# How do human brains vary?

The newly launched Center for Human Brain Variation seeks to understand biological diversity in the brain.

### The Center for Human Brain Variation

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# ABSTRACT

The mission of the Center for Human Brain Variation is to address an unmet need in cell census research: to understand the cell-type-specific mechanisms and tissue-level biological principles that generate inter-individual variation in brain biology. To fully understand the brain's function and vulnerabilities, we must know and be instructed by its biological diversity across people. In this work, we will leverage new technologies in single-cell and spatial genomics, including many developed in our labs, to construct an atlas of human brain cell variation.



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CENTER FOR HUMAN BRAIN VARIATION





### MOTIVATION

An inventory of the human brain's cellular components and their associated molecular repertoires – a cell atlas – will provide a powerfully enabling platform for translational neuroscience. Our atlas will simultaneously inform our understandings of:

- The common, shared cellular features that make all of our brains work
- The ways in which these features vary and co-vary across individuals
- The relationship of this biological variation to genes, alleles and biological function
- The tissue-based mechanisms of genetic risk for neurodevelopmental and neuropsychiatric disorders

# **RESEARCH GOALS**

### 1. Construct **a comprehensive atlas** of human brain cell variation

To understand biological variation, we are analyzing brain tissue from >250 people across 50 diverse brain regions. Selected regions include key associational, motor, and sensory areas, major amygdalar divisions, major monoaminergic regions, and several non-gray matter areas.



### 2. Characterize human brain biological variation

Define cell type abundance and spatial distribution, transcriptome, and DNA accessibility

Identify how these features vary and co-vary across individuals



### 3. Use variation to reveal and understand biological function

How does genetic variation shape the biology of cell types, brain tissue and brain vulnerability?



Scalable and rigorous data generation is critical.

Our laboratory workflow (*figure* on the right) had the best performance<sup>2</sup> in a comparison of BRAIN Initiative Cell Census Network (BICCN) protocols.

These results have dispelled our initial concerns that peri- or post-mortem circumstances might obscure biologically meaningful relationships.

We are developing advanced ways to analyze single-cell and spatialgenomics data. We will **optimize** and share field-advancing laboratory practices and analysis workflows using FAIR principles.





### **DATA GENERATION**

### DATA ANALYSIS





## PLAN FOR ENHANCING DIVERSE PERSPECTIVES (PEDP)

environment where all members flourish.

- **Recruitment goals** • 12/14 (86%) of new hires are from
- underrepresented groups in biomedical research, greatly surpassing our goal of 30%
- Hiring committee will receive training in inclusivity and implicit bias in collaboration with the IDEA Office

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