Stony Brook University
The Graduate School

Doctoral Defense Announcement

Abstract

Targeting the lncRNA *MALAT1* in patient-derived breast tumor organoid xenografts using antisense oligonucleotides

By

Disha Aggarwal

Understanding the molecular drivers of breast cancer progression and metastasis continues to be a challenge in oncology. Long non-coding RNAs (lncRNAs) are increasingly recognized as key regulators of tumor biology but have not yet translated to clinical therapies. In this study, we investigated the role of the lncRNA *MALAT1* using patient-derived organoid xenograft (PDO-X) models. We successfully established multiple PDO-X models that recapitulate the intrinsic features of the patient tumors. Using antisense oligonucleotides (ASOs), we achieved efficient *in vivo* knockdown of *MALAT1* across three independent PDO-X models. Transcriptomic analyses revealed that *MALAT1* depletion led to significant changes in gene expression and alternative splicing patterns, underscoring a regulatory role in transcriptional and post-transcriptional processes. Furthermore, *MALAT1* knockdown also led to changes in the tumor microenvironment and a marked reduction in metastasis to the lungs in PDO-X models. Taken together, these findings highlight the therapeutic potential of a *MALAT1*-targeted therapy in breast cancer and demonstrate the utility of PDO-X models for functional studies.

Date: April 23, 2025 **Program**: Genetics
Time: 1:00 PM **Dissertation Advisor**: Dr. David L. Spector
Place: Plimpton Conference Room, Beckman Building, Cold Spring Harbor Laboratory
To attend virtually, contact the Program Director at martha.furie@stonybrook.edu.