



## Ph.D. DISSERTATION DEFENSE

**Candidate:** Sarah Alshehri  
**Degree:** Doctor of Philosophy  
**School/Department:** Charles V. Schaefer, Jr. School of Engineering and Science / Chemistry and Chemical Biology  
**Date:** Wednesday, May 3rd, 2023.  
**Time/Location:** 12:00 – 1:30 pm / Babbio Center, Room 221.  
**Title:** Extracellular Matrix Modulates Outgrowth Dynamics in Ovarian Cancer.

**Chairperson:** Dr. Marcin Iwanicki, Assistant Professor, Department of Chemistry and Chemical Biology.

**Committee Members:**

Dr. Patricia Muisener, Associate Chair of Undergraduate Education, Department of Chemistry and Chemical Biology.  
Dr. Ansu Perekatt, Assistant Professor, Department of Chemistry and Chemical Biology.  
Dr. Kenny Wong, Associate Chair of Graduate Education, Department of Chemistry and Chemical Biology.

### ABSTRACT

Ovarian carcinoma (OC) forms outgrowths that extend from the outer surface of an afflicted organ into the peritoneum. OC outgrowth formation is poorly understood because there is limited availability of OC cell culture models to examine the behavior of cell assemblies that form outgrowths. Prompted by immunochemical evaluation of extracellular matrix (ECM) components, laminin  $\gamma 1$  and collagens, in human tissues representing untreated and chemotherapy-recovered OC, we developed laminin- and collagen-rich ECM-reconstituted cell culture models amenable to studies of cell clusters that can form outgrowths. We demonstrate that ECM promotes outgrowth formation in fallopian tube non-ciliated epithelial cells (FNE) expressing mutant p53-R175H and various OC cell lines. Outgrowths were initiated by cells that had undergone outward translocation and, upon mechanical detachment, could intercalate into mesothelial cell monolayers.

Electron microscopy, optical coherence tomography (OCT), and small amplitude oscillatory shear experiments revealed that high ECM concentration increased ECM fibrous network thickness and led to high shear elasticity in the ECM environment. These physical characteristics were associated with the suppression of outgrowth.

A culture environment with low ECM concentration mimicked viscoelasticity of malignant peritoneal fluids (ascites) and supported cell proliferation, cell translocation, and outgrowth formation. These results highlight the importance of ECM microenvironments in modulating OC growth and could provide an additional explanation of why primary and recurrent ovarian tumors form outgrowths that protrude into the peritoneal cavity.