

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

The Impact of Urinary Tract Infections, Pregnancy and Aging on Mammary Tissue

Homeostasis

By

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The majority of breast cancer cases are sporadic, meaning they occur without a known genetic predisposition or familial inheritance pattern. Various risk factors such as age, reproductive history, hormonal levels, lifestyle choices, infections, and environmental exposures influence breast cancer predisposition. Therefore, understanding how these factors impact mammary tissue health in general, before the development of cancer, is crucial. Here, I explored two significant factors affecting mammary tissue health: urinary tract infections (UTIs) and age at first pregnancy. UTIs are highly prevalent among women, especially those of young age. Through a combination of histological tissue analysis and single-cell transcriptomics, we observe alterations in tissue architecture, collagen deposition, and cellular signaling within the mammary gland in UTI-bearing mice. Additionally, we identified an increase in the systemic factor TIMP1. Inhibiting TIMP1 restores mammary tissue homeostasis, suggesting a link between never suspected systemic host response during UTIs and mammary gland alterations. Pregnancy has a more defined role on breast cancer risk. Previous epidemiological studies indicate an onco-protective effect of pregnancy before the age of 25 and an onco-promotive effect after the age of 35. Using single-cell transcriptomics, 3D organoid cultures, and histological analysis, we observe age-dependent alterations in response to pregnancy stimuli, including changes in luminal cellular function. Altogether, my dissertation studies highlighted alterations in normal mammary gland homeostasis influenced by frequently experienced risk factors, specifically UTIs and age at first pregnancy, thus raising the rationale for further studies of how these differences influence breast cancer development

Date: July 25th, 2024

Program: Genetics

Time: 1:00 p.m.

Dissertation Advisor: Camila dos Santos

Place: Cold Spring Harbor Laboratory, Hawkins Building, Wendt Conference Room

To attend virtually, contact the Program Director at martha.furie@stonybrook.edu.