ASHBi SEMINAR

Transcriptome plasticity & progressive lineage restriction in stem cell systems

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Date Thursday, 9 June 2022

Time 11:00 – 12:00 [JST]

Venue Zoom Online Meeting*

*Register via the right QR code

Abstract

Within the Weissman lab (Stanford School of Medicine) my major focus has been on elucidating the role of global transcriptome plasticity that governs the progressive lineage restriction of the stem/progenitor fractions within the developing fetal brain and blood systems during ontogeny and post-natal aging.

Normal hematopoiesis: I have used single-cell RNA sequencing (scRNAseq) to thoroughly study first, the development, then aging within the stem cell compartments of brain and blood.
In the hematopoietic system I confirmed the existence of diverse hematopoietic stem cell (HSC) subsets based on mRNA expression in young mice. As the mice aged, the diversity of HSCs diminished with most HSCs expressing mRNAs indicative of myeloid biased HSCs.
A parallel study where I profiled HSC and progenitor fractions during multiple stages of human fetal development and 7 decades of post-natal life also revealed clonal selection and expansion of certain HSC subsets that were present in young individual.

Normal neuropoiesis: The human brain undergoes rapid development at midgestation from a pool of neural stem and progenitor cells (NSPCs), which give rise to the neurons, oligodendrocytes, and astrocytes of the mature brain. Functional study of these cell types has been hampered by a lack of precise purification methods. We describe a method for prospectively isolating nine distinct NSPC types from the developing human brain using combinations of cell surface markers. CD24−THY1−/lo cells were enriched for radial glia, which robustly engrafted, migrated, and differentiated into all three neural lineages in the mouse brain. THY1hi cells marked unipotent oligodendrocyte precursors committed to an oligodendroglial fate, and CD24+THY1−/lo cells marked committed excitatory and inhibitory neuronal lineages. Notably, we identify and functionally characterize a transcriptomically-distinct THY1hiEGFRhiPDGFRA− bipotent glial progenitor, which is lineage-restricted to astrocytes and oligodendrocytes, but not neurons. Our study provides a framework for the functional study of distinct cell types in human neurodevelopment.

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