Building and rebuilding the retina and hypothalamus, one cell at a time

Summary

Our lab aims to identify the molecular mechanisms that control the generation of the major cell types of the vertebrate retina and hypothalamus, which both arise from the ventral embryonic forebrain. We aim to identity genes that pattern progenitors in time, and regulate their ability to proliferate and give rise to specific types of retinal cells at different stages during the course of neurogenesis. To do this, we have generated single-cell RNA and ATAC-Seq profiles of developing mouse retina, and have used this to identify NFI family transcription factors as key regulators of cell cycle exit and generation of late-born retinal bipolar and Müller glia. We have used similar approaches to identify the gene regulatory networks that control spatial patterning and cell fate specification in the developing mammalian hypothalamus. By identifying genes that control how major cell types of the hypothalamus are formed, we gain the ability to selectively manipulate their function and determine their contribution to a broad range of innate behaviors. I will describe insights we have gained into control of progenitor competence and neurogenesis, hypothalamic patterning, and control of sleep. Finally, I will discuss recent comparative work that has identified gene regulatory networks controlling proliferative and neurogenic competence in radial glia of the retina and hypothalamus. Mature glial cells of both the retina and hypothalamus retain the ability to give rise to neurons in certain species. In zebrafish, retinal Müller glia do this readily following injury, while hypothalamic tanycytes of mammals retain limited neurogenic competence. By generating single cell RNA and ATAC-Seq data from zebrafish and mammals, we have identified genes that control this process, and are now able to induce these cells to give rise to neurons. This may ultimately allow replacement of rod and cone photoreceptors lost to disease and rewiring hypothalamic circuitry that controls core homeostatic processes.