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Cell Type Diversity and Organization in the Mammalian Brain

Hongkui Zeng

Brain Science Management, Allen Institute for Brain Science, USA

Email: hongkuiz@alleninstitute.org

To understand the function of the brain and how its dysfunction leads to brain diseases, it is essential to uncover the cell type composition of the brain, how the cell types are connected with each other and what their roles are in circuit function. At the Allen Institute, we have built multiple technology platforms, including single-cell transcriptomics, spatial transcriptomics, single and multi-patching electrophysiology, 3D reconstruction of neuronal morphology, and brain-wide connectivity mapping, to characterize the molecular, anatomical, physiological, and connectional properties of brain cell types in a systematic manner, towards the creation of multi-modal cell atlases for the mouse and human brains.

We have now generated a comprehensive and high-resolution transcriptomic and spatial cell type atlas for the whole adult mouse brain, based on the combination of two single-cell-level, whole-brain-scale datasets by scRNA-seq and MERFISH. The atlas is hierarchically organized into four nested levels of classification: 34 classes, 338 subclasses, 1,201 supertypes and 5,322 clusters. We systematically analyzed the neuronal, non-neuronal, and immature neuronal cell types across the brain and identified a high degree of correspondence between transcriptomic identity and spatial specificity for each cell type. We also found that transcription factors are major determinants of cell type classification in the adult mouse brain and identified a combinatorial transcription factor code that defines cell types across all parts of the brain. This study reveals extraordinary cellular diversity and underlying rules of brain organization. It establishes a benchmark reference atlas and a foundational resource for deep and integrative investigations of cellular and circuit function, development, and evolution of the mammalian brain.