Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Coordination of Proliferative and Invasive Cellular Fates:

Insights from *C. elegans* Somatic Gonad Development

By

Taylor N. Medwig-Kinney

A growing body of evidence suggests that cell division and basement membrane invasion are mutually exclusive cellular behaviors; but how cells switch between proliferative and invasive states remains poorly understood. Here, I investigate this dichotomy in cellular behavior *in vivo* by examining two cell types in the developing *Caenorhabditis elegans* somatic gonad that arise from a stochastic Notch-mediated cell fate decision: the anchor cell (AC) and ventral uterine (VU) cells. The post-mitotic AC, the default state of the AC/VU cell fate decision, goes on to invade the underlying basement membrane during morphogenesis of the reproductive system, while the VU cells remain proliferative. I show that invasive differentiation of the AC is dependent on the function of a gene regulatory network comprised of four conserved transcription factors: FOS-1 (Fos), EGL-43 (EVI1/MEL), HLH-2 (E/Daughterless), and NHR-67 (NR2E1/Tailless/TLX). While the FOS-1 sub-circuit regulates cell cycle-independent targets, EGL-43 and HLH-2 form a feed-forward loop with NHR-67, which controls cell cycle arrest through regulation of CKI-1. Furthermore, in the VU cells, the default invasive state is suppressed through two distinct modes of regulation of NHR-67. NHR-67 transcription is downregulated in VU cells following post-translational degradation of its upstream regulator, HLH-2. Strikingly, remaining NHR-67 protein forms putative nuclear condensates in VU cells that are dynamic over cell cycle and co-localize with Groucho orthologs, UNC-37 and LSY-22, as well as the TCF/LEF homolog POP-1. Through functional perturbations, I demonstrate that UNC-37, LSY-22, and POP-1 facilitate repression of the default invasive state. Together, these mechanisms coordinate robust control of the proliferative-invasive cellular switch and provide evidence that genes thought to promote differentiated cell behaviors can have opposite roles depending on biological context.

Date: April 4, 2022
Time: 12:00 PM
Place: Laufer Center Lecture Hall 101

Program: Genetics Graduate Program
Dissertation Advisor: Dr. David Matus