Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

SWI/SNF chromatin remodeling and an invasive gene regulatory network:
Insights from *C. elegans* anchor cell invasion

By

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Cellular invasion through basement membranes (BM) is a critical step in metazoan development and is important for human health and fitness. Atypical activation of invasive behavior requires dysregulation of the expression of pro-invasive transcription factors (TFs) and is associated with metastasis, one of the hallmarks of cancer. Cancer metastasis is also associated with mutations in subunits of chromatin regulating factors (CRFs), such as the SWItching defective/Sucrose NonFermenting (SWI/SNF) ATP-dependent chromatin remodeling complex, which coordinates metazoan development through broad regulation of chromatin accessibility and transcription. Here we utilize *Caenorhabditis elegans* anchor cell (AC) invasion as an *in vivo* model to both decode the transcription factor (TF) gene regulatory network (GRN) that governs AC specification and invasion and to identify the suite of CRFs that promote cellular invasiveness. We show that the AC expresses TFs common to metastatic cancers, namely, *egl-43* (EVI1/MEL), *fos-1* (FOS), *hlh-2* (E/Daughterless), and *nhr-67* (TLX/Tailless), initially to contribute to AC specification via regulation of LIN-12 (Notch). Following AC specification, these TFs are then recycled and cooperate together in two parallel subcircuits, one cell cycle- independent and the other cell cycle-dependent, which together activate pro-invasive gene expression and ensure G_0 cell cycle arrest in the AC. Moreover, we identify the suite of chromatin agents and CRFs that promote cellular invasiveness and specifically characterize the SWI/SNF ATP-dependent chromatin remodeling complex as a critical regulator of the AC GRN and AC invasion, with pleiotropic effects on both the cell cycle-independent activation of invasive machinery and maintenance of G_0 cell cycle arrest. The *C. elegans* AC therefore requires coordination of genome-wide chromatin remodelers and lineage-specific TFs to specify, adopt and maintain G_0 cell cycle arrest, and breach the BM *in vivo*.

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Time: 12:00 pm **Dissertation Advisor**: David Q. Matus, Ph.D.
Place: Virtual Conferencing
(*If an outside member of the community would like to attend the defense, please contact the Program Director at Martha.Furie@stonybrookmedicine.edu)