

A woman is lying on a table in a clinical setting, receiving an ultrasound scan on her abdomen. A medical professional is using a probe on her skin. In the background, a monitor displays a blue-toned ultrasound image. The scene is overlaid with decorative elements: a dark blue horizontal band on the left containing text, and several light blue and white circular and organic shapes scattered across the image. The background features a pattern of light blue, interconnected, organic shapes.

Tissue and Organ Mechanobiology (R2)

Wendy Liu, University of California, Irvine

Our Team Spans Disciplines & Schools



Wendy Liu, UCI

Biomedical Engineering, Chemical & Biomolecular Engineering, Materials & Microfabrication, Regulating Cell Behavior, Multicellular Behavior, Cardiovasculature



Naomi Chesler, UCI

Biomedical Engineering, Cardiovascular Mechanobiology & Biomechanics, Engineering Education, Diversity, Equity & Inclusion in STEM



X. Edward Guo, CU

Biomedical Engineering, Mechanics of Soft Tissues, Preterm Birth, Hydrated Biomaterials



Helen Lu, CU

Biomedical Engineering, Biomaterials and Tissue Engineering



Joshua Mauney, UCI

Urology, Tissue Engineering, Medical Device Testing



Kristin Myers, CU

Mechanical Engineering, Mechanics of Soft Tissues, Preterm Birth, Hydrated Biomaterials



Christine O'Brien, WUSTL

Radiology, Raman Spectroscopy, Maternal Hemorrhage, Wearable Devices



Joy-Sarah Vink, CU

OB/GYN, Preterm Birth Prevention



Gordana Vunjak-Novakovic, CU

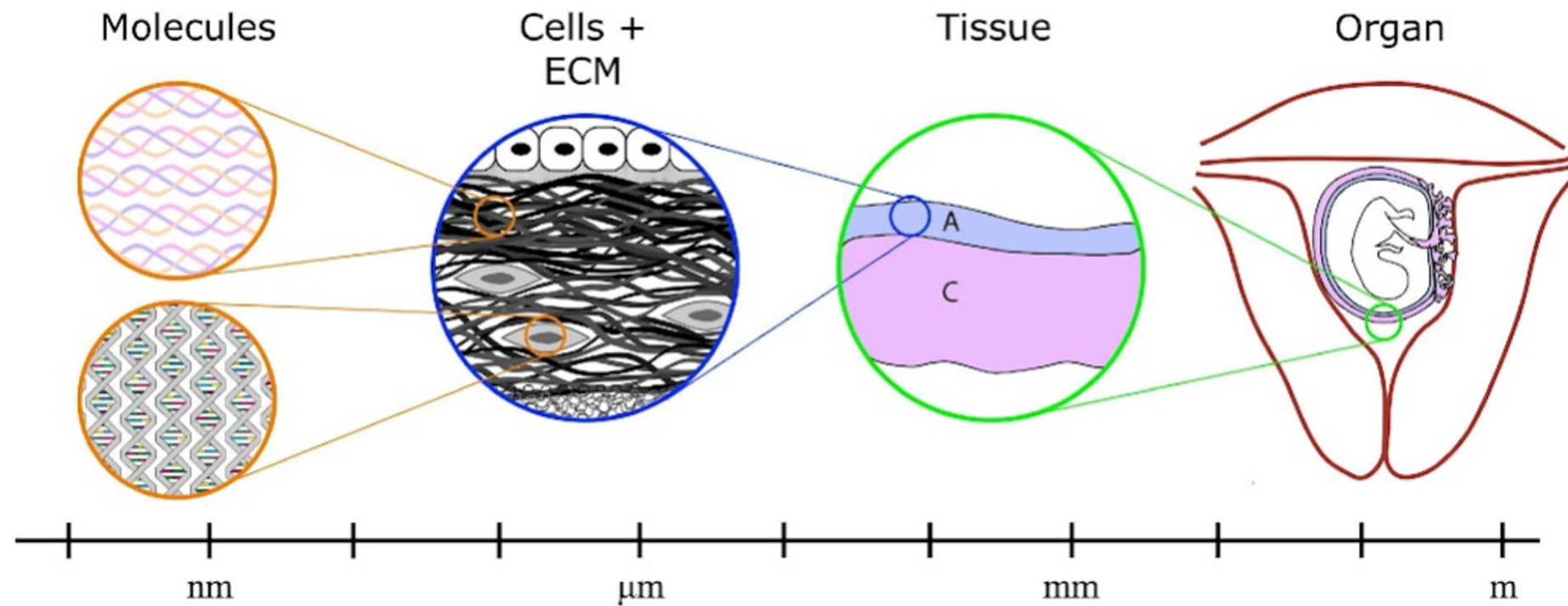
Biomedical Engineering, Medicine, Dental Medicine, Regenerative Medicine, Tissue Engineering, Organs on a chip



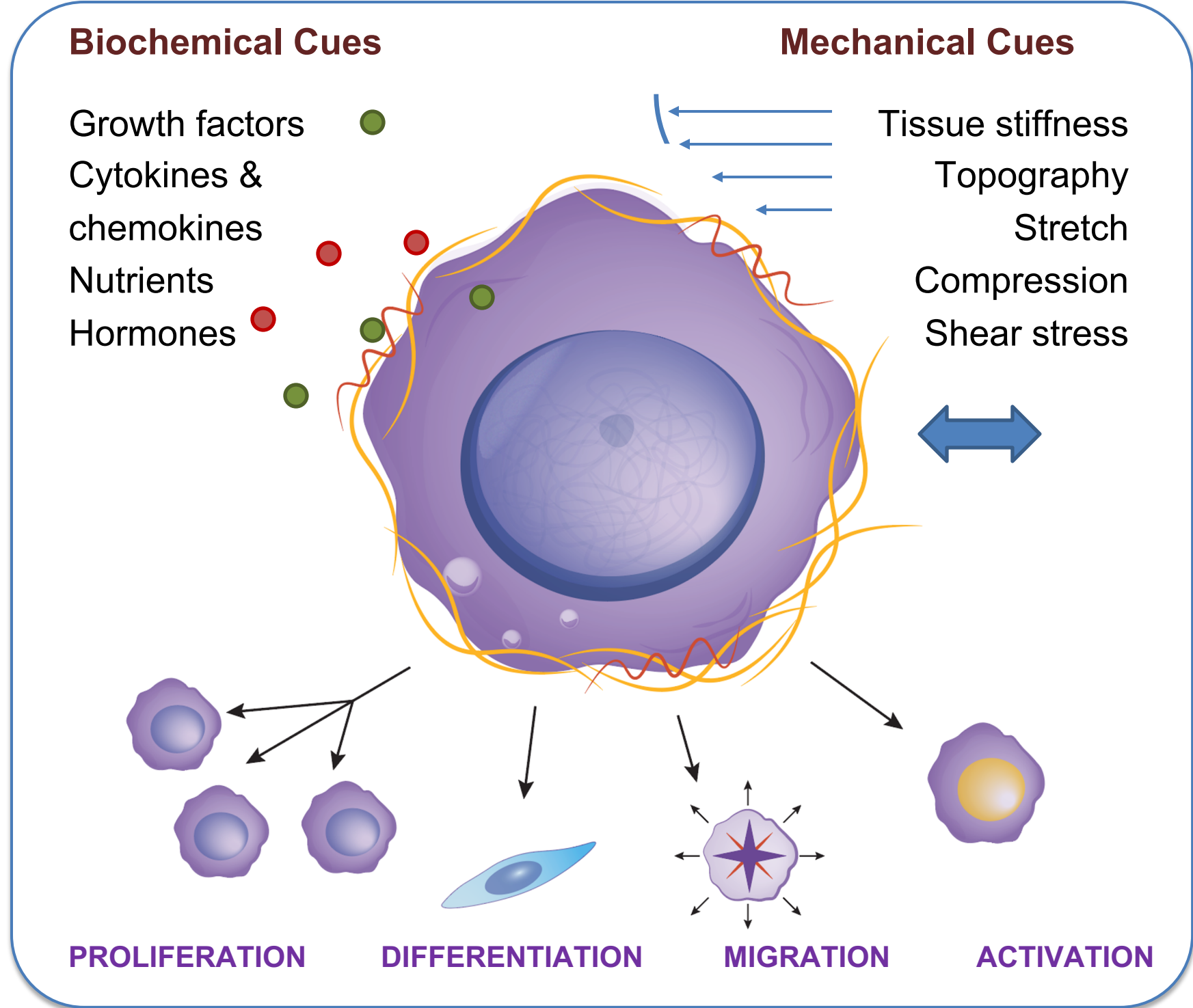
Yong Wang, WUSTL

OB/GYN, Radiology, Biomedical Engineering, Uterine Functional Imaging, Electrophysiology

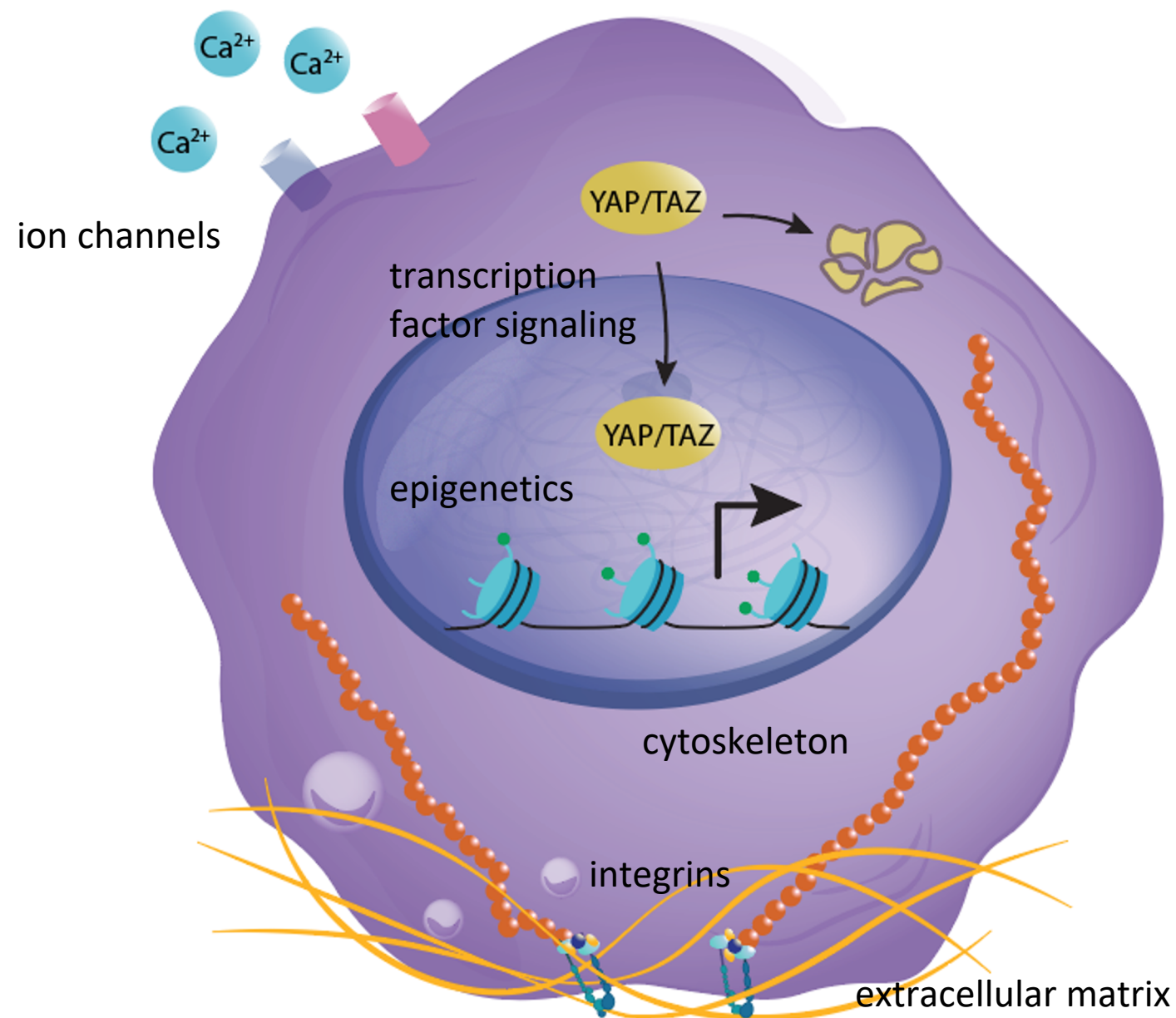
Multiscale mechanobiology



Mechanical forces drive and modulate biological function



How do cells transduce mechanical forces into biochemical signals that regulate cell function?

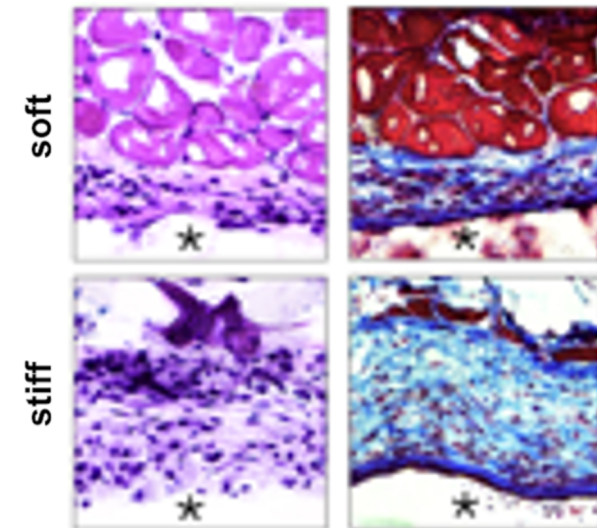
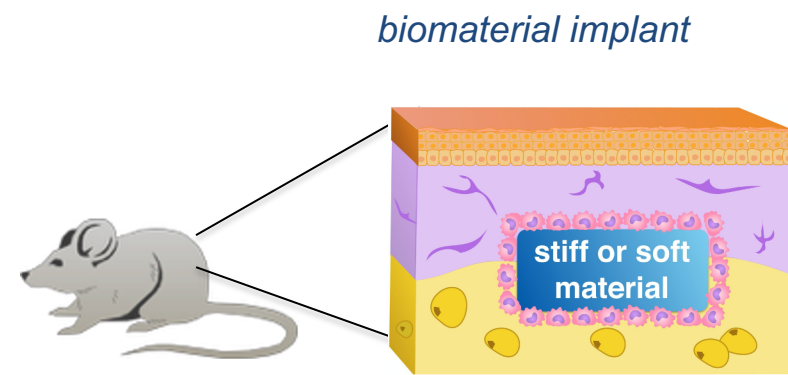


- Adhesion molecules
- Ion channels*
- Cytoskeletal components
- Adhesion-related signaling
- Transcription factor signaling
- Epigenetic mechanisms

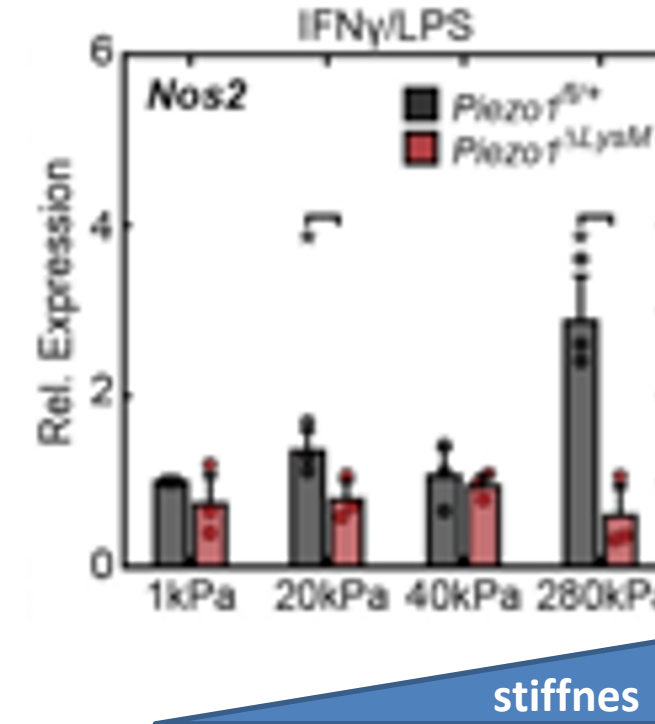
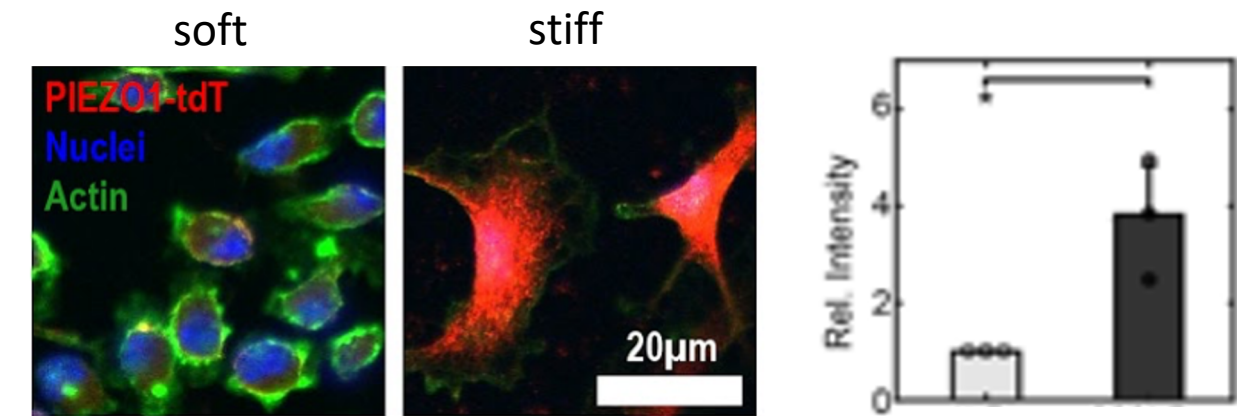


* 2021 Nobel Prize in Physiology or Medicine

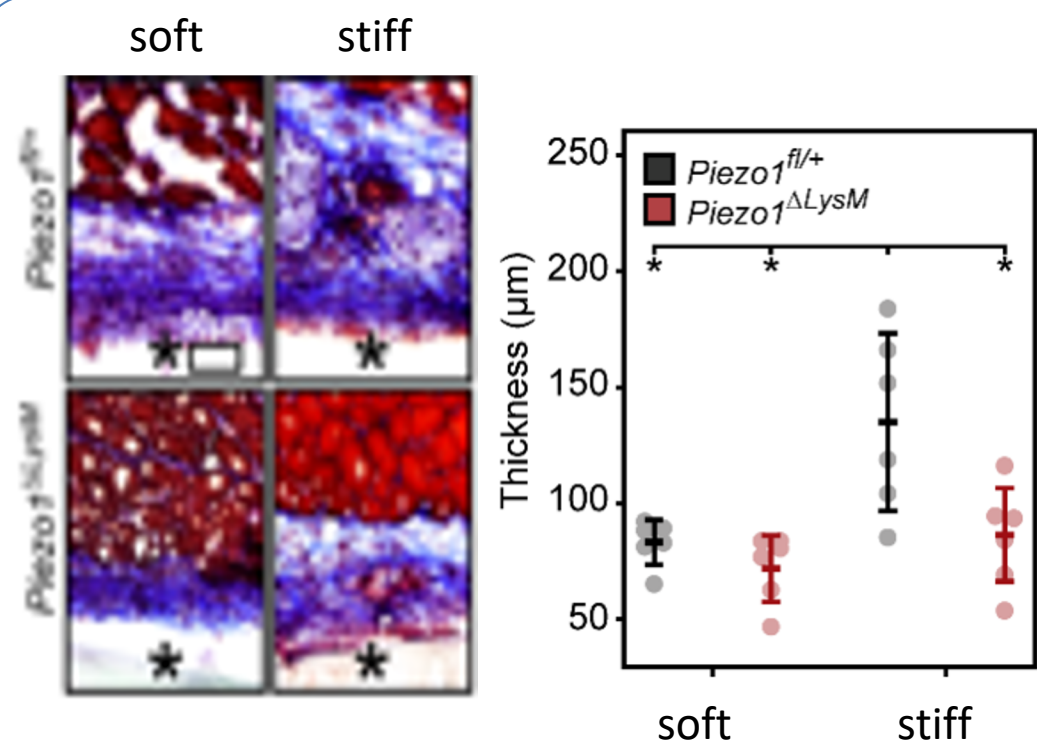
Mechanical cues in the repair response to biomaterials



Meli et al., *Science Advances* 2020



- Stiffer materials enhance Piezo1 expression
- Blocking Piezo1 abrogates stiffness-dependent cell responses



- Blocking Piezo1 prevents fibrosis response to stiff implants

Grand challenges



How do the unique mechanical forces present during pregnancy and childbirth affect cells and tissues of the reproductive system and pelvic floor?

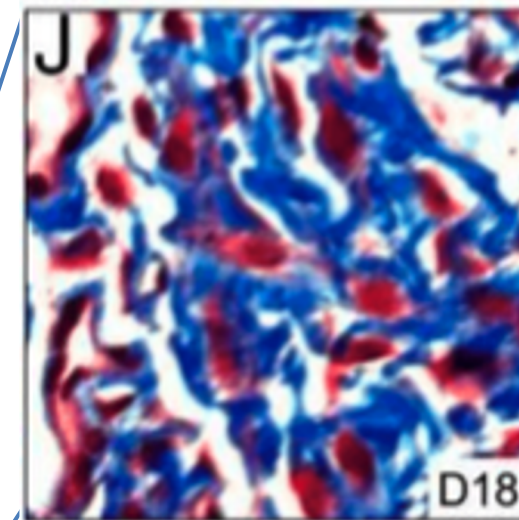
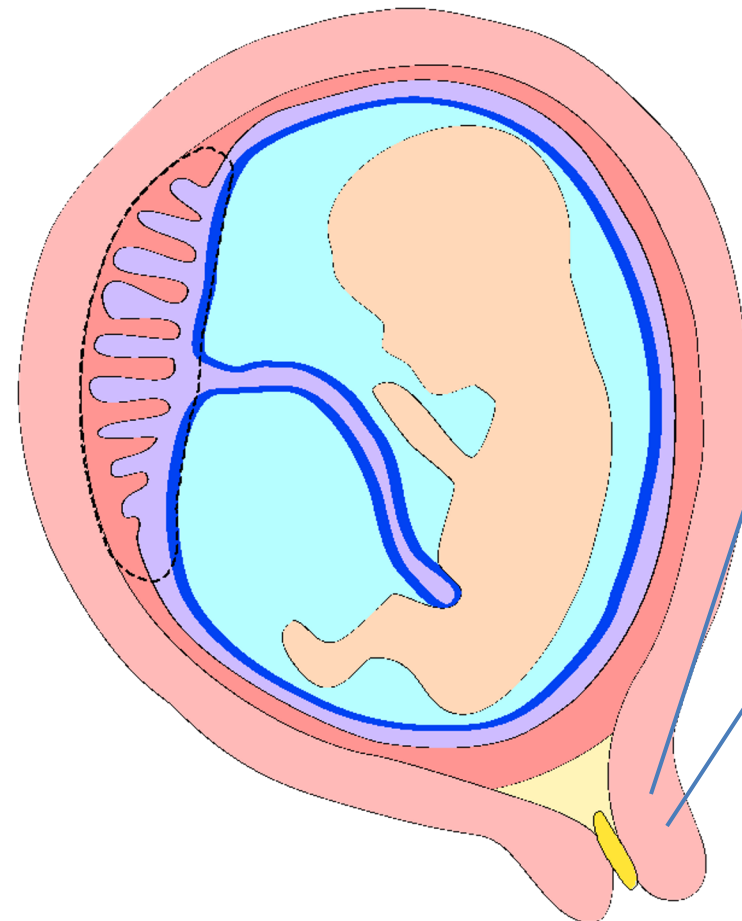


What is the role of age, sex, and race in mechanobiology of the cardiovascular and musculoskeletal systems?

Mechanoregulation of uterine and cervical tissues



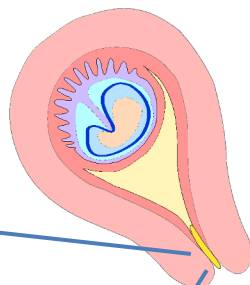
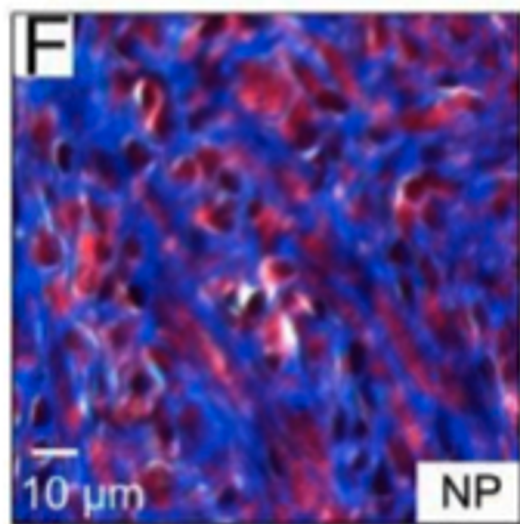
The uterine wall grows and **stretches to over 300% the non-gravid size** during pregnancy



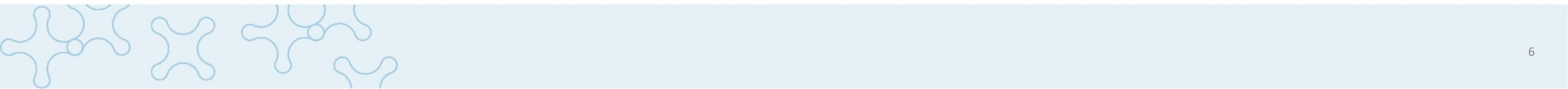
How do **stretch** and **stiffness** contribute to:

- Cellular composition?
- Function of cells?
- Remodeling of the matrix?

What are the **molecular mechanisms** underlying these responses?

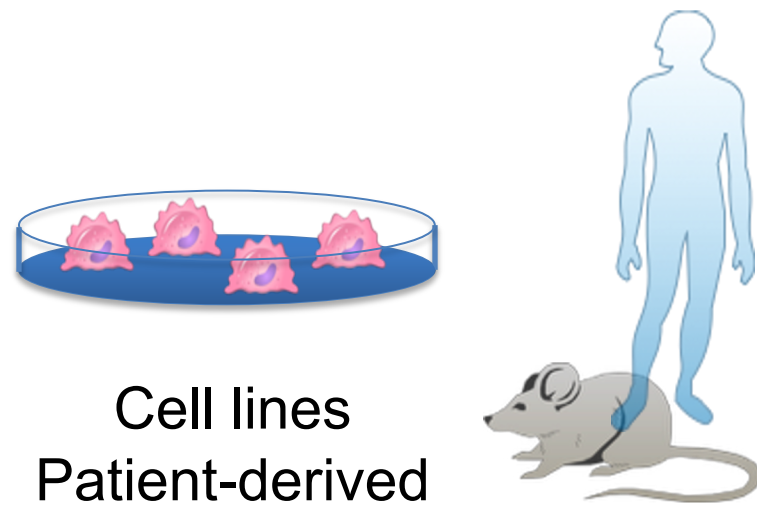


The cervix **softens 3 orders of magnitude** in stiffness prior to the onset of childbirth



Mechanobiology workflow

Uterine and cervical cells and tissues



Cell lines
Patient-derived
iPSC

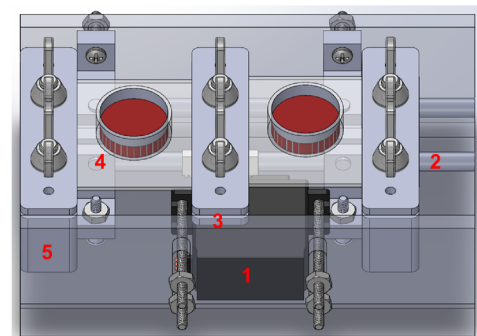
Animal
models
Patients



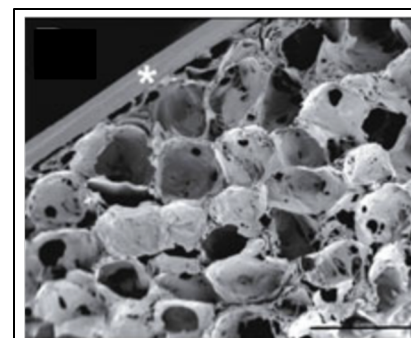
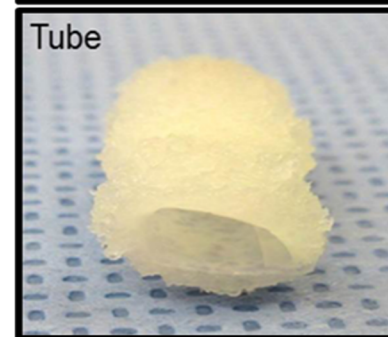
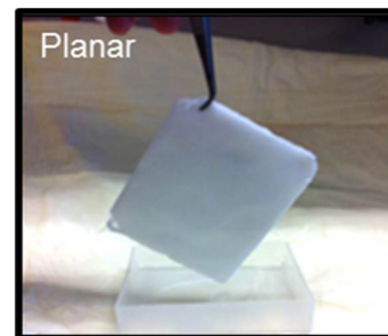
T2

Bioengineered platforms to mimic physiology and manipulate mechanical cues

Mechano-organs/devices



Biomaterials

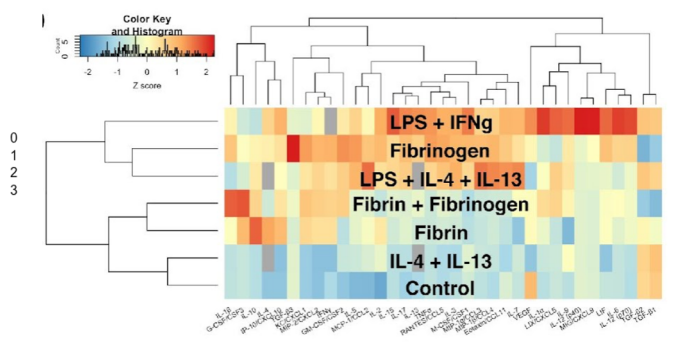
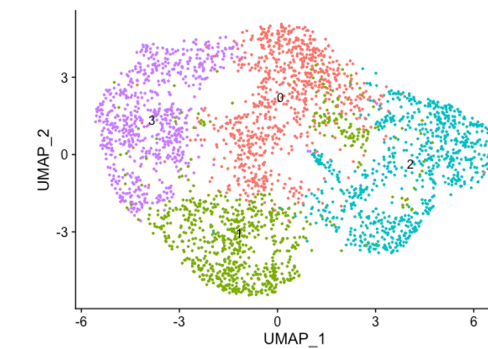


R1

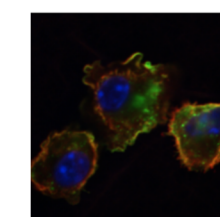
T1

T2

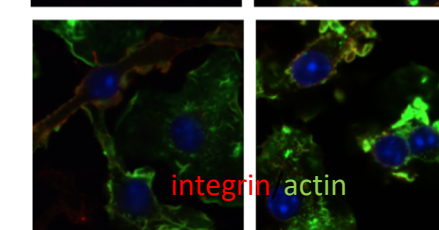
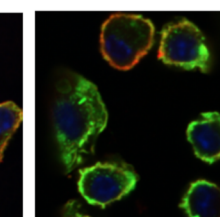
Functional analysis and biological understanding



crosslinked fibrin



fibrin



- Cell composition
- Cell and tissue function (growth, remodeling)
- Adhesion molecules, ion channel activity, signaling pathway activation, etc.



R4

T4

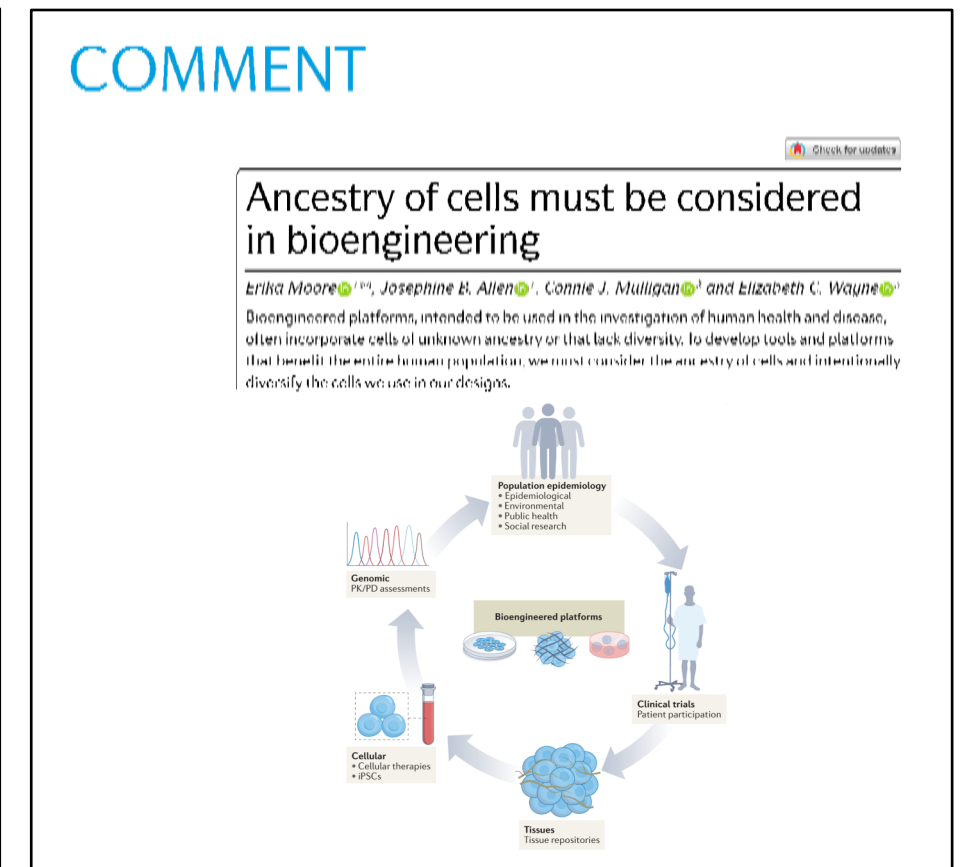
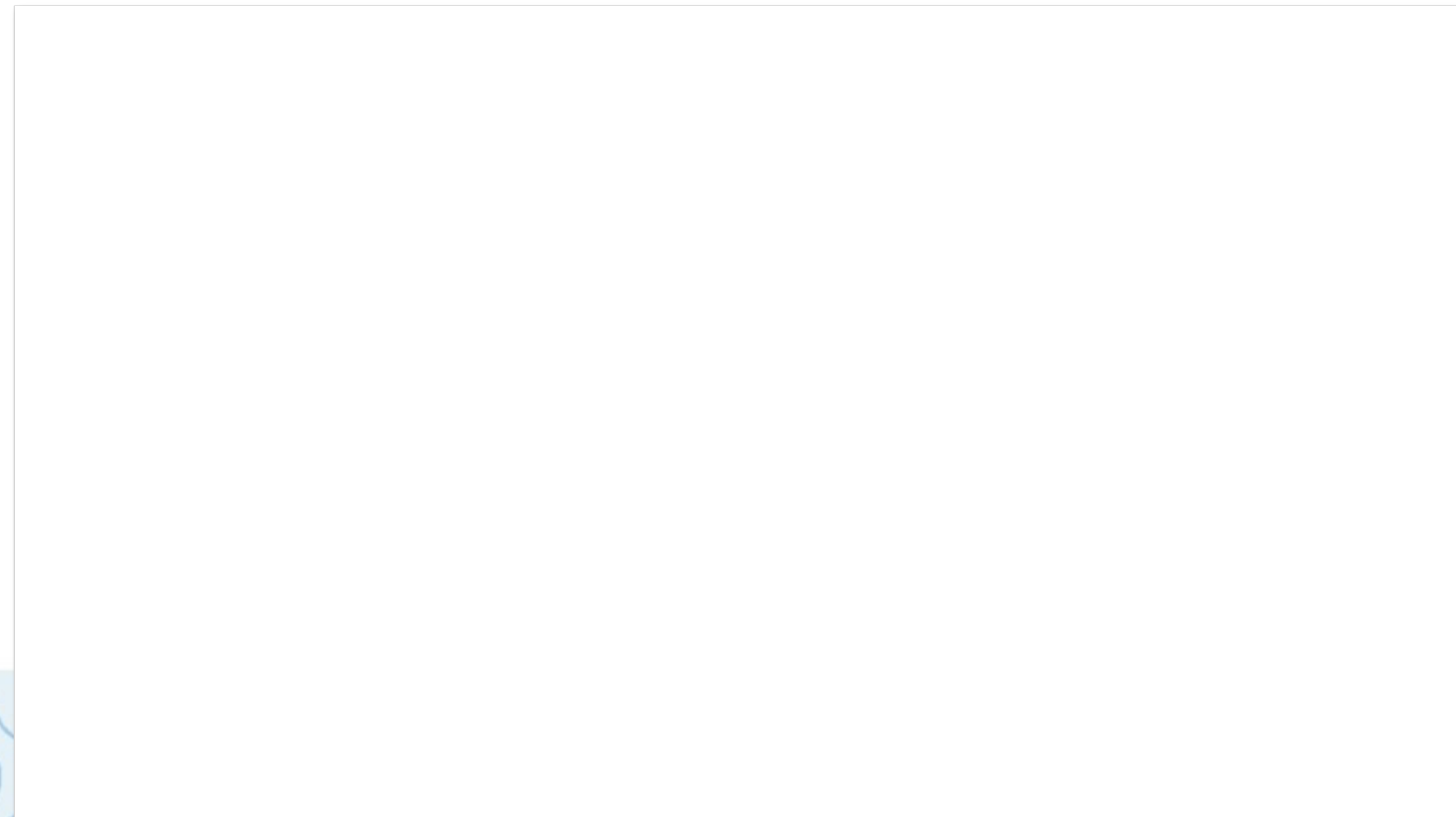
Hormonal regulation of cardiovascular and musculoskeletal mechanobiology



heart



bone



What are the effects of age, sex, and hormones on musculoskeletal and cardiovascular systems?

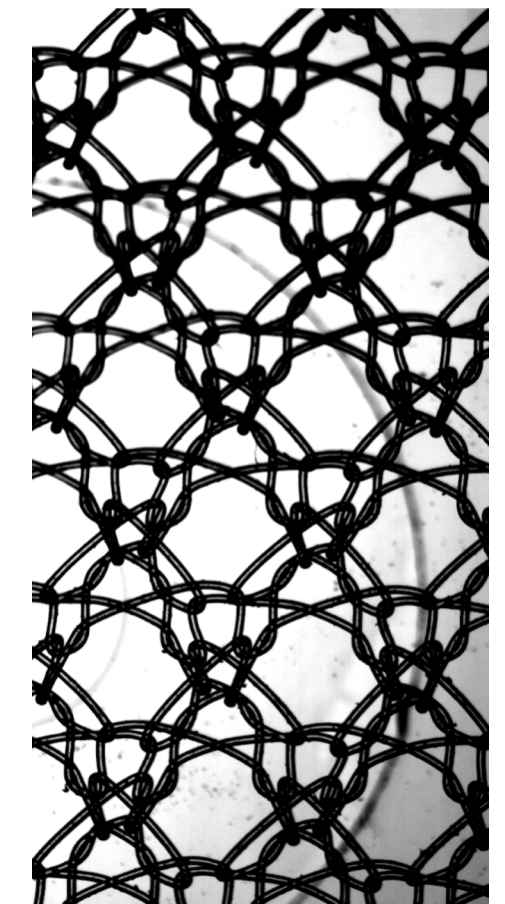
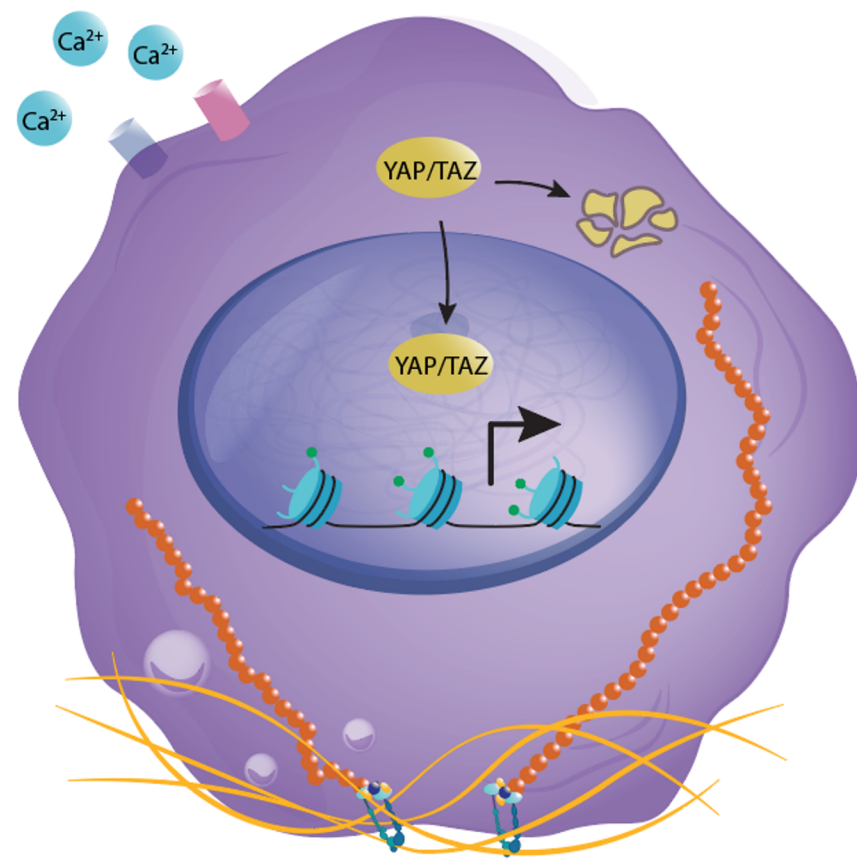
What are the mechanisms underlying women's musculoskeletal health declines with age?

Goals & Milestones

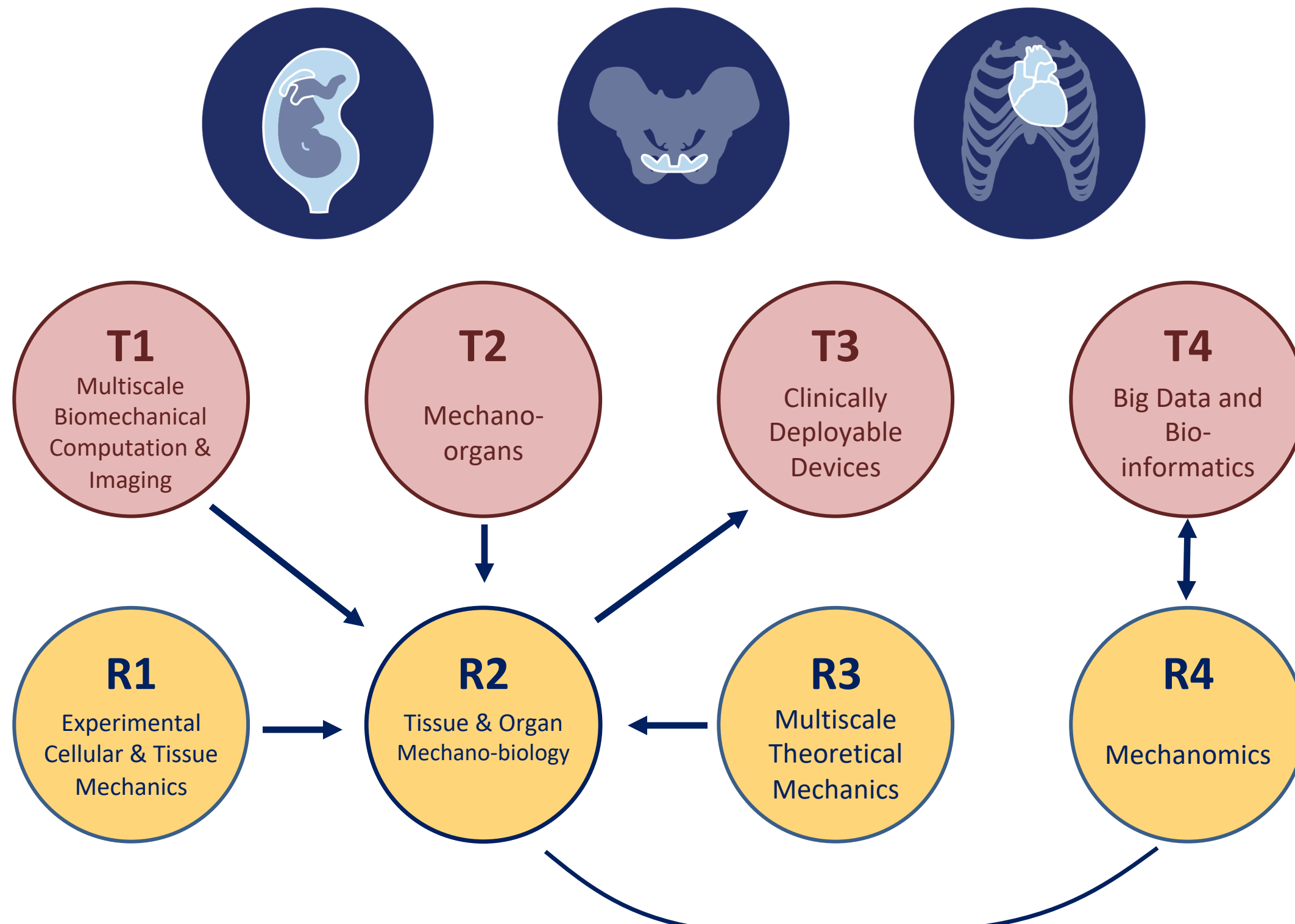
YEARS 1-2	YEARS 3-5	YEARS 5-10
<ul style="list-style-type: none">• Evaluate effects of mechanical forces on commercially available cell lines and tissue-derived cells<ul style="list-style-type: none">– Uterine smooth muscle and epithelial cells, cervical fibroblasts– 300% stretch, stiffness• Collect cells from male and female, different ancestry, and different age patients• Analyze patient data to corroborate and motivate in vitro studies	<ul style="list-style-type: none">• Integrate new technologies and knowledge into mechanobiology studies:<ul style="list-style-type: none">– Patient-derived iPSC– New information from computational models and experimental measurements– Advanced mechano-organ systems• Identify new mechanisms of mechanotransduction unique to female patients and/or different ancestries	<ul style="list-style-type: none">• Identify new mechanotransduction mechanisms unique to the female reproductive system during pregnancy and childbirth• Leverage new knowledge for design of new drugs and treatments for preterm birth and pelvic floor disorders• Develop sex, ancestry, and age-specific treatments based on mechanobiological principles

Mechanomedicine for women's health

- Enable prediction of preterm birth or pelvic floor disorders by sampling cells and tissues
- Target molecular pathways to manipulate cell function in order to prevent or treat preterm birth or pelvic floor disorders
- Create devices or treatments that leverage mechanobiology to support healthy pelvic, cardiovascular, and musculoskeletal function



Convergence (R2)



1. **Multiscale Biomechanical Computation & Imaging (T1)** and **Experimental Cellular and Tissue Mechanics (R1)** will determine relevant forces to study
2. Development of new **MechanoOrgans (T2)** will enable in vitro studies of mechanobiology
3. **Mechanomics (R4)** and **Big Data and Bioinformatics (T4)** will enable probing of mechano-systems and nuclear mechanotransduction mechanisms
4. New knowledge gained will advance **Clinically Deployable Devices (T3)** and treatments for pre-term birth and pelvic floor disorders, and promote healthy cardiovascular and MSK aging

Mechanomics (R4)



Our Team Spans Disciplines & Schools



Lance Kam, CU

Biomedical Engineering, Immune Engineering, Microfabrication



Elham Azizi, CU

Biomedical Engineering, Machine Learning, Genomics, Tumor Cell Composition



Timothy Downing, UCI

Biomedical Engineering, Tissue Engineering, Regenerative Biology, Mechanobiology



X. Edward Guo, CU

Biomedical Engineering, Mechanics of Soft Tissues, Preterm Birth, Hydrated Biomaterials



Kam Leong, CU

Biomedical Engineering, Advanced Tissue Biofabrication



Kristin Myers, CU

Mechanical Engineering, Mechanics of Soft Tissues, Preterm Birth, Hydrated Biomaterials



Itsik Pe'er, CU

Computer Science, Computational Methods in Germline Human Genetics



Joy-Sarah Vink, CU

OB/GYN, Preterm Birth Prevention



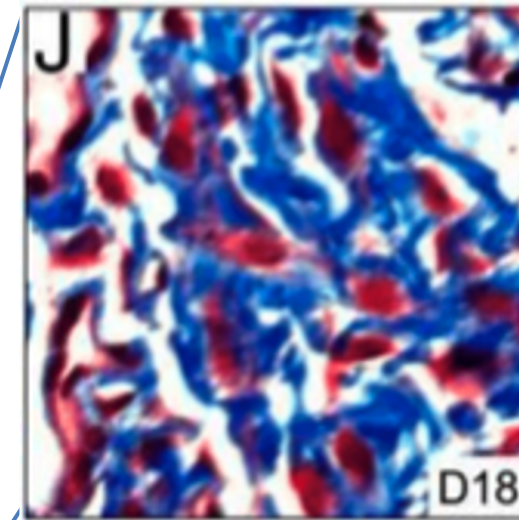
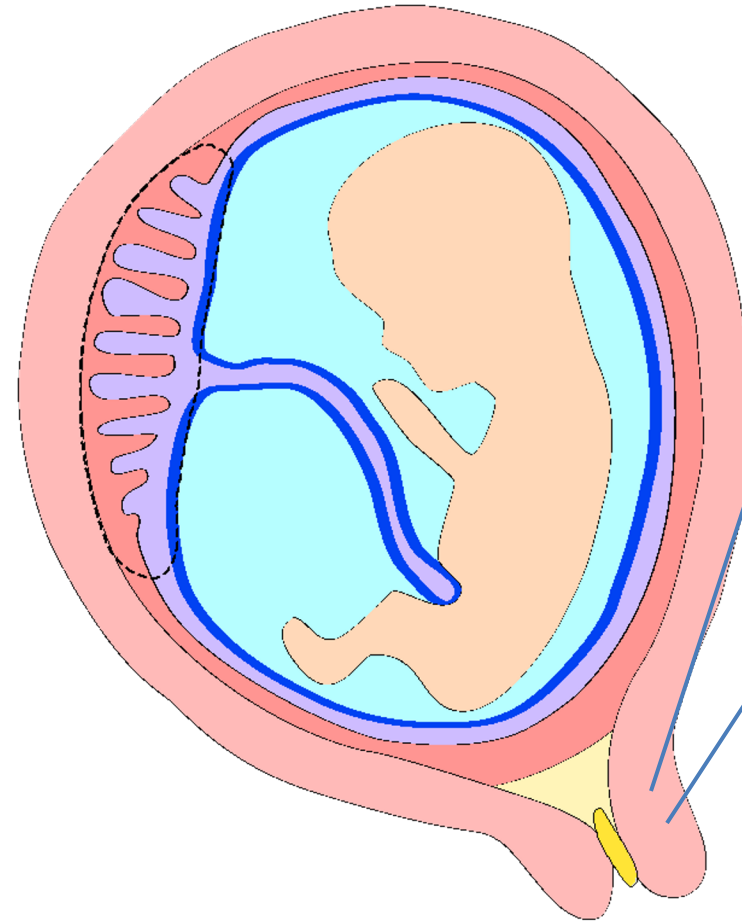
Ronald Wapner, CU

OB/GYN, Fetal Genetic Testing

A global view of mechanobiology



The uterine wall grows and **stretches to over 300% the non-gravid size** during pregnancy

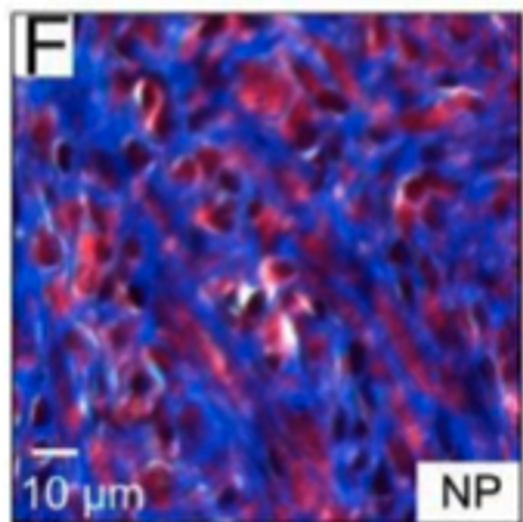


How do **stretch** and **stiffness** contribute to:

- Cellular composition?
- Function of cells?
- Remodeling of the matrix?

What are the **molecular mechanisms** underlying these responses?

The cervix **softens 3 orders of magnitude** in stiffness prior to the onset of childbirth



Grand challenges



Interpret mechanobiology in core IMWEL physiology

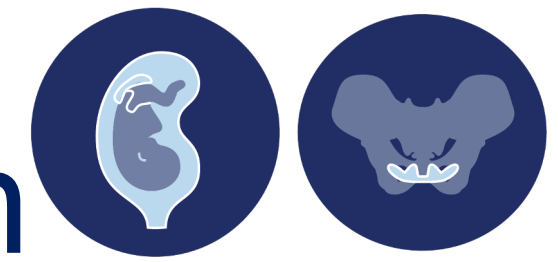


Develop –omic signatures that capture mechanobiology in complex systems

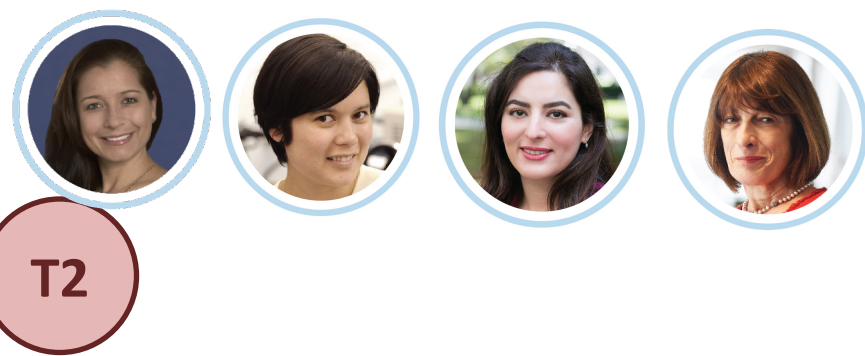
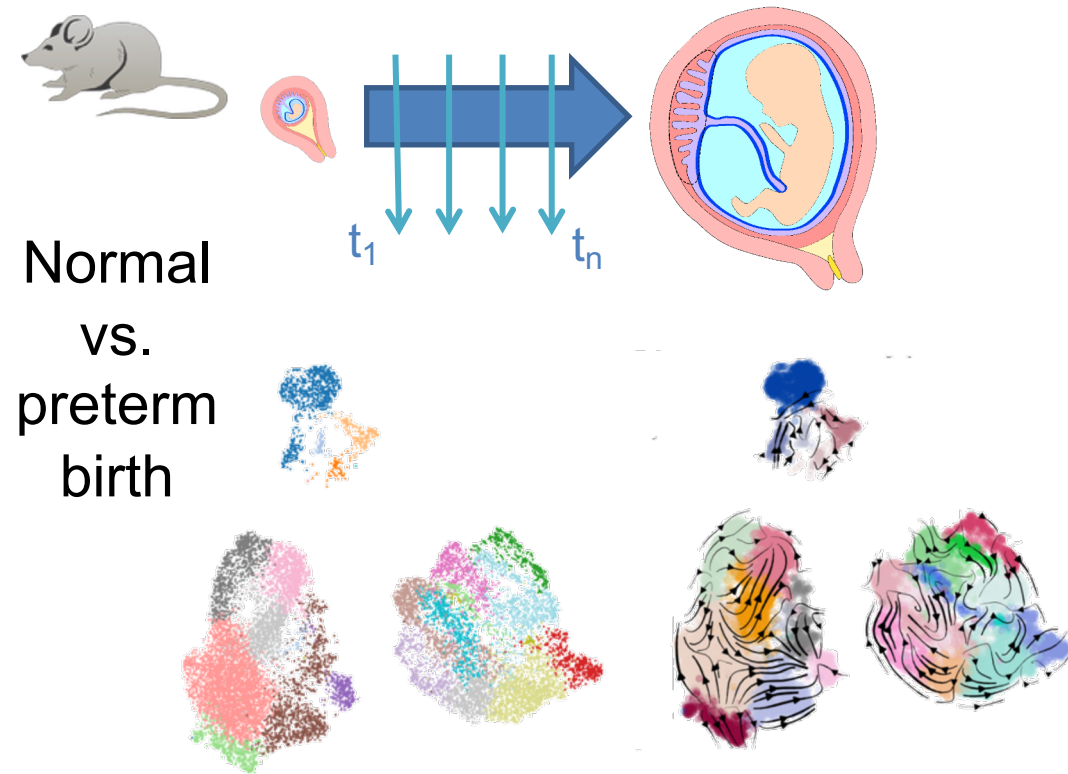


Develop user-oriented systems for sample collection

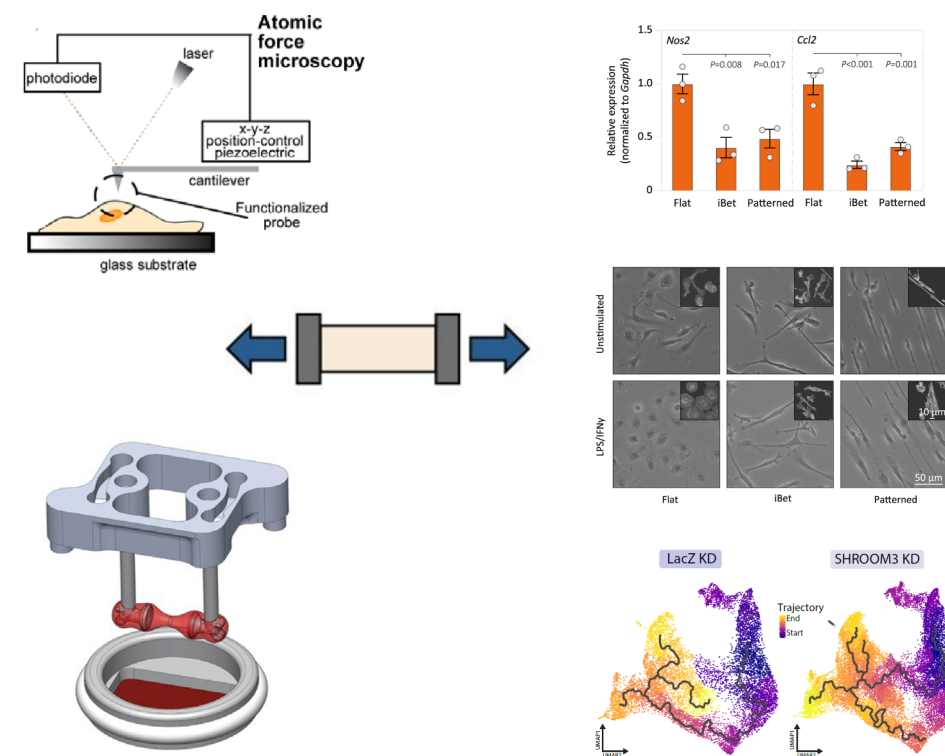
Mechanomics workflow in preterm birth



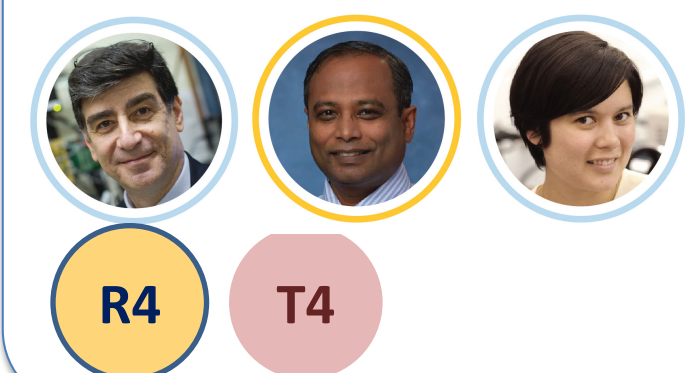
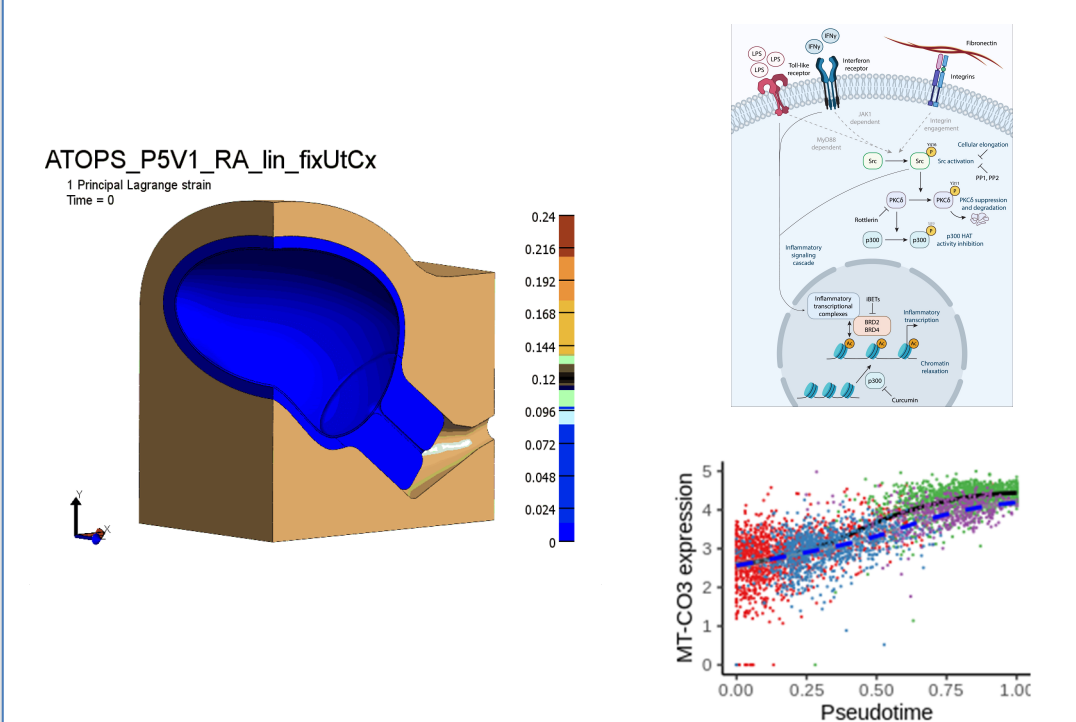
Profiling in tissues: time and space



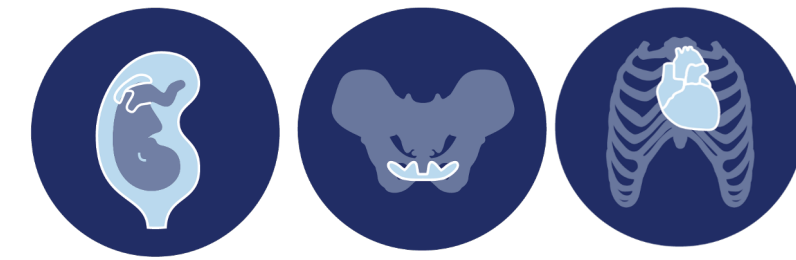
Guidance and validation of ex vivo models Fundamental mechanobiology



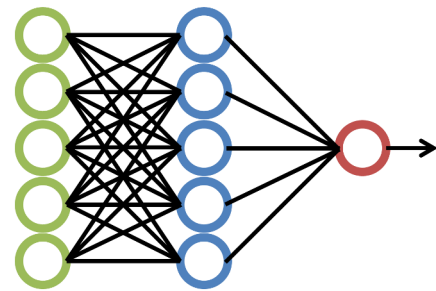
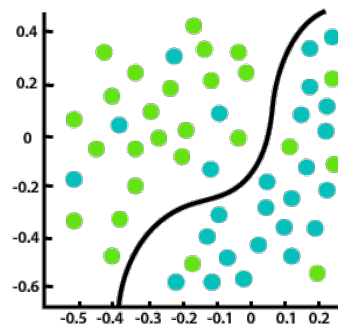
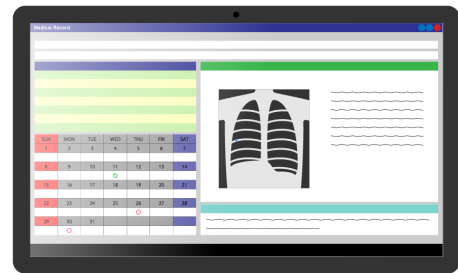
Computational models System-level mechanobiology



Creating tools for women's health



Identification of strategic cohorts

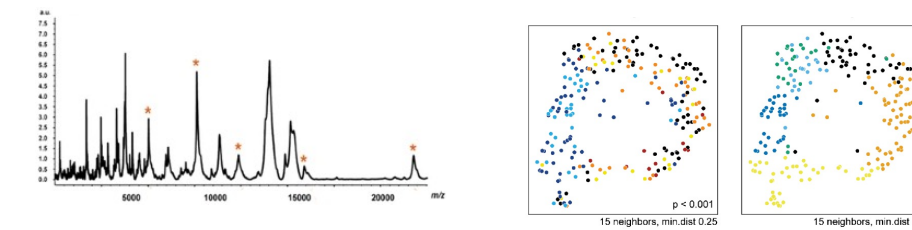


- Interviews
- Demographic
- Ancestry
- Clinical measurements
- Surveys
- Home tests
- Biospecimens
- **Biomechanics** **checkup/monitor**



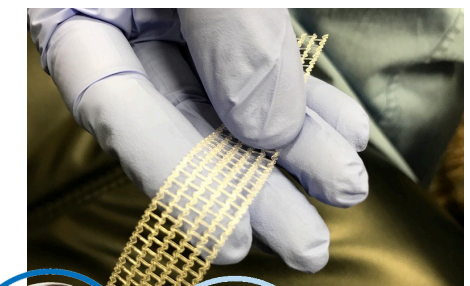
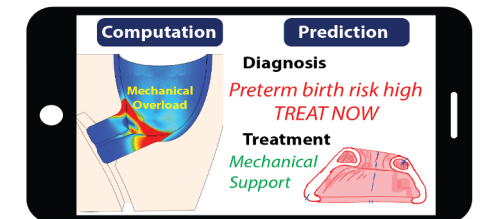
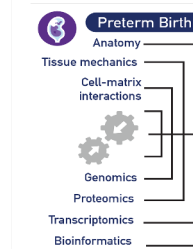
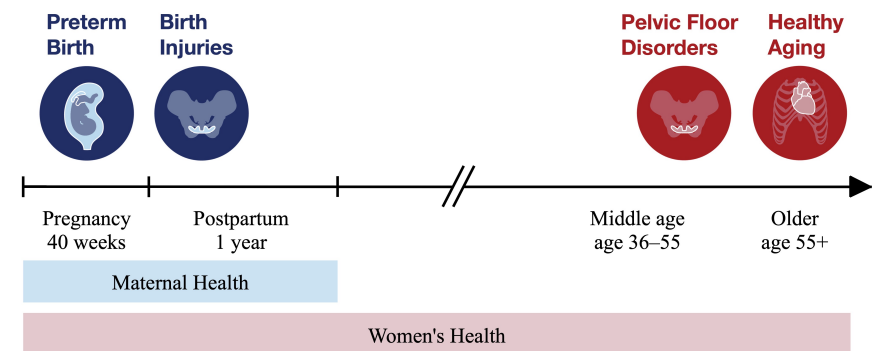
T2

Deployable sample collection and analysis



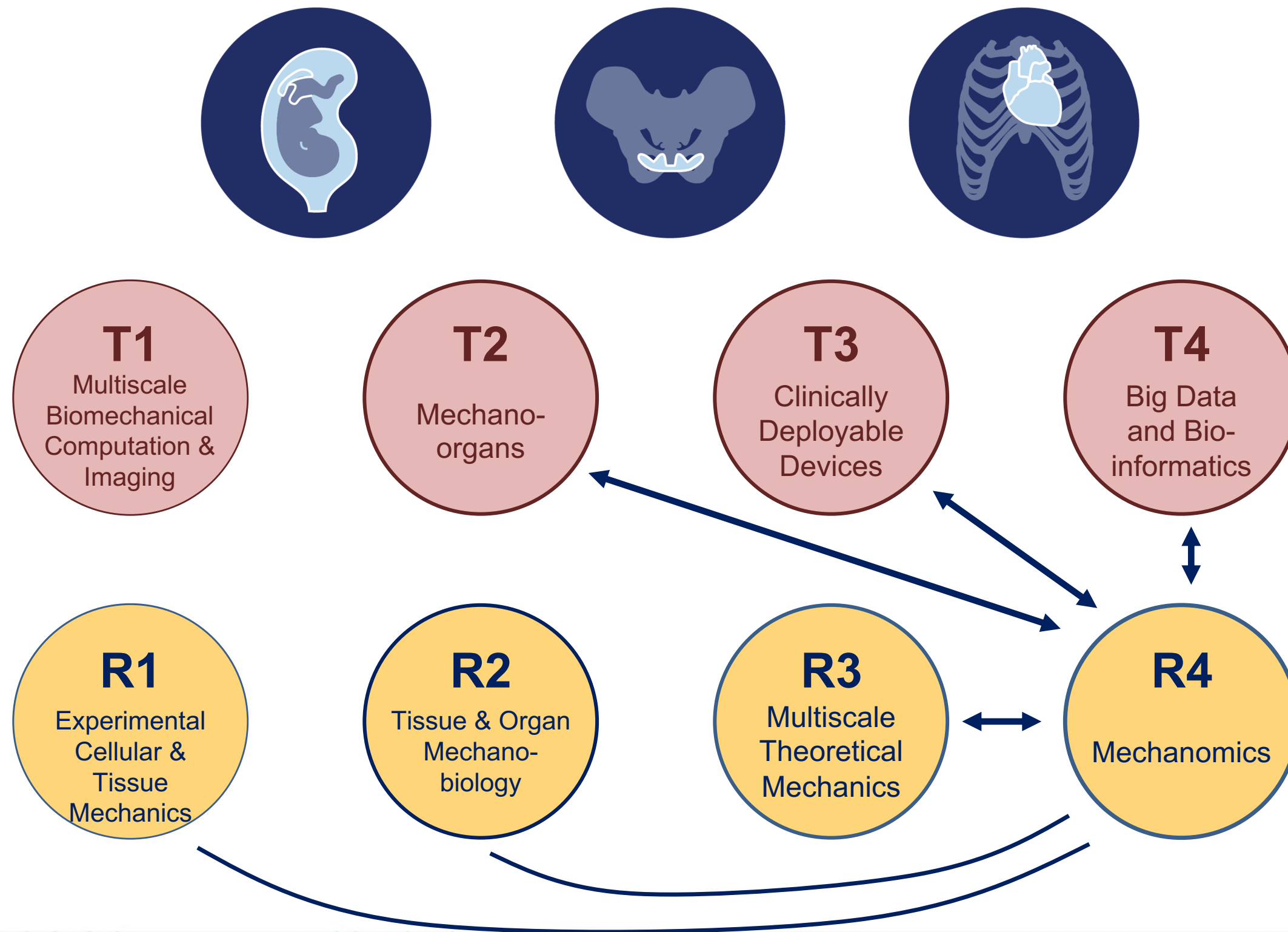
R1 T1 T2

Devices and systems



R4 T4

Integration (R4)



Education & outreach modules

- Data science
- Mechanical forces in women's health
- Data & Diversity

Goals and Milestones

YEARS 1-2	YEARS 3-5	YEARS 5-10
<ul style="list-style-type: none">• Mechanobiology experiments on controlled systems• New tool development• Profile cell populations in IMWEL-specific tissues• Establish workflows	<ul style="list-style-type: none">• Identify signatures of mechanical function in target tissues.• Guide ex vivo experiments of cervical tissue• Develop sample collection systems	<ul style="list-style-type: none">• Workflows for sample collection• Collection of biomechanics checkup data across wide sections of the IMWEL community• Sample collection for exercise, interpreting data over the course of a new exercise regimen.• Biomechanics profile during checkup / at home

IMWEL Research Thrusts Q&A

