**A high-resolution transcriptomic and spatial atlas of cell types in the whole mouse brain.**

Yao, Z., van Velthoven, C.T.J., Kunst, M. et al. *Nature* 624, 317–332 (2023).

Presenter: Tzu-Chia Lin Date/Time: 2024/03/07, 16:10 -17:00

Commentator: Yu-Min Kuo, Ph.D. Location: Room 601, Med College Building

**Background:**

The mammalian brain's anatomical structure and related functions are extremely complicated and still under investigation. So far, millions and billions of cells of different cell types in the mammalian brain form extraordinarily complex neural circuits that play important roles in a wide variety of the organism’s activities, such as vitality, homeostasis, goal-directed behavior, learning, and memory. With the emergence of single-cell RNA sequencing (scRNA-seq) technology, a concordance between morphological and physiological properties has been revealed. However, as the most widely used mammalian model organism, a comprehensive and high-resolution transcriptomic cell-type atlas with clear spatial distribution defining anatomical context covering the entire mouse brain is still lacking.

**Objective/Hypothesis:**

To create a complete, brain-wide cell-type atlas of a mammalian brain and determine how the brain-wide transcriptomic landscape of cell types relates to the anatomical organization with the coordinated gene expression specifies cell-type identity and functional properties.

**Results:**

Through combining a scRNA-seq dataset of around 4.0 million cells passing quality control and a spatial transcriptomic dataset of 4.3 million cells using multiplexed error-robust fluorescence in situ hybridization (MERFISH), a cell-type atlas of mouse brain organized to 4 nested levels of classification was produced, and the authors also set up an interactive online platform. Among different neuronal subclasses, the transcriptomic identity has corresponded with spatial specificity. The results also indicated the extraordinary diversity in intercellular communications in the brain via examining the neurotransmitter and neuropeptide expression. Compared to anterior and dorsal brain regions, cells from the ventral part of the brain had restricted spatial localization. They formed many small clusters closely related to each other, which were hypothesized to be responsible for survival function. Finally, the cell atlas demonstrated the specific neuron-glia and glia-vasculature interactions, especially for astrocytes and ependymal cells. In addition, the trajectories of immature to mature neuronal types in the olfactory bulb and dentate gyrus were highlighted.

**Conclusion:**

In summary, the transcriptomic and spatial cell-type atlas of the whole mouse brain provide the reference genomes for deep investigations of cellular and circuit functions of the brain. However, due to the tremendous scale of the atlas, it will be critical to engage the neuroscience community to refine the atlas collectively.