”How does the genome encode the brain connectome?”

Abstract: Complex neural networks consist of many neurons with distinct identities. Important aspects of neuronal identity include which genes are expressed (transcriptome), the cell’s shape (morphology) and its connection to other neurons (connectome). A majority of these features are generated during development. In the Drosophila brain, we have shown that neural stem cells produce morphologically distinct neurons in an invariant order. Lineage mapping, together with genetic mosaic molecular studies, indicate that neuronal diversity is generated by a series of fating events, including lineage, temporal and binary sister fate specification. We are now working toward incorporating single-cell transcriptomics with lineage tracing, by using dynamic developmental recording. We begin with lineages that have been morphologically mapped at a high temporal resolution. We ultimately strive to build a genome-to-connectome brain map.

Tzumin Lee earned his PhD at Johns Hopkins Medical School where he acquired the power of Drosophila genetics from Dr. Denise Montell. He then studied the development of the nervous system in Liqun Luo’s lab at Stanford. Lee set out to develop a way to label specific neurons based on cell lineage. The technique, called mosaic analysis with a repressible cell marker, or MARCM, is used to discover the functions of genes, as well as trace the lineages of neurons and the paths of neural impulses. Besides uncovering genes critical for lineage-guided neural development, Lee has taken MARCM further, creating twin-spot MARCM and lineage-restricted genetic drivers. These refinements make it easier to identify individual neurons and their origins. At Janelia, Lee aims to reconstruct the development of the fruit fly brain at both cellular and molecular levels and extend similar analyses to higher brains.