The Hippocampal Aging Clock

College Alumni Society
Undergraduate Research Grant

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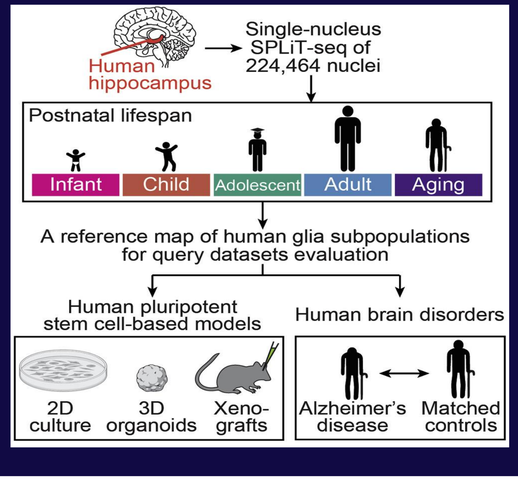
Overview

The project aims to build transcriptome-based cell type-specific aging clocks of the human hippocampus.

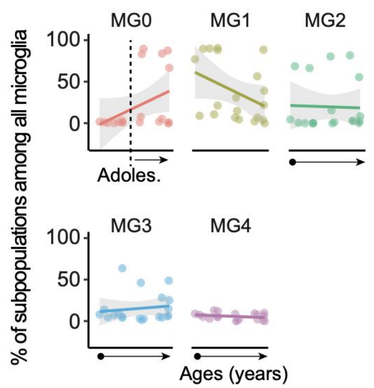
The goal of this study is to identify:

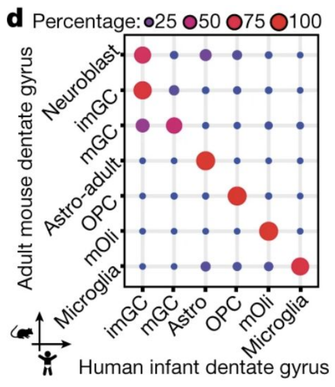
- Whether different cell types age at different rates.
- Which cell types accurately predict age.
- Any constraints associated with cells and aging, such as gender, region, or species.

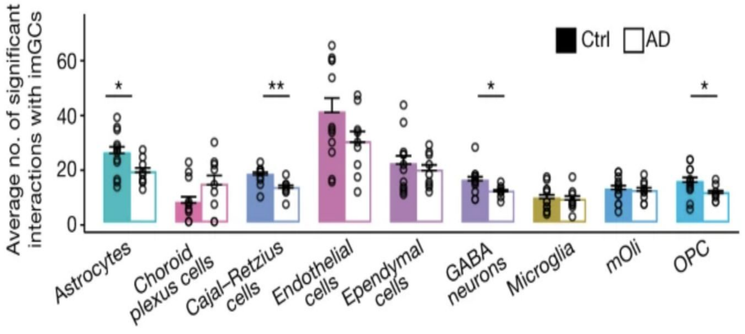
The project involves working with **human hippocampal samples** obtained **post-mortem** and utilizes **single nuclei RNA sequencing** (snRNA-seq) to generate a dataset of 30-50 human hippocampus samples across the lifespan. The division of the hippocampal cells dependent on their cell types and stages allows for a more precise quantification of aging. Additionally, this project also incorporates **machine learning approaches** and the analysis focuses on the **molecular signature** of immature neurons and glia (sub)types.



Results







Significance

The cell type-specific aging clocks built by this project will provide us with insights into the aging process of specific cell types and their contribution to aging. This will accelerate our understanding of existing interventions and provide valuable tools to assess health states, such as more precise aging biomarkers, and evaluate the effectiveness of anti-aging interventions.

Conclusions

By conducting this experiment, a comprehensive single-nucleus transcriptome atlas of a specific human brain region across the postnatal lifespan has been developed. This atlas enables the understanding of cellular mechanisms underlying brain homeostasis and disorders across different ages and has helped us conclude the following:

- Alzheimer's Disease affects various cell types and glial subpopulations differently. Only certain glial subpopulations exhibit transcriptomic dysregulation, with distinct genes affected. Nonetheless, there are common pathways and biological processes affected by these diverse genes across different brain regions and degenerative disorders. This suggests that there is a convergence of pathological features in various disease contexts
- Alzheimer's Disease only affects certain glial subpopulations, and there is minimal overlap in the genes that are dysregulated in each subpopulation.

References

Su, Yijing et al. A Single-Cell Transcriptome Atlas of Glial Diversity in the Human Cell Stem Cell, Volume 29, Issue 11, 1594 - 1610.e8. https://www.cell.com/cell-stem-cell/fulltext/S1934-5909(22)00418-0.

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