

Single Cell Epigenomics

scMultiomics exercises

Learning Objectives of this week

Basic principles of 10x Genomics multiome kit

Understanding of early brain organoid development

Mapping early development using multiomics

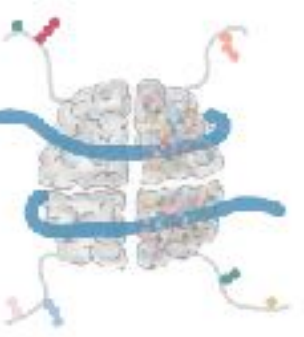
Understanding Human Brain Development



How does cellular diversity arise in the brain?

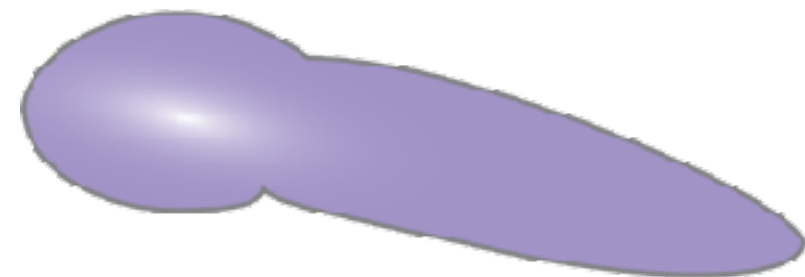


Understanding Human Brain Development



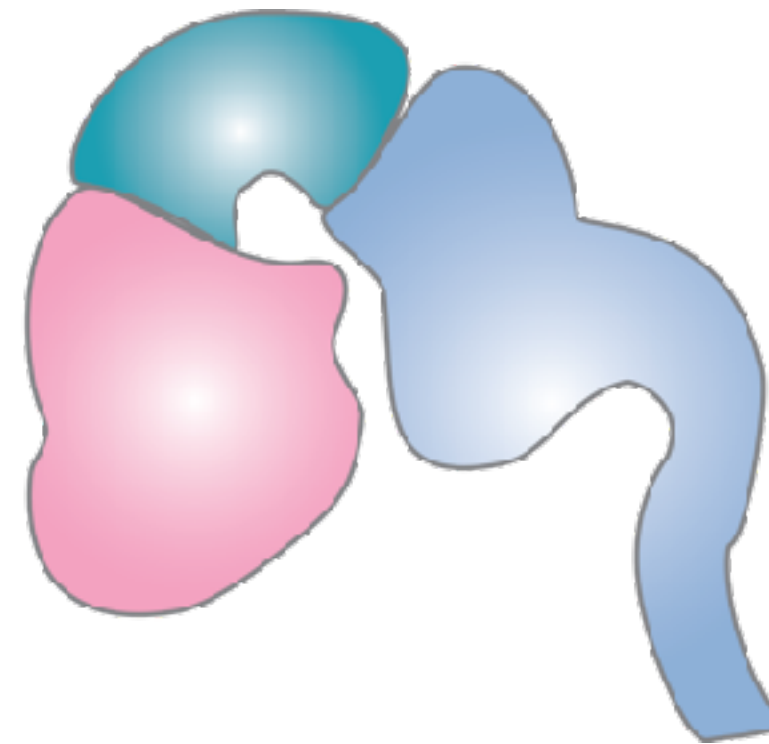
Understanding Human Brain Development

21 Days



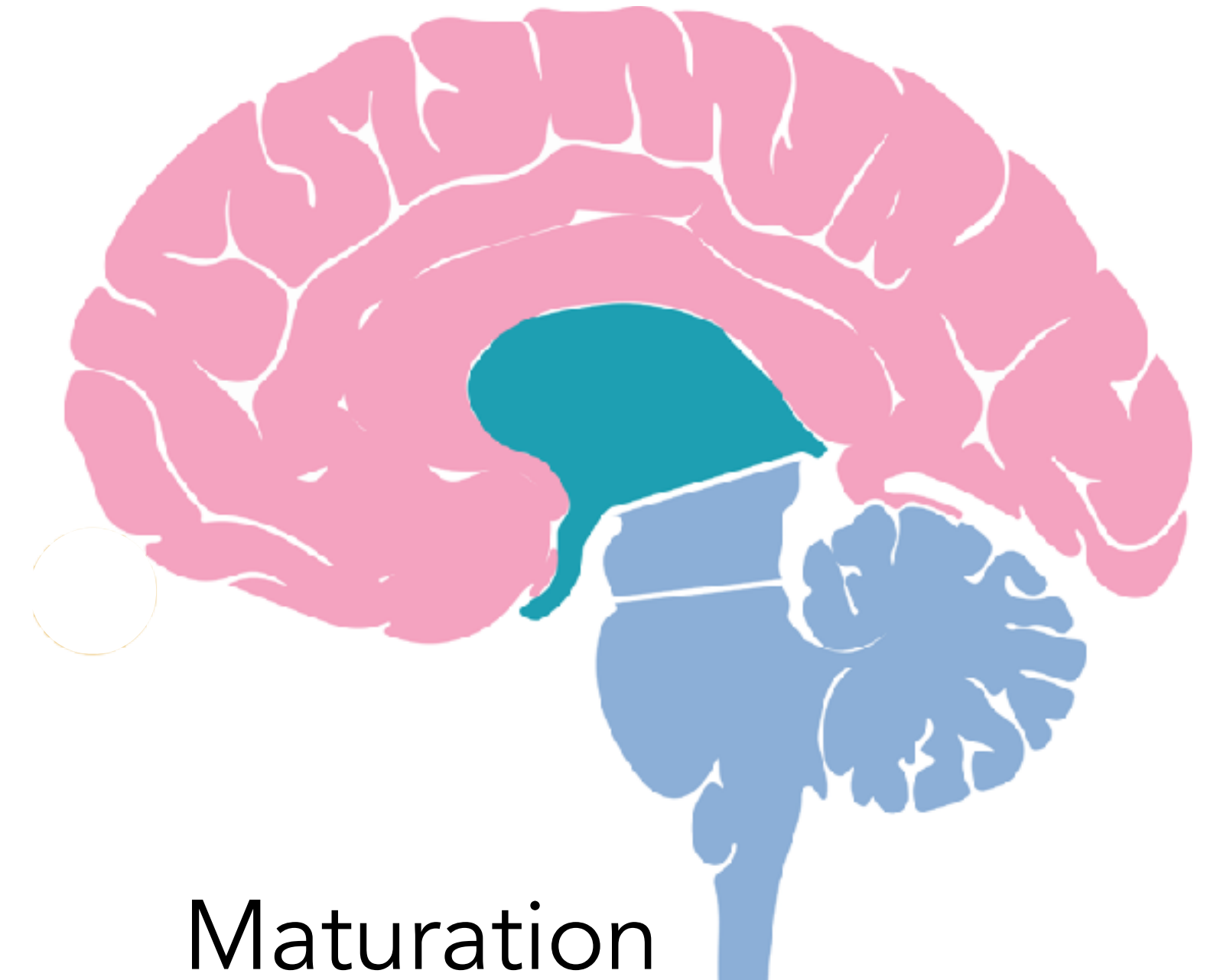
Formation of Neural Tube

35-40 Days



Regionalization

9 Months

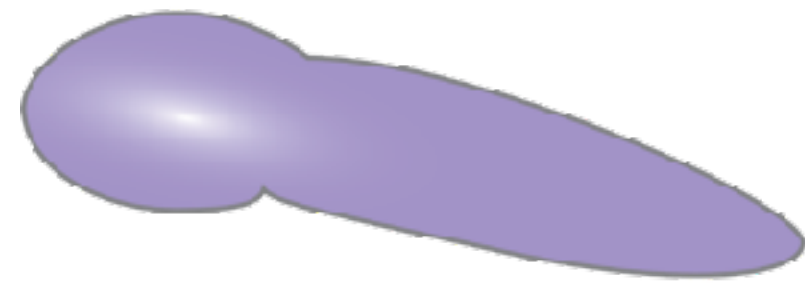


Maturation

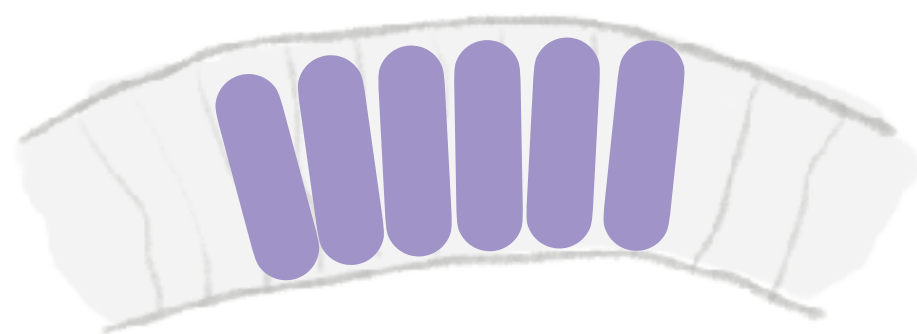


Understanding Human Brain Development

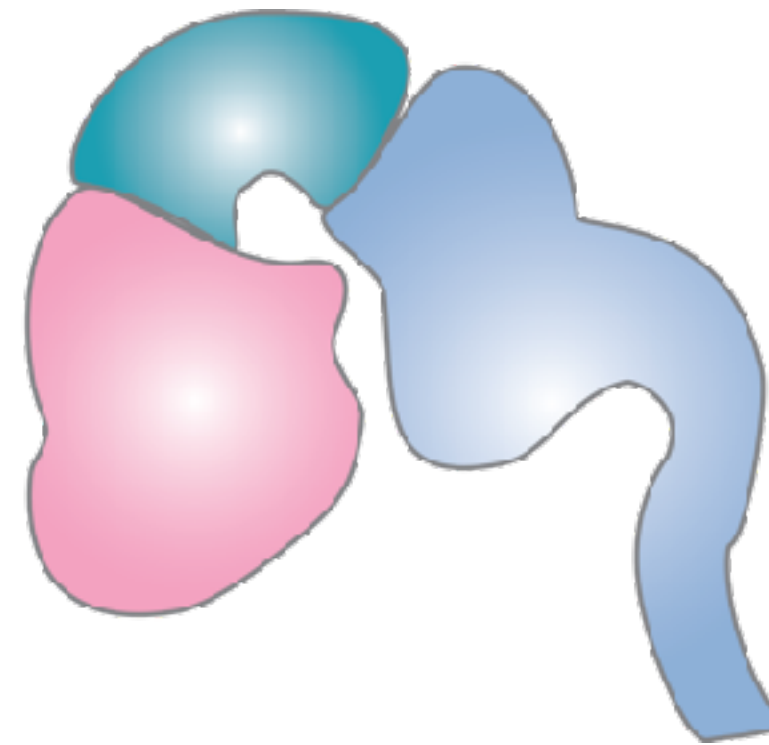
21 Days



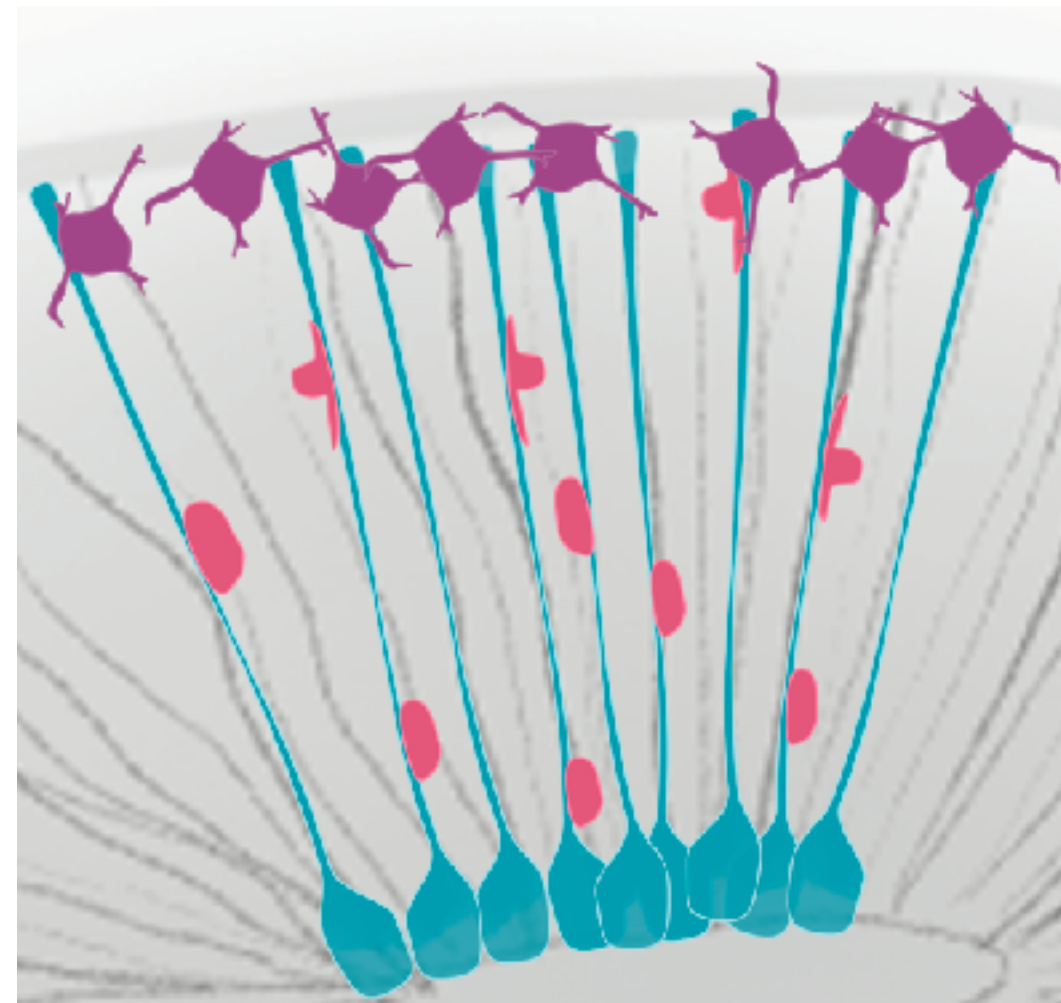
Formation of Neural Tube



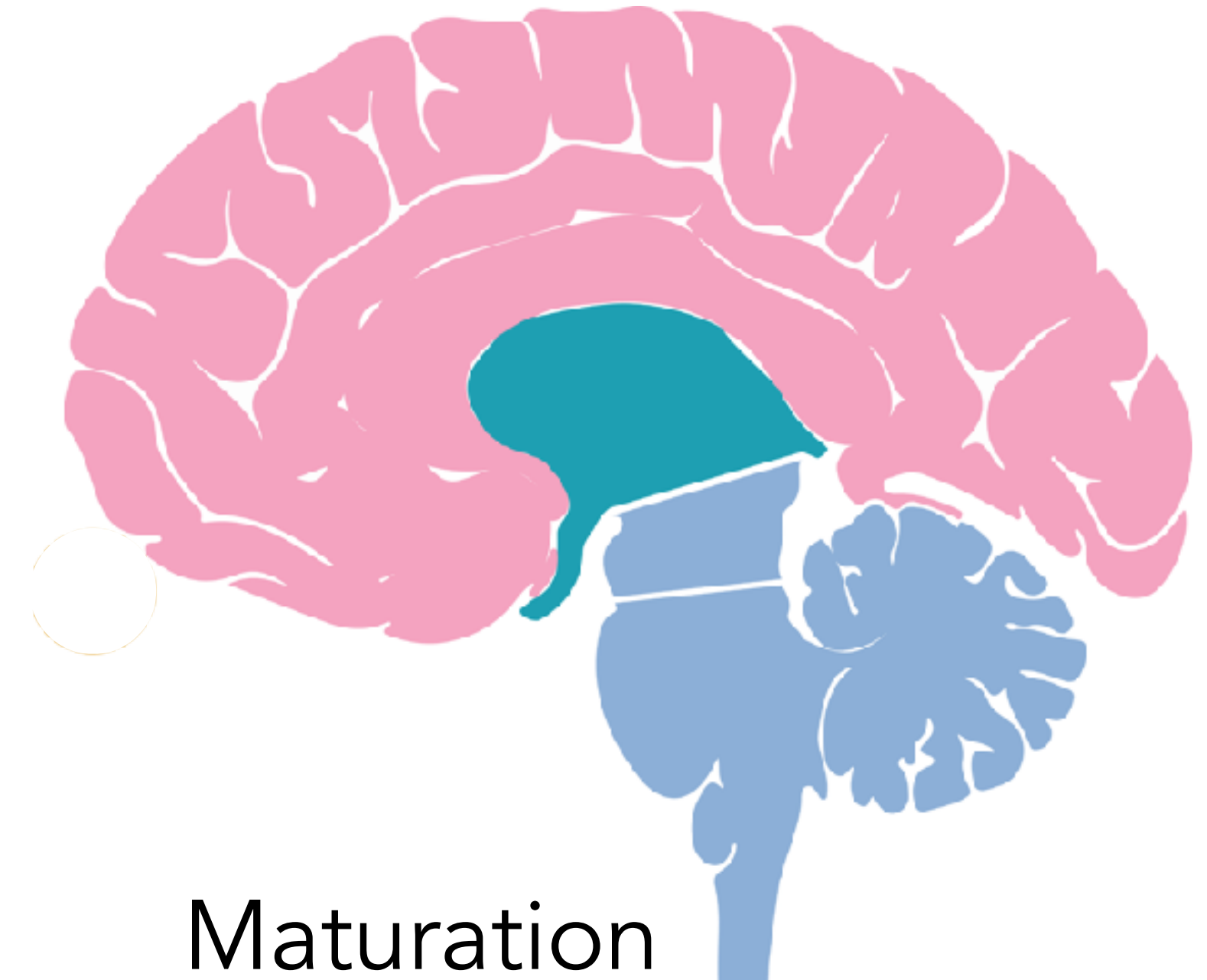
35-40 Days



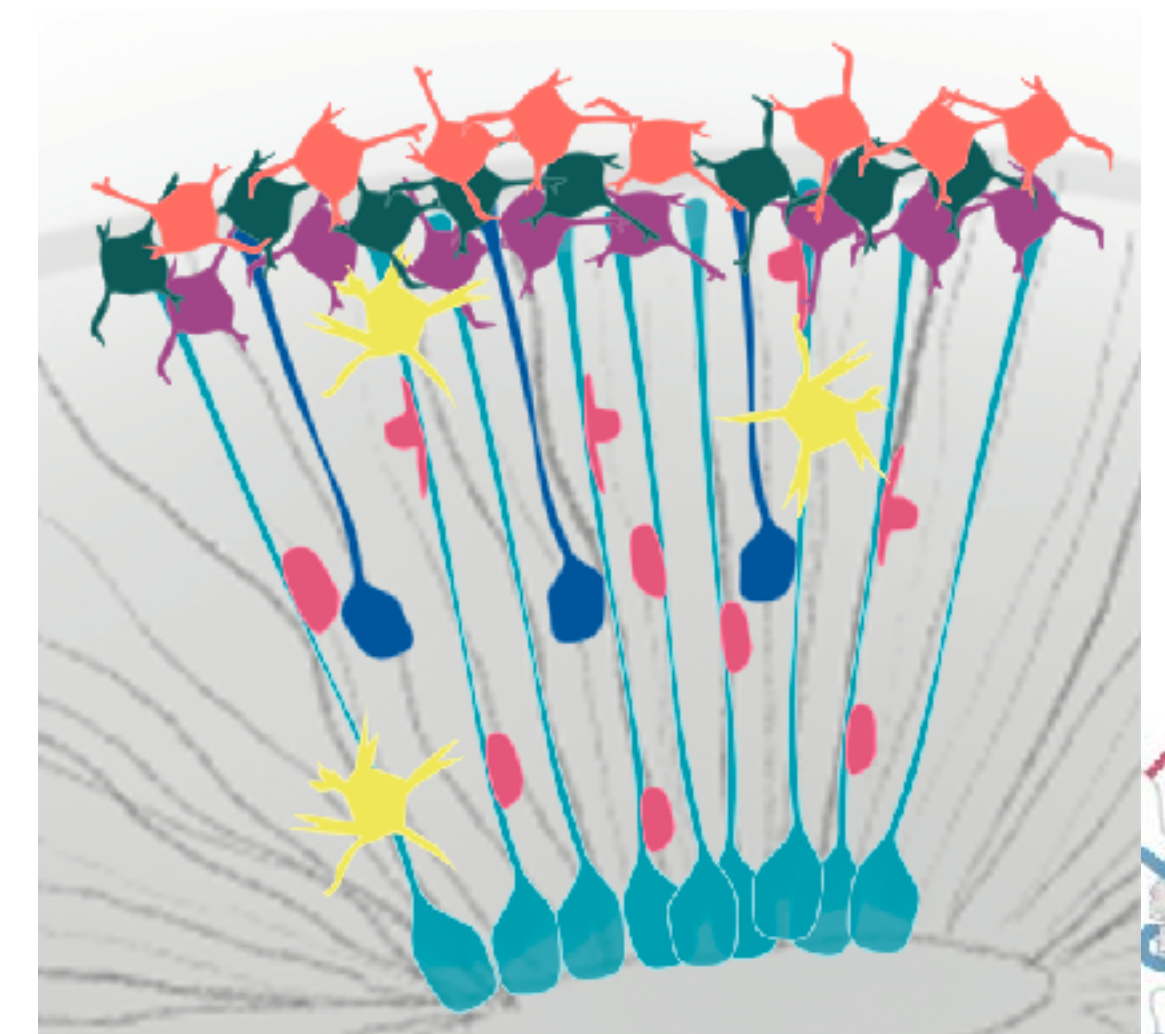
Regionalization



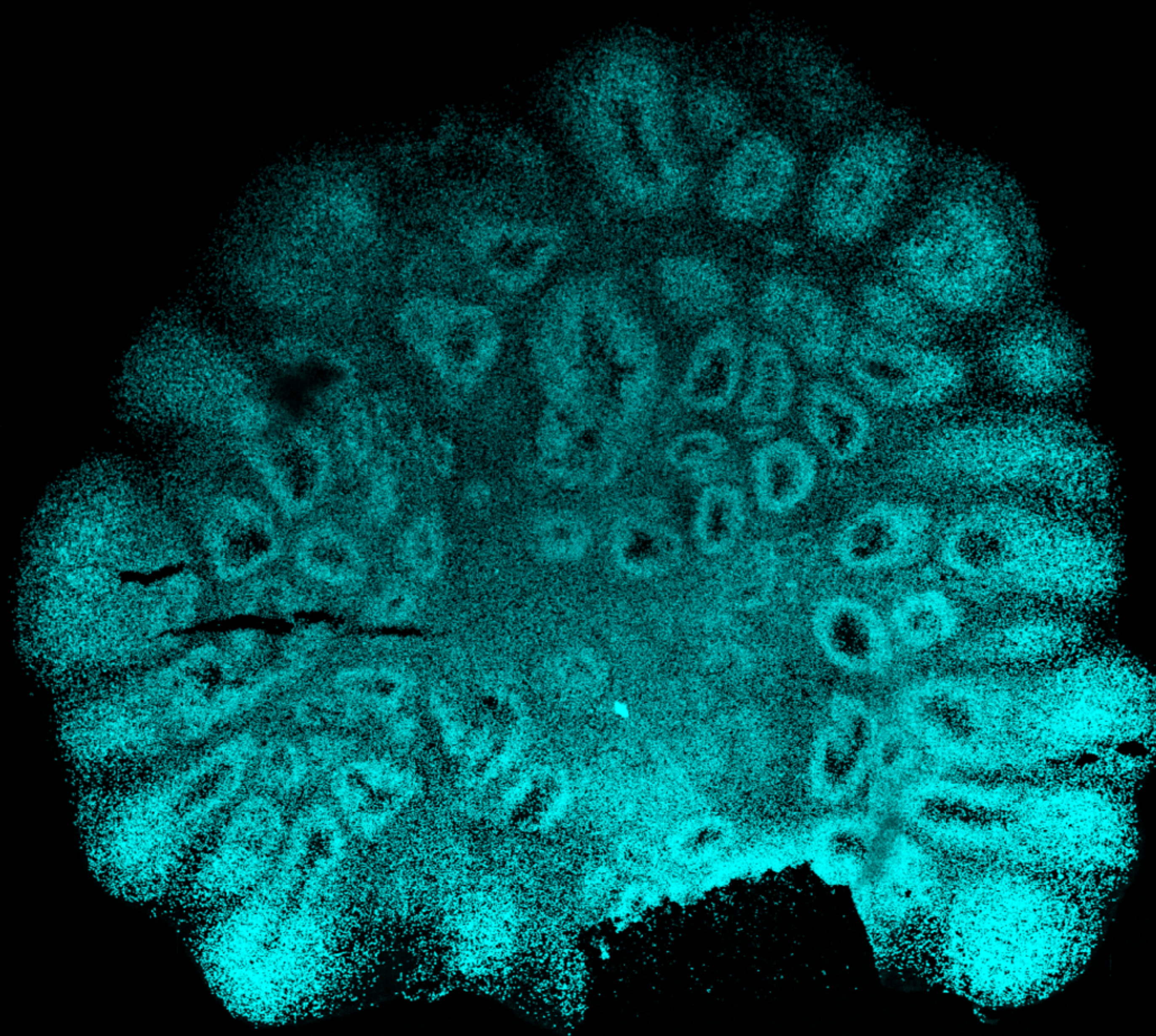
9 Months



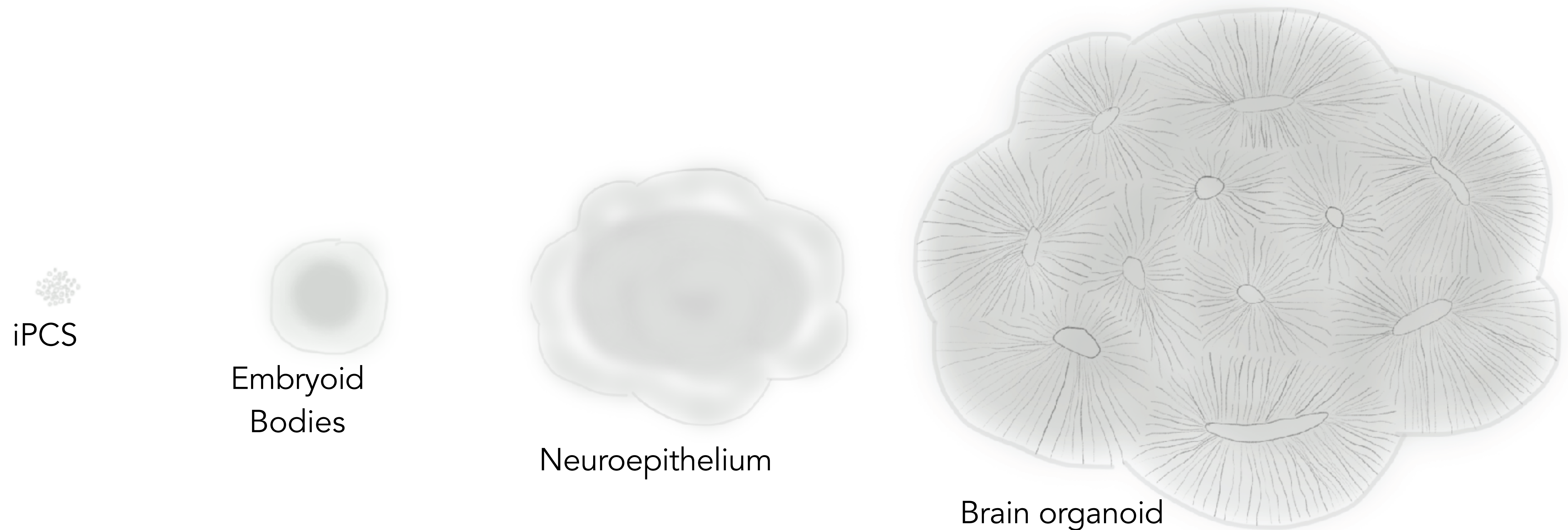
Maturation



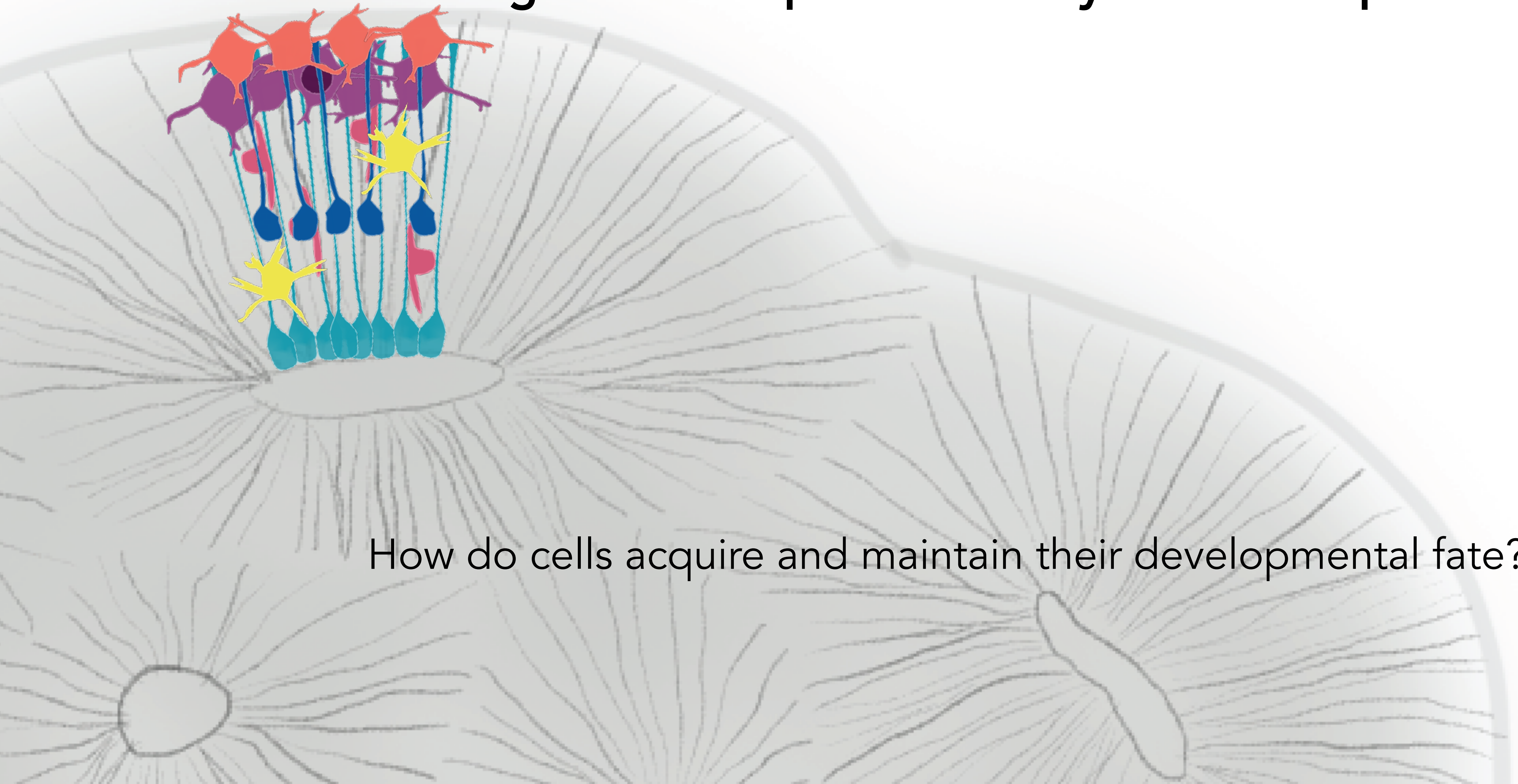
Understanding Human Brain Development using Neural Organoids



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>

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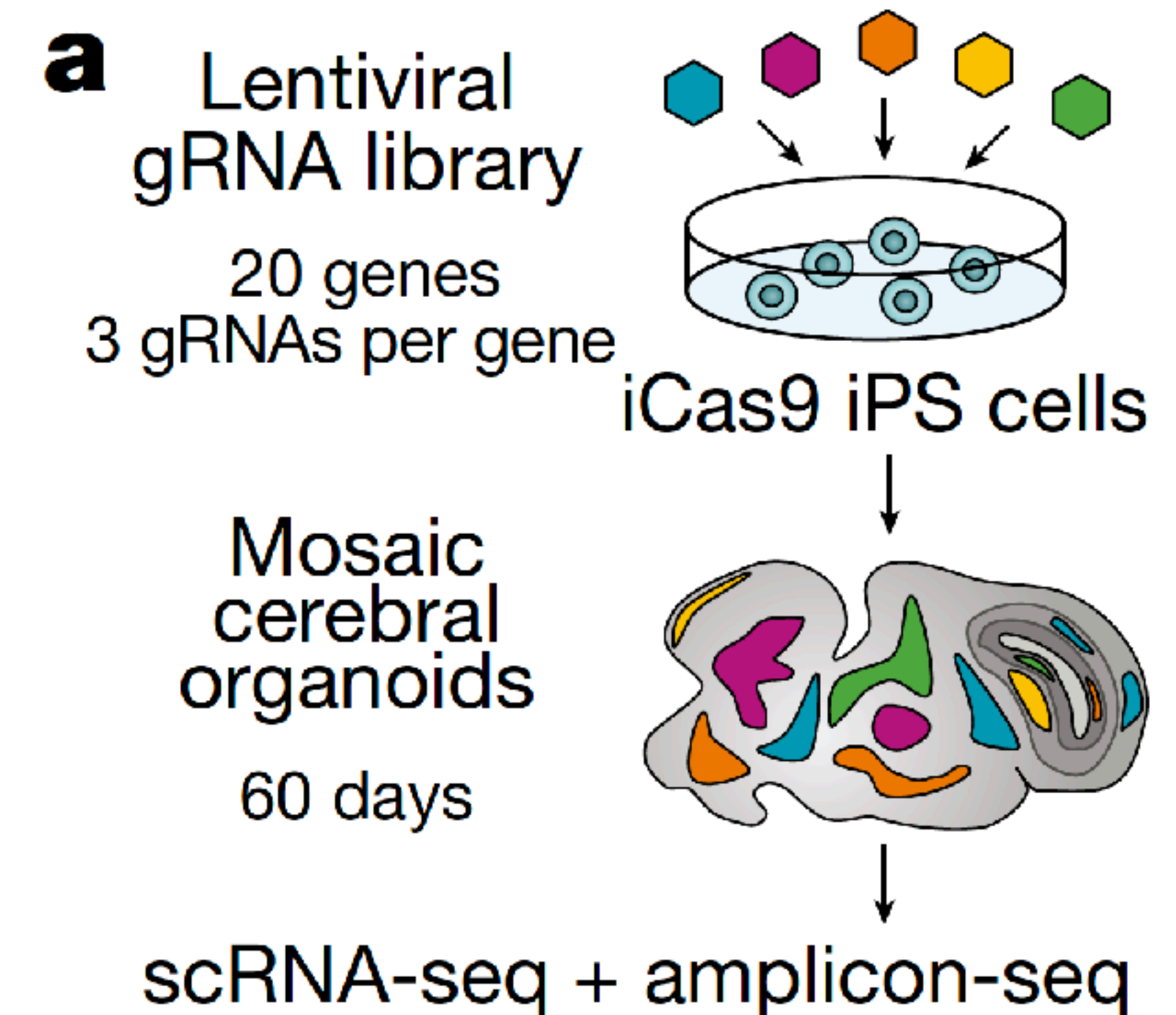
Published online: 05 October 2022

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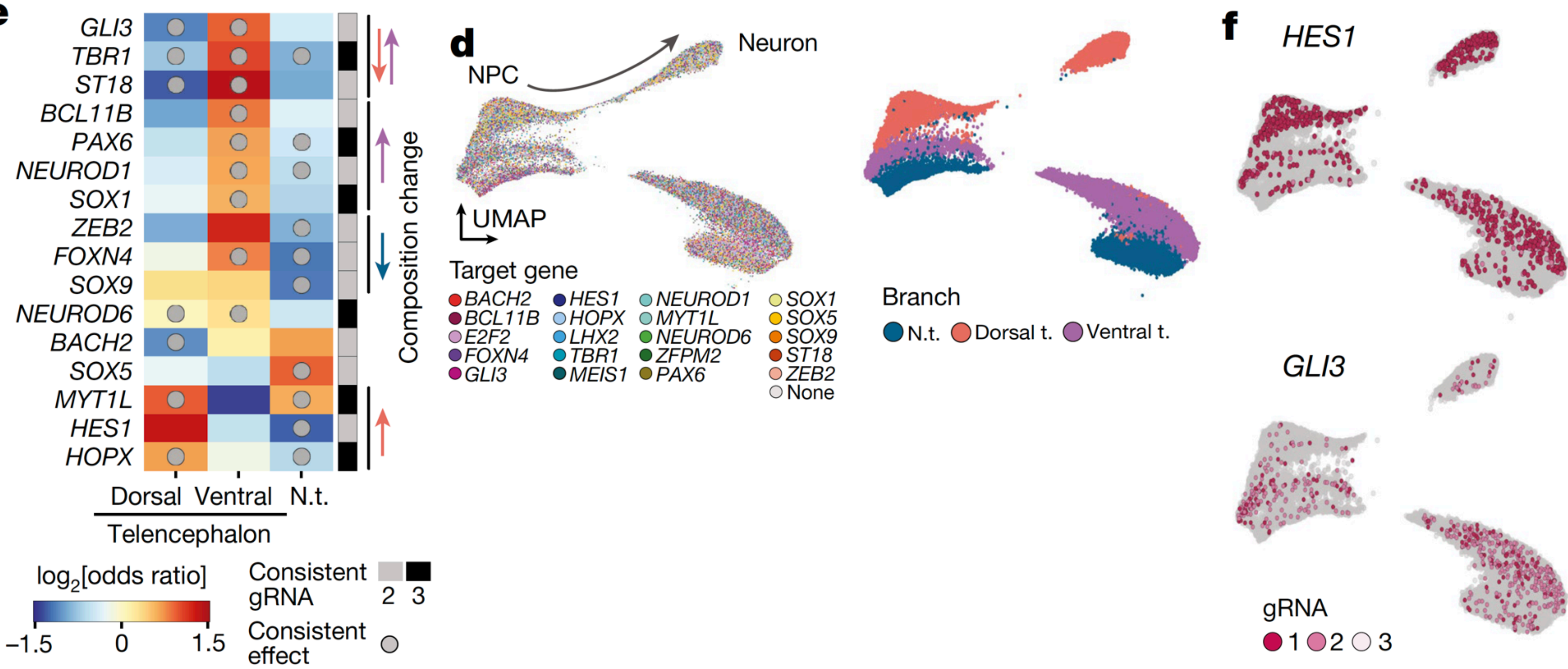
 Check for updates

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

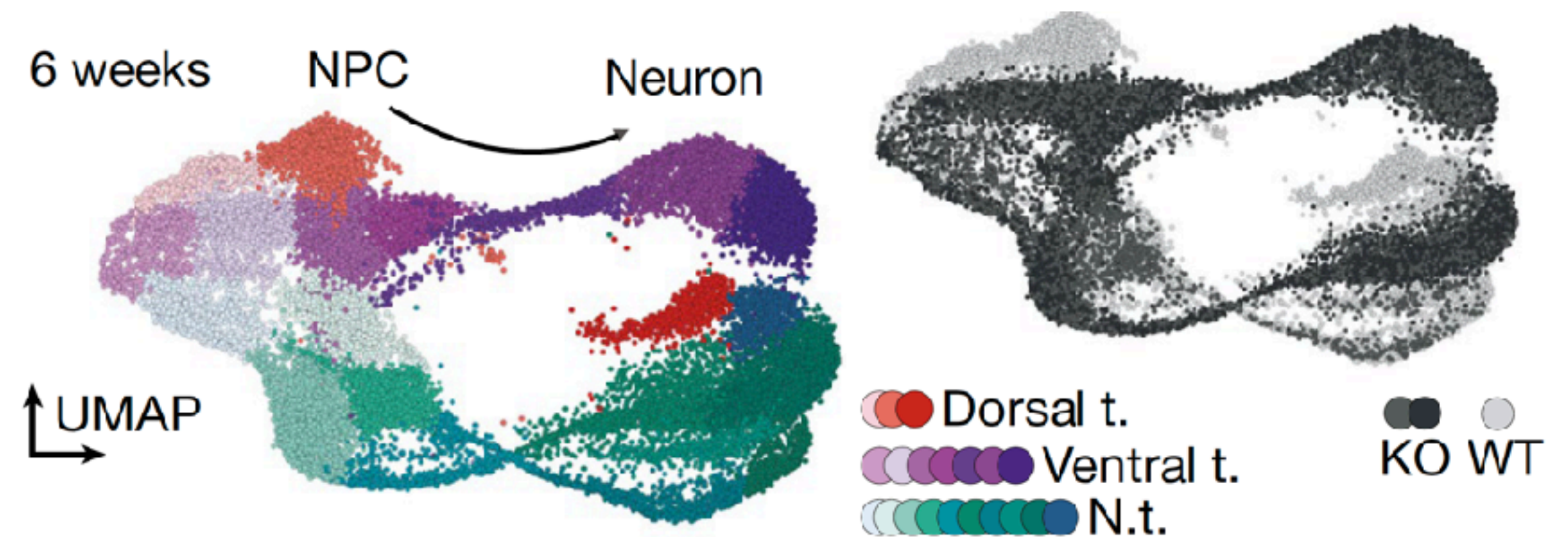
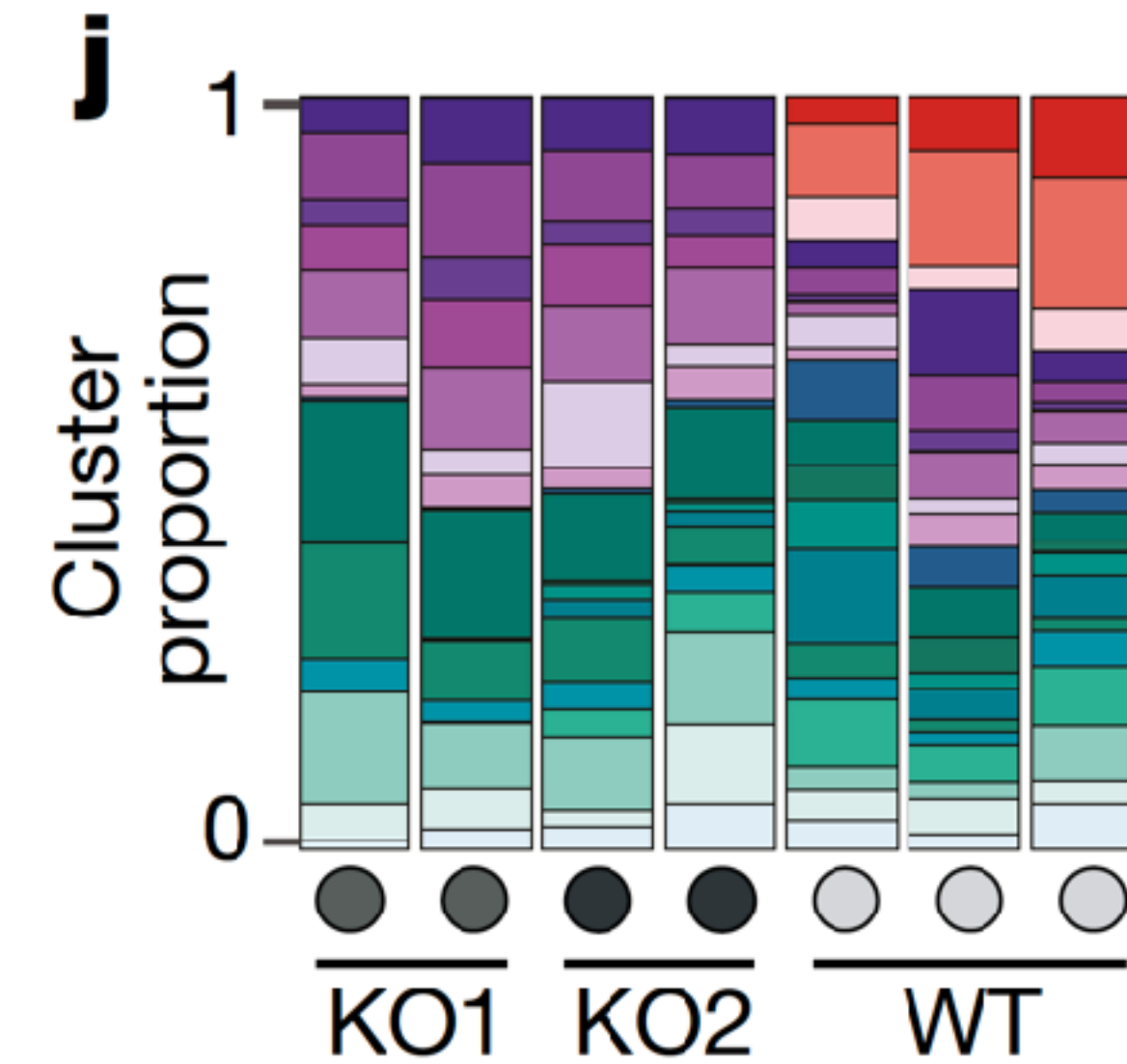
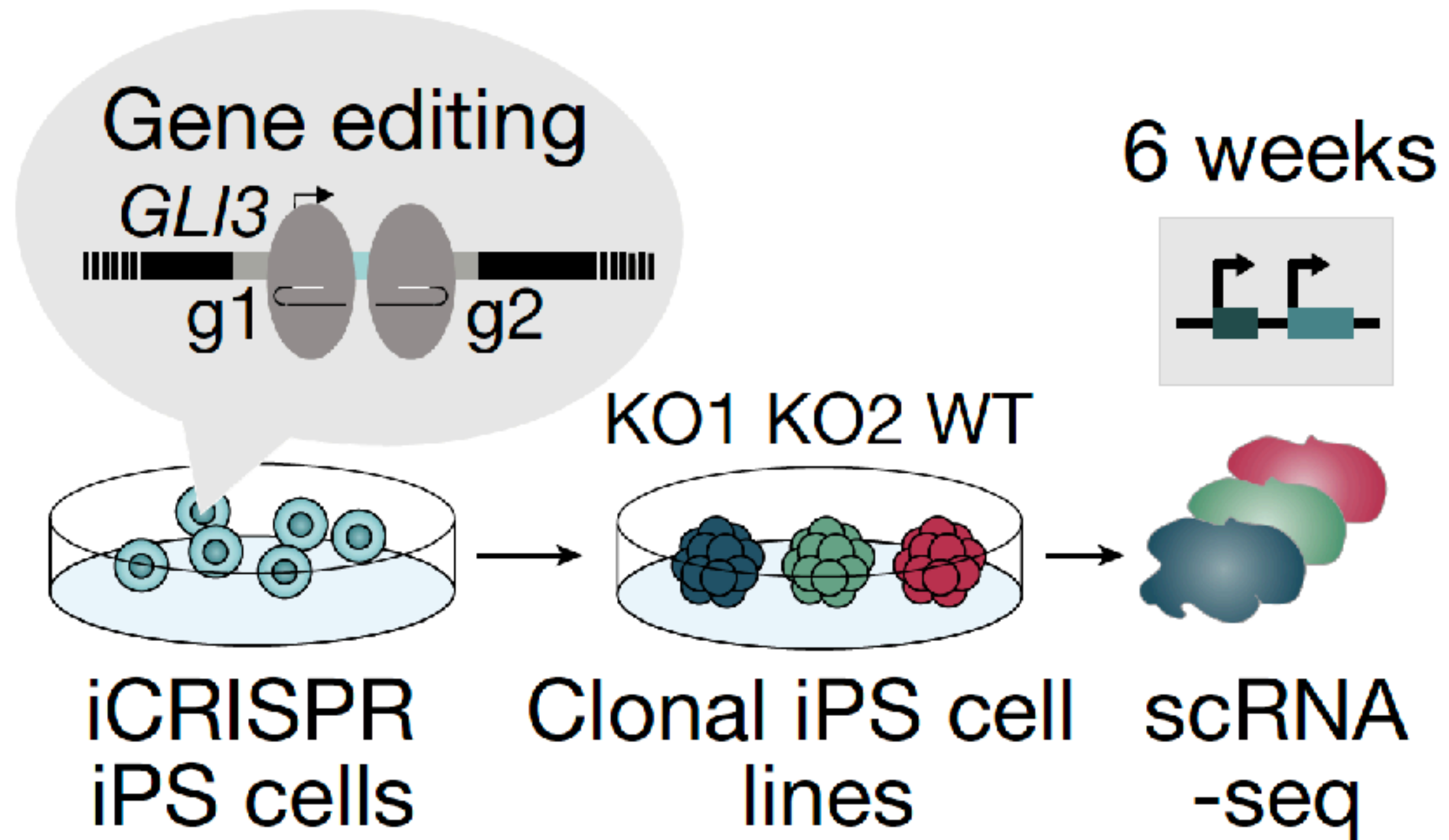
Self-organizing neural organoids grown from pluripotent stem cells^{1–3} combined with single-cell genomic technologies provide opportunities to examine gene regulatory networks underlying human brain development. Here we acquire single-cell transcriptome and accessible chromatin data over a dense time 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



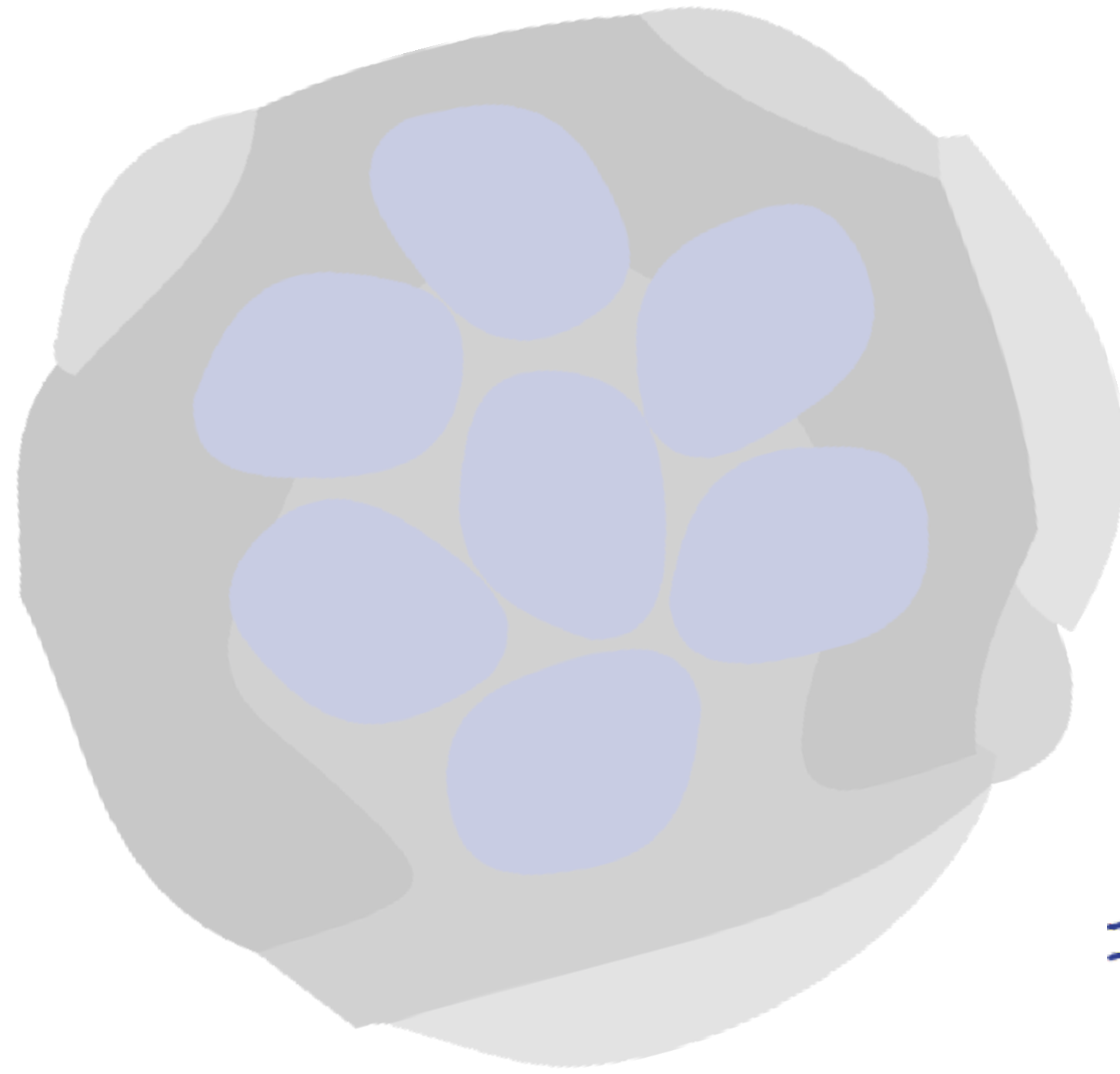
GLI3 regulates dorsal forebrain development



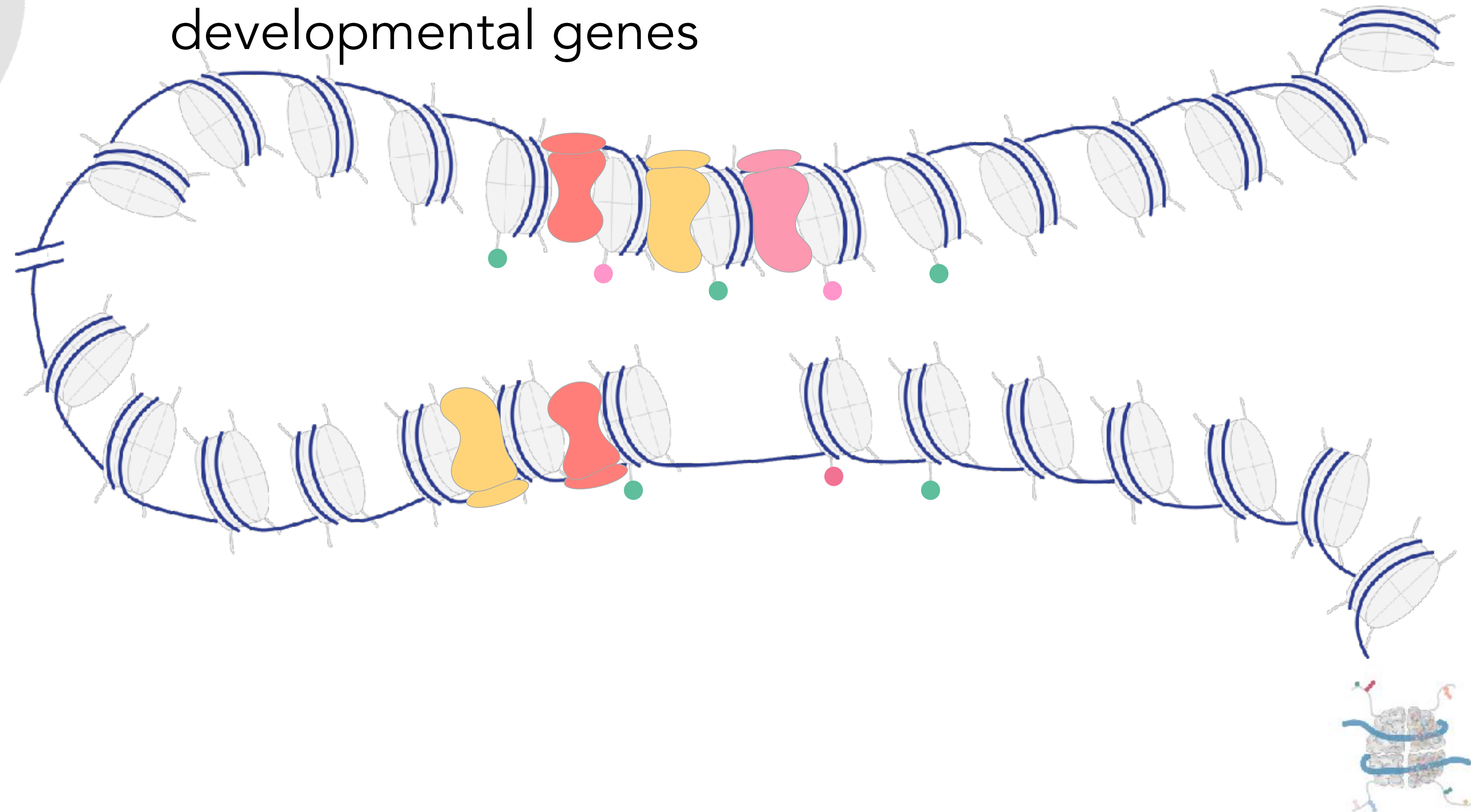
GLI3 regulates dorsal forebrain development



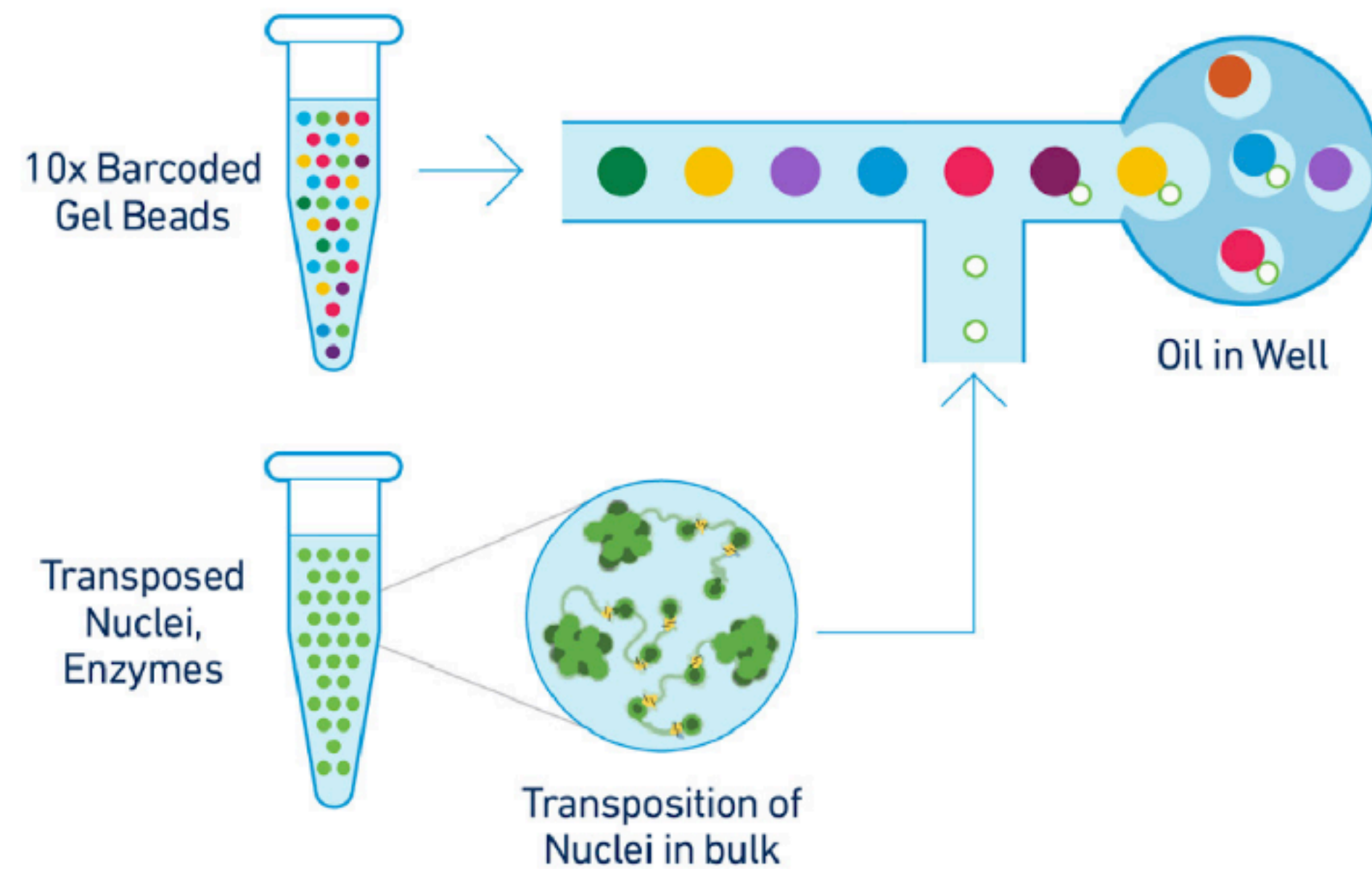
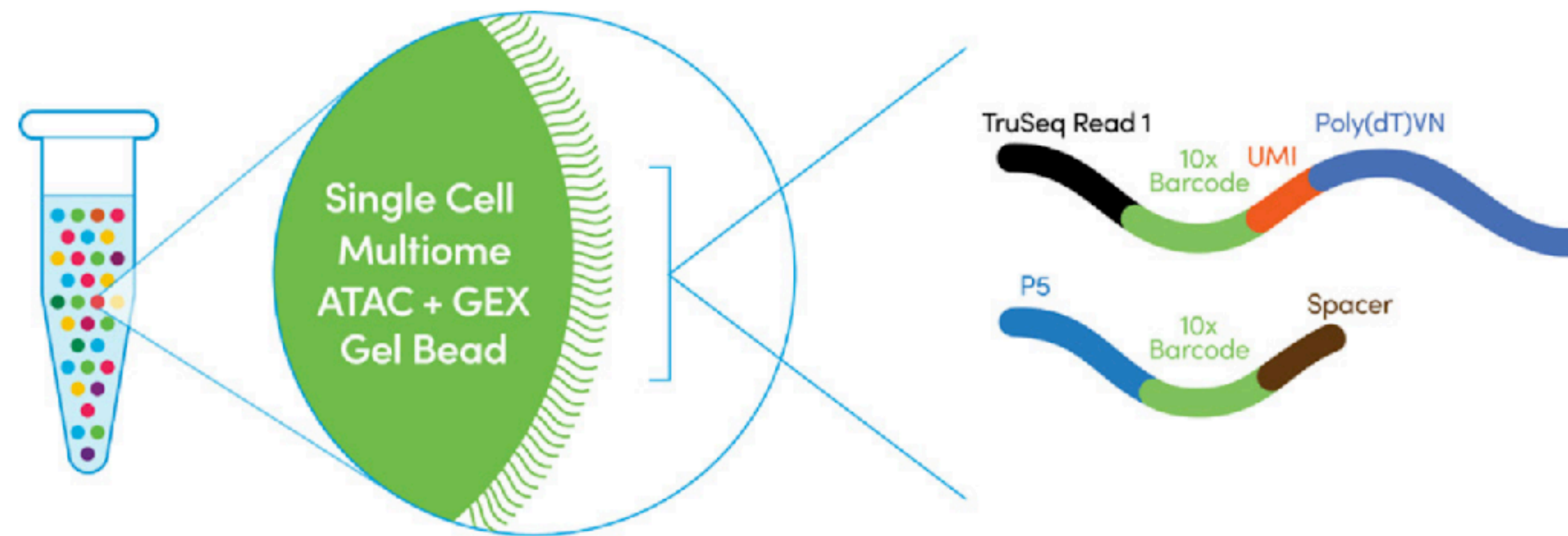
What are the molecular mechanisms of GLI3 regulation?



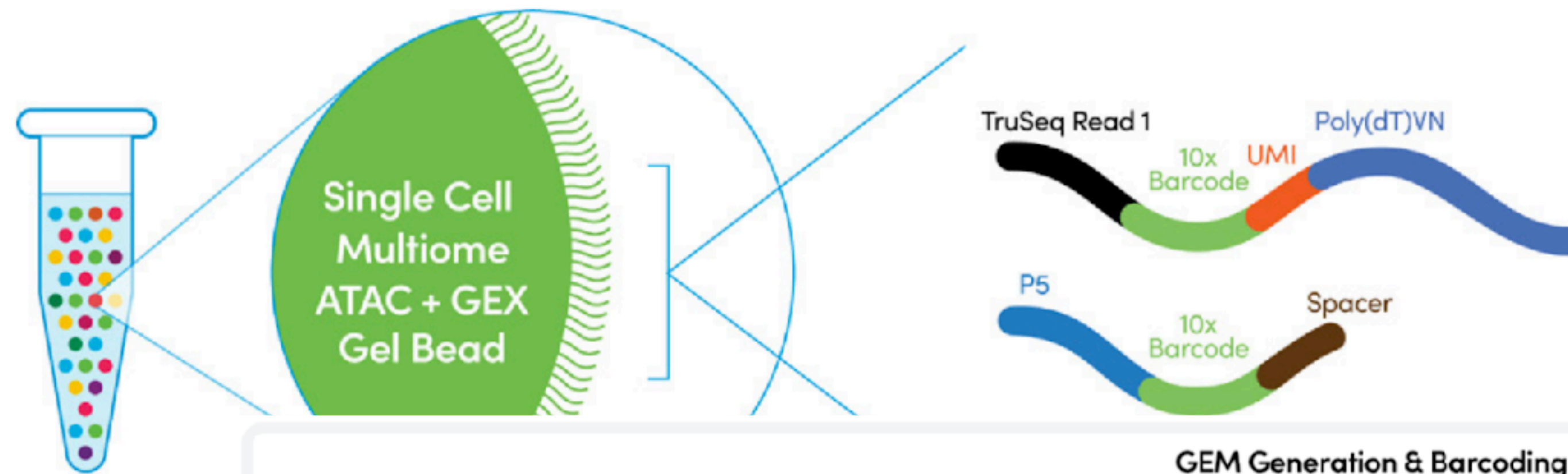
GLI3 is a transcription factor that regulated developmental genes



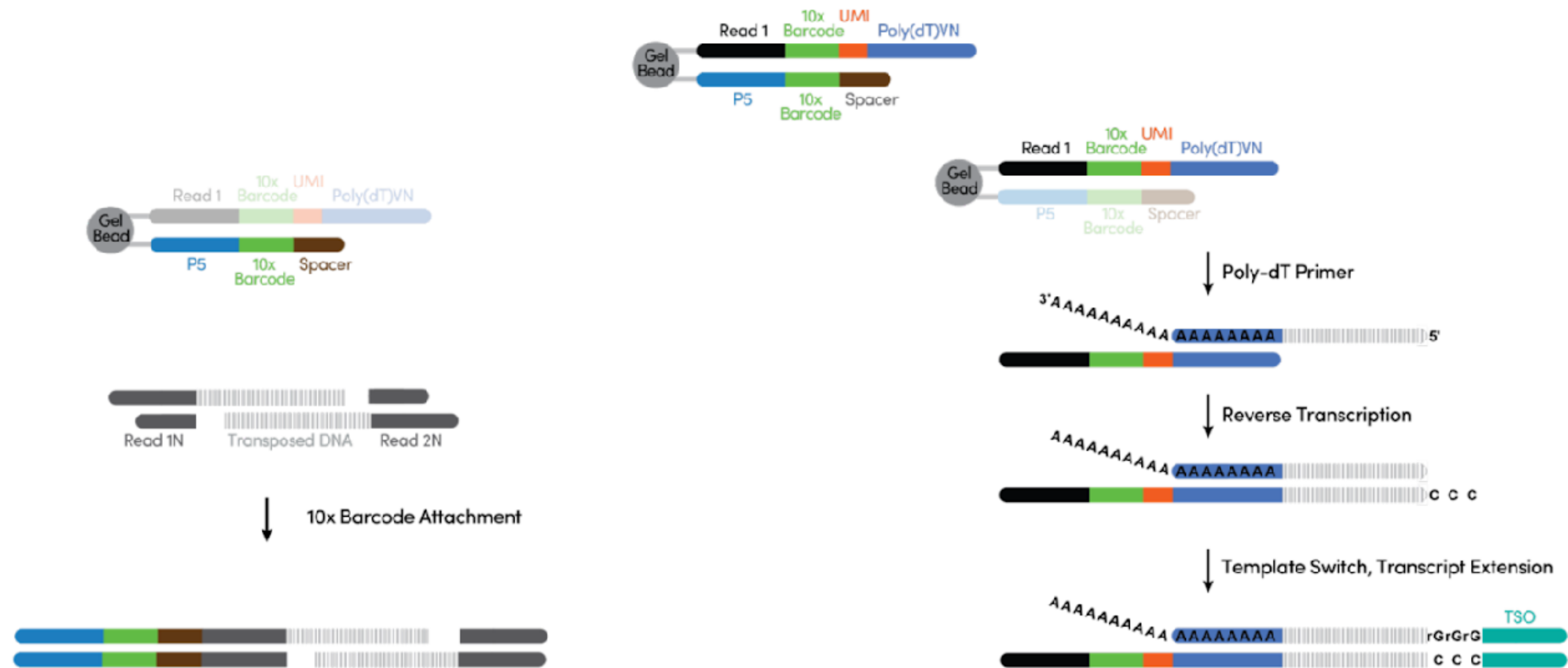
10 x Genomics multiome kit



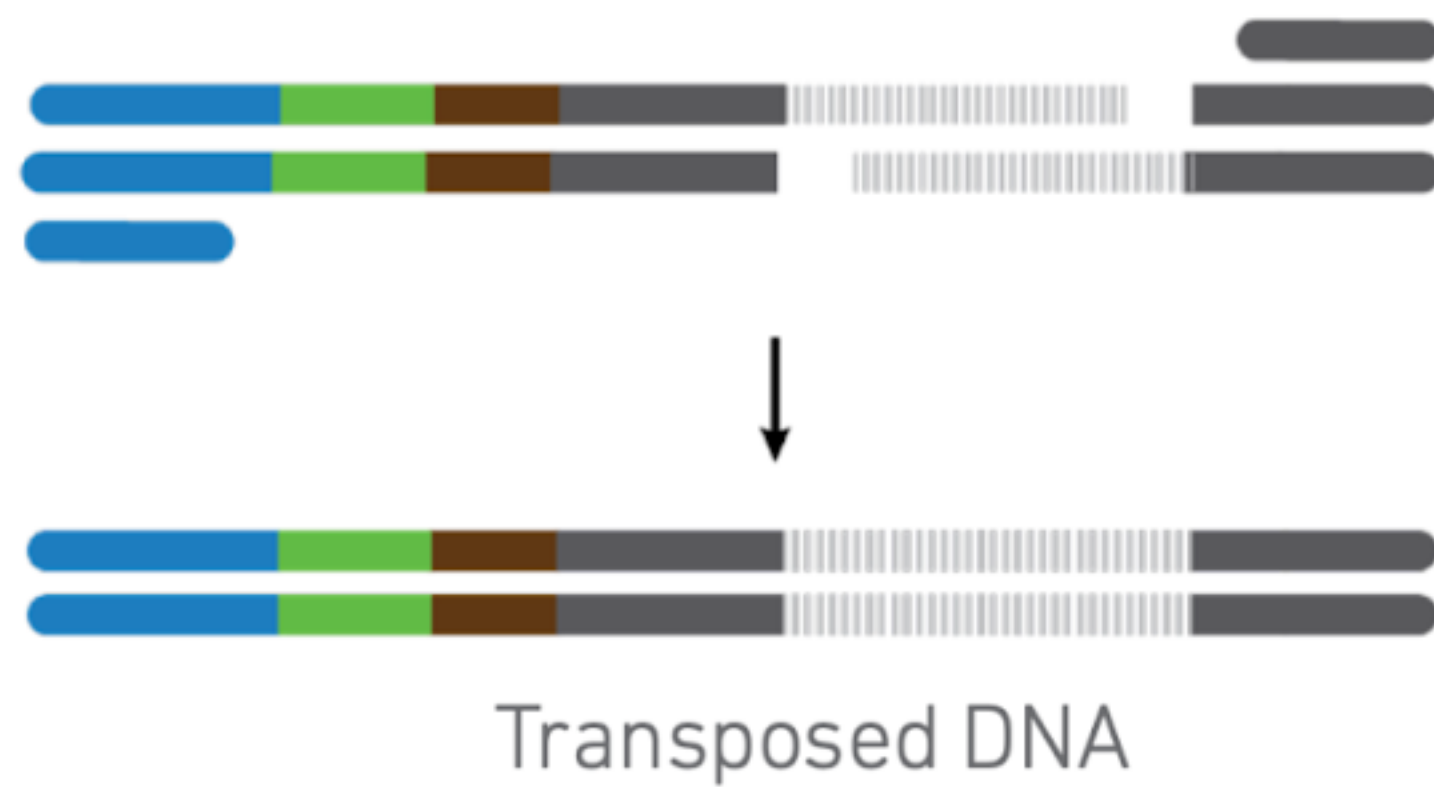
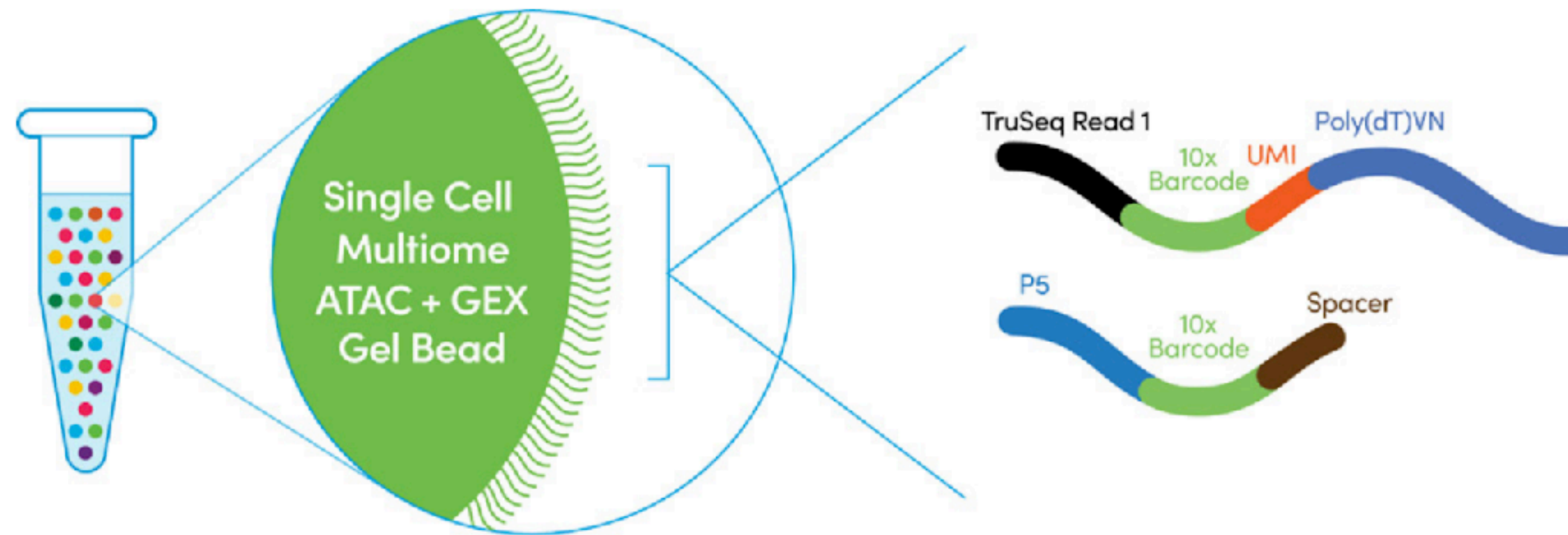
10 x Genomics multiome kit



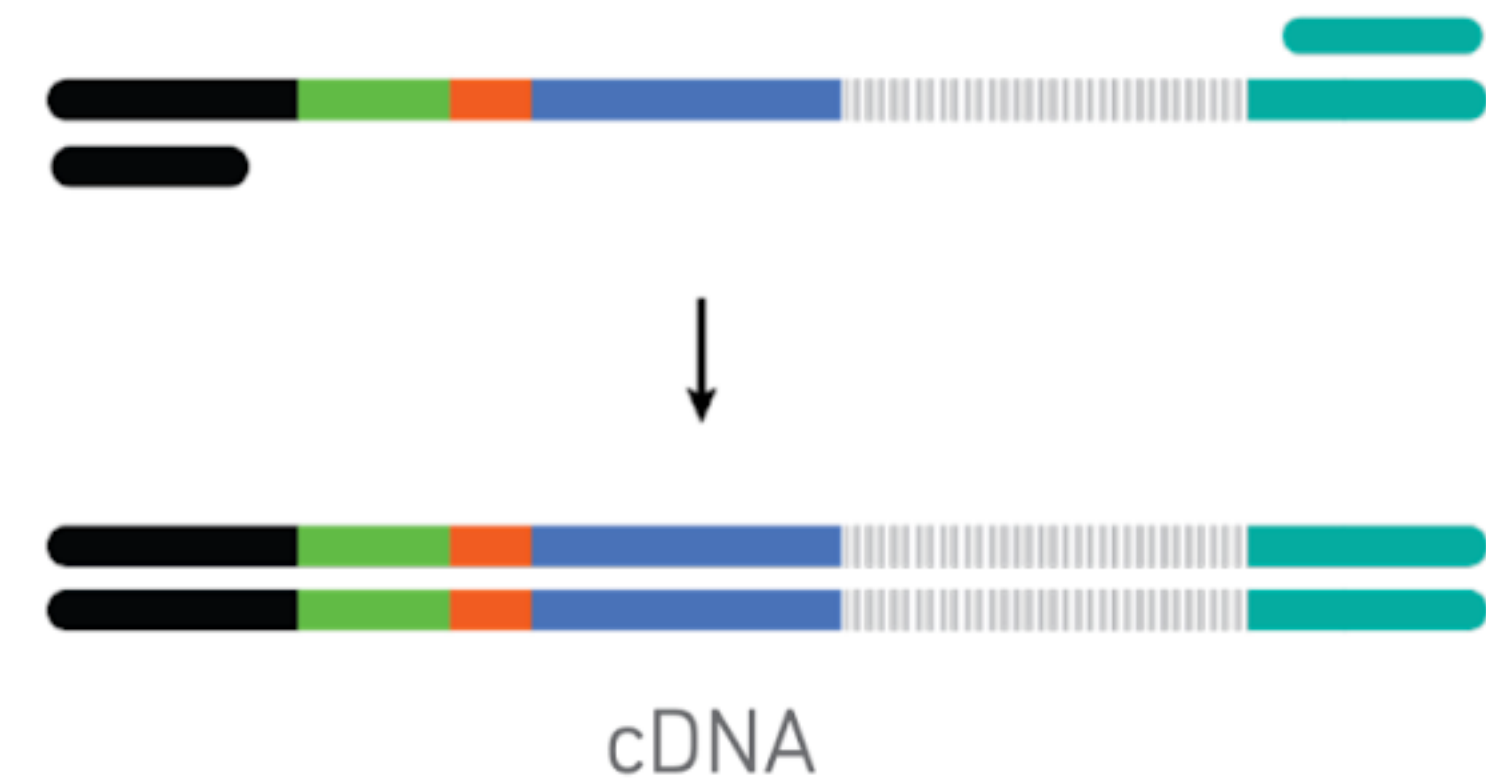
GEM Generation & Barcoding



10 x Genomics multiome kit



Pre-Amplification PCR



10 x Genomics multiome kit

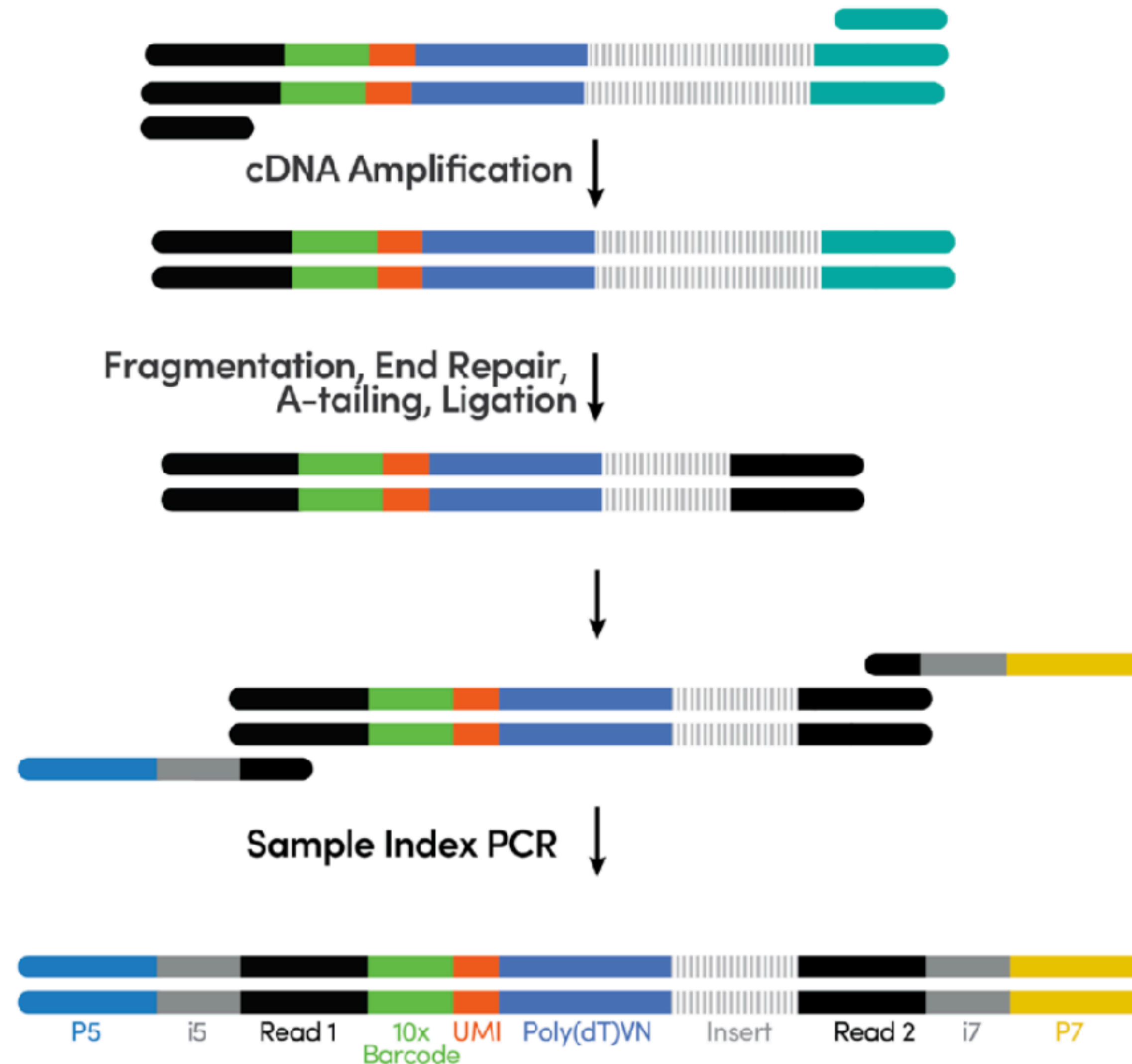


Sample Index PCR ↓



Chromium Single Cell Multiome ATAC Library

10 x Genomics multiome kit

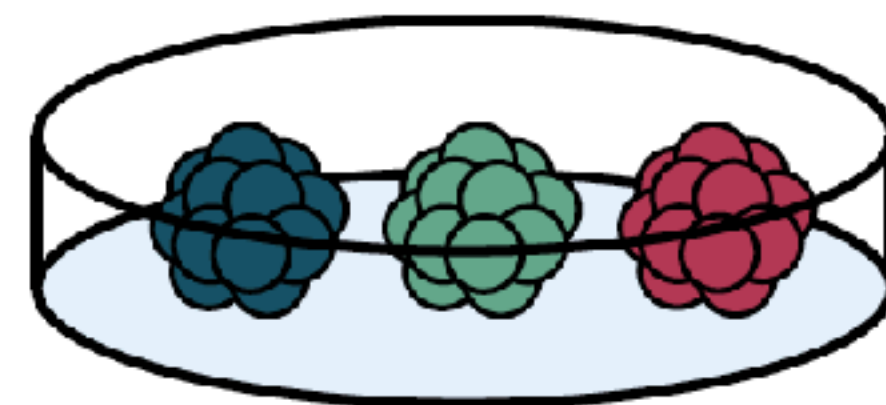


Chromium Single Cell Multiome Gene Expression Library

What are the molecular mechanisms of GLI3 regulation?

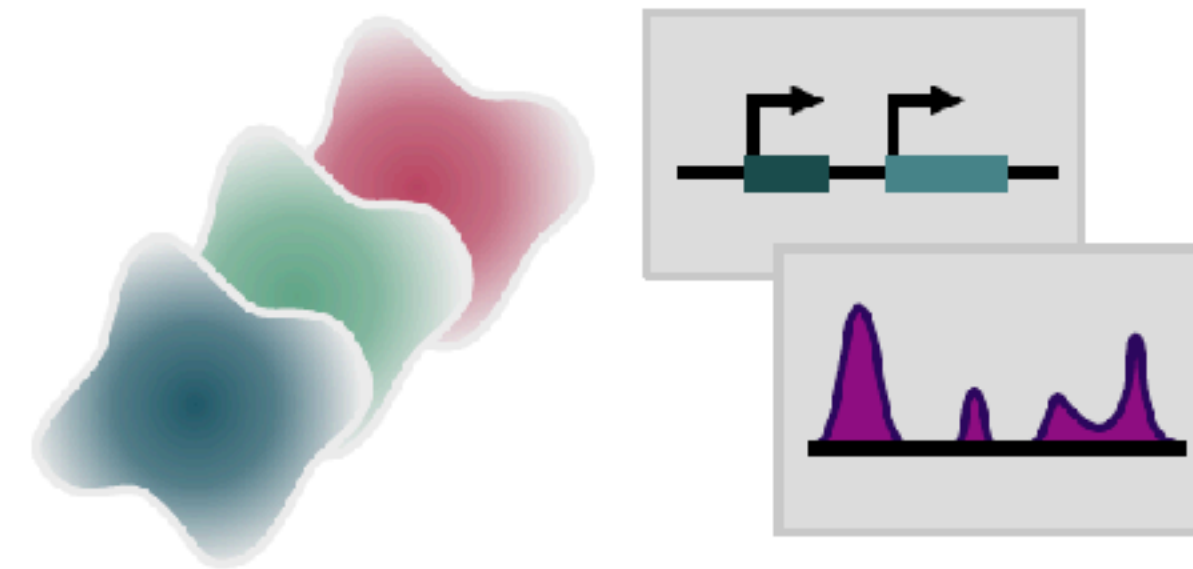
a

GLI3-KO
and control
iPS cell lines



KO1 KO2 WT

Week 3
Single-cell multiome



This is the dataset you will be working on!