# Johns Hopkins University

## Department of Biology- Special Seminar

For more information go to: *https://bio.jhu.edu/events*

**November 27th, 2023 - Mudd 100**

## Kiara Eldred

Department of Biological Structure

University of Washington School of Medicine

**Host: Bob Johnston**

# "Visualizing progenitor cell trajectories in the developing human retina"

The diverse complement of neurons in the retina sense, process, and relay light information from the eye to the brain. All of these cells are generated from a common pool of progenitors. While significant progress has been made in understanding the genetic elements required to generate retinal cell types, our understanding of the mechanisms responsible for specifying and maintaining cell identity remains incomplete. Chromatin structure plays a central role in defining cell identity by regulating gene expression. During development, shifts in chromatin structure facilitate changes in gene expression needed to specify distinct cell types. To understand how changes in chromatin structure influence the developmental trajectory of retinal progenitor cells, we developed a technique termed CUT&TIME, that uses a hyperactive 6-methyl adenosine (6mA) methyltransferase to map ancestral chromatin accessibility genome-wide. We show that CUT&TIME is able to produce a record of the chromatin landscape of retinal progenitor cells that are competent to produce POU4F2+ retinal ganglion cells. We further show that this method is compatible with single cell profiling technologies, which allows us to visualize and capture the diversity of chromatin states that are competent to produce RGCs. This method allows us for the first time to nondiscriminatory track gene accessibility over developmental trajectories on a single cell level. Additionally, we investigate the temporal progression and maintenance of retinal progenitors in the retina. Retinal cell types are specified in defined temporal windows, with early cell types born at early timepoints and late cell types born at later time points. We have identified a region of the developing retina in the far periphery that continues to proliferate long after the rest of the retina is quiescent, which we refer to as the Late Proliferative Zone (LPZ). We show that this region contains both early and late progenitor cells, and produces both early and late born cell types at very late developmental stages. Ongoing studies using various small molecule treatments are underway to understand if proliferation of retinal progenitors and cell fate specification can be modulated. These findings describe a unique model system to study retinal progenitor dynamics and cell type determination factors.