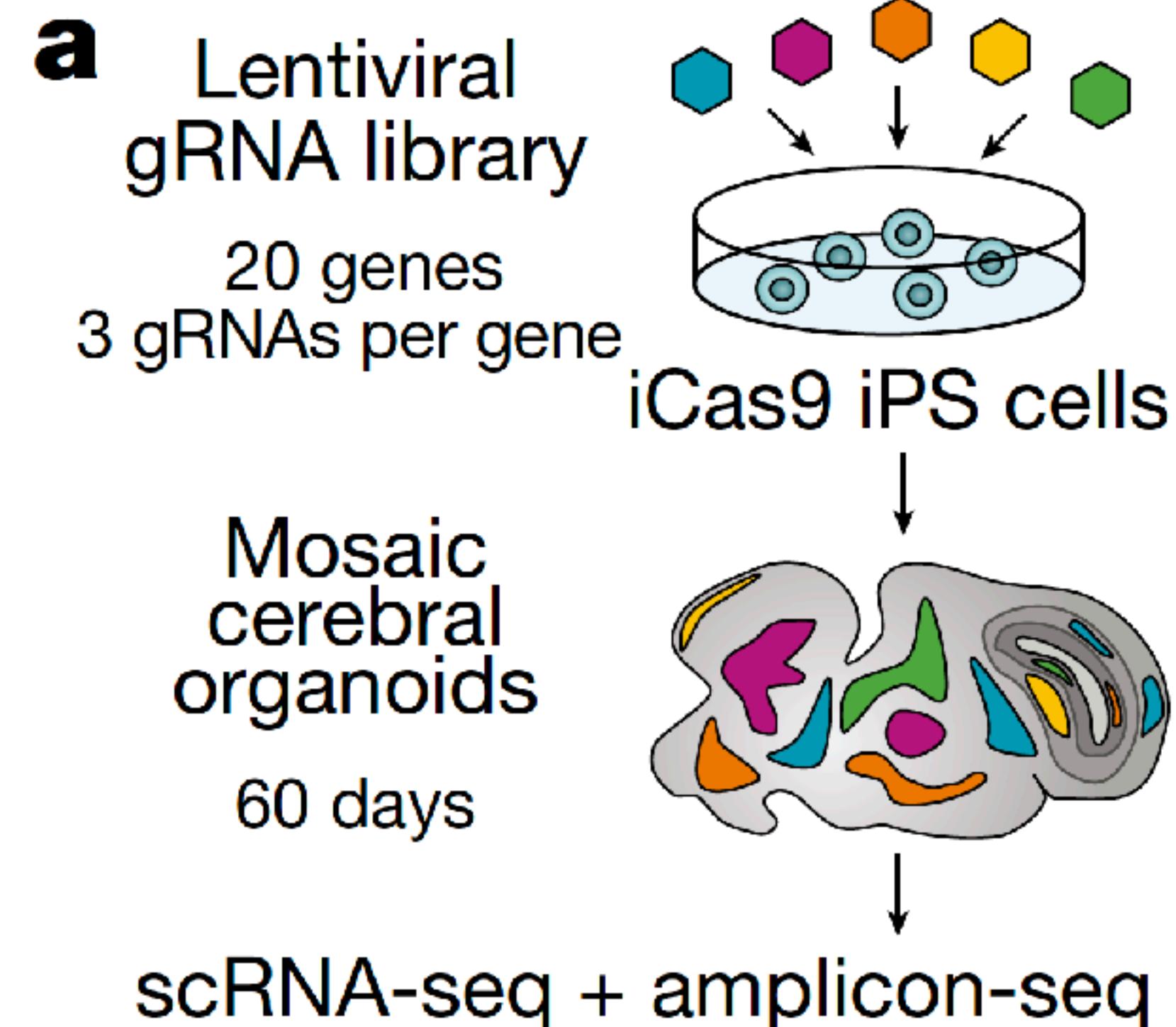
Published online: 05 October 2022

Open access

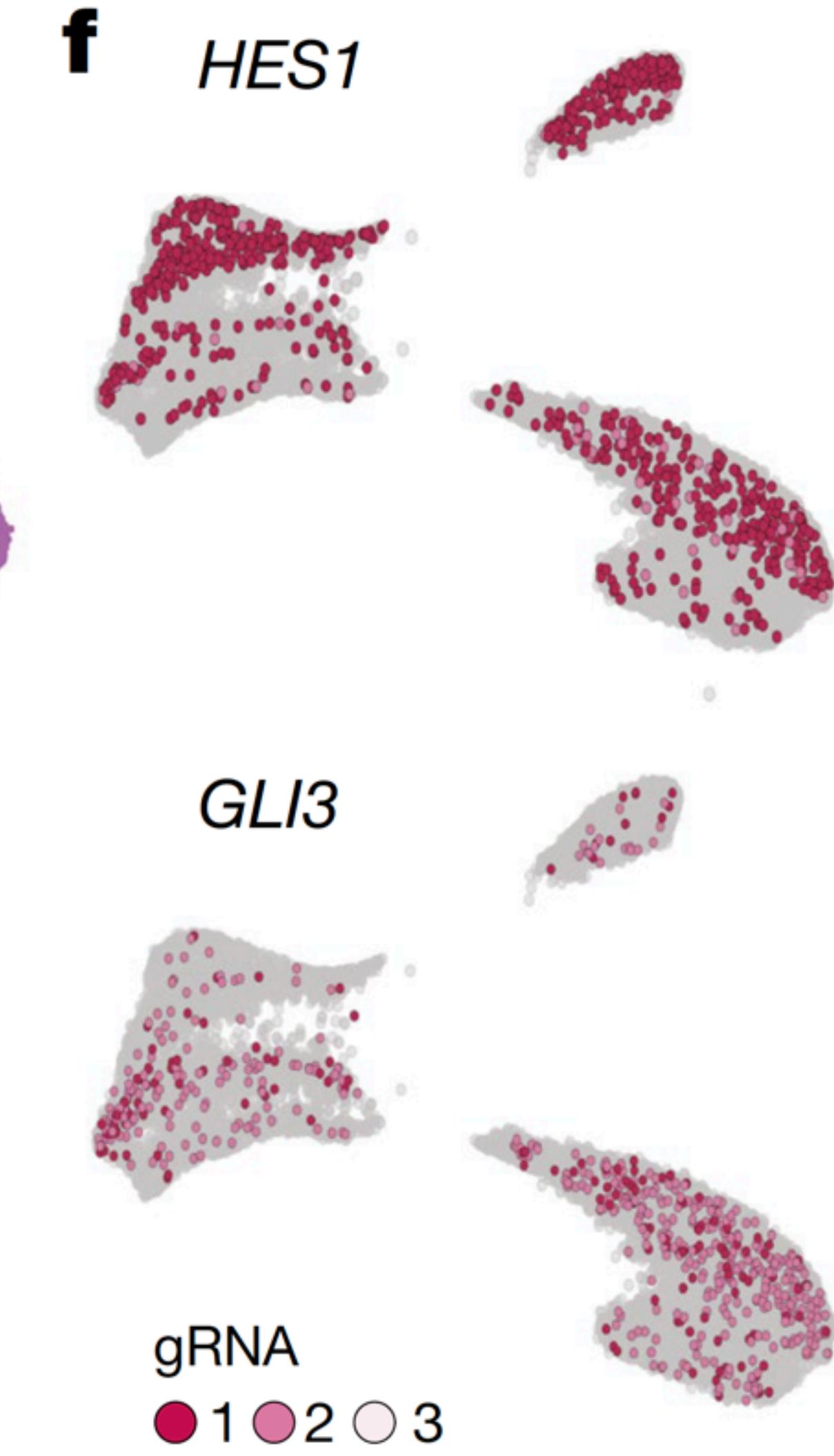
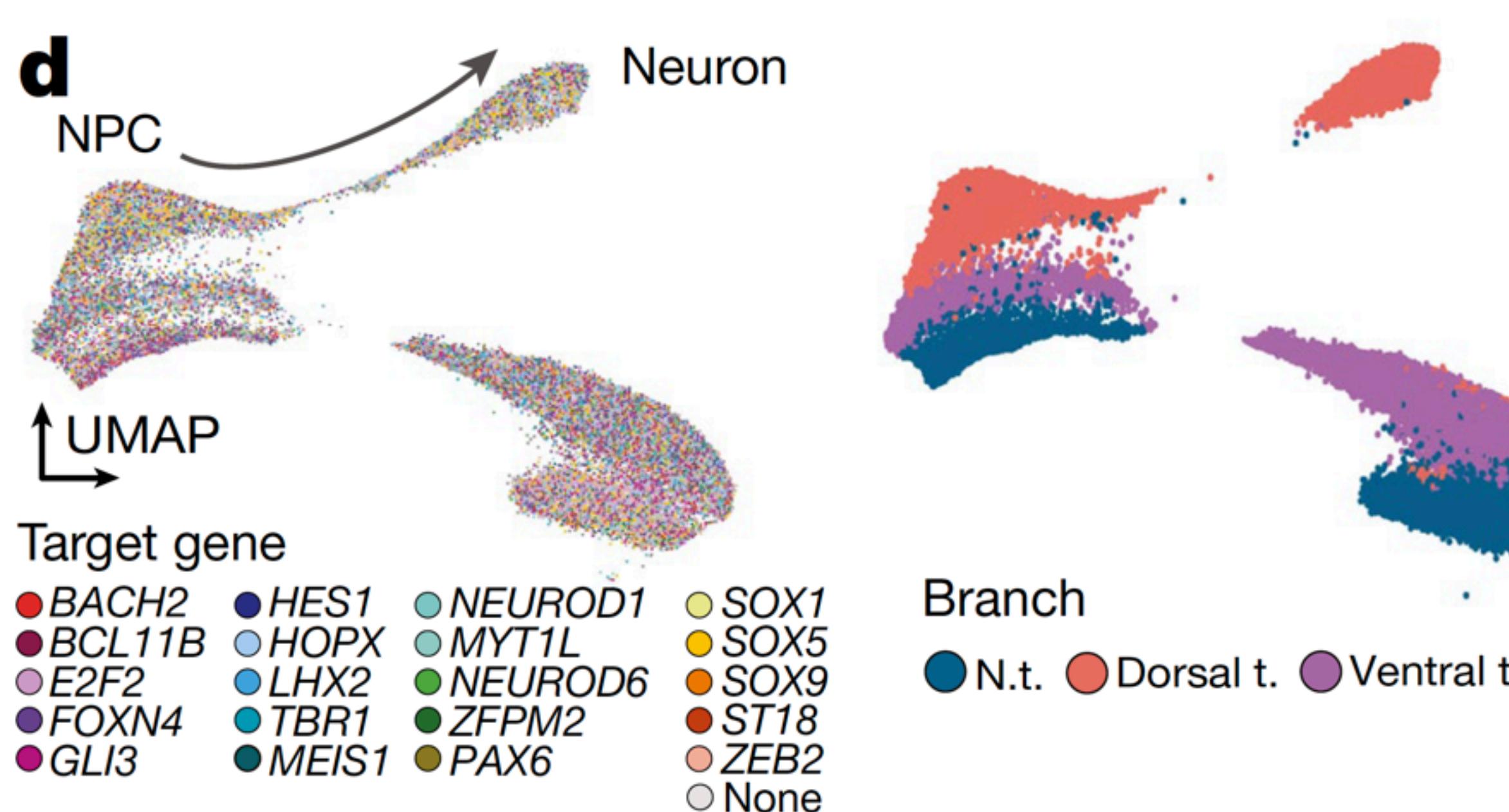
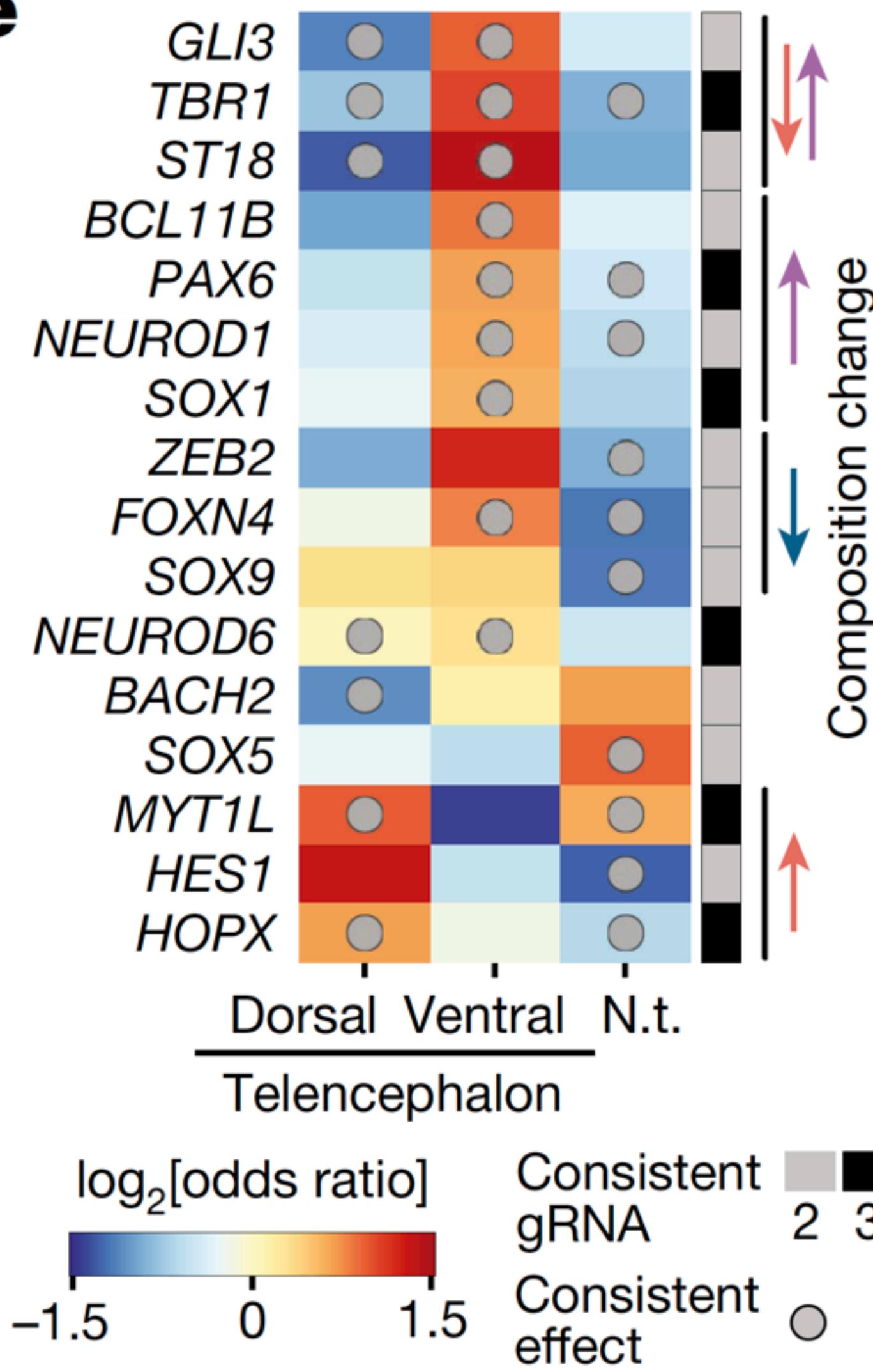
 Check for updates

Jonas Simon Fleck^{1,6}, Sophie Martina Johanna Jansen^{1,6}, Damian Wollny², Fides Zenk¹, Makiko Seimiya¹, Akanksha Jain¹, Ryoko Okamoto¹, Małgorzata Santel¹, Zhisong He¹✉, J. Gray Camp^{3,4,5}✉ & Barbara Treutlein¹✉

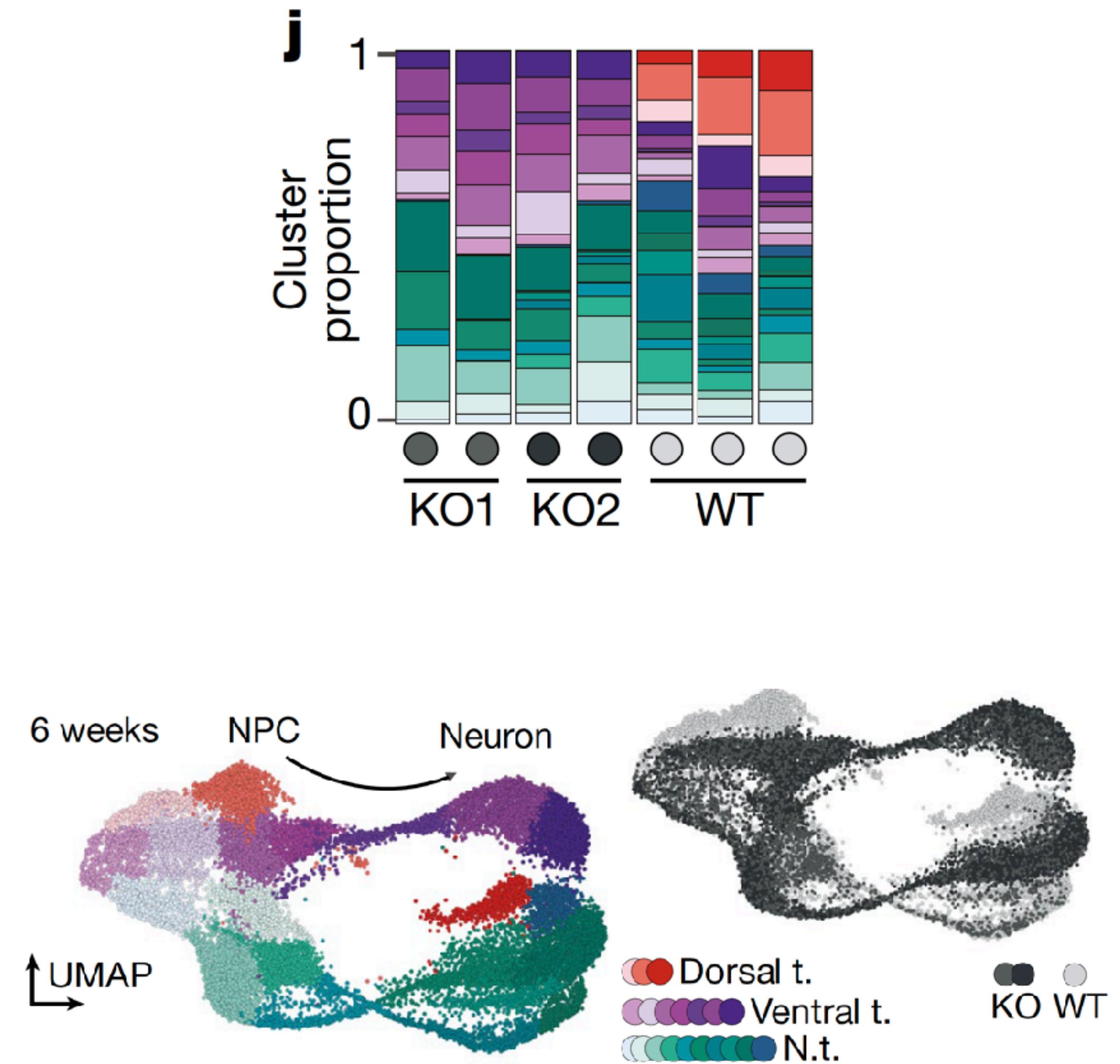
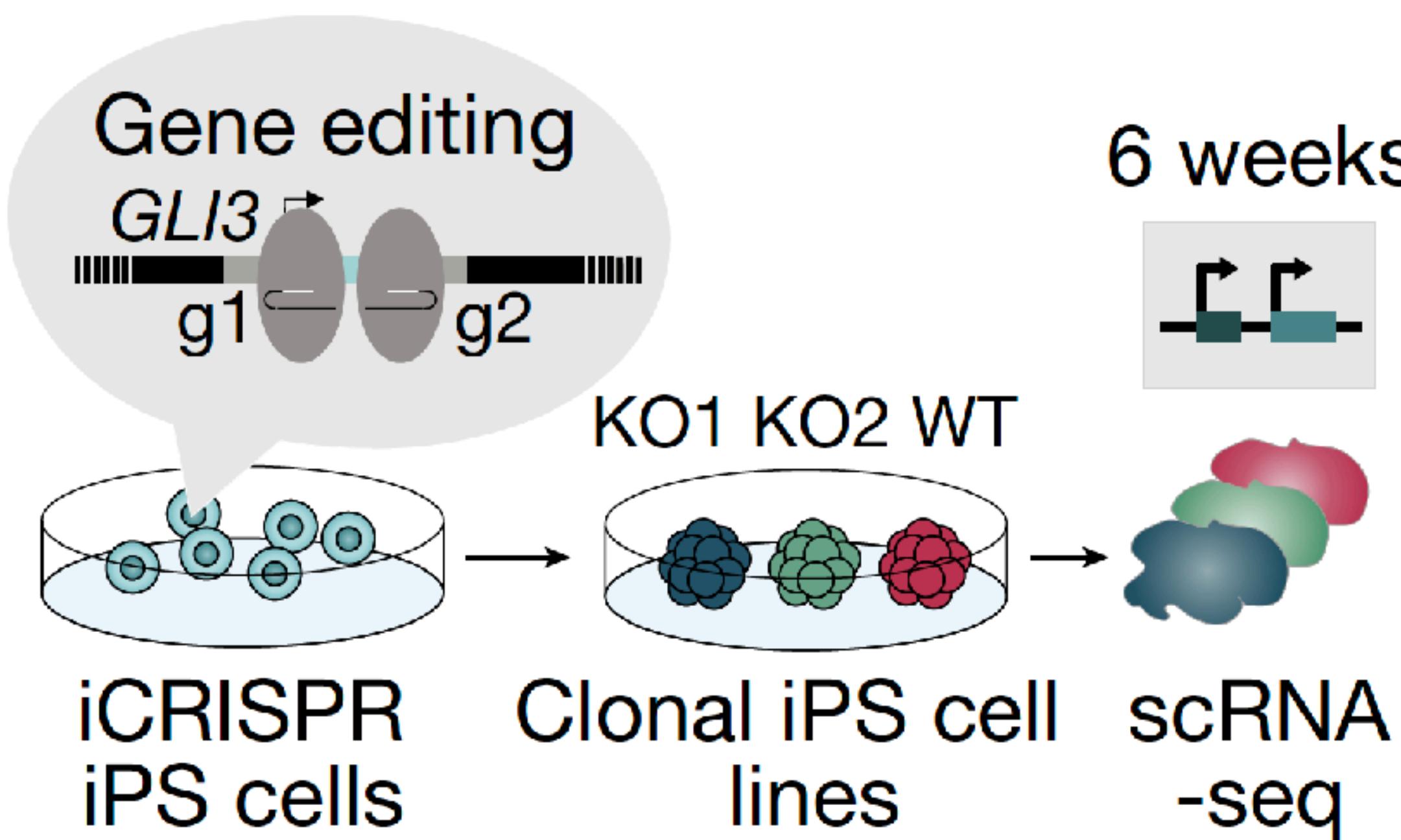
Self-organizing neural organoids grown from pluripotent stem cells^{1–3} combined with single-cell genomic technologies provide opportunities to examine gene regulatory networks underlying human brain development. Here we acquire single-cell transcriptome and accessible chromatin data over a dense time course in human organoids covering neuroepithelial formation, patterning, brain regionalization and neurogenesis, and identify temporally dynamic and brain-region-specific regulatory regions. We developed Pando—a flexible framework that incorporates multi-omic



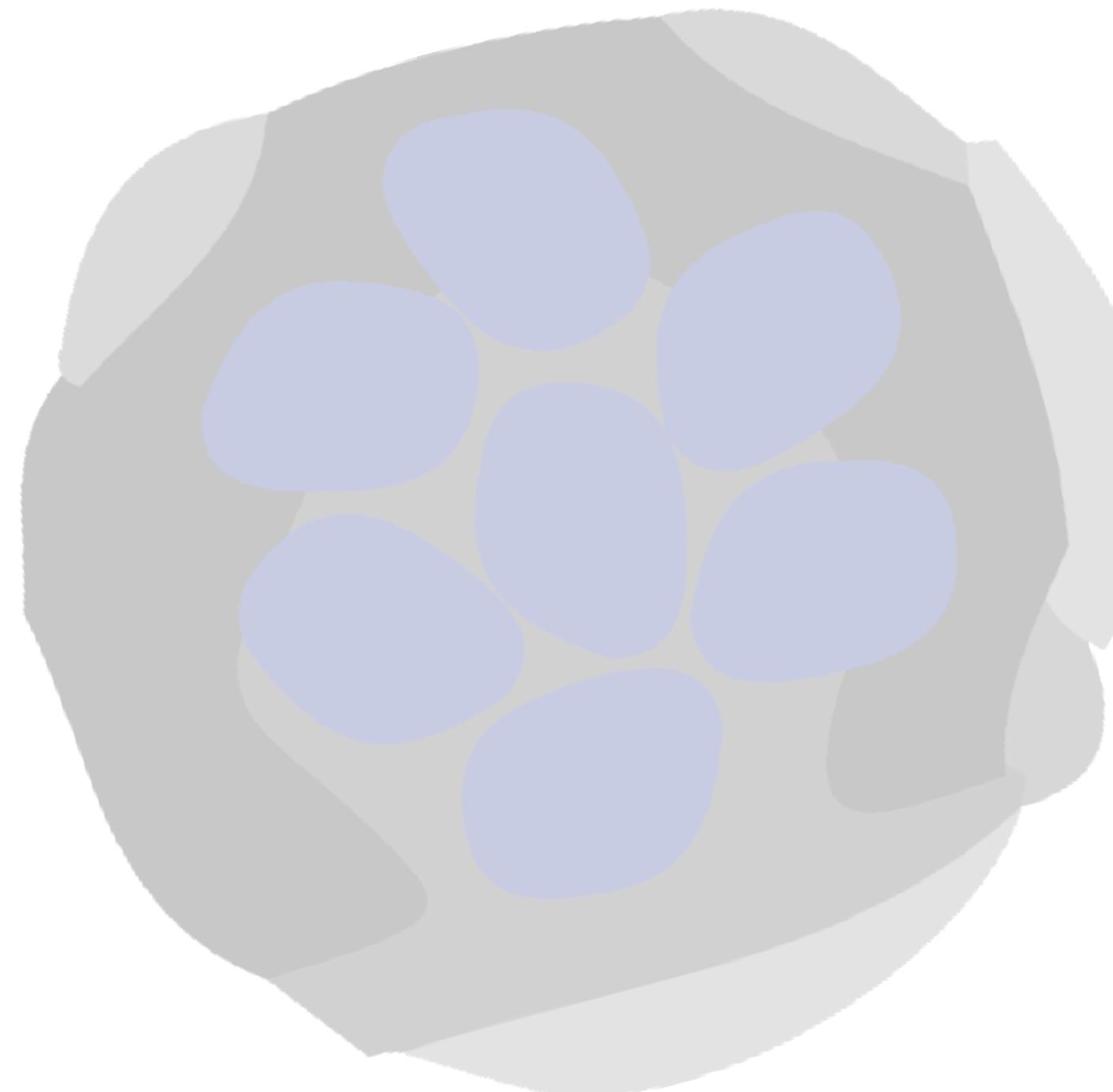
GLI3 regulates dorsal forebrain development



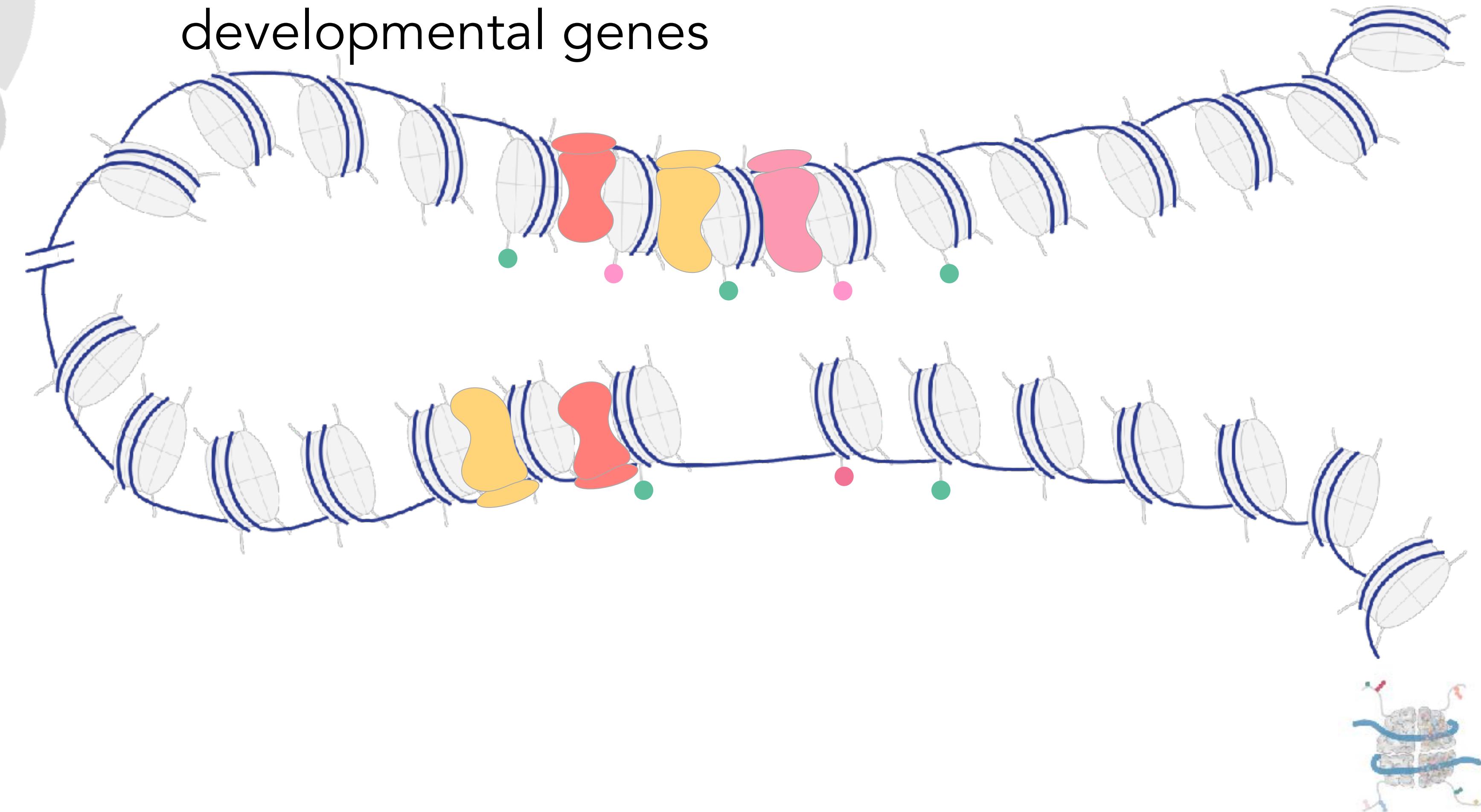
GLI3 regulates dorsal forebrain development



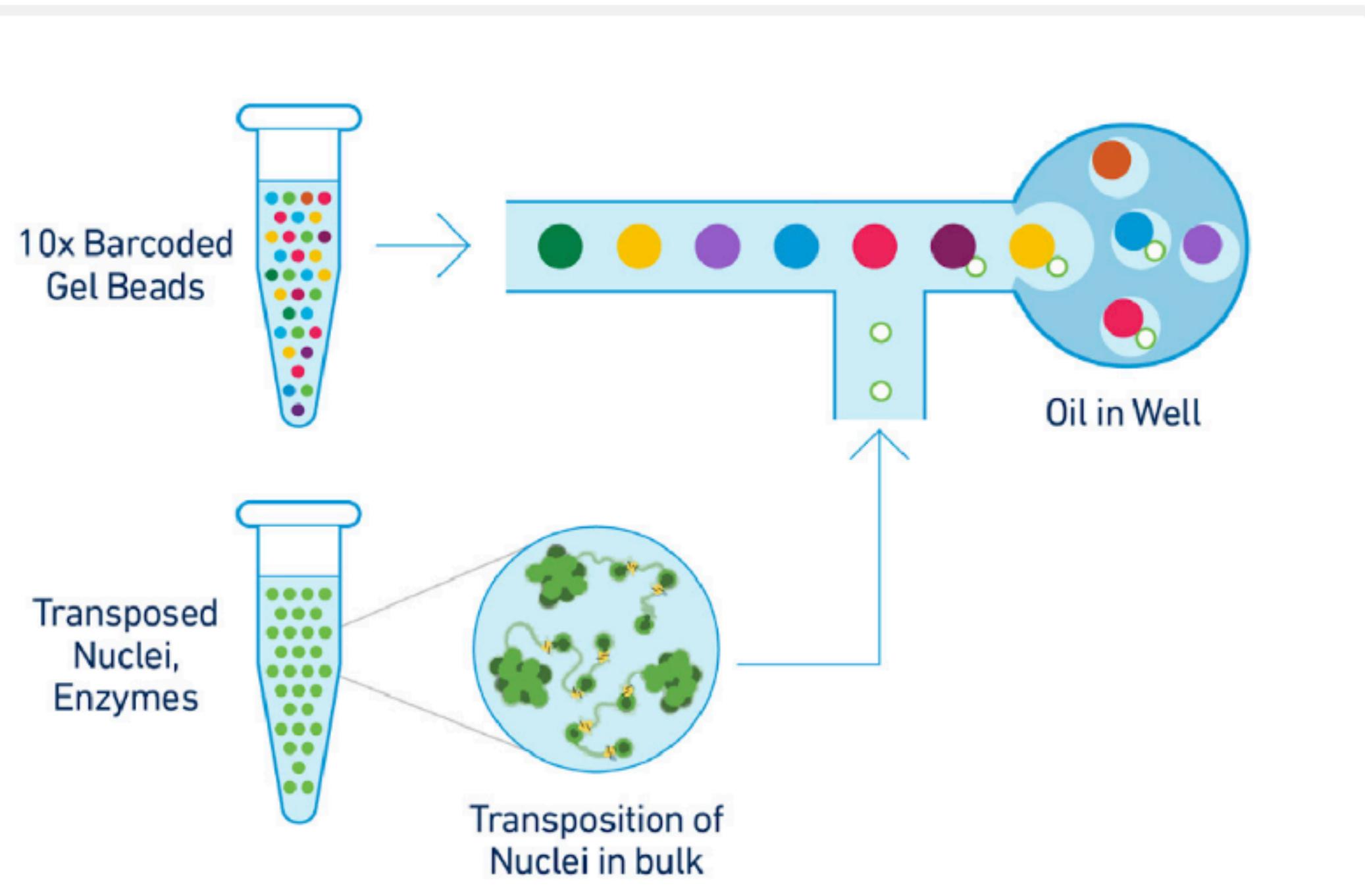
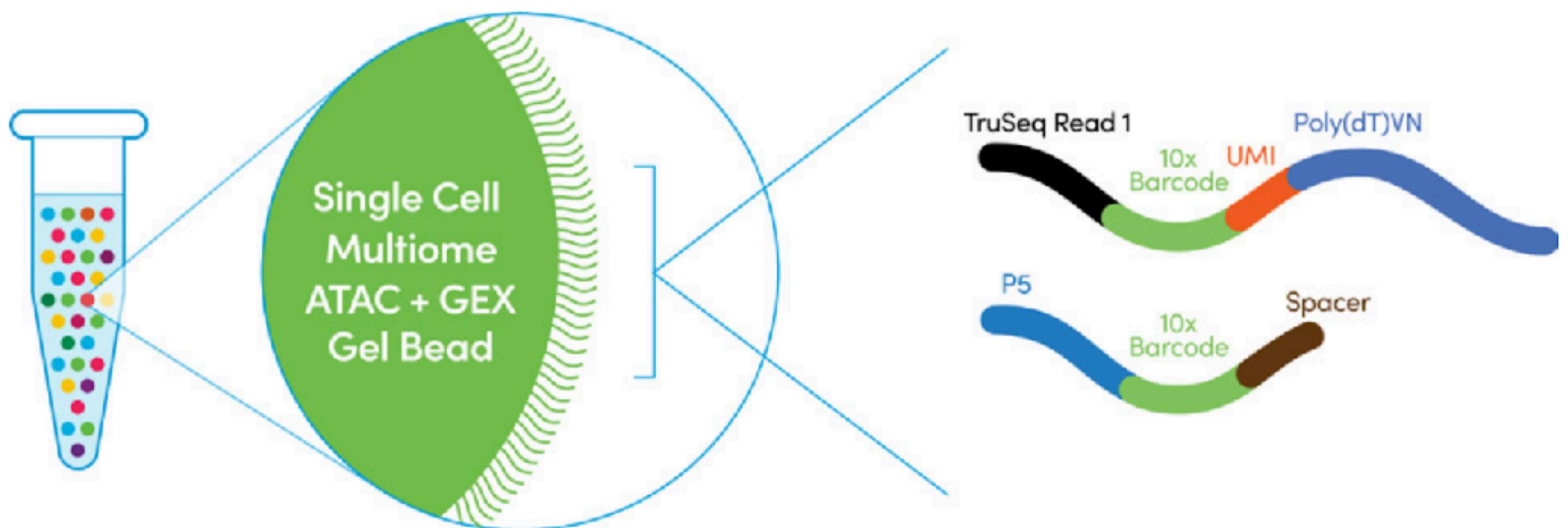
What are the molecular mechanisms of GLI3 regulation?



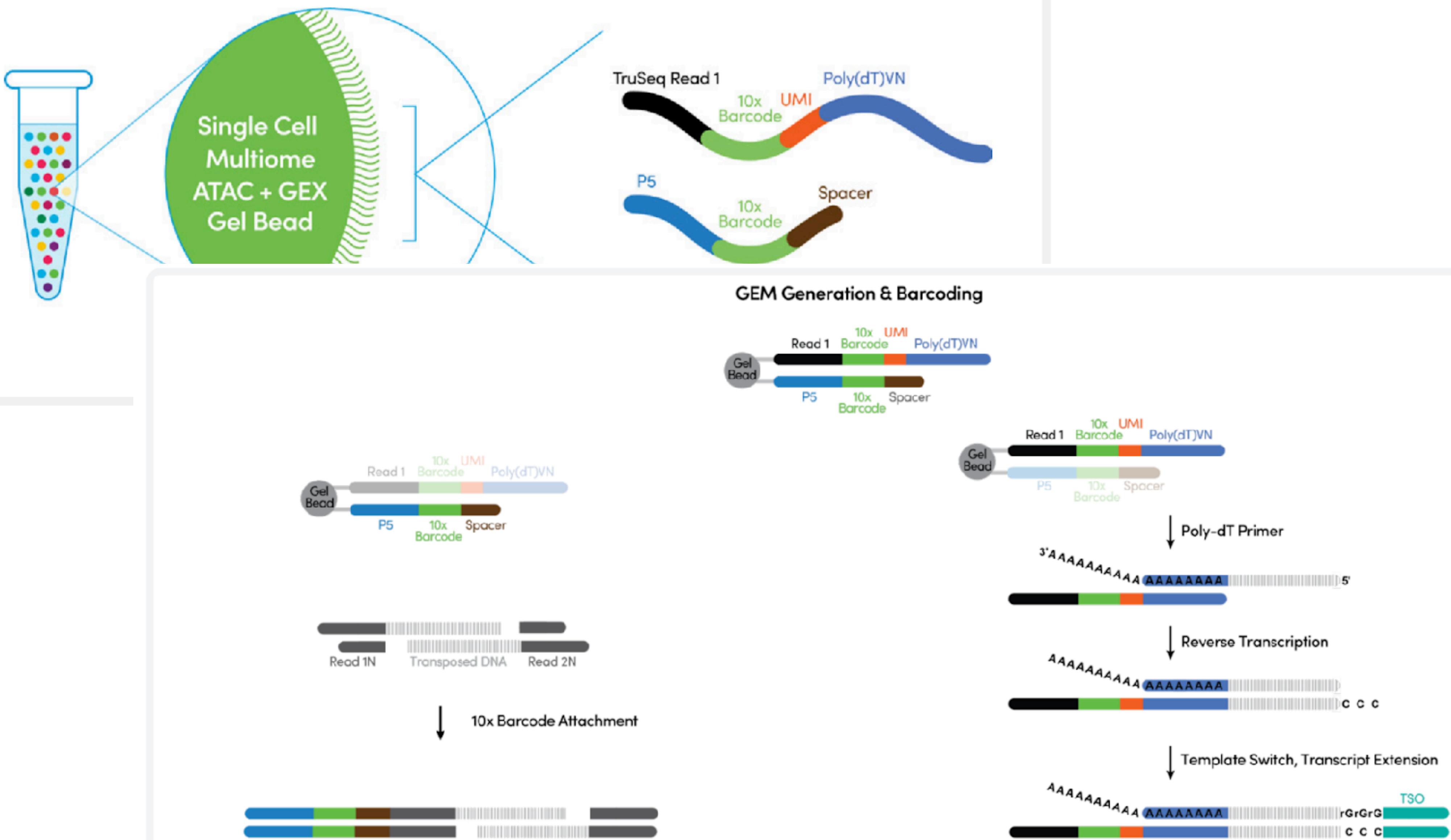
GLI3 is a transcription factor that regulates developmental genes



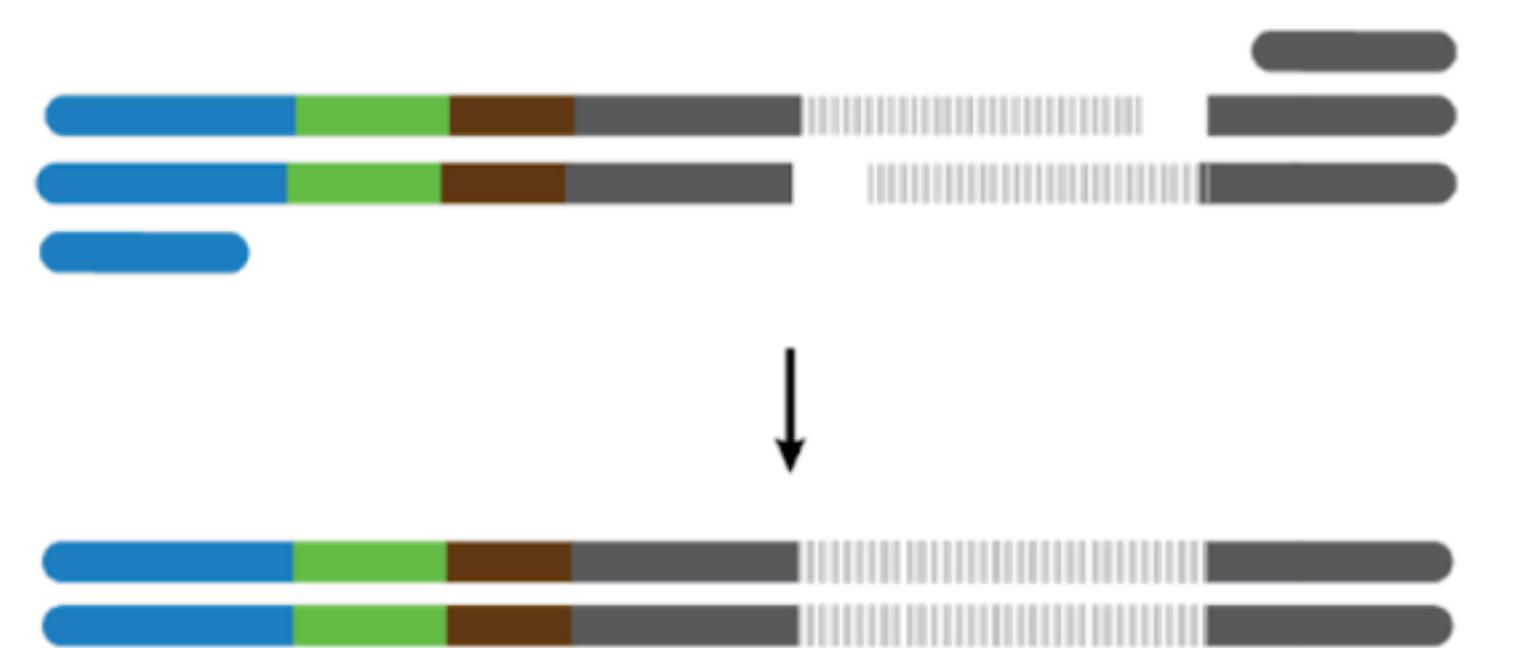
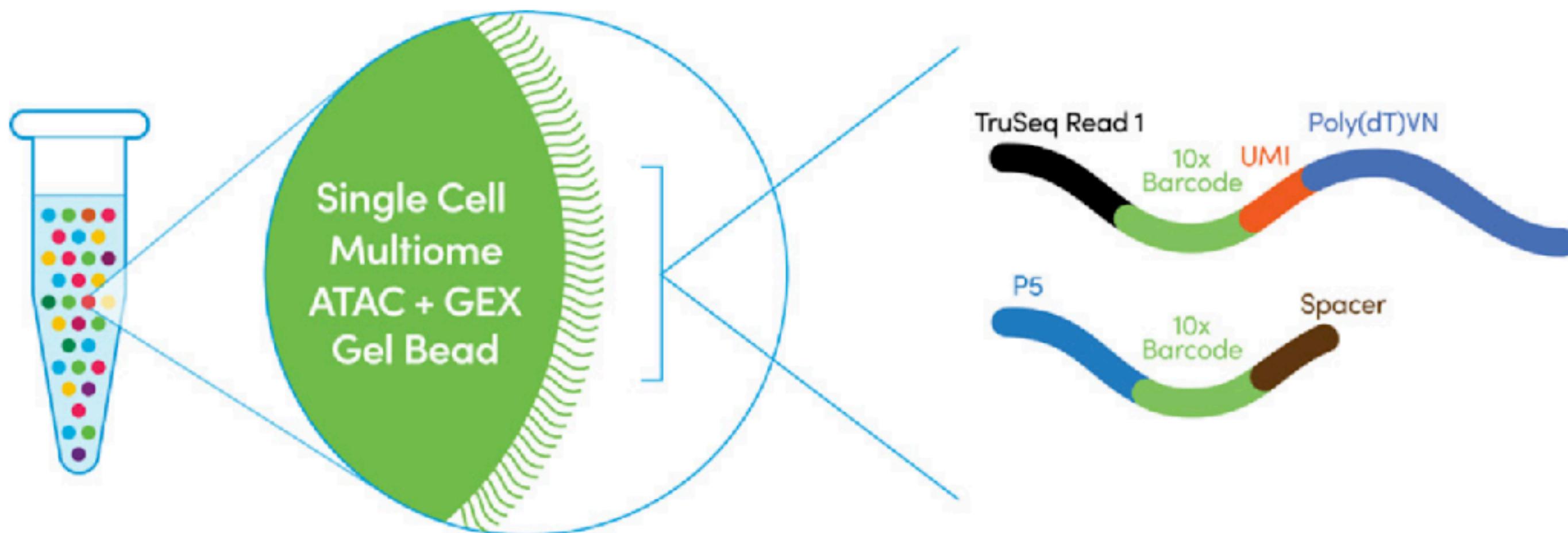
10 x Genomics multiome kit



10 x Genomics multiome kit

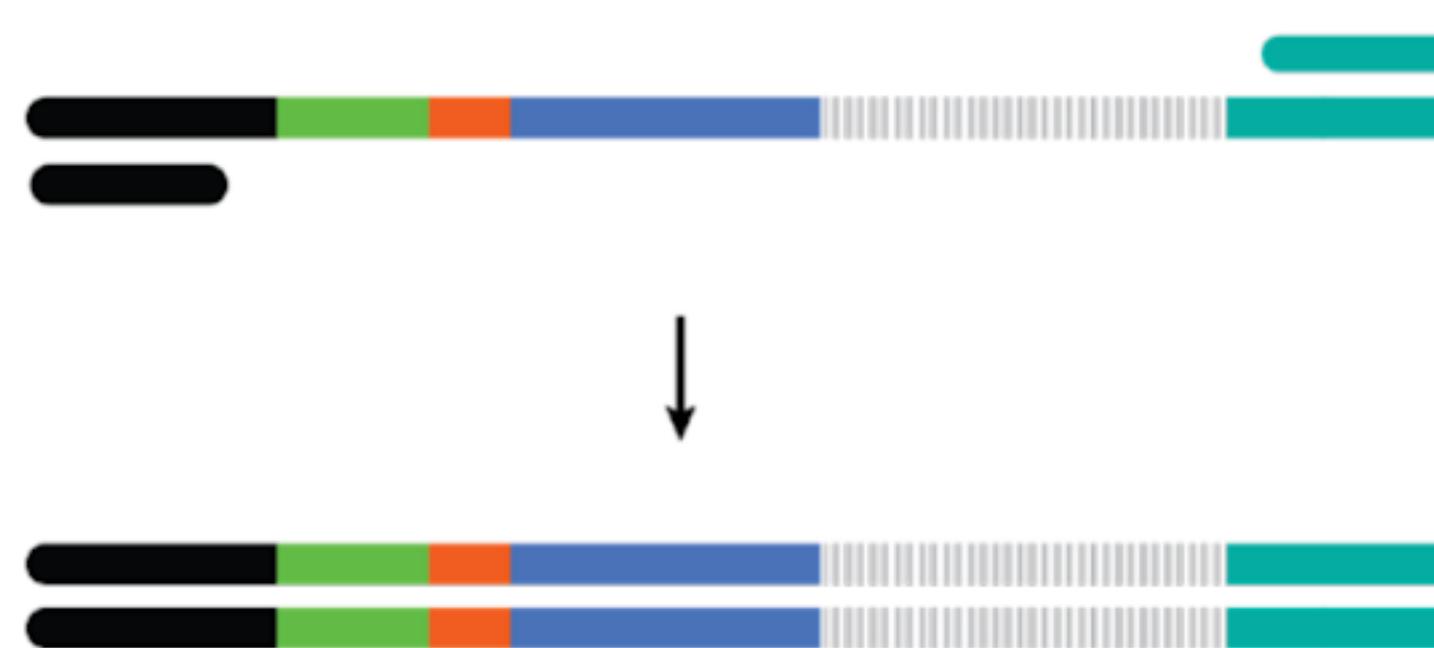


10 x Genomics multiome kit



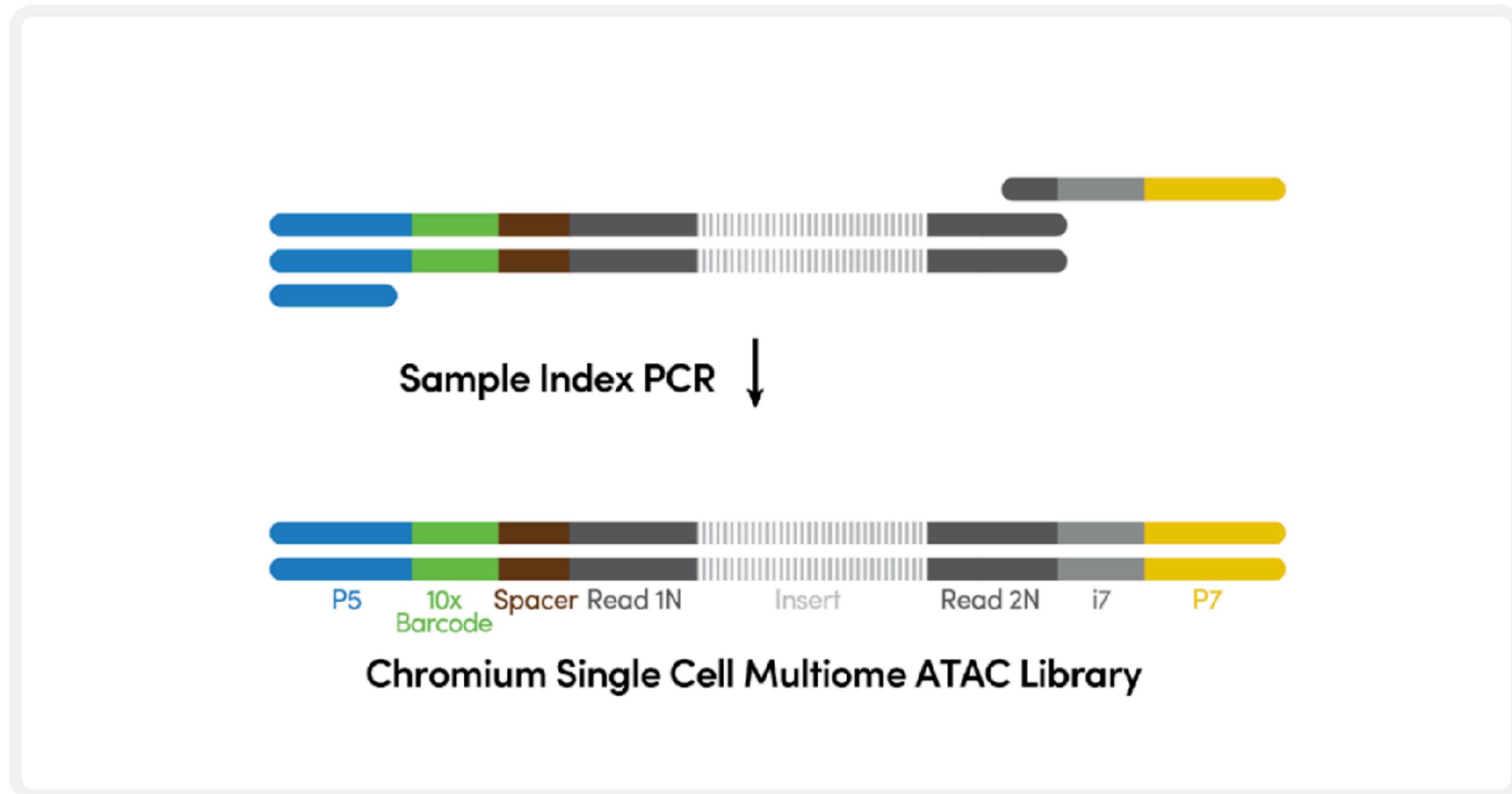
Pre-Amplification PCR

Transposed DNA

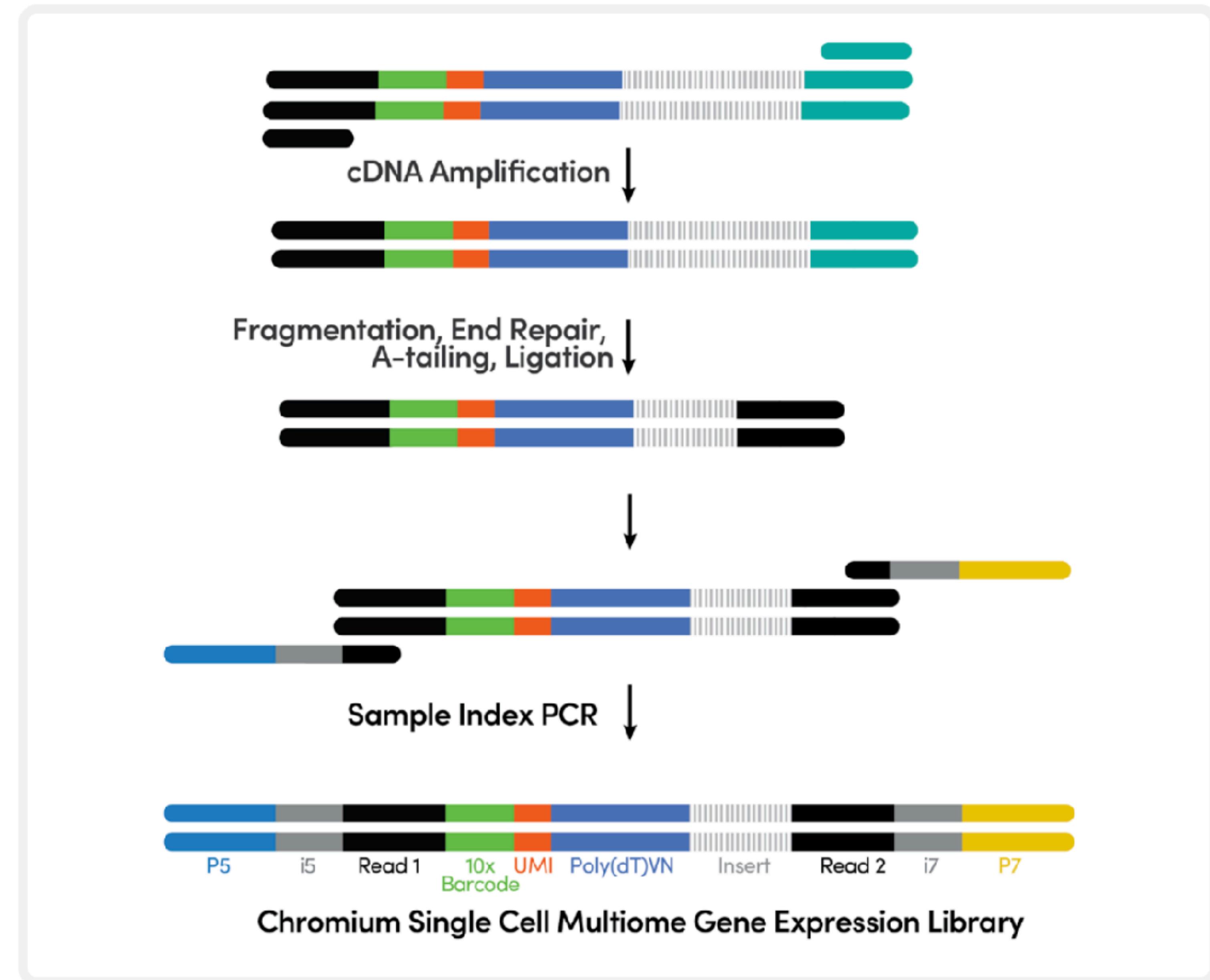


cDNA

10 x Genomics multiome kit



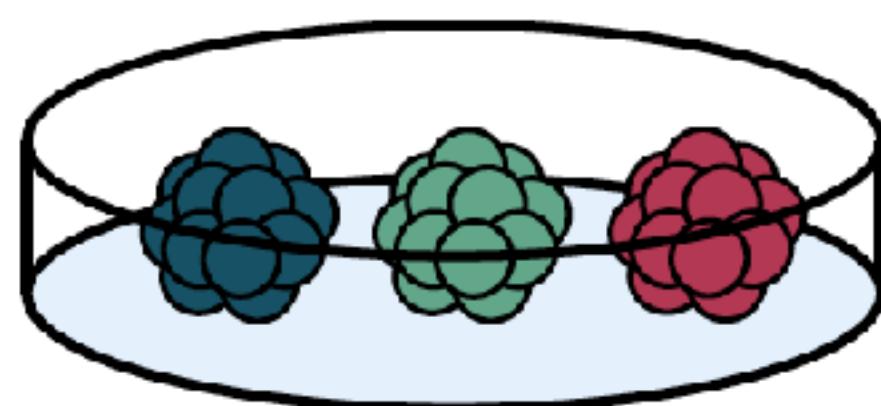
10 x Genomics multiome kit



What are the molecular mechanisms of GLI3 regulation?

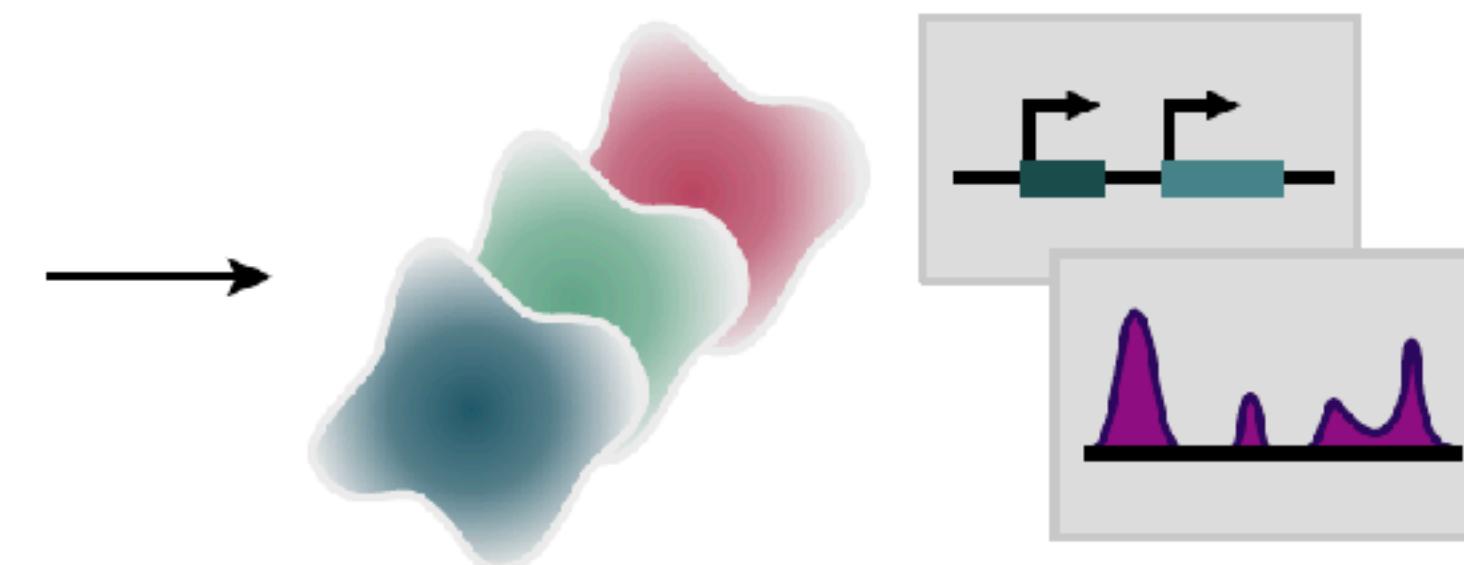
a

GLI3-KO
and control
iPS cell lines



K01 K02 WT

Week 3
Single-cell multiome



This is the dataset you will be working on!