

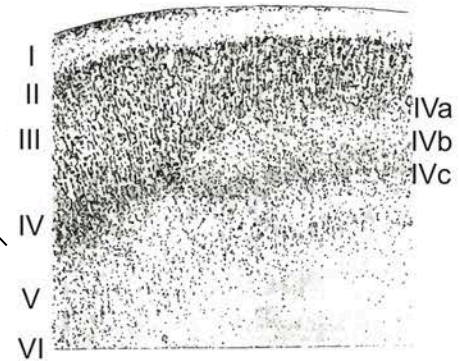
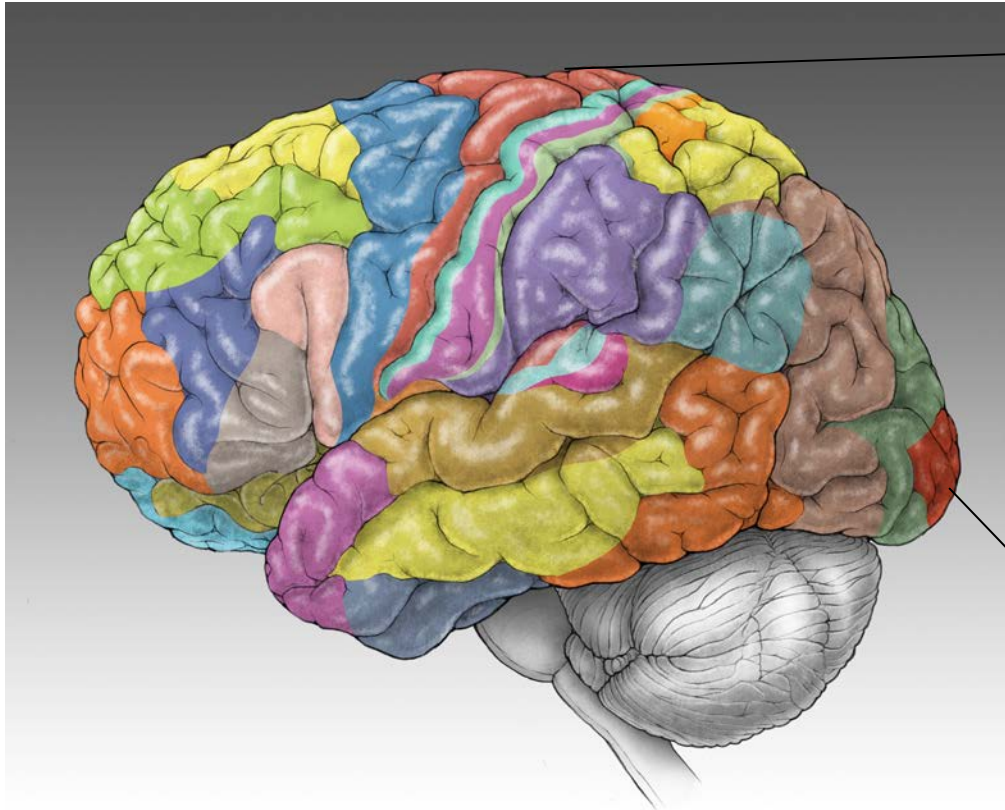
CIRM Genomics Stem Cell Hub: Experimental-Computational Collaboration to Characterize Cortical Organoids

Aparna Bhaduri and Max Haeussler

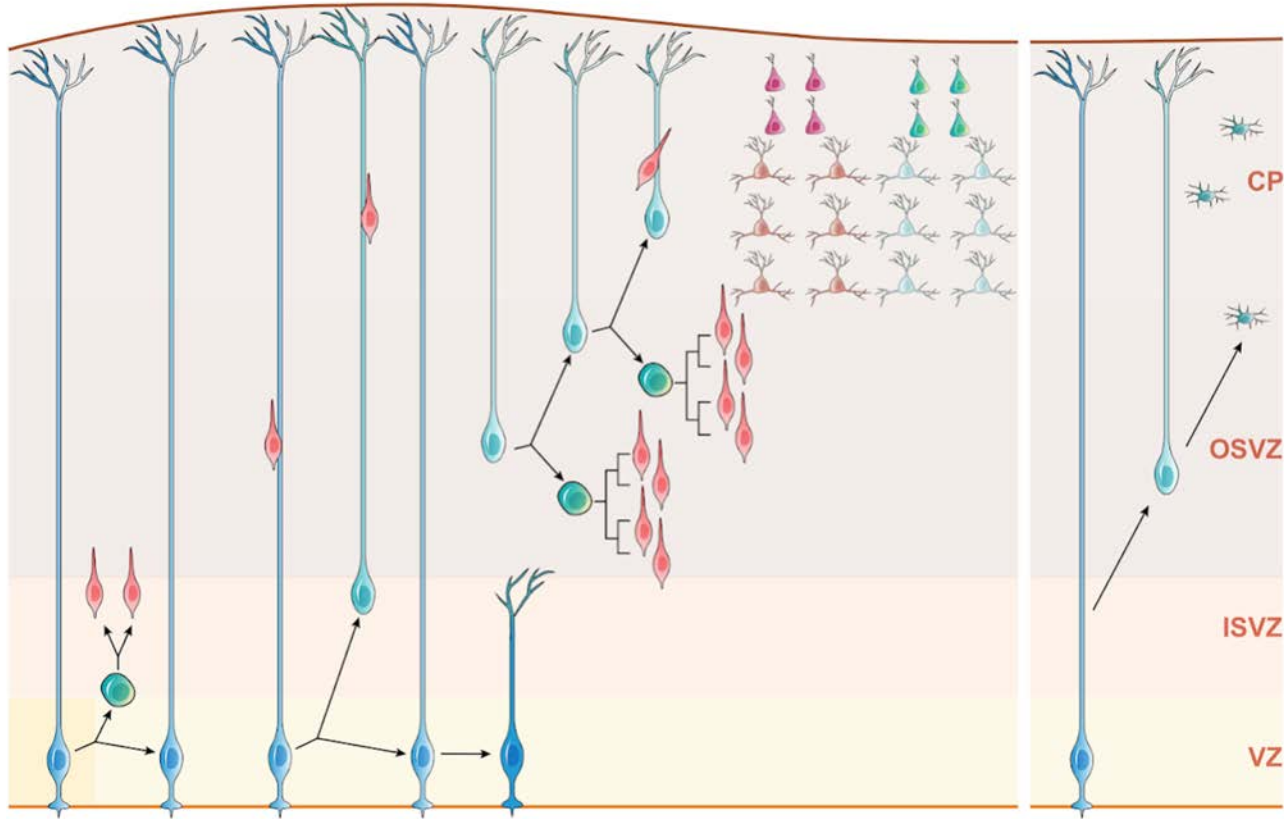
February 24, 2022



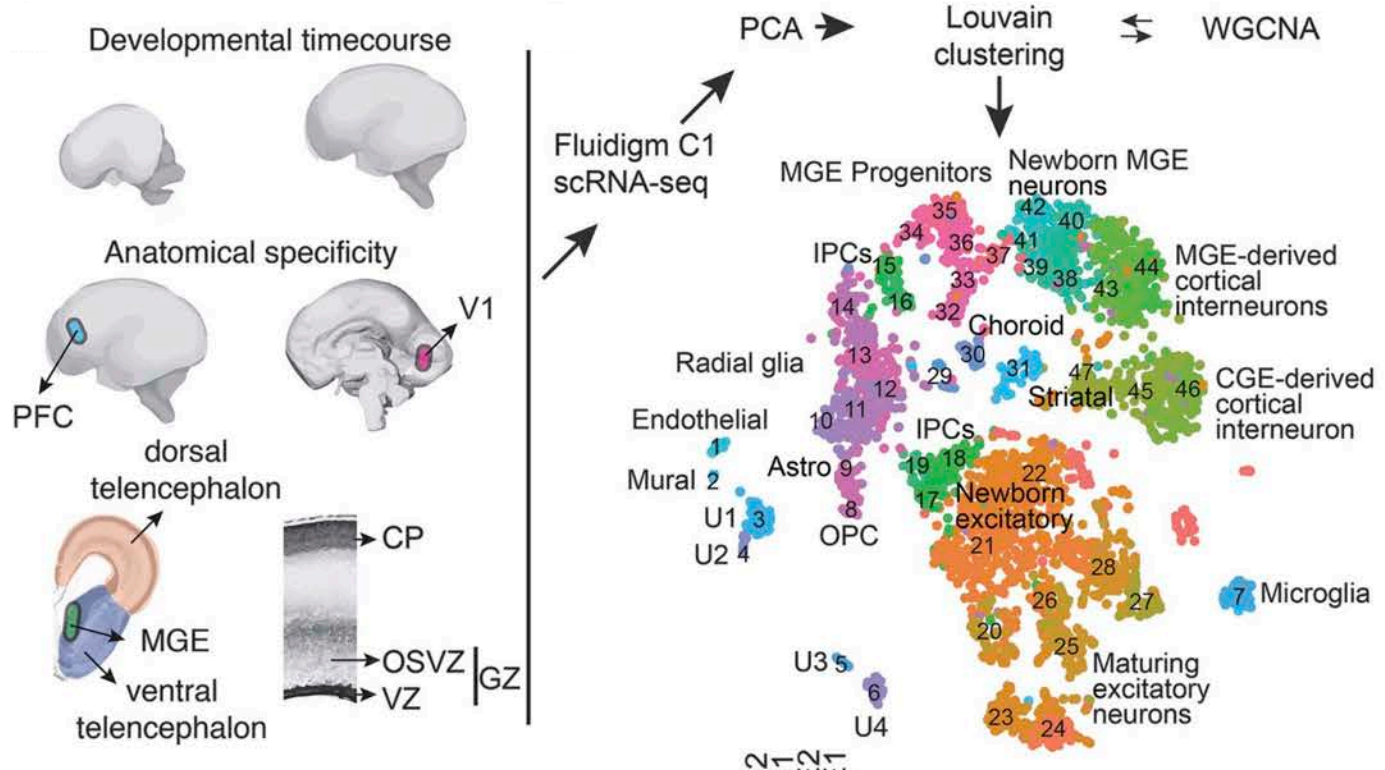
The Human Brain



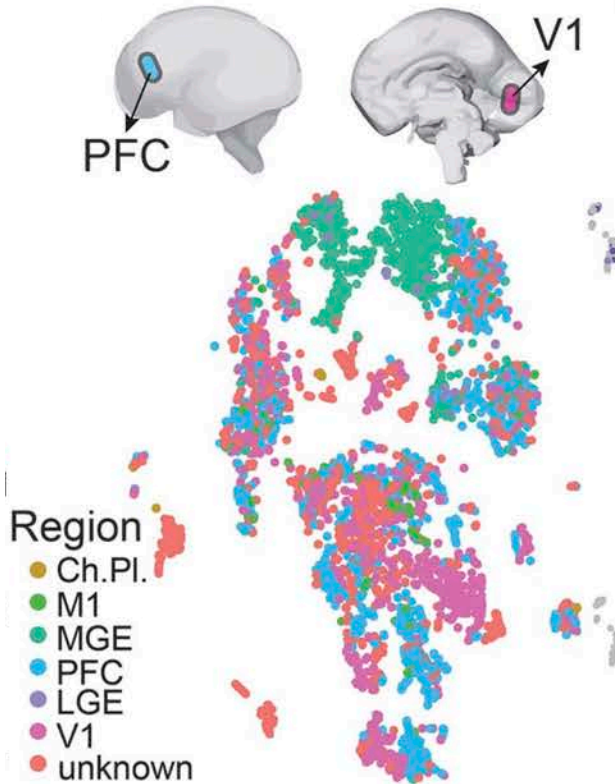
Overview of Cortical Development



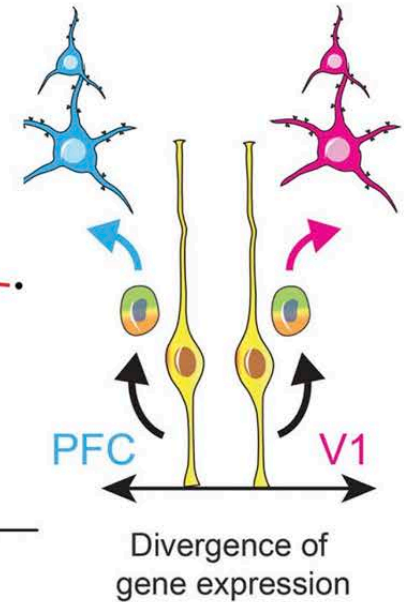
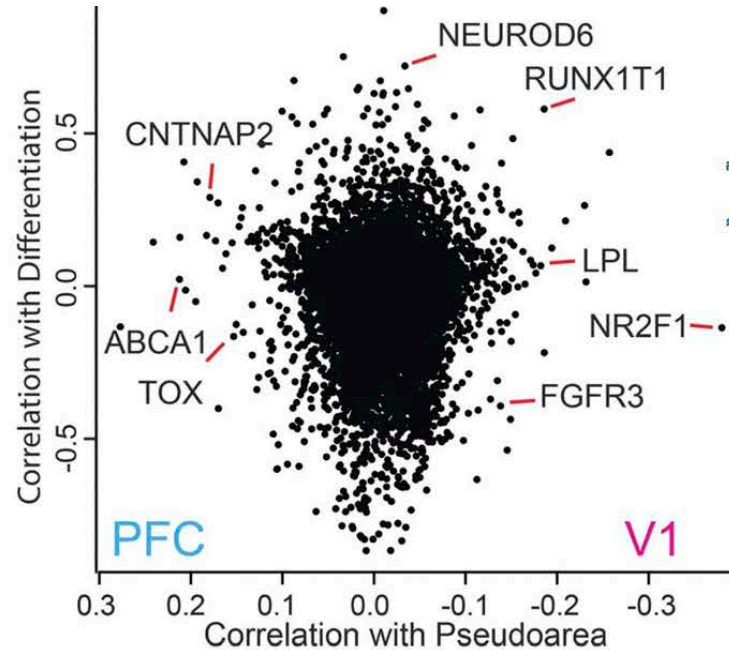
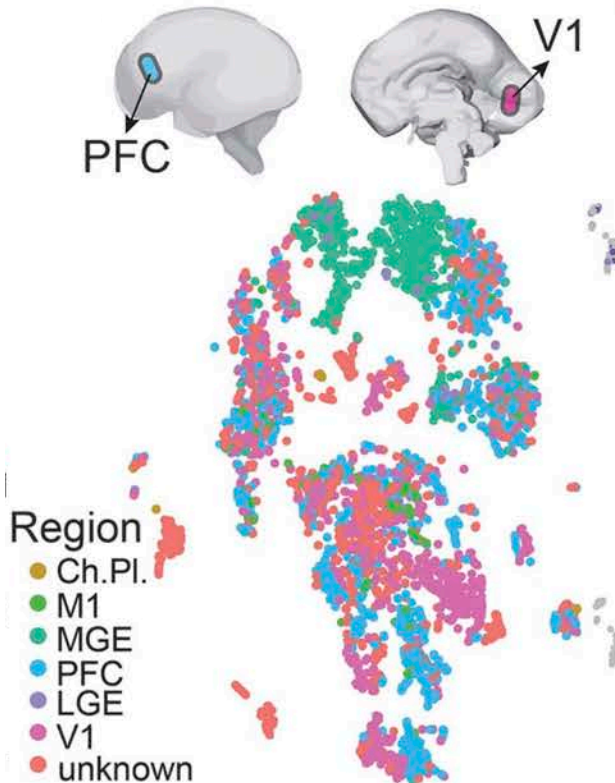
Landscape of Cell Diversity



Area – Specific Cell Types

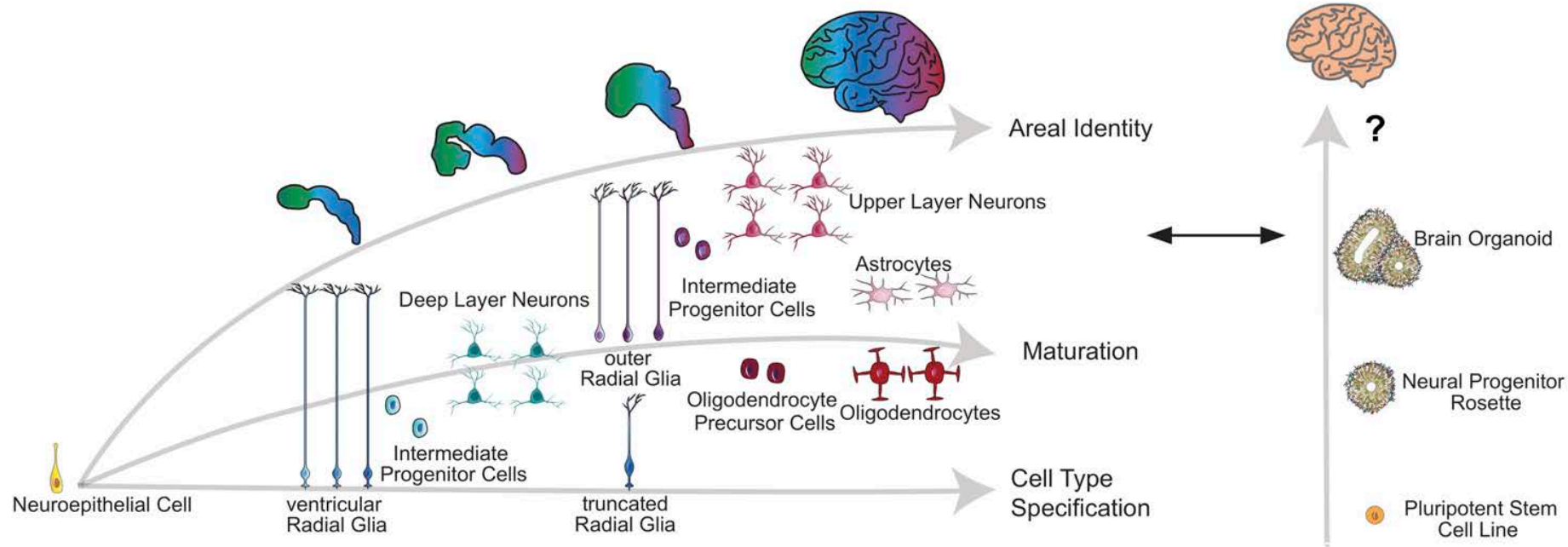


Area – Specific Cell Types

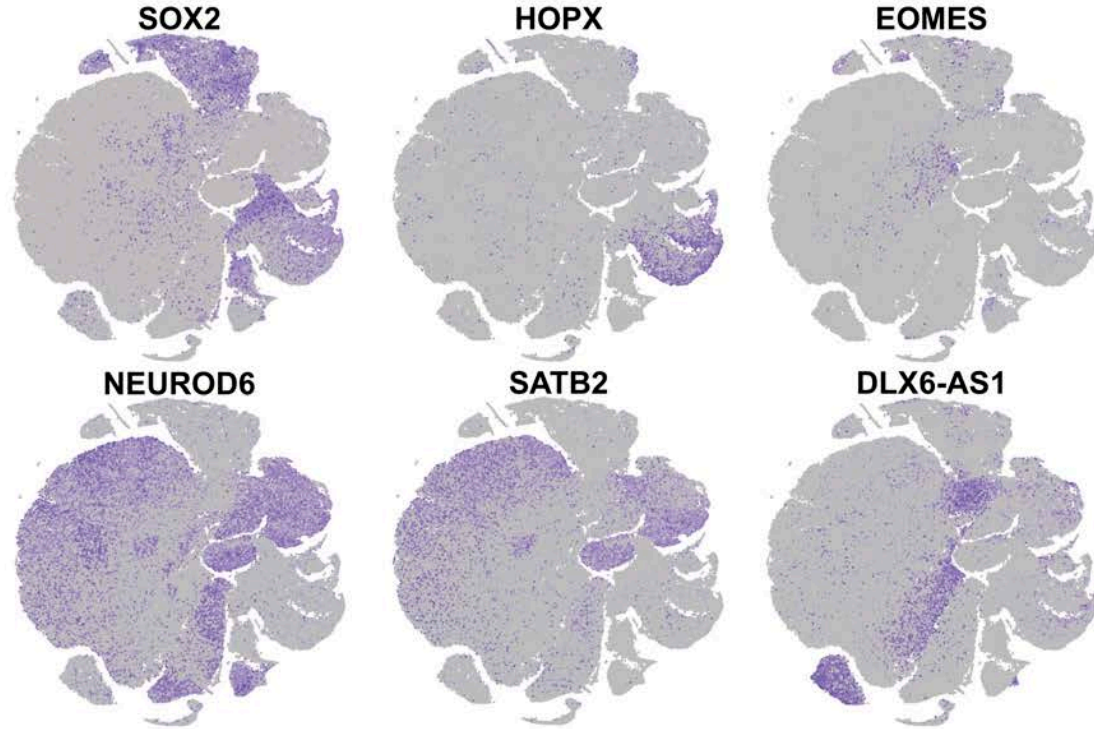
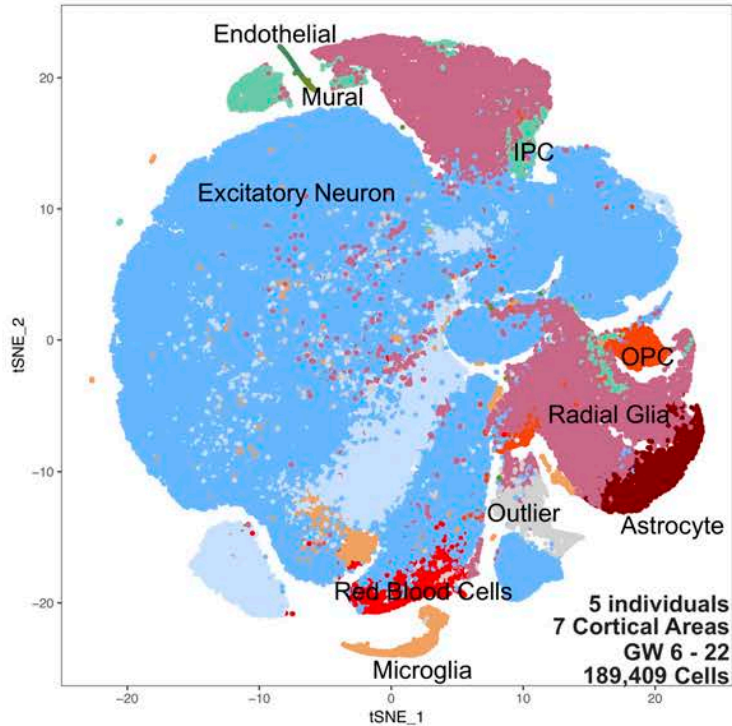


Modeling Cortical Development with Organoids

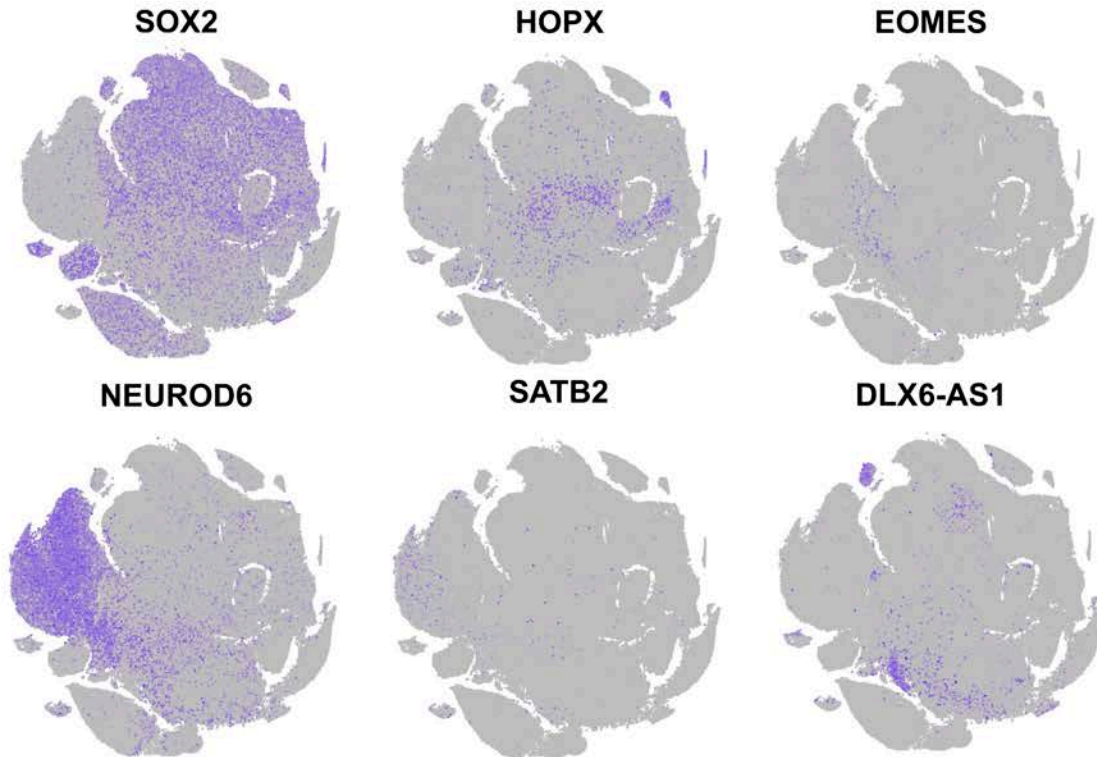
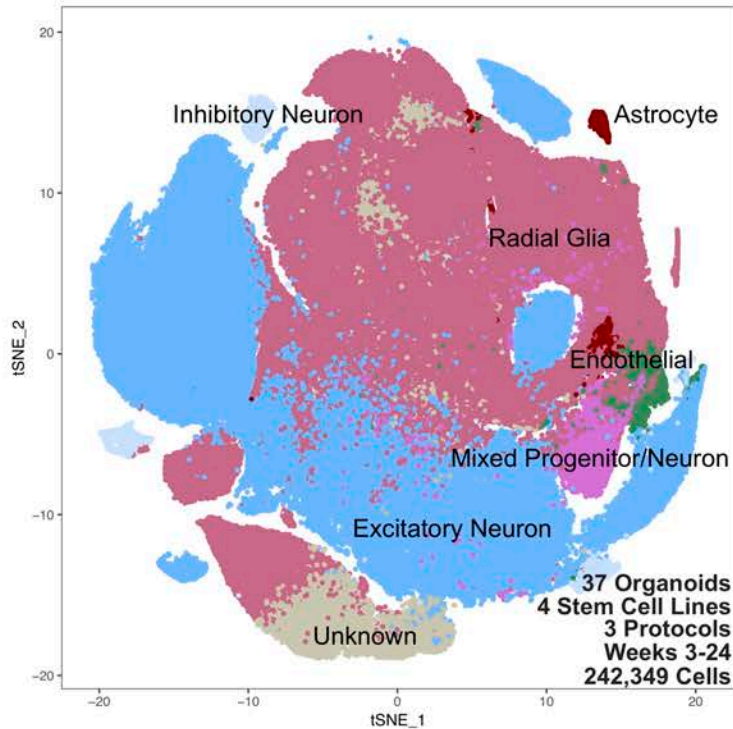
Studying Primary Human Development and Cortical Organoids



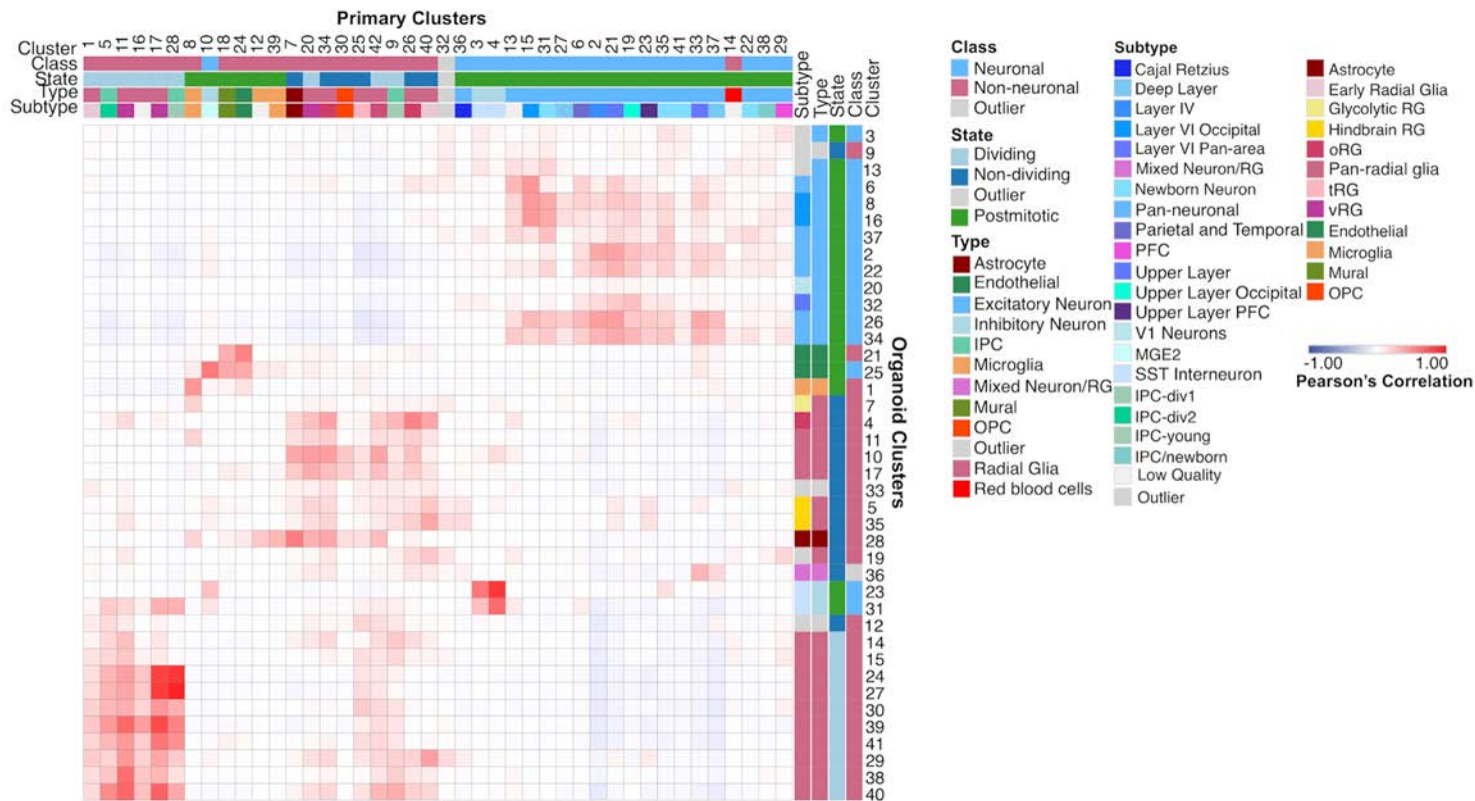
Cortical Development During Peak Neurogenesis



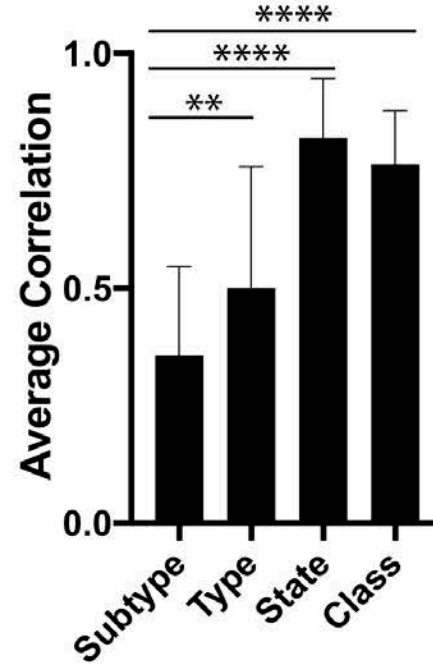
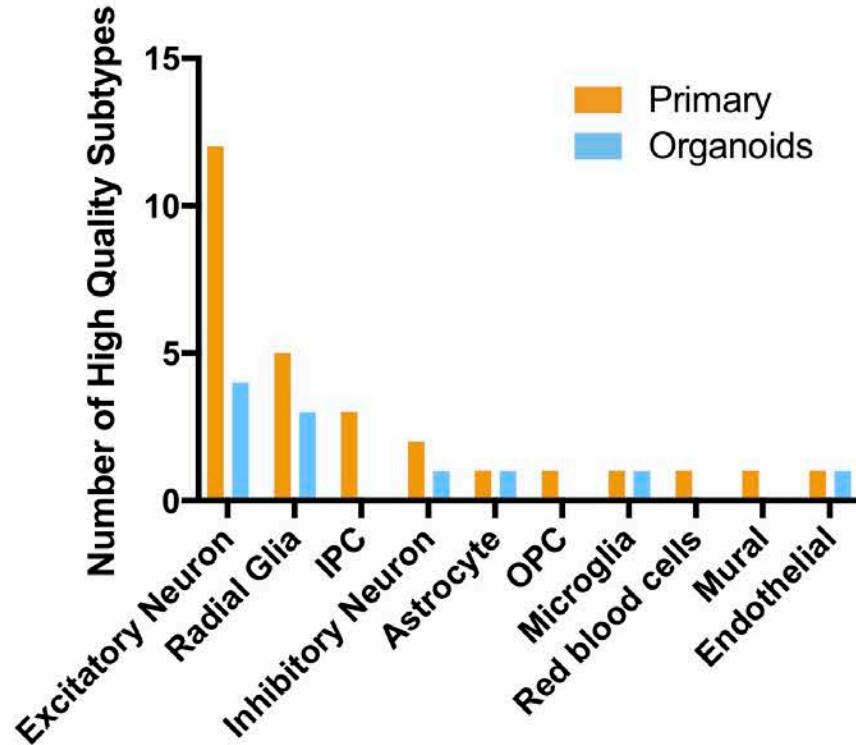
Cortical Development in the Organoid



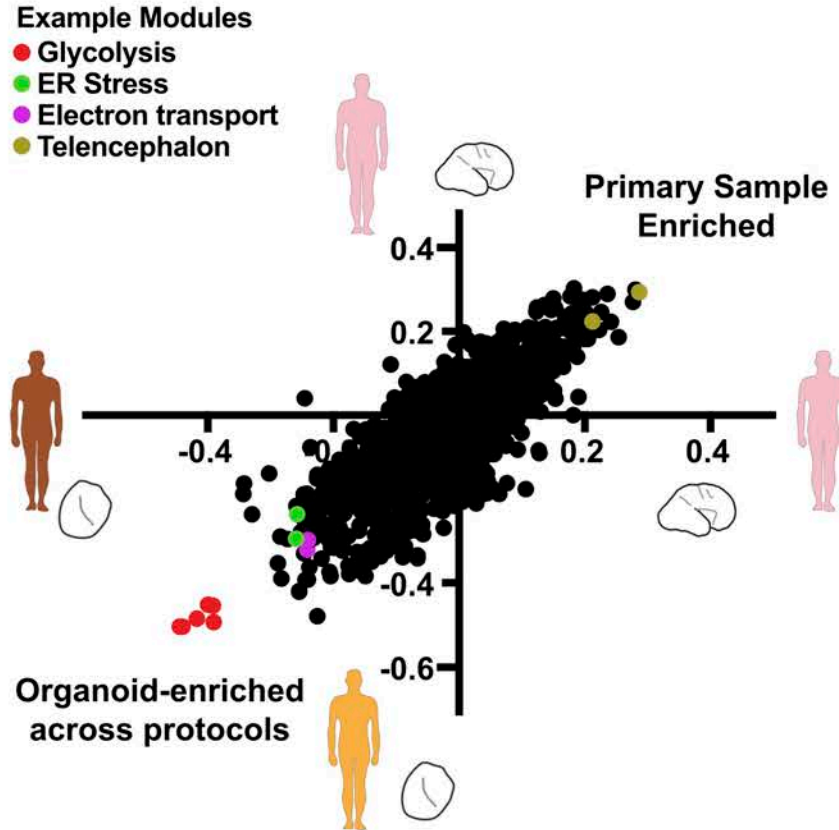
Comparison of Organoid and Primary Clusters



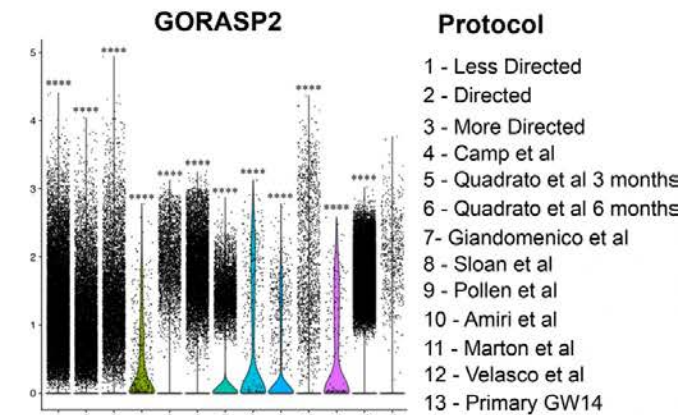
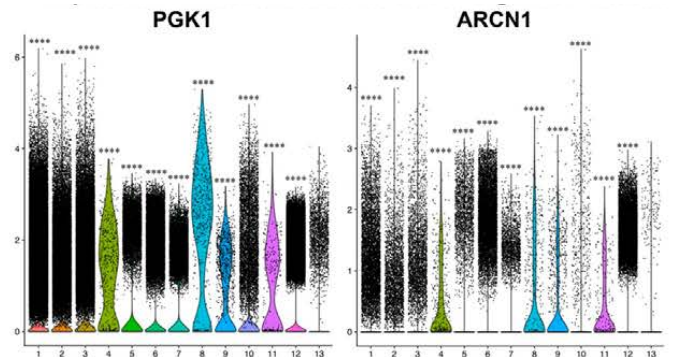
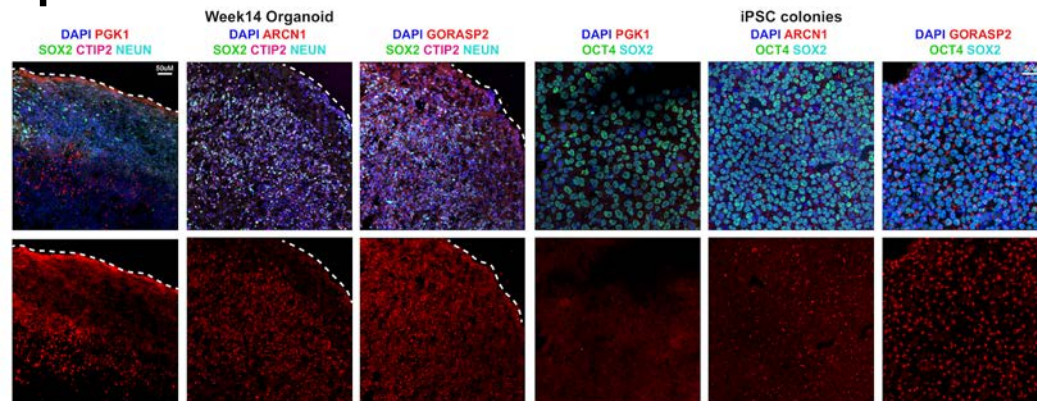
Quantification of Correspondence



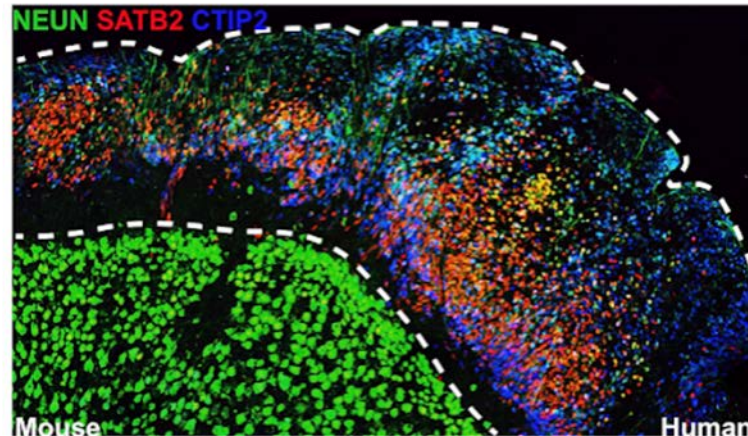
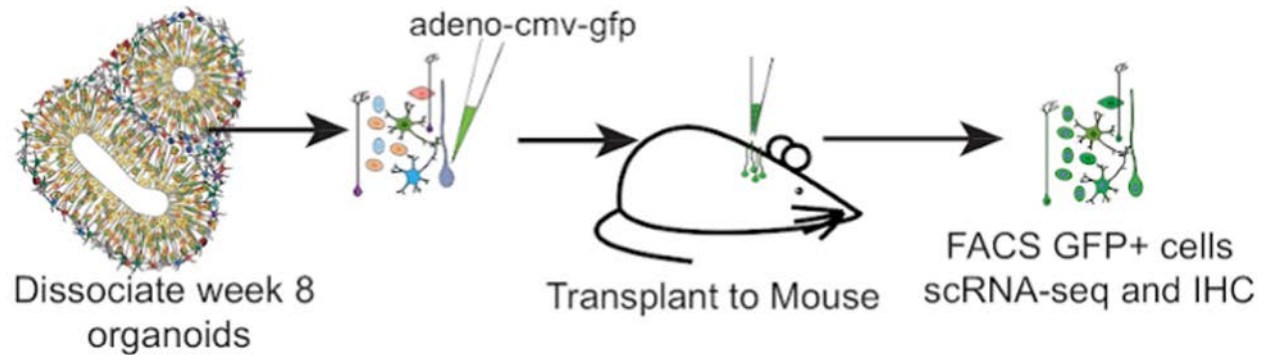
Stress Pathway Expression in Organoids



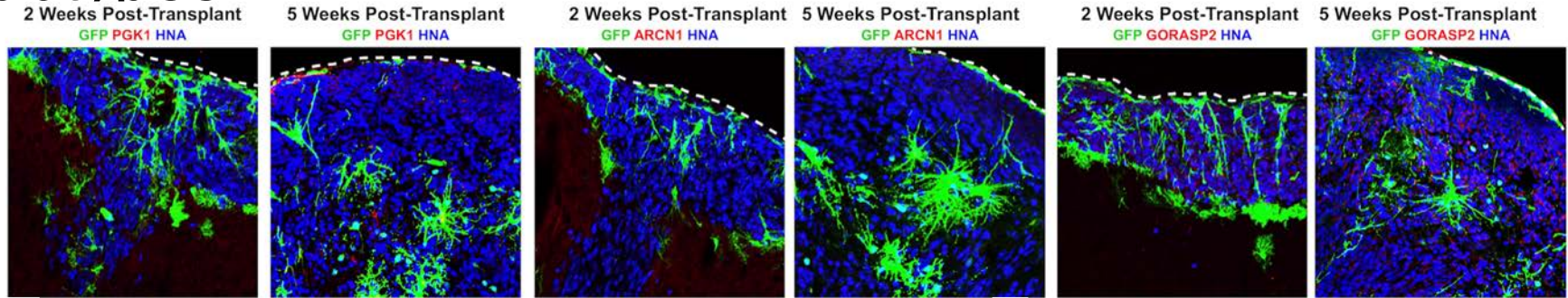
Expression of Stress Genes



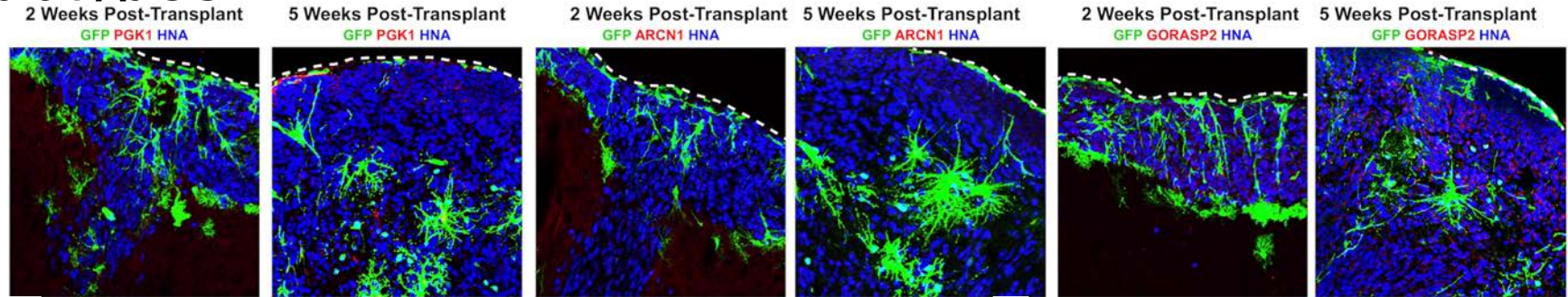
Transplantation of Organoids into Mouse Cortex



Transplanted Cells Decrease Stress and Improve Subtypes

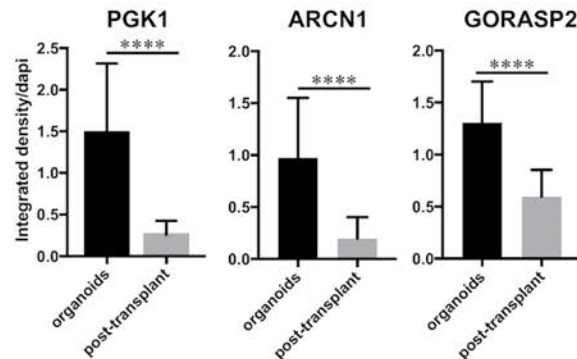


Transplanted Cells Decrease Stress and Improve Subtypes

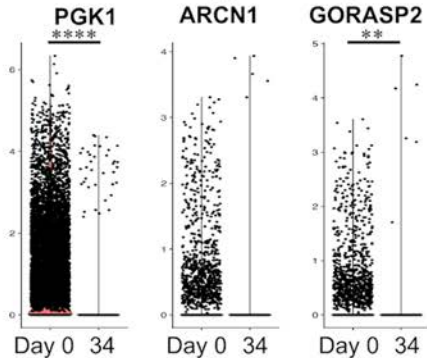


Decreased Metabolic Stress in Transplanted Organoid Cells

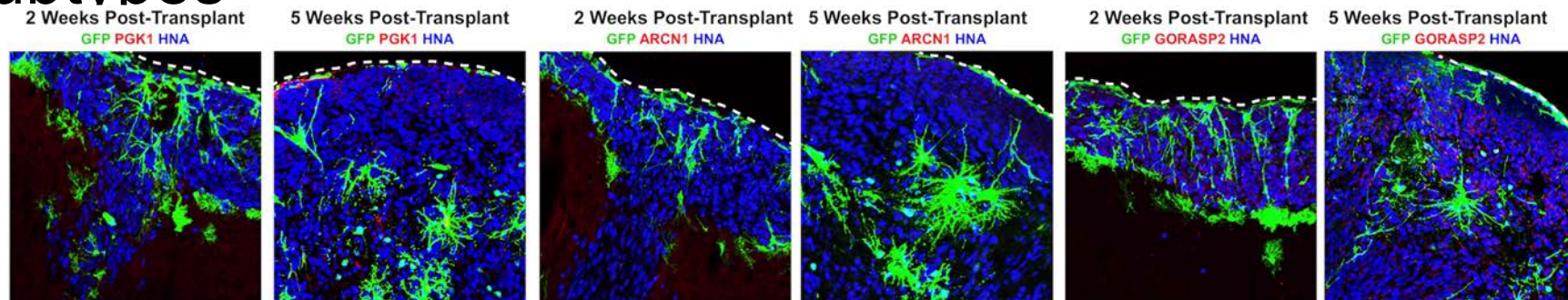
Quantification of Immunostaining



Quantification of Single-Cell Sequencing

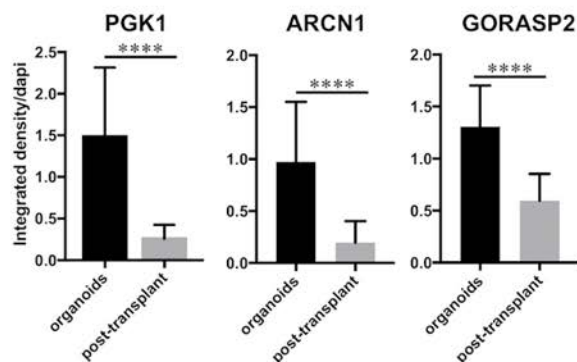


Transplanted Cells Decrease Stress and Improve Subtypes

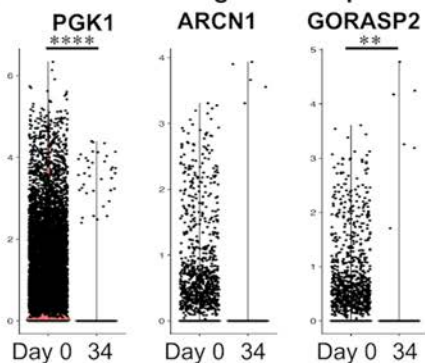


Decreased Metabolic Stress in Transplanted Organoid Cells

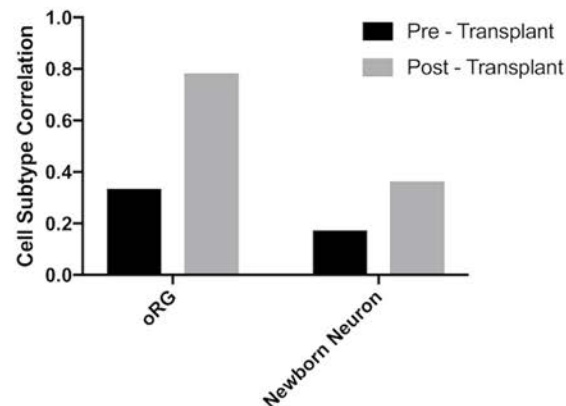
Quantification of Immunostaining



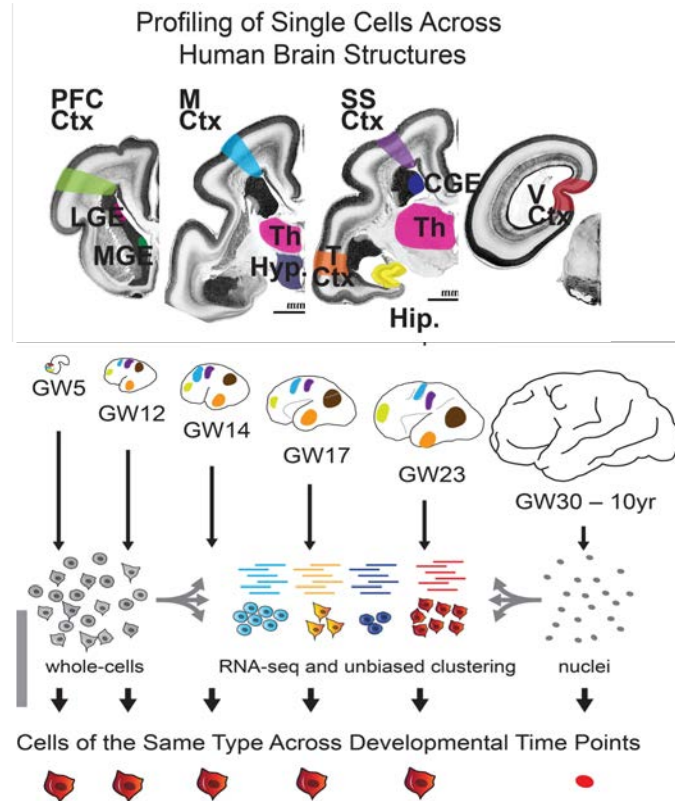
Quantification of Single-Cell Sequencing



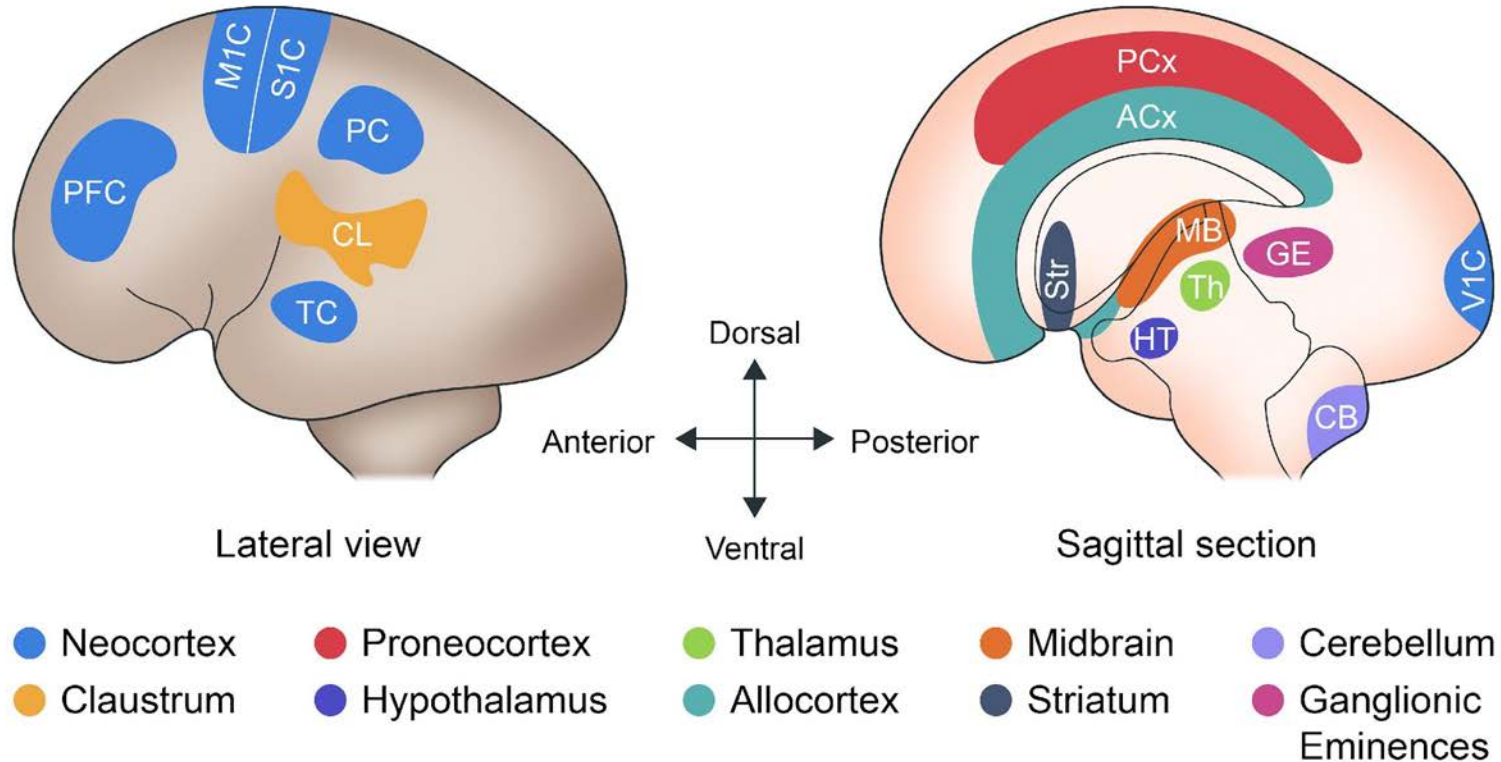
Organoid Cell Subtypes After Mouse Transplant



Developing Human Brain Cell Atlas

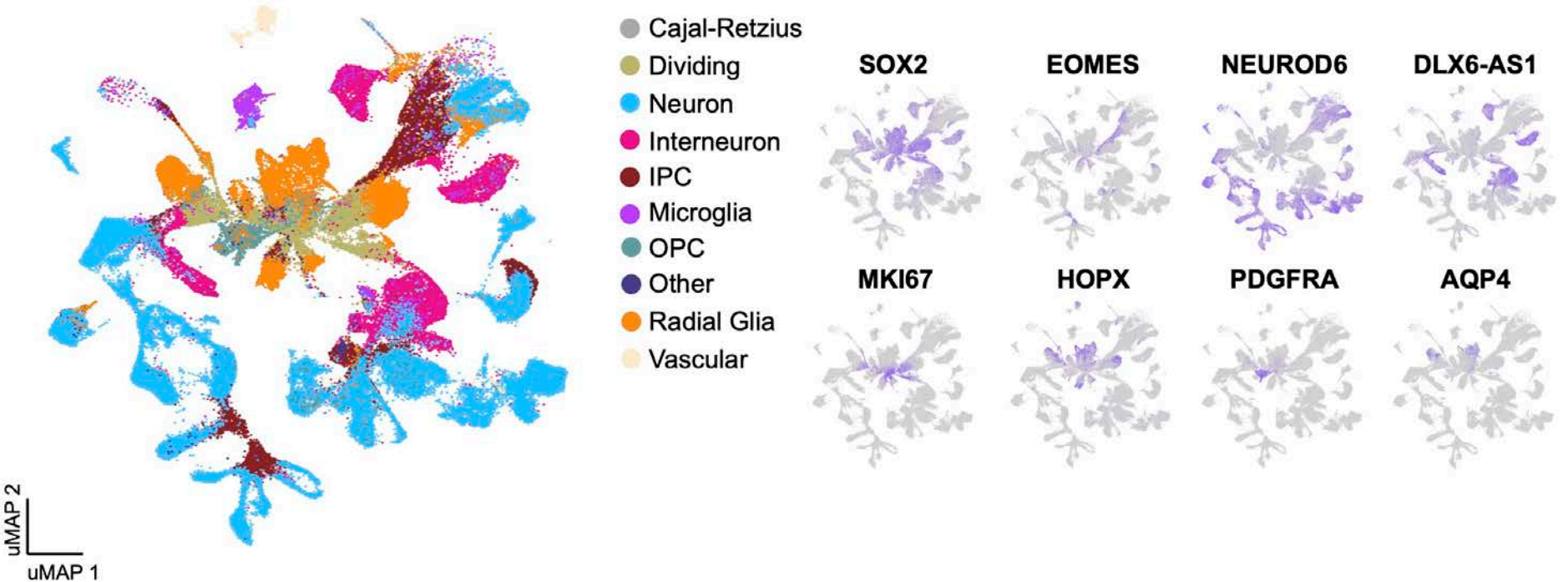


Atlas During Peak Stages of Neurogenesis



Neocortex Cell Types

Developing Neocortex Clustering By Cell Type



The Data Browser

Max Haeussler, UCSC

CIRM-funded data warehouse (cirm.ucsc.edu)



The
Stem Cell Hub
Center for Excellence in Stem Cell Genomics

CIRM

[Home](#) [Data](#) [Projects](#) [Tools](#) [Standards](#) [Help](#) [About](#) ▾

[Overview](#) [Browse](#) ▾ [Analysis](#) ▾ [Metadata Query](#)

Click on file's name to see full metadata. Links in ucsc_db go to the Genome Browser.

Search

50111 files found.

species

- ☐ [Homo sapiens \(42413\)](#)
- ☐ [Mus musculus \(3936\)](#)
- ☐ [Pan troglodytes \(2579\)](#)
- ☐ [Macaca mulatta \(1114\)](#)
- ☐ [n/a \(45\)](#)
- ☐ [Pongo pygmaeus abelii \(24\)](#)

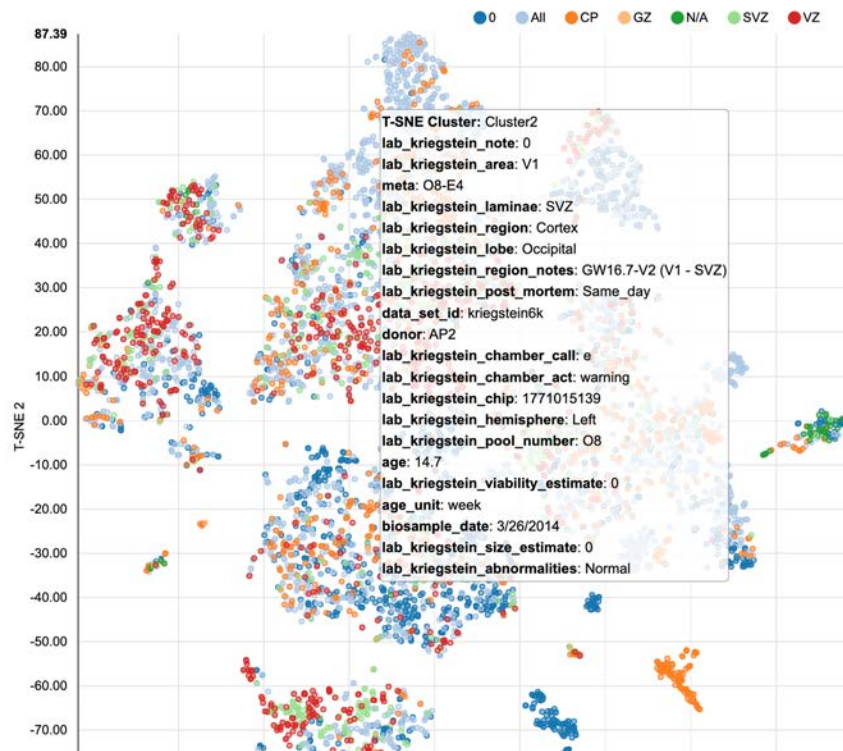
assay

- ☐ [sc-RNA-seq \(43144\)](#)
- ☐ [long-RNA-seq \(5062\)](#)
- ☐ [Frac-seq \(932\)](#)

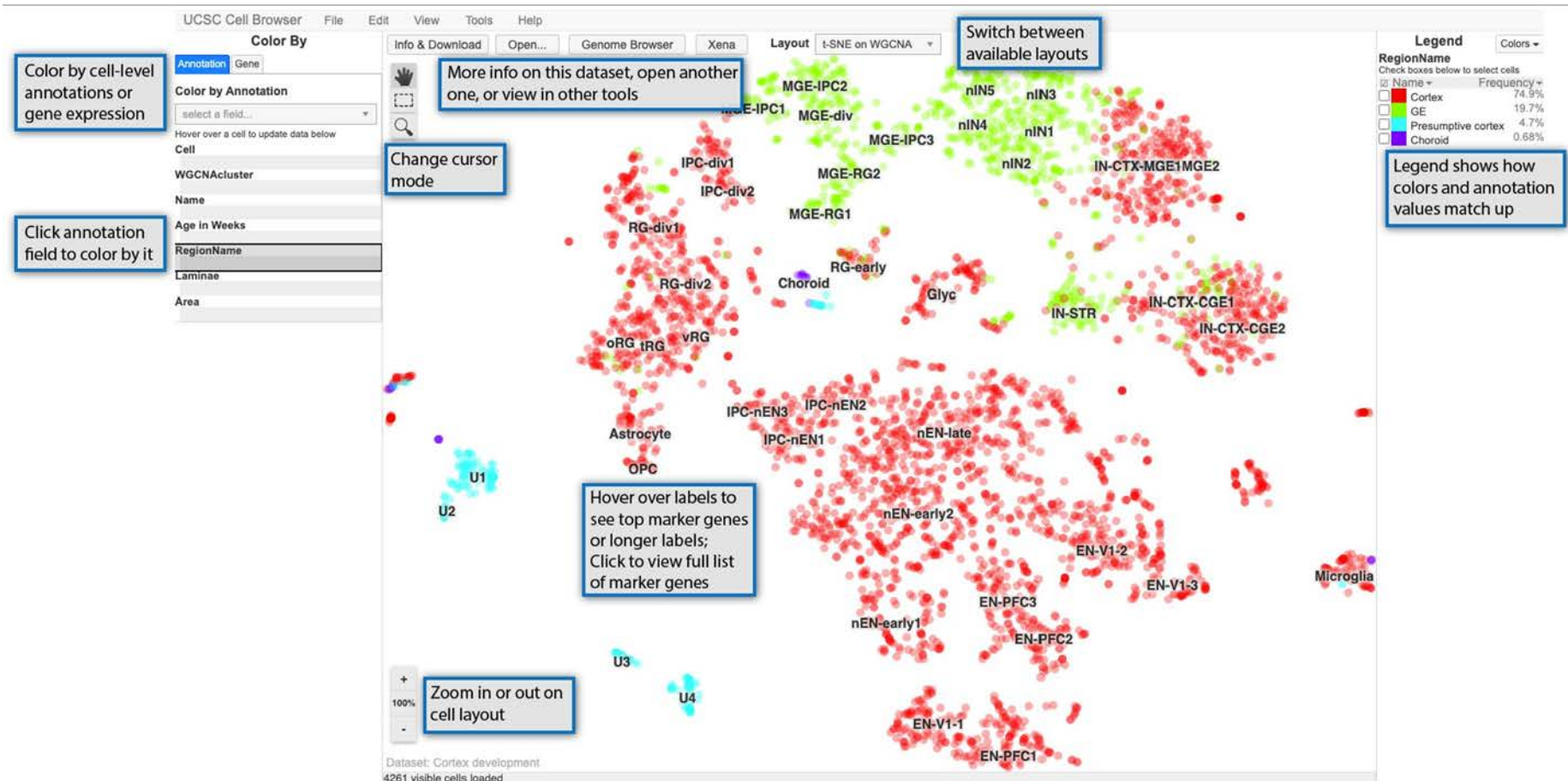
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sc007RTV.fastq.gz	32 MB	hg38	Homo sapiens	sc-RNA-seq	fastq	reads	pancreas	quake	quakeAdultAging...	alpha cell	:
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sc007RTM.fastq.gz	53 MB	hg38	Homo sapiens	sc-RNA-seq	fastq	reads	pancreas	quake	quakeAdultAging...	alpha cell	:

Initial data browser on UCSC CIRM Data Warehouse

Seurat T-SNE: gene list trimming and non-linear dimensional reduction



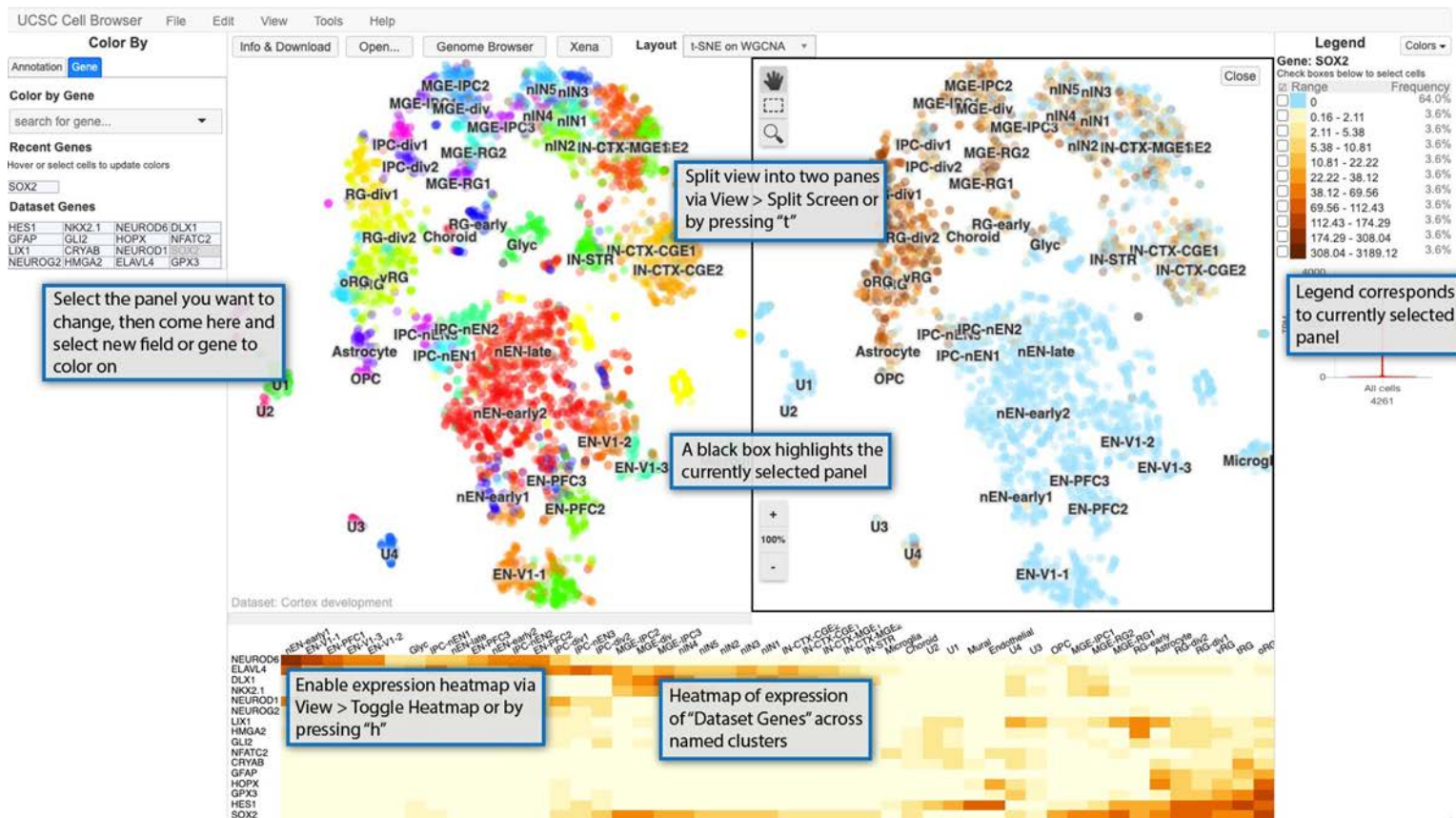
Post-2018: cortex-dev.cells.ucsc.edu



Features of the data browser

- No heavy server needed - cheap to run (end of CIRM data funding)
- Can be used for any single cell dataset - added non-CIRM datasets
- Uses lab-provided results, no analysis - easy to use
- One dataset, one URL - find mentions in Google Scholar
- Documentation at cellbrowser.readthedocs.org

Added features over time



More than 100 datasets

The screenshot shows the UCSC Cell Browser interface. On the left, there's a sidebar titled "Choose Cell Browser Dataset" with a search filter and a list of datasets. Each dataset entry includes its name, technology (e.g., smartseq2, 10x, Drop-Seq), sample size, and an "Open" button. The main content area on the right is titled "Overview" and contains an introduction to the UCSC Cell Browser, instructions on how to use it, and a "News" section with dates and links to new datasets.

UCSC Cell Browser File Edit View Tools Help

Choose Cell Browser Dataset

Filter datasets by organ:

Overview
Cortex development smartseq2 4.3k Open
HCA Datasets via Xena 10 datasets Open
Adult Pancreas smartseq2 4.0k Open
Autism 10x 105k Open
Alexandria Project from the Shalek Lab 2 collections 3 datasets Open
Lifespan Nasal Atlas 3 datasets Open
Human Lung Airway 2 datasets Open
Mouse Hematopoietic Stem Cells 2 datasets Open
Dental Cells 2 datasets Open
Adult Testis 8.2k Open
Glioblastoma 33k Open
Head and Neck Cancer smartseq2 3.6k Open
Melanoma Drop-Seq 10x 3 datasets Open
Choroid Plexus Organoids 32k Open
Macrophage Development 1.2k Open
Mouse Nervous System 20 datasets Open

Overview

UCSC Cell Browser Intro

The UCSC Cell Browser is an interactive viewer for single-cell expression. You can find a few datasets converted at UCSC in the list on the left.

You can also set one up yourself, by [installing the package](#). Exporters to create a Cell Browser from your own data are integrated into [Seurat](#) or [Scanpy](#) and we provide one for [Cell Ranger](#) and for [text files](#).

We are very happy about bug reports or feedback: cells@ucsc.edu.

Or open an issue in our [GitHub Repo](#)

If you use the UCSC Cell Browser in your research, please cite [our Bioinformatics paper](#). If you are also using data from a specific dataset we host, please also cite the original authors of that dataset (visible under 'Info & Download').

News

Jan 24, 2022

New datasets:

- [Human Cortical Lineage](#)
- [Developing Human Brain and Neocortex](#)

Dec 13, 2021

New datasets:

- [snATAC-seq of Human Retina](#)

Nov 29, 2021

New datasets:

- [EvoCell Project](#)

Nov 15, 2021

New datasets:

- [Vasculature in the developing brain](#)

Oct 18, 2021

But Kriegstein-lab CIRM brain datasets still almost 25% of site's usage

Relatively popular website

- > 3000 monthly users as of Jan/Feb 2021
- Mentioned in 180 publications

Typical usage in papers

“We extracted genes that have been found to carry common and rare genetic variants detected in the most recent studies and analyzed the expression pattern of these genes in different cells in the developing human cortex using publicly available database (<http://cortex-dev.cells.ucsc.edu/>). “

[Yang et al, Dev Dynamics 2019](#)

The BrainSpan Atlas of the Developing Human Brain has an extensive collection of such data including transcriptomic and microarray atlases as well as an in situ hybridization resource (<http://www.brainspan.org/>). Single-cell transcriptomic resources are also available to query cell-type-specific gene expression in the developing human neocortex (e.g. <https://cortex-dev.cells.ucsc.edu/>, <http://solo.bmap.ucla.edu/shiny/webapp/>).

[Khakipoor et al, Brain Res 2020](#)

Data from RNA sequencing of isolated single nuclei, performed on surgical specimens of healthy, non-affected lung tissue from 12 lung adenocarcinoma patients, were analysed for AR, TMPRSS2 and ACE2 expression using Eils Lab UCSC Cell browser (<https://eils-lung.cells.ucsc.edu>)

[Leach et al, Nature Comm 2021](#)

...and 178 other publications...

Why did this collaboration work?

- CIRM mandated data sharing
- Kriegstein group extremely successful single-cell lab
 - Cutting-edge domain knowledge available
- Kent group has been doing visualization for 20 years, no single cell at all
 - no competition
- Kent group: long-term staff, Kriegstein: mostly post-docs
 - Long-term IT staff is less cutting-edge than post-docs but expensive
 - 2-3x more expensive than postdocs, but covered by CIRM (-> Schmidt Foundation)
- CIRM had specific funding for data browsing (Stephen Lin encouraged)

Acknowledgments

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Maureen Galvez

Mo Mostajo-Radji

Olivia Meyerson

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Wei Huang

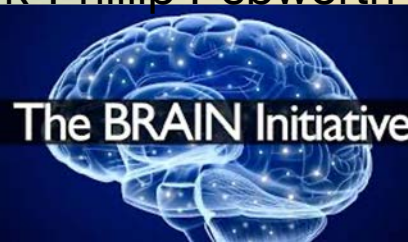
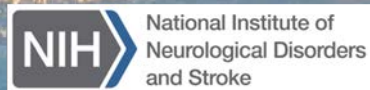
Mark-Phillip Pebworth

Funding:

F32 NRSA Postdoctoral Fellowship

K99/R00 Pathway to Independence

L'Oreal For Women in Science Fellowship



Acknowledgements UCSC

Jim Kent - CIRM PI

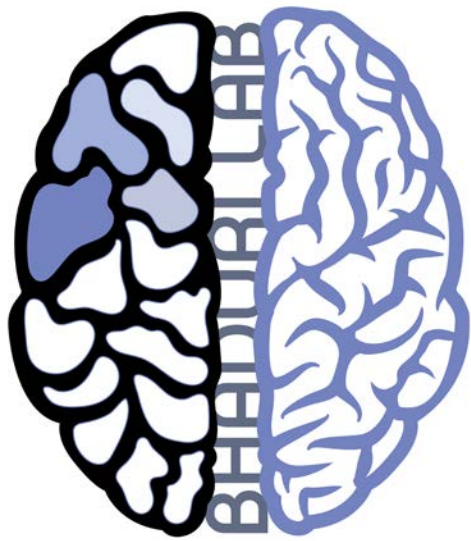
Max Haeussler - Programming, CZI PI

Matt Speir, Brittney Wick - Data Wranglers

Brian Raney, Lucas Seninge, Nikolay Markov (Northwestern Univ) - Programming and support

Jorge Garcia, Erich Weiler – server administration





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Early Medical
Research Trust