OCRA Research Grant Executive Summary

Examining the Early Events in Fallopian Tube Transformation
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Grant: Mentored Investigator Grant (MIG-2023-1-1012)

Why This Research Matters

High-grade serous ovarian cancer is the deadliest gynecologic cancer and is often diagnosed too late for cure. Unlike other cancers, there is no effective screening test. New evidence shows that most ovarian cancers actually begin in the fallopian tube, as a microscopic pre-cancer called serous tubal intraepithelial carcinoma (STIC). Today, clinicians lack reliable tools to determine which STIC lesions are dangerous and which are not—leaving patients with uncertainty about treatment and follow-up care.

What This Project Set Out to Do

This research aims to identify the **earliest biological changes** that drive the transition from STIC to invasive ovarian cancer, with the goal of developing **markers that identify high-risk patients** and inform clinical decision-making.

Key Accomplishments to Date

- **Identified early stress signals linked to cancer risk.** The team discovered abnormal activation of cellular stress pathways in STIC lesions associated with invasive disease. In one case, this finding directly contributed to identifying early-stage cancer requiring chemotherapy.

- **Found evidence that cancer-enabling genome instability begins early.** Advanced single-cell and spatial genomic analyses revealed chromosomal abnormalities in some STIC lesions before invasion, suggesting cancer development may begin earlier than previously thought.
- **Detected early immune dysfunction.** The presence of exhausted immune cells within STIC lesions indicates that immune escape may start at the pre-cancer stage.
- **Built new tools for future discovery.** The project established innovative laboratory models and applied cutting-edge sequencing technologies to archived patient tissue—capabilities that did not exist at the project's start.

Impact Beyond the Lab

- Supported the launch of a **longitudinal clinical program** to better monitor and care for patients diagnosed with STIC lesions.
- Enabled an early-career physician-scientist to pursue high-impact, translational research at a critical career stage.
- Generated findings with direct implications for **future clinical guidelines**.

What's Next

The team is expanding the study to larger patient cohorts, refining methods to isolate high-risk STIC cells, and continuing to integrate genomic and immune data. The long-term goal is to develop **practical biomarkers** that guide treatment decisions and reduce both under- and over-treatment.

Why Donor Support Is Essential

This work targets ovarian cancer at its **earliest and most treatable stage**. Donor support has accelerated discoveries that may ultimately save lives by enabling earlier detection, better risk stratification, and more personalized care for women at risk.