# MIGS 26

55TH GLOBAL CONGRESS ON MIGS

BOSTON, MASSACHUSETTS
NOVEMBER 13-16, 2026

# Syllabus

## PG-26040

Improving Endometriosis Outcomes Through Translational Research: Advancing Awareness of New Directions


HONORARY CHAIR
Charles H. Koh, MD

SCIENTIFIC PROGRAM CHAIR
Nash S. Moawad, MD

PRESIDENT
Michael Hibner, MD, PhD




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**PG-26040: Improving Endometriosis Outcomes Through Translational Research: Advancing Awareness of New Directions**

**Chair:** Danielle E. Luciano
**Co-Chair:** Kelly Wright
**Faculty:** Elise Courtois, Linda Griffith, Danielle E. Luciano, Kelly Wright

**Course Description**

Endometriosis remains the least funded and studied conditions per quality adjusted life years (QALYs), according to National Institutes of Health data. As a result, research into endometriosis is well behind other disease states, and relies not only on basic scientists, but also surgical experts. This course, led by basic scientists and surgeon researchers, will update the audience on future advancements in endometriosis research and define the role of the endometriosis surgeon in translational research. The goal of the course is to demonstrate how collaborative relationships between endometriosis surgeons and basic scientists can advance our understanding of this complex disease and advocate for our patient community with better treatments.

**Learning Objectives:** *At the end of this course, the participant will be able to:* 1) Discuss the importance of research in understanding the pathophysiology of endometriosis and the difficulties in defining outcomes in endometriosis research; 2) Examine the important role of a surgeon in basic science and how to set up contemporary collaborative models for advancing research that do not detract from clinical responsibilities; and 3) Evaluate recent advancements in Endometriosis Research and the pitfalls in current diagnostic tests and treatments.

**Course Outline**

| | | |
|---|---|---|
| 2:00 pm | Welcome, Introduction and Course Overview | D. Luciano |
| 2:05 pm | Why Is Translational Research Important to Advance the Care of Endometriosis Patients and How Can the Endometriosis Surgeon Help? | D. Luciano |
| 2:30 pm | How Can an Endometriosis Surgeon and Basic Scientist Collaborate to Advance Research without Detracting from Clinical Responsibilities? | K. Wright |
| 2:55 pm | What Information Are We Lacking about Endometriosis Pathophysiology and How Does Single Cell Spatial Transcriptomics Help Us to Better Understand It? | E. Courtois |
| 3:20 pm | How Can Models of Endometriosis Lesions Help Us to Better Study the Disease and What Have We Learned so Far? | L. Griffith |
| 3:45 pm | Discussion Questions & Answers | All faculty |
| 4:00 pm | Adjourn | |

**ADA Statement:** In accordance with the Americans with Disabilities Act (ADA), please contact CMEsupport@aagl.org should you require any special assistance.

**Disclosure of Relevant Financial Relationships**

As an ACCME-accredited provider, AAGL is responsible for ensuring that accredited education is fair, balanced, free of commercial bias, and supports safe, effective patient care. AAGL maintains control over all aspects of educational planning, content, faculty selection, delivery, and evaluation.

All individuals in a position to control educational content are required to disclose financial relationships with ACCME-defined ineligible companies within the past 24 months. AAGL identifies and mitigates all relevant financial relationships before individuals assume their respective roles. Educational content is also subject to independent peer review by individuals without relevant financial relationships.

Disclosure information and acknowledgment of any commercial support are provided to learners before the activity to promote transparency and maintain the independence and integrity of the education.

Asterisk (*) denotes no financial relationships with ACCME-defined ineligible companies to disclose.

**PLANNER DISCLOSURES**

**The following members of AAGL have been involved in the educational planning and/or review of this course (listed in alphabetical order by last name).**

**PROFESSIONAL EDUCATION COMMITTEE**

Harold Wu, MD* - Chairman
Adrian Balica, MD*
Jamal Mourad, DO – Proctor: Intuitive Surgical
Jude Okohue, MD*
Steven Radtke, MD*
Anna Reinert, MD*
Jean Uy-Kroh, MD*
Linda Bradley, MD, AAGL Medical Director*
Linda Michels, AAGL Executive Director*
Linda Bell, AAGL Admin Support*
Nancy Williams, COO, CME Consultants*

**SCIENTIFIC PROGRAM COMMITTEE**

Nash Moawad, MD, MS, Chairman – Consultant (ended 12/2024): Medtronic, Womed, Integra Life Sciences
Amani Harris, MD*
Ted Lee, MD – Advisory/Consultant: Johnson & Johnson, Regeneron Pharmaceuticals
Nucelio Lemos, MD, PhD – Speakers Bureau: Pfizer, Inc., Medtronic; Advisory Board: Knight Therapeutics, Vecfer Pharma
Mario Malzoni, MD*
Emad Mikhail, MD – Consultant: Johnson & Johnson
Hannah Palin, MD*
Megan Wasson, DO*
Michael Hibner, MD, PhD*
Jose "Tony" Carugno, MD*
Angela Chaudhari, MD - Consultant: Tag/Dream Medical, Johnson & Johnson; Speakers Bureau: Johnson & Johnson
Linda D. Bradley, MD, Medical Director*
Linda Michels, Executive Director, AAGL*

**COURSE CHAIR DISCLOSURE**

Danielle E. Luciano, MD*

**COURSE CO-CHAIR DISCLOSURE**

Kelly Wright, MD – Consultant: Karl Storz, Aqua Therapeutics

**FACULTY DISCLOSURES**

**The following faculty have agreed to support their presentations and clinical recommendations with the best available evidence from the medical literature (in alphabetical order by last name).**

Elise Courtois, PhD*
Linda Griffith, MD – Contracted Research: Novo Nordisk, Amgen; Consultant: RA Capital, Emm
Danielle E. Luciano, MD*
Kelly Wright, MD – Consultant: Karl Storz, Aqua Therapeutics

**MITIGATION OF RELEVANT FINANCIAL RELATIONSHIPS**

**All relevant financial relationships have been mitigated.**

Drs. Lee, Lemos, Mikhail, and Chaudhari's planning decisions, as part of the Scientific Program Committee (SPC), were peer reviewed by other planners on the SPC who had disclosed no financial relationships with ineligible companies, and found to be fair, balanced, and free of commercial bias. Dr. Moawad's financial relationships ended 12/2024, thus mitigating them. For most of his AAGL Professional Education Committee service, Dr. Mourad had no financial relationships to disclose. He recently disclosed a new relationship as a Proctor for Intuitive Surgical. Since then, he has not participated in activities involving control or influence over accredited educational content; therefore, no additional mitigation was necessary.

Dr. Wright's role as Course Co-Chair was limited primarily to course oversight and moderation, rather than development of educational content. Any planning decisions or content under her influence were subject to independent peer review by individuals without relevant financial relationships.

The presentation content for course faculty, Drs. Griffith and Wright, has been peer reviewed and found to be fair, balanced, and free from commercial bias.

# Improving Endometriosis Outcomes through Translational Research: Advancing Awareness of New Directions

November 13, 2026

NOVEMBER 13-16, 2026 · BOSTON · #AAGL26

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## Definitions

- **Endometriosis Outcomes**:
  - Improve Pain
  - Improve Fertility
  - Excise all lesions
  - Prevent Recurrence
  - CURE Endometriosis
- **Translational Research**: is the conversion of basic research into results that directly benefit human life. The term has been used most commonly in life sciences and biotechnology. In the context of biomedicine, translational research is also known as **bench to bedside**. (Wikipedia)
- **New Directions**:
  - Adjustments to our Surgical Approach
  - Targeted Therapies
  - Preventing Recurrence/Fibrosis/Scar
  - Early Diagnostic Testing

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## Course Objectives

- Discuss the importance of research in understanding the pathophysiology of endometriosis and the difficulties in defining outcomes in endometriosis research
- Examine the important role of a surgeon in basic science and how to set up contemporary collaborative models for advancing research that do not detract from clinical responsibilities
- Review the recent advancements in Endometriosis Research and the pitfalls in current diagnostic tests and treatments

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## Course Outline

| | Discussion Topic | Faculty |
|---|---|---|
| 10 min | Introductions and Course Overview | |
| 20 min | Why is translational research important to advance the care of endometriosis patients and how can the endometriosis surgeon help? | Danielle Luciano, MD<br>Professor and Chair of OBGYN at UConn Health |
| 25 min | What information are we lacking about endometriosis pathophysiology and how does single cell spatial transcriptomics help us to better understand it? | Elise Courtois, PhD<br>Assistant Professor and Single Cell Lab Director at The Jackson Laboratory |
| 25 min | How can models of endometriosis lesions help us to better study the disease and what have we learned so far? | Linda Griffith, PhD |
| 20 min | How can an endometriosis surgeon and basic scientist collaborate to advance research without detracting from clinical responsibilities? | Kelly Wright, MD |
| 20 min | Question and answer session | Presenters |

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# Why is translational research important to advance the care of endometriosis patients and how can the endometriosis surgeon help?

Danielle Luciano, MD
Professor and Chair of OBGYN at UConn Health
Adjunct Faculty Jackson Laboratory

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## Disclosure

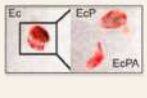
- I am Co-Director of a State-funded Endometriosis Data and Biorepository and Education Program (CTEndoRISE)

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## Objectives

- Describe the unique characteristics of endometriosis which necessitate translational research to understand the disease
- Explore the Role of the Endometriosis Surgeon in Basic Science Research---in other words---

HOW IN THE WORLD CAN a SURGEON HELP a BASIC SCIENTIST?

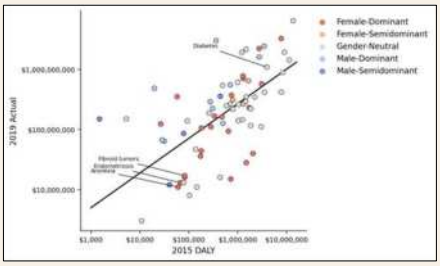





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## Research Funding

(or lack there of)




- Endometriosis affects **11% of US women** in their lifetime, only **$2.00/patient per year** is allocated for research.
- **Diabetes** impacts 12% of US women in their lifetime & funding allocation is **$31.30 per woman**, **over 1,500% more than for endometriosis**
- **Erectile Dysfunction** affects **19% of men**, and receive **5 times** more funding than **Pre-menstrual symptoms that impact 90%** of menstruating individuals.

Gender Disparity in the Funding of Diseases by the U.S. National Institutes of Health, **Mirin. et al, 2021**

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## Endometriosis Presentation

- It presents in all different shapes/colors
- It can be superficial, ovarian, deeply infiltrating, or adenomyosis
- It causes pain in some and infertility in others, and both pain and infertility in some and no symptoms in others
- It is systemic and inflammatory and is associated with many overlapping conditions



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## Models of Endometriosis








**"The pain I have would make Darth Vader squirm"**

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## The Study of Endometriosis



**Animal Models?**

- Non-human primates specifically baboons spontaneously get endometriosis
- Rats/mice/pigs etc do not menstruate and don't spontaneously make endometriosis
- To induce endometriosis in these animals we have to inject endometrial tissue into the peritoneum

**Heterogenous Presentation**

- Endometrioma
- Fibrosis
- Superficial Lesions
- Deeply Infiltrating Lesions

**Ambiguous Outcomes**

- Fertility?
- Pain?
- Recurrence?

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## Why Collaboration is Important






UCONN HEALTH

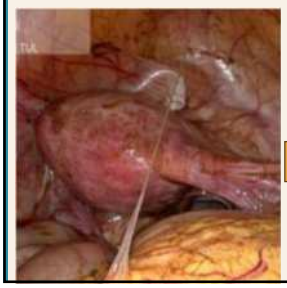


The Jackson Laboratory

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## Asking the Questions

- What is in the stain?
- What is in the OMA fluid?
- Are we leaving active tissue behind?





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## Collecting Biospecimens

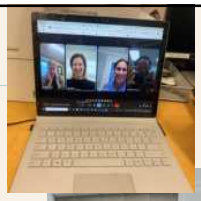
- **Trial and Error**
  - EMB with a pipelle better tissue than a curette
  - Peritoneal Fluid has more cells than peritoneal lavage
- **Better tissue specimen for research**
  - NO telfa, right into the tube
  - Less char/bigger margins
  - Full thickness uterine pieces marking the serosa
- **New ways of collecting biospecimens**
  - OMA fluid with a foley and syringe
  - Peritoneal fluid "neat"…with a foley and a syringe and gravity/pressure



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## Translational Research Collaboration

- We shouldn't be working in silos
- We should be helping each other ask the right questions and learn from each other
- Multi-center trials
- Supporting each other getting started





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## Raise Awareness/Educate and Advocate








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## Disparities in Endometriosis Care, Diagnosis and Treatment

- Historically, endometriosis was commonly known to affect White women while being seen as a "rare condition" for other races, leading to misdiagnoses for chronic pelvic pain in non-Whites
- White women had higher rates of minimally invasive procedures versus open abdominal surgeries than non-White women
- Black women had higher rates of perioperative complications, higher mortality, and spent more time in the perioperative stage than any other race or ethnicity



Westwood S, Fannin M, Ali F, et al. (May 09, 2023) Disparities in Women With Endometriosis Regarding Access to Care, Diagnosis, Treatment, and Management in the United States: A Scoping Review. Cureus 15(5): e38765. DOI 10.7759/cureus.38765

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## How can an Endometriosis Surgeon Help with Disparities in Care?

- Apple et al JMIG 2024: Increasing fellowship in MIGS/CBG trained gynecologic surgeons and providing more opportunities in robotic/laparoscopic training for academic specialists improves access to MIH for Black patients and reduces disparities.
- Allen et al JMIG 2022: Patients who underwent primary surgery for endometrioma by MIGS/CBG needed a second (10.4%) and third surgery (1.1%) vs General OBG 2nd (18.2%) and 3rd (6.8%) p<0.01
- Conversion to Open: General OBG vs MIGS/CBG : 1st surgery (54.8% vs. 31.7%), second surgery (73.2% vs. 16.1%), third surgery (84.6% vs. 7.7%) p<0.01

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## Why is the Endometriosis Surgeon Important for Advancing Endometriosis Research?

- We know how to diagnose and manage endometriosis
- We know what questions are important about the disease and what needs to be understood
- We know how to collect the tissue
- We improve surgical outcomes for patients with endometriosis and increase access to care
- **We can educate our colleagues and advocate for our patients**

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## Acknowledgements



EndoRISE Team




**Courtois Lab**
Jasmina Kuljancic
Jessica Cheung, MD
Caroline Haley, PhD
Joshua Lee



**UConn COE Team:**
Surgeons, Nurses, Staff, and Clinical Research

**All Patients who enrolled in the Biorepository/Research**

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## References


- Allen SE, Su S, Wegner I, Lee TTM, Knekre T, Donnellan N. Minimizing Repeat Surgeries for Endometrioma: Impact of Surgical Intervention by Minimally Invasive Gynecologic Surgeons. JMIG 2022;29(11):S5-6.
- Gender Disparity in the Funding of Diseases by the U.S. National Institutes of Health, Mirin. et al, 2021
- Westwood S, Fannin M, Ali F, et al. (May 09, 2023) Disparities in Women With Endometriosis Regarding Access to Care, Diagnosis, Treatment, and Management in the United States: A Scoping Review. Cureus 15(5): e38765. DOI 10.7759/cureus.38765
- Braundmeier, Fazleabas The non-human primate model of endometriosis: research and implications for fecundity. 2009. PMID: 19633013


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## Elise Courtois

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## Linda Griffith

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## Kelly Wright

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# How can an endometriosis surgeon and basic scientist collaborate?

Kelly Wright, MD, FACOG, FACS
Vice Chair, Gynecology
Division Director, Minimally Invasive Gynecologic Surgery
Program Director, CBGF
Cedars-Sinai

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## Disclosures

- Financial relationships:

Consultant: Aqua Therapeutics, Karl Storz

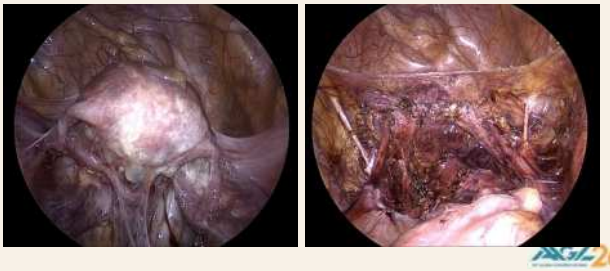
2

## Objectives

- 1. Discuss the importance of research in understanding the pathophysiology of endometriosis and the difficulties in defining outcomes in endometriosis research
- 2. Examine the important role of a surgeon in basic science and how to set up contemporary collaborative models for advancing research that do not detract from clinical responsibilities
- 3. Review the recent advancements in Endometriosis Research and the pitfalls in current diagnostic tests and treatments

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## We have the tissue!



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## Others have the expertise

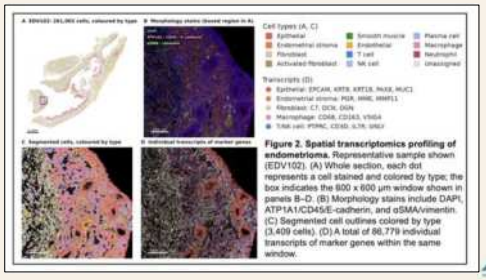
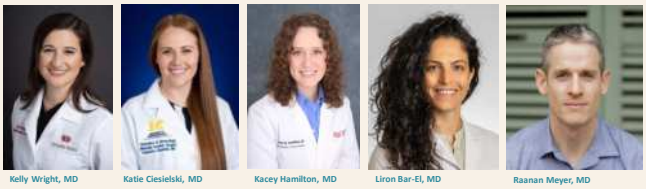


**Figure 2. Spatial transcriptomics profiling of endometrioma.** Representative sample shown (EDV102). (A) Whole section, each dot represents a cell stained and colored by type; the box indicates the 800 x 600 µm window shown in panels B–D. (B) Morphology stains include DAPI, ATP1A1/CD45/E-cadherin, and αSMA/vimentin. (C) Segmented cell outlines colored by type (3,409 cells). (D) A total of 86,779 individual transcripts of marker genes within the same window.

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## Start with dedicated high-volume surgeons



| Kelly Wright, MD | Katie Ciesielski, MD | Kacey Hamilton, MD | Liron Bar-El, MD | Raanan Meyer, MD |
|---|---|---|---|---|
| Brigham/MGH Newton-Wellesley | USC Univ Michigan | Abington Jefferson Cedars-Sinai | Lenox Hill Hospital Cleveland Clinic | Sheba Medical Center Cedars-Sinai |

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## Create an Endometriosis Center

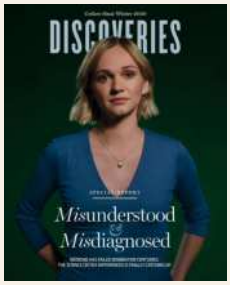
Multidisciplinary team caring for complex patients:

- MIGS
  - High surgical volume
- Urogynecology
- GI
- Pelvic floor physical therapy
- Pain management
- Pain psychiatry
- Social work – Peer support group
- Pathology




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## Build some publicity




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## Find a biobank

- Collect tissue
- Just start – find a way to do it

- 901 – the Gilda Radner hereditary ovarian cancer program



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## Find your scientists

- Researchers working on the same mechanistic problems
  - Ovarian cancer
  - IBD
  - Allergy/immunology
  - Derm
  - Rheum
  - Pain
- Use your clinical connections for scientific connections

| Endometriosis Type | Standardized Incidence Ratios (95% CI) | | | |
|---|---|---|---|---|
| | Serous EOC | Mucinous EOC | Endometrioid EOC | Clear cell EOC |
| Ovarian endometrioma | 1.62 (0.99–2.49) | 1.29 (0.42–3.01) | 4.72 (2.75–7.56) | 10.1 (5.50–18.9) |
| Peritoneal endometriosis | 1.21 (0.79–1.79) | 0.8 (0.26–1.86) | 2.03 (1.05–3.54) | 2.67 (0.98–5.81) |
| Deep infiltrating endometriosis | 2.05 (0.25–7.41) | 0 (0.00–9.58) | 3.35 (0.08–18.7) | 0 (0.00–28.2) |

**Table 2. Risk of ovarian cancer, by histotype, in women with different types of endometriosis.** Adapted from Saavalainen *et al.*, 2018. EOC, epithelial ovarian cancer.

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## Write grants

- Get help
- We need money!
- Apply for all the grants

- Started with a $200,000 internal grant
- Received $750,000 private donation
- Received two R01s
- Donor committed another $750,000
- Private donors x 3, $100,000




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## Assemble a research team




- With funding, we were able to hire a research team who keep the projects running

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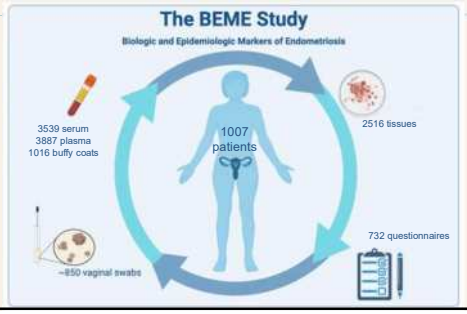
## BEME Study

- Inclusion Criteria
  - Scheduled for surgery for pelvic pain and/or infertility
- Individuals aged 18 – 60 years

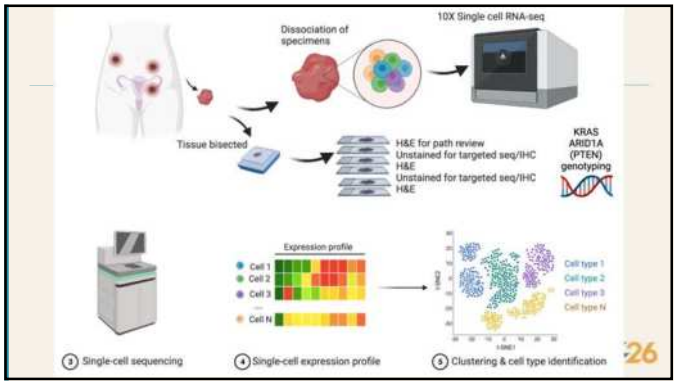
- Exclusion Criteria
  - Suspected pregnancy or malignancy

13

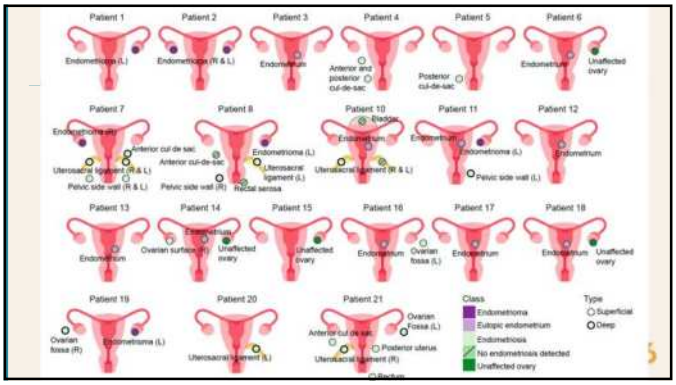
## Accrual is high




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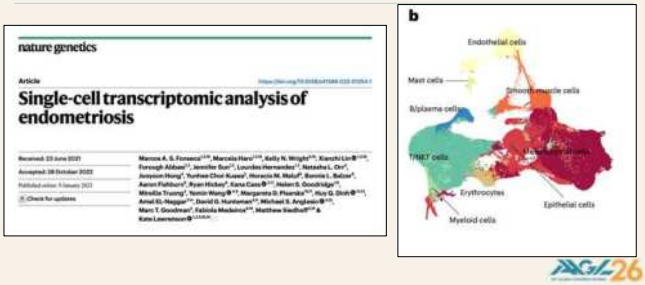



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## Understand the foundations of the disease




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## Build in research for the next generation



**Ida Dhanuka, MD**
1st year Fellow
SUNY Downstate

**Connie Liao, MD**
2nd year Fellow
Abington Jefferson Health

**Maya Shats, MD**
2nd year Fellow
Sheba Medical Center

**Oge Ezike, MD**
3rd year Fellow
Women & Infants
Brown University

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## Build in research

| | | Aug-26 | Sep-26 | Oct-26 | Nov-26 | Dec-26 | Jan-27 | Feb-27 | Mar-27 | Apr-27 | May-27 | Jun-27 | Jul-27 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| First Year Fellow | ID | Research | MIGS* | MIGS | MIGS | REI* | Research* | MIGS | MIGS | Research* | MIGS | MIGS | MIGS |
| Second Year Fellow | CL | MIGS | Research | Urogyn | MIGS* | MIGS | MIGS | Research* | MIGS | MIGS | MIGS/Pain & PFPT | Research* | MIGS |
| Second Year Fellow | MS | Research | MIGS | MIGS* | Urogyn | MIGS* | MIGS | MIGS | MIGS/Pain & PFPT | Research* | MIGS | MIGS | MIGS |
| Third Year Fellow | OE | MIGS* | MIGS | Research* | MIGS* | MIGS* | Research | MIGS | Colorectal | MIGS | MIGS/Ambulatory/US | Elective (TVUS in Canada) | MIGS* |
| Off service fellow | | | | | | REI Fellow | | | | | | | |

*fellow requested vacation in that block; * conference that block

| MIGS Service: | Clinic/OH/TVUS | OR | Research | Notes: |
|---|---|---|---|---|
| First Year FID | 0.5-1 | 3 - 3.5 | 1 | Clinical Scholars, Surgicenter 1x/wk, Attending clinic 1x/wk |
| Second Yr CL | 0.5-1 | 3 - 3.5 | 1 | Rotating Fellows Clinic 1x/wk, Pain & PFPT 2nd half of year 2x/each |
| Second Yr CL | 0.5-1 | 3 - 3.5 | 1 | Rotating Fellows Clinic 1x/wk, Pain & PFPT 2nd half of year 2x/each |
| Third Year OE | 0.5-1 | 3 - 3.5 | 1 | Rotating Fellows Clinic 1x/wk |

Goals = More senior fellows will staff more complex cases. Goal = balance of LSC, robotics, and faculty exposure.

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## Use the money creatively






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## Partnering with industry

- Developing ways to measure progression and composite outcomes

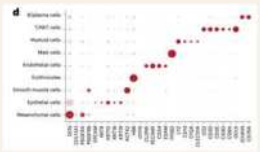
**Assessment of endometriosis angiogenesis using $^{99m}$Tc-maraciclatide imaging (DETECT): a single-centre, exploratory, open-label, non-randomised, phase 2 study**



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## When industry won't partner …

- Drug trials
- Tissue studies for patients already on targeted therapies



- CGRP (erenumab, galcanezumab)
- TNF (adalimumab, infliximab, golimumab)
- IgE (omalizumab)
- IL-4 (dupilumab)
- IL-17 (ixekizumab)
- IL-23 (risankizumba, ustekinumab)



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## Hurdles

- Pathology – working with a senior pathologist to get a clear and thorough protocol for tissue collection (with high-level sign off)
- Cell annotation – gyn tissues are absent/underrepresented in databases used for 'automated' cell annotation
- Study size and inclusion – population-scale studies are needed to disentangle role of hormones, disease context, germline genetics, somatic genetics
- Limited options for funding
- Once you have all the tissue, what do you do with it?

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## Conclusion

We MUST participate in research or else we won't have therapies for our patients

"The current gold standard for diagnosis does little to facilitate early diagnosis or avoid long-term sequelae."
- Lancet, 2025

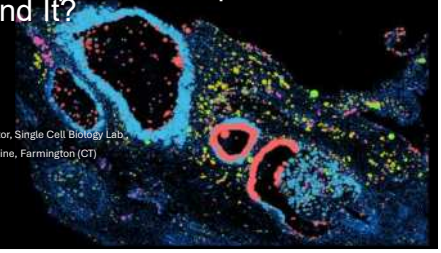
24

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25

# 16157 - What Information Are We Lacking about Endometriosis Pathophysiology and How Does Single Cell Spatial Transcriptomics Help Us to Better Understand It?

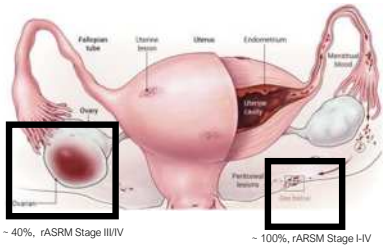


Elise Courtois, Assistant Professor & Director, Single Cell Biology Lab,
The Jackson Laboratory for Genomic Medicine, Farmington (CT)

AAGL
Nov. 2026, Boston, USA

1

## The Heterogeneous Nature of Endometriosis




~ 40%, rASRM Stage III/IV

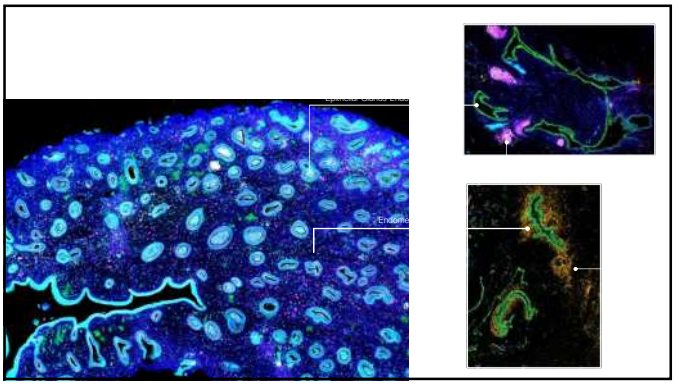
~ 100%, rARSM Stage I-IV

Generate an **integrated single-cell and spatial atlas** to resolve cellular states and lesion architecture

Identify **conserved versus lesion-specific pathways** across anatomical sites

Identify **drivers of pain** across lesion types and anatomical sites

2

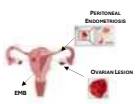


3

## Single Cell Atlas of Endometriosis



Yuliana Tan, PhD

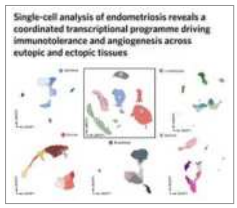


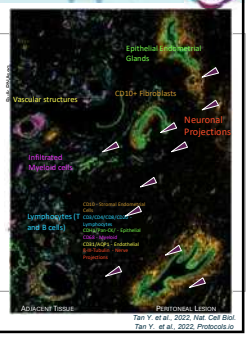

**rASRM Stage III/IV, OC**

EMB (endometrium Biopsy) from both Ctrl and Endometriosis patients

Hormonal Contraceptive Treatment
Treatment matched

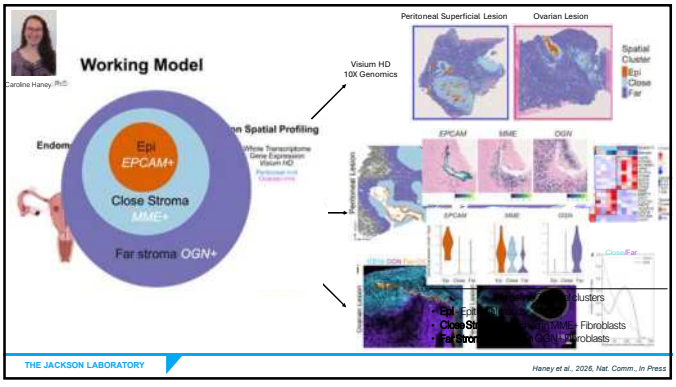
**Single-cell analysis of endometriosis reveals a coordinated transcriptional programme driving immunotolerance and angiogenesis across eutopic and ectopic tissues**






Tan Y. et al., 2022, Nat. Cell Biol.
Tan Y. et al., 2022, Protocols.io

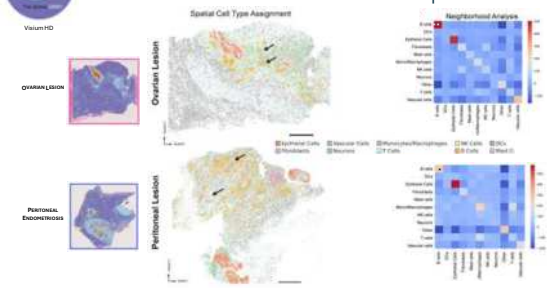
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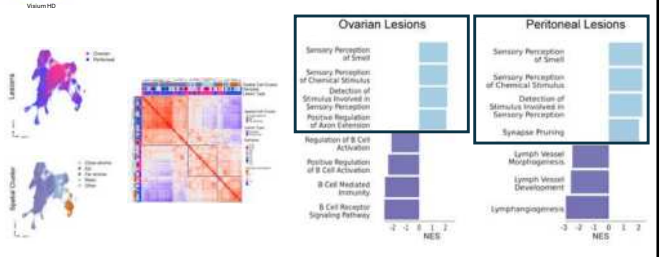
## Spatial Single Cell Atlas of Endometriosis Lesions: Immune Landscape




THE JACKSON LABORATORY
Haney et al., 2026, Nat. Comm., In Press

6

## Shared Spatial Transcriptomic Programs Across Lesion Types

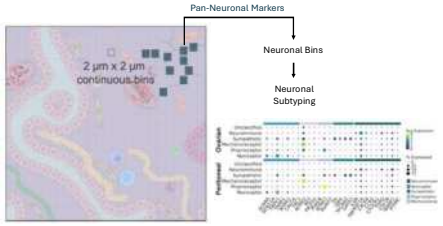




Elaheh Alizadeh, Brian White
Haney et al., 2026, Nat. Comm., In Press

7

## Sensory Neuron Diversity Across Endometriosis Lesions Types and Spatial Clusters




We identified 3 **subtypes of sensory neurons** across lesions:

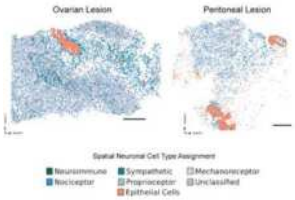
- Nociceptors
- Mechanoreceptors
- Propioceptors

Haney et al., 2026, Nat. Comm., In Press

8

## Distribution of Sensory Neurons Across Lesions

Visium HD

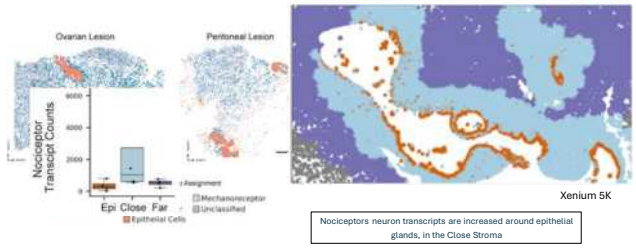




Haney et al., 2026, Nat. Comm., In Press

9

## Nociceptor Neurons Locate Close to Epithelial Glands, Across Lesions




Nociceptors neuron transcripts are increased around epithelial glands, in the Close Stroma


Haney et al., 2026, Nat. Comm., In Press

10

## Defining Spatial Distribution of Neurogenic Immune Cells

Visium HD



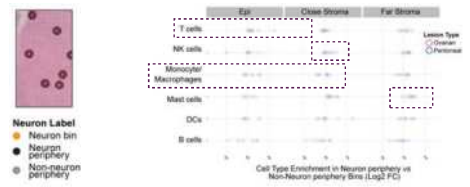

- Increased presence of (Activated) Macrophages in Close Stroma
- Increased Cell interactions (L/R) between Macrophages and Neurons in Close Stroma


Tan et al., 2022, Nat Cell Biol
Haney et al., 2026, Nat. Comm., In Press

11

## Neuro–Immune Spatial Distribution

Enrichment of immune cells in the immediate neuron periphery (within 16 µm distance) and relative to all other bins

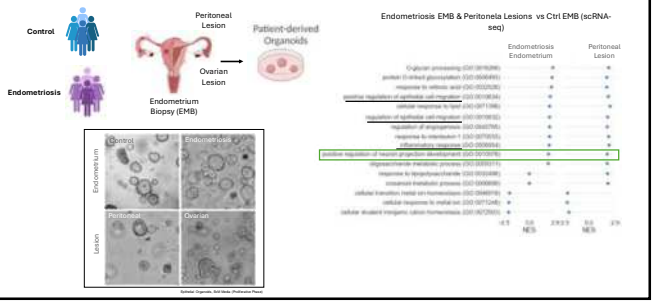



- **T & NK** cells position closely to neuronal bins in **Epi and Close Stroma**
- **Macrophages/Monocytes** close to neurons in **Epi** spatial layer
- **Mast** cells close to neurons in **Far Stroma** across lesion types

Haney et al., 2026, Nat. Comm., In Press

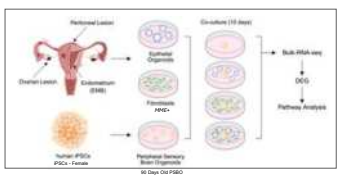
12

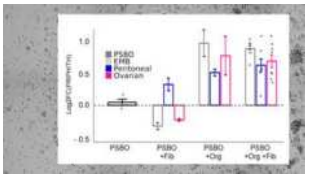
## Patient-Derived Endometrium and Lesion Epithelial Organoid




13

## Mechanistic Insights Into Neuron–Fibroblast–Epithelial Crosstalk in 3D Models of Lesions



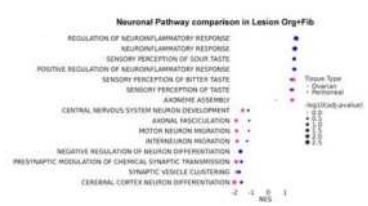

Epithelial Presence Promote Sensory/Nociceptor Neurons and Decreases Sympathetic Neurons in 3D Models of Lesion

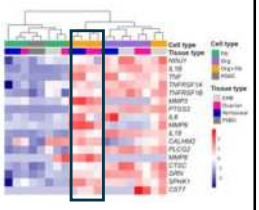
THE JACKSON LABORATORY

*Haney et al., 2026, Nat. Comms.*
*Bozal et al., 2024 SLAS Discovery*

14

## Neuron–Fibroblast–Epithelial Crosstalk: The Neuro-Inflammation Link



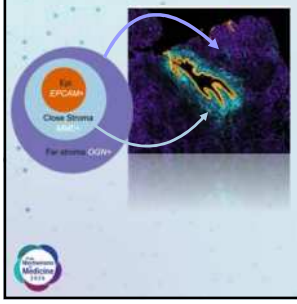

Epi/Fibro Presence induces **neuro-inflammation** signaling pathways

THE JACKSON LABORATORY

*Haney et al., 2026, Nat. Comms.*
*Bozal et al., 2024 SLAS Discovery*

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## Take Home Message




- Heterogeneous Lesions Types Share Spatial Stromal Layers Relative to Epithelial Glands Across Lesions: **Close** and **Far Stroma**
- Innervation is Spatially Defined and Sensory Neurons Specifically Distribute Close to Epithelial Glands and Close Stroma
- We Define Neuronal Diversity and Neuro-Immune Spatial Distribution
- The Presence of Epithelial and CD10+ Fibroblasts Promote Sensory Neurogenesis and Neuro-inflammatory Pathways



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Shruthi Soh

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Brian White (CS)
Elaheh Alizadeh

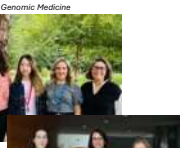
Sun Lab (Renji hospital, Shanghai, China)
Kommagani Lab (Baylor College of Medicine Tx)
Lawrenson Lab (UT San Antonio)
Greaves Lab (Warwick, UK)

JAX Support
Scientific Services: Histology, Flow, Microscopy, RIT, External & Gov Affairs

Dr. Luciano's Team
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Makayla Murphy
Amanda Ulrich, MD
Alexis Newmark, MD
Danielle Luciano, MD

UConn REI /CARS
Lawrence Engmann, MD
Daniel Grow, MD

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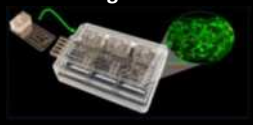


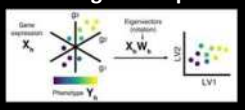




All patients who generously donated tissues, blood and time for these studies

# Move over, Mice
## Humanizing Models for Endometriosis Drug Development





**AAGL 2026**

**Linda Griffith**

**Biological & Mechanical Engineering MIT**

1

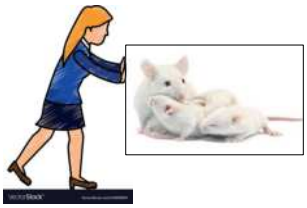
## Disclosures

- LGG is co-inventor on a patent for synthetic hydrogel for organoid culture, which is licensed to BioTechne
- New Jun kinase inhibitor compounds patented by Steve Palmer/Baylor and licensed to Gedeon Richter are provided to our MIT NIH-funded NAMs Center for efficacy evaluation
- LGG consults for RA Capital on use of NAMs in preclinical endometriosis drug development

2

2

## Move over, Mice!
*but don't you (and NHP, etc.) leave altogether, just yet...*



- **Phenomena are often similar in animals & humans**
  - → *animals can be informative*
- **Devil is in the details – molecules, and networks often don't translate**
  - → *animals can be misleading*
  - → *humanized alternatives needed*

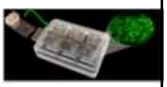
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## NAMs for Clinical Translation of Therapies for Systemic Gynecology Diseases

MIT | U Mich | Case Western | Brigham & Women's | Certara | "TDC – Women's Health" NIH UM1 TR006029 Member, Complement-ARIE Consortium



**Candidate drugs**
industry partnerships
clinical compounds as benchmarks



**Endometriosis patients**
**Clinical & molecular/ cellular phenotyping**
(2 active sites + public data)





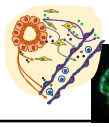
**DATA**

**QSP Models**
MPS operating features
**Drug effects**
**Hormone effects**

**Systems Biology**
In vivo- in vitro-in vivo translation

**DATA**

**Living Patient Avatars**
designed to capture drug MOA
**Microvascularized immune-competent Endometriosis lesions**
***+ sex specific liver***







**Pain /symptoms**
**Lesion burden**
**Tissue/cell-omics**
***+ patient metadata etc.***

**Predictions of Clinical Outcomes**

4

**Overarching question:**
Can we capture key features of endometriosis lesions using in vitro models (made from patient cells), to test therapeutic efficacy??

**First question (from analysis of lesions, -omics and other features):**
What are key features to capture, for a proposed mechanism of action (MOA)? *And how variable are patient populations/lesions for a given MOA?*

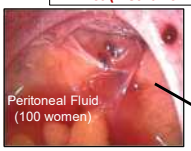
**Second Question (from analysis of in vitro models)**
Can we benchmark in vitro models against in vivo lesion (or other) data?

5

5

## Endometriosis Computational Systems Biology NAMs v1 (2014):
M/L Analysis of Peritoneal Fluid Targeted Immune Proteomics

**First (Mechanism-based) Molecular Classification *+ new drug target (!!)***



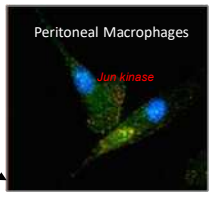

Targeted (immuno) proteomics

Machine learning analysis
(patient groups & biomarkers)

Immune network inference

Bioinformatic prediction of key disease enzyme: JNK

validation




Beste, Pfaeffle-Doyle, Prentice, Lauffenburger, Isaacson, Griffith, *Sci. Transl. Med.* (2014).

6

## A JNK Inhibitor Cured Diverse Patient Populations of Endometriosis! (alas, no humans)




Palmer* et al., Reprod Sci. 2016



Hussein & Palmer* , Fertil Steril. 2016

**Preglem clinical trial of a JNK inhibitor = unsuccessful -** Low potency, patient heterogeneity

7

STEVE PALMER EXPLAINS

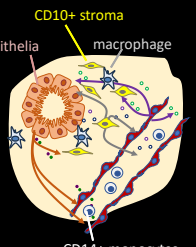
## "What's Next" for JNK Inhibitors.... Besides New Molecules




"We need HUMAN efficacy models... patient-on-a-chip"

ASRM CONFERENCE 2014, HONOLULU

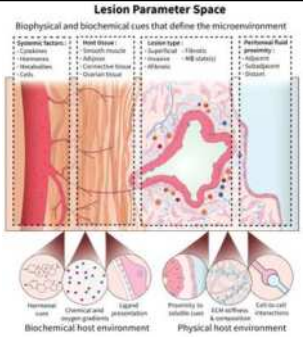
*Human LESION*




8

## Lesion Parameter Space

Biophysical and biochemical cues that define the microenvironment




**What are crucial features of lesions? (Depends on MOA)**

For JNKi: Epithelia, Stroma, macrophages (+??) What proportions?

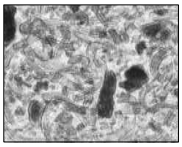
ADD photo of lesion from Colgrave et al

9

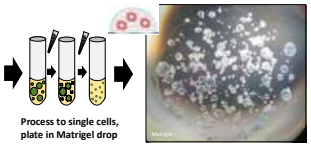
## Building endometriosis lesions models using patient cells

Images from Juan Gnecco (Asst Prof Tufts)

**Isolated endometrial glands from biopsy**



**Endometrial epithelial organoids in Matrigel droplet**




**Matrigel is widely used for organoid culture, but :**

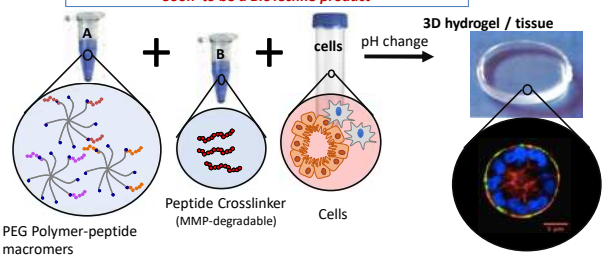
- is derived from a tumor extracellular matrix, many confounding biological signals
- degrades quickly, limits culture period
- Significant lot to lot variation
- Cannot use for culture of stromal and immune cells, vascularization of lesions

10

## Modular Synthetic Hydrogel for 3D Tissue Engineering

The devil is in the (many) details – ligands, mechanics, etc
***Soon to be a BioTechne product***

Jeff Hubbell + the universe

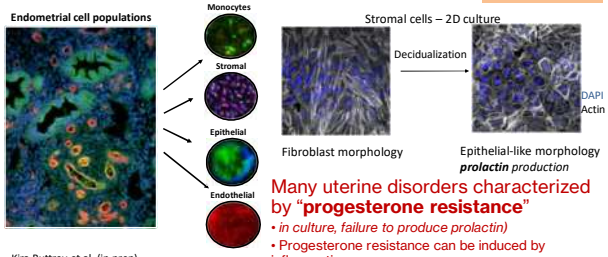



*Valdez et al, Biomaterials 2017; Cook et al, Integrative Biol. 2017, Hernandez-Gordilla 2020, Below et al 2021; Gnecco et al Cell Med 2023.*

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## Progesterone induces a "decidualization response" in healthy endometrial cells

Patient-derived cells

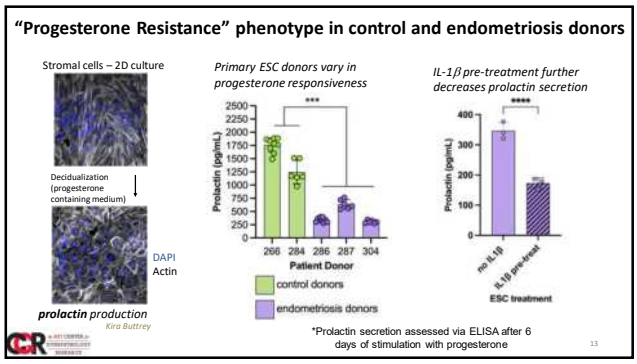



Many uterine disorders characterized by "**progesterone resistance**"

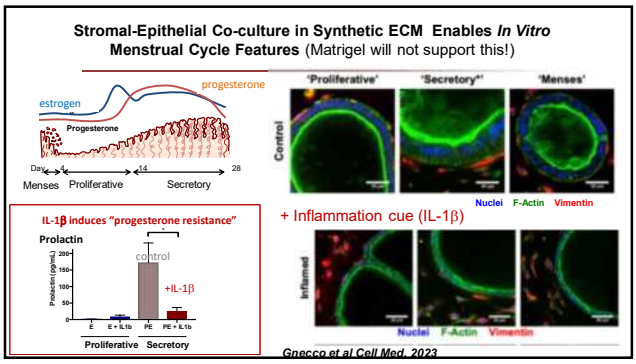
- *in culture, failure to produce prolactin)*
- Progesterone resistance can be induced by inflammation

Kira Buttrey et al, (in prep)

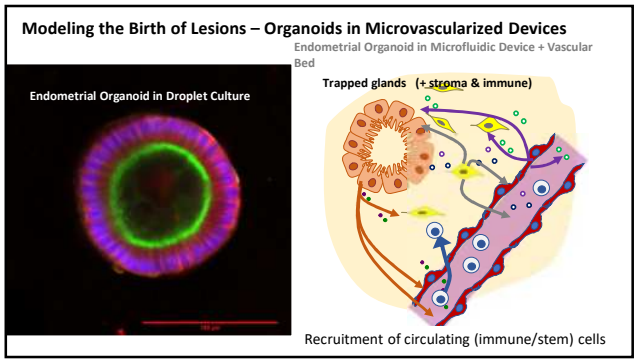
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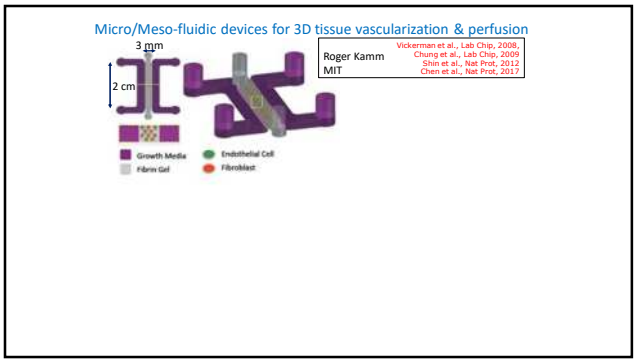

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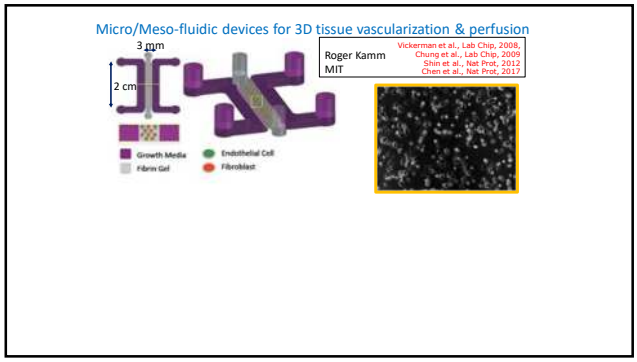

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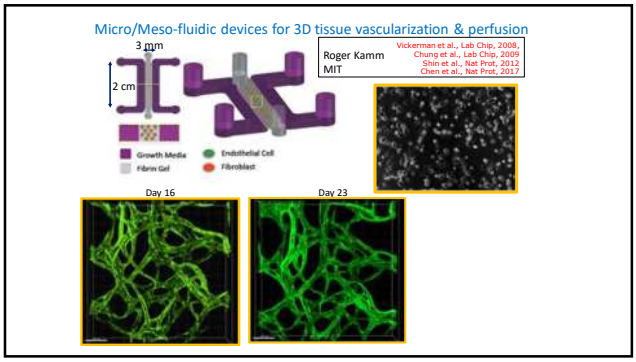

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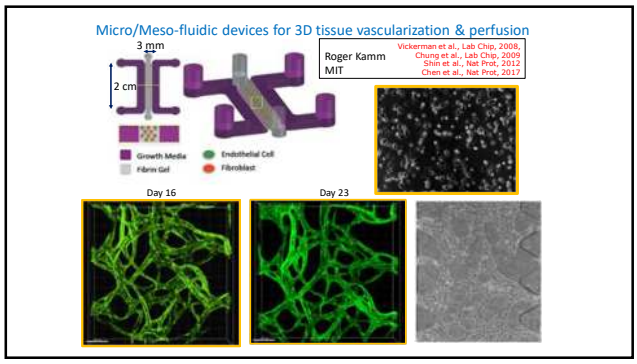

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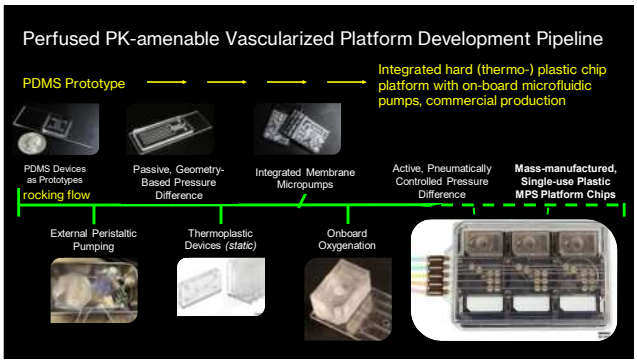

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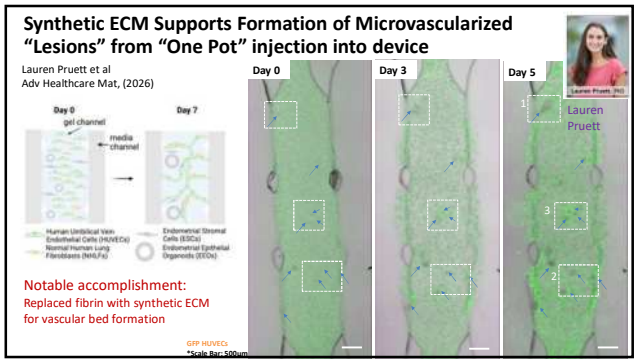

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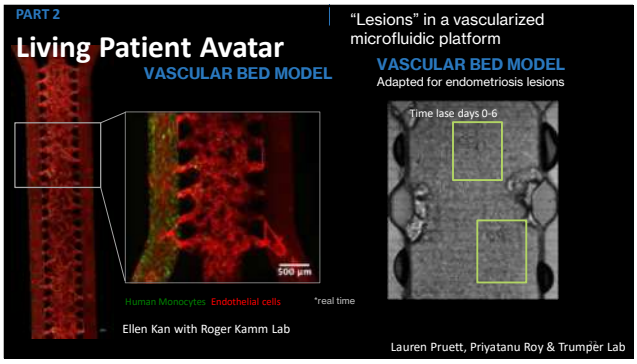

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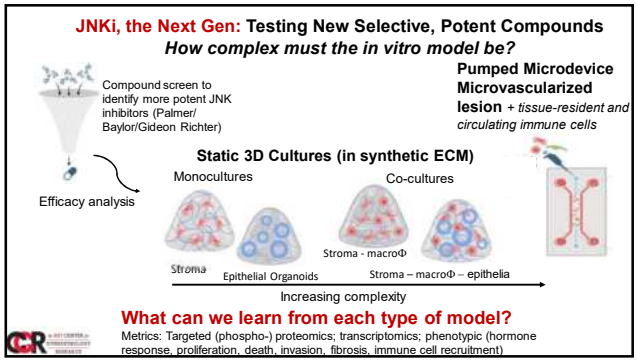

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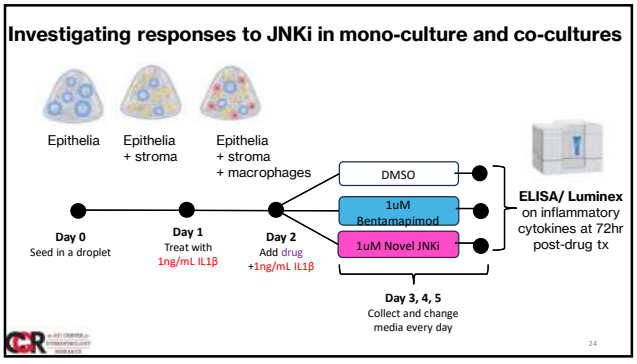

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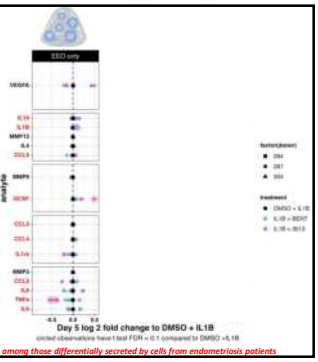



24

**Triculture model highlights the increased ability of novel JNKi to reduce inflammation compared to Bentamapimod**

Sean Pascoe (Lauffenburger Lab),Griffith, Palmer, unpublished



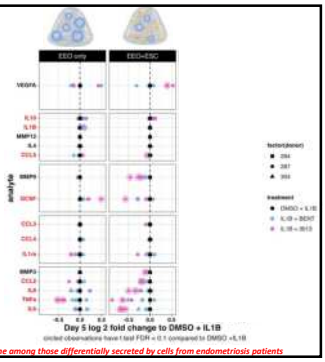

*Cytokine among those differentially secreted by cells from endometriosis patients

25

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Sean Pascoe (Lauffenburger Lab),Griffith, Palmer, unpublished



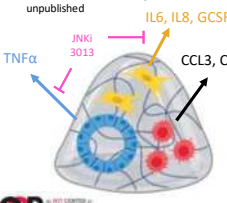



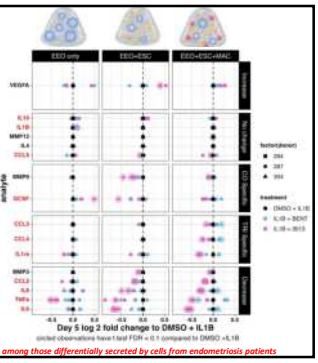

*Cytokine among those differentially secreted by cells from endometriosis patients

26

**Triculture model highlights the increased ability of novel JNKi to reduce inflammation compared to Bentamapimod**

Sean Pascoe (Lauffenburger Lab),Griffith, Palmer, unpublished




*Cytokine among those differentially secreted by cells from endometriosis patients

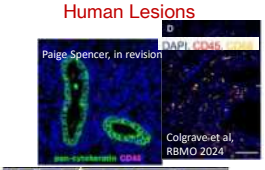
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**Frontier:** Controlling soluble cues in the medium

***In Endometriosis:***

- Systemic **steroid** hormones – especially **ANDROGENS!** -- are dysregulated
- Lesions (often) exhibit progesterone resistance (inflammation-induced)
- Steroid hormone ***metabolism*** in lesions can be highly pathological
- local synthesis of ***estradiol,*** associated with ***lesion growth***
- immune cell functions are regulated by (sex) steroids
- ***Yet, patients are being prescribed progestins****, to "oppose estradiol" – but many fail to respond and have terrible side effects*

Human Lesions



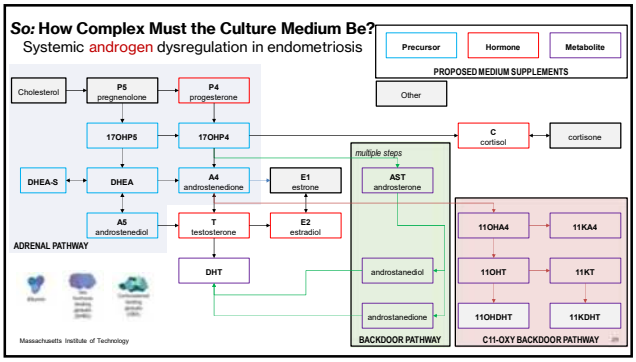




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**So: How Complex Must the Culture Medium Be?**

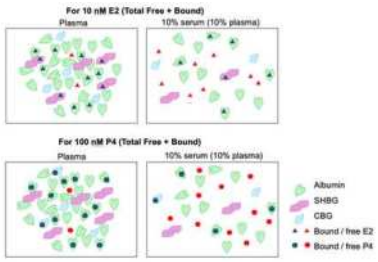
Systemic androgen dysregulation in endometriosis




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Dilution of protein in culture medium (compared to plasma) drives HUGE increase in free steroid concentratation

*(same TOTAL hormone concentration)*

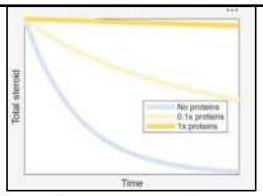


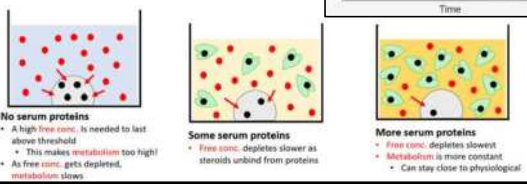

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## Binding proteins buffer metabolic depletion

*unknown how this affects function*

Metabolism is first order
(proportional to free concentration)




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## Treatment landscape evolution: (Symptom relief) -> disease-modifying

***Diverse MOA in pipelines/clinical trials***

- Immune/inflammation-targeting (e.g.)
  - anti-IL8 (Chugai); anti-IL1 (academic)
  - JNK inhibitor (Gideon Richter)
- Angiogenesis inhibitors
- anti- Prolactin receptor (Phase II/III)
- HDAC inhibitors
- DCA (repurposed from cancer)
- Cannabinoid receptor (Nalu Bio, others)
- Pain – CRGP, mPEGS
- GLP-1 drugs, *chatter on patient Facebook groups*

**Start-ups AND established ("Big") Pharma now very engaged with endometriosis as a TA**

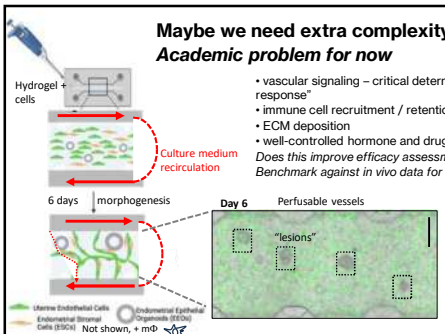
An Ad on my FB!! AbSci Anti-Prolactin Receptor




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## Maybe we need extra complexity?

***Academic problem for now***




- vascular signaling – critical determinant of "progesterone response"
- immune cell recruitment / retention / inflammation
- ECM deposition
- well-controlled hormone and drug PK

*Does this improve efficacy assessment?*
*Benchmark against in vivo data for clinical drugs*

Pruett et al, Adv Healthcare Mat, 2026

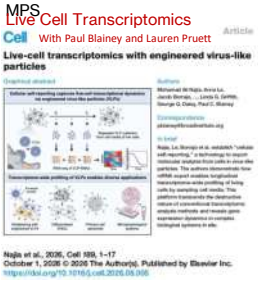
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## In Progress:

Many New Non/Minimally Invasive Technologies to Probe Function of MPS

**Live Cell Transcriptomics**

With Paul Blainey and Lauren Pruett




**Computational Biophotonics + AI**

With Sixian You




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## NAMs TDC for Women's Health: Team & Core Expertise

*PI/PD led Centerwith Co-Investigator Joint Steering Committee Overseeing Clinical-to-NAMs Integration*




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## Thanks to!

**@Griffith Lab**

Postdocs
Dr. Samantha Holt
*Dr Priyatanu Roy*
Dr Lauren Pruett

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*Jacob Hochfelder*
*Ellen Kan*
*Erin Tevonian*
*Matthew Johnson*

Undergraduates
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Sydney Kim
Maria

Technicians
Heather George
Ryan Ogi
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Roger Kamm lab
Mikki Tal lab



Dave Trumper lab

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*Lauren Baugh*
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Victor Hernandez-Gordilla
Natasha Hardcastle
*Allison Lenhard*
*Duncan O'Boyle*
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Hilde Jørgensen, MD

**@U. Edinburgh**
Hilary Critchley, MD Lab



Peter Movilla, MD



Megan Loring, MD *(Currently Seattle)*

**@Wellcome-Sanger**
Roser Vento-Tormo Lab

**GUT Engineering**

**@Northeastern University**
Rebecca Carrier Lab

**@Harvard Medical School**
David Breault

***Current Funding***

NIH U01 Immune Chips
NICHD R01, Endometriosis
NICHD R01, Endometrium
NIH NAMs Center Grant
NIEHS Tox Training Grant
NovoNordisk
Fairburn Foundation
Begg Foundation

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NEW Endometriosis Documentary from the Endometriosis Collective




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# CULTURAL AND LINGUISTIC COMPETENCY & IMPLICIT BIAS

The California Medical Association (CMA) outlines standards for Cultural Linguistic Competency and Implicit Bias in CME. The goal of the standards is to support the role of accredited CME in advancing diversity, health equity, and inclusion in healthcare. These standards are relevant to ACCME-accredited, CMA-accredited, and jointly accredited providers located in California. AAGL is ACCME-accredited and headquartered in California.

CMA developed the standards in response to California legislation (Business and Professions (B&P) Code Section 2190.1), which directs CMA to draft a set of standards for the inclusion of cultural and linguistic competency (CLC) and implicit bias (IB) in accredited CME.

The standards are intended to support CME providers in meeting the expectations of the legislation. CME provider organizations physically located in California and accredited by CMA CME or ACCME, as well as jointly accredited providers whose target audience includes physicians, are expected to meet these expectations which began on January 1, 2022. AAGL has been proactively adopting processes that meet and often exceed the required expectations of the legislation.

CMA CME offers a variety of resources and tools to help providers meet the standards and successfully incorporate CLC & IB into their CME activities, including FAQ, definitions, a planning worksheet, and best practices. These resources are available on the CLC and IB standards page on the CMA website.

**Important Definitions:**

**Cultural and Linguistic Competency (CLC)** – The ability and readiness of health care providers and organizations to humbly and respectfully demonstrate, effectively communicate, and tailor delivery of care to patients with diverse values, beliefs, identities and behaviors, in order to meet social, cultural and linguistic needs as they relate to patient health.

**Implicit Bias (IB)** – The attitudes, stereotypes and feelings, either positive or negative, that affect our understanding, actions and decisions without conscious knowledge or control. Implicit bias is a universal phenomenon. When negative, implicit bias often contributes to unequal treatment and disparities in diagnosis, treatment decisions, levels of care and health care outcomes of people based on race, ethnicity, gender identity, sexual orientation, age, disability and other characteristics.

**Diversity** – Having many different forms, types or ideas; showing variety. Demographic diversity can mean a group composed of people of different genders, races/ethnicities, cultures, religions, physical abilities, sexual orientations or preferences, ages, etc.

**Direct links to AB1195 (CLC), AB241 (IB), and the B&P Code 2190.1:**

Bill Text – AB-1195 Continuing education: cultural and linguistic competency.
Bill Text – AB-241 Implicit bias: continuing education: requirements.
Business and Professions (B&P) Code Section 2190.1

**CLC & IB Online Resources:**

Diversity-Wheel-as-used-at-Johns-Hopkins-University-12.png (850×839) (researchgate.net)
Implicit Bias, Microaggressions, and Stereotypes Resources | NEA
Act, Communicating, Implicit Bias (racialequitytools.org)
https://www.contemporaryobgyn.net/view/overcoming-racism-and-unconscious-bias-in-ob-gyn
https://pubmed.ncbi.nlm.nih.gov/34016820/
https://hr.ucdavis.edu/departments/learning/certificate/implicit-bias
https://pmc.ncbi.nlm.nih.gov/articles/PMC7011228/