Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Clonal Dynamics and Luminal Intermediate Cells in Prostate Homeostasis and Cancer

By

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The most common prostate disorders, benign prostate enlargement and prostate cancer, are associated with aging and attributed to hormonal imbalances and loss of glandular homeostasis. Given the major impact prostate pathologies have on men's health and their significant burden on healthcare systems, it is important to elucidate the barriers posed by normal homeostasis to deregulated clonal growth. A precise understanding of the cellular and population *dynamics* at play in adult prostate homeostasis, and how its fine balances change with aging and contribute to malignant hyperproliferations, has not emerged so far. Advances in this area would be extremely beneficial for identifying deregulated prostate populations in aged tissues and for designing prophylactic therapies. Using *in vivo* lineage-tracing in genetically engineered mouse models and single cell transcriptomics, my studies uncovered a novel "luminal intermediate" transcriptional state (**LumI**) with unique Wnt/p63 signaling which is a major contributor to the long-term prostate homeostasis. Moreover, LumI cells greatly expand during early stages of tumorigenesis in several mouse models of prostate cancer. In accord, I have also validated the LumI cell state in human aging prostate and prostate cancer samples. Eliminating the p63 signaling *in vivo* has reduced the formation of aggressive clones in mouse prostate tumor models.

Taken together, my studies provide a comprehensive understanding of population growth dynamics and cellular heterogeneity in the luminal layer of prostate tissue and provide potential new venues for identifying early markers of hyperproliferative lesions and preventive cancer therapies.

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Program: Genetics
Dissertation Advisor: Flaminia Talos, MD, PhD

(*If an outside member of the community would like to attend the defense, please contact martha.furie@stonybrook.edu.)