

Modeling Female Reproductive Tract Diseases

J. Julie Kim, PhD

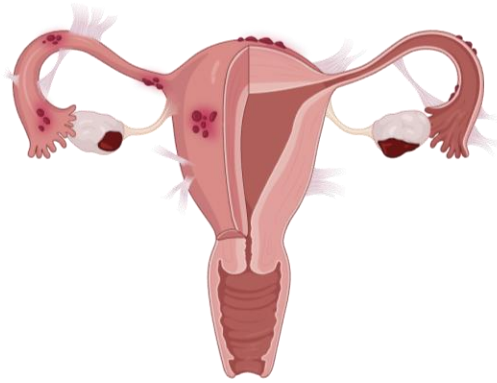
Professor of Obstetrics and Gynecology

Northwestern University

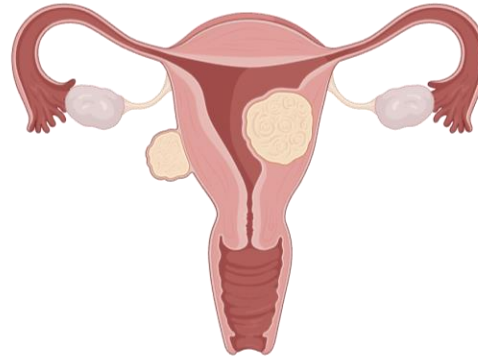
Kim Lab: Understanding Development and Growth of Uterine Diseases

Sex Hormones, Obesity, Genetics, Race

Northwestern
University



Endometriosis

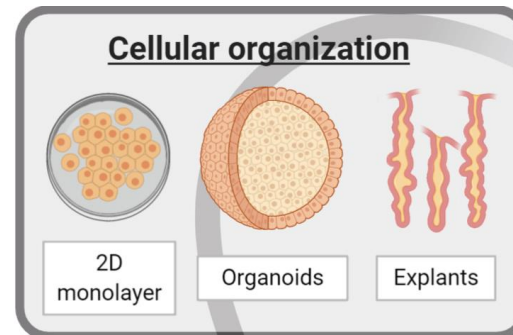
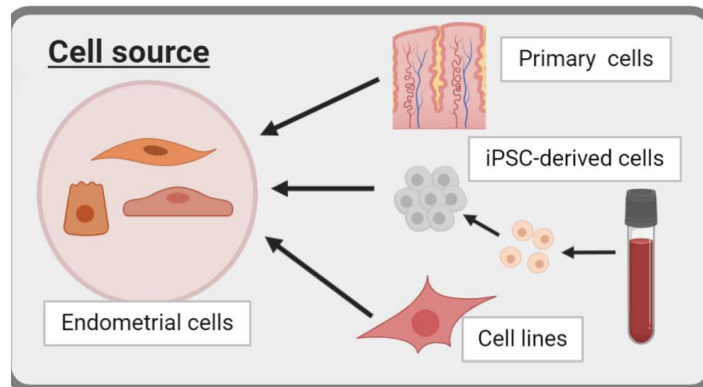


Uterine fibroids



Endometrial Cancer

In vitro physiological modeling



Organ connections
- Microfluidics

Medicine is failing women's health

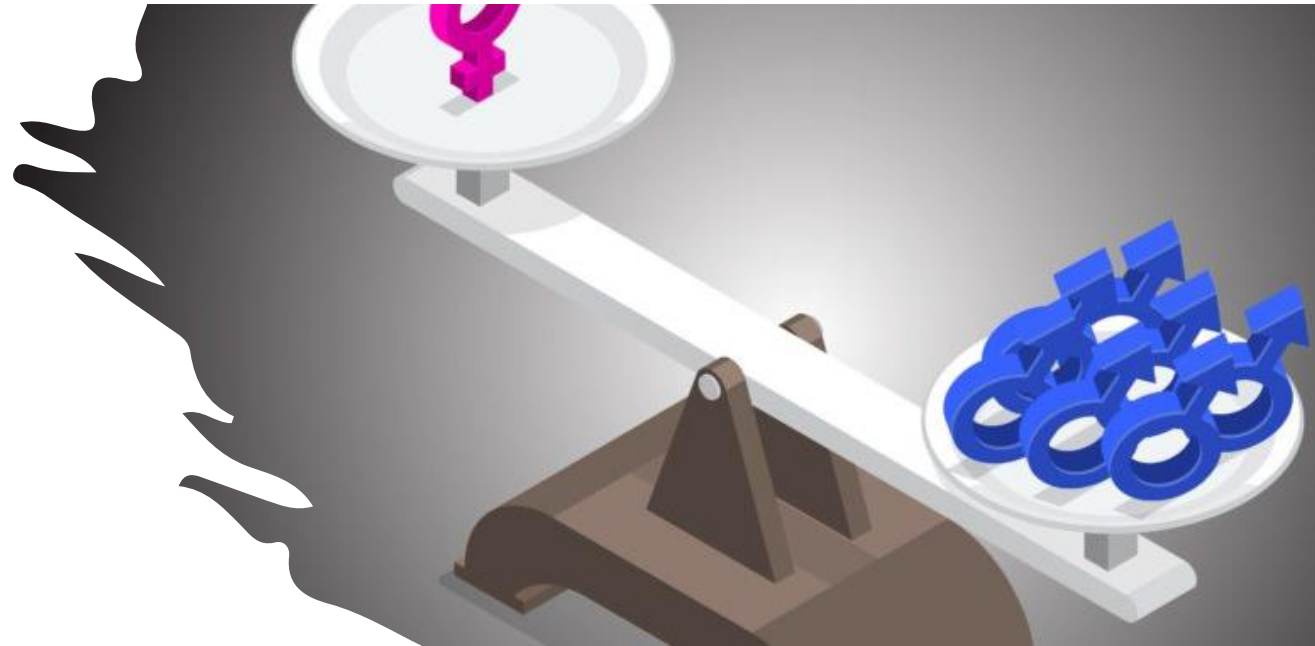
Toxicity with new drugs

Menopause

Gynecologic diseases

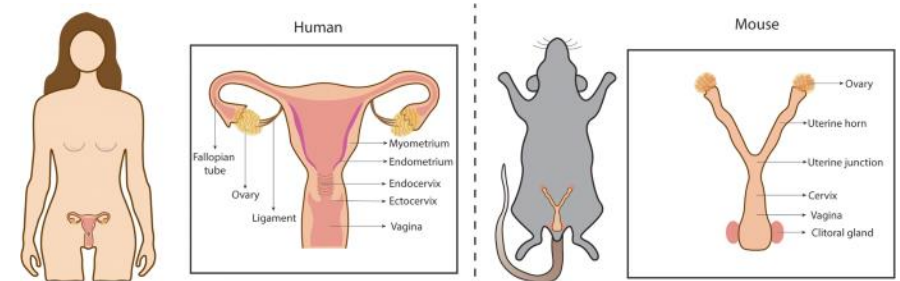
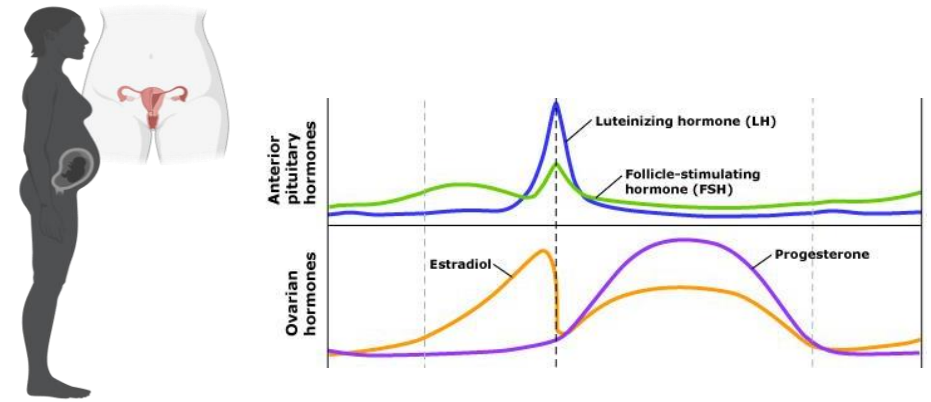
Age-related fertility

Freezing eggs



Challenges in Research of the Female Reproductive Tract

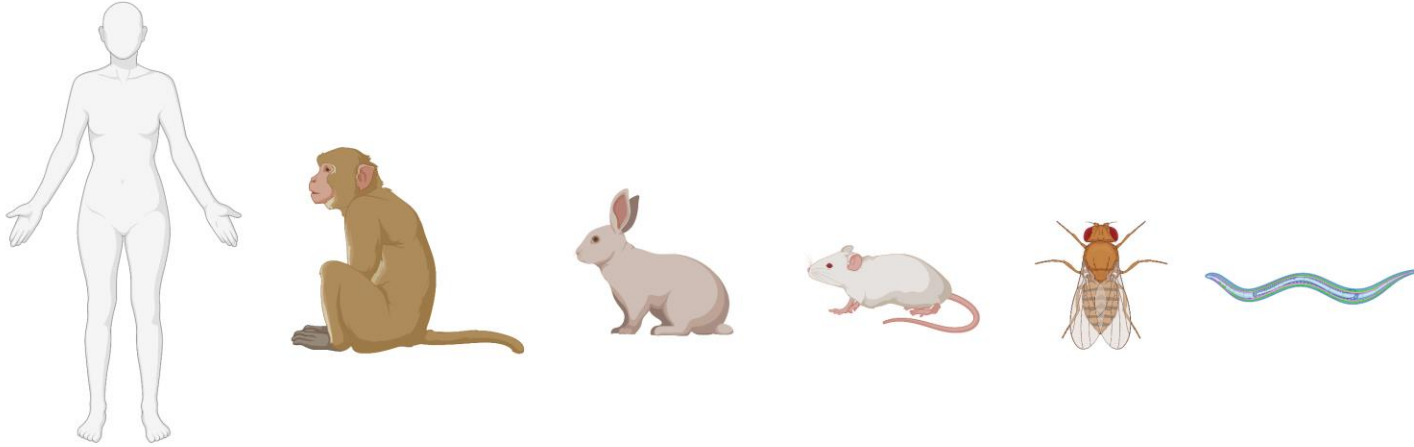
- Ethical issues associated with research in women of reproductive age/pregnancy
- Hormones are complicated – context dependent, whole body effects, fluctuations are key.
- Vast species differences in reproductive processes



Grskovic et al *Nat Rev Drug Discov* 2011

Models to Study Reproductive Biology

In vivo



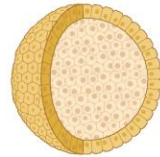
In vitro



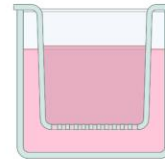
Tissue
explants



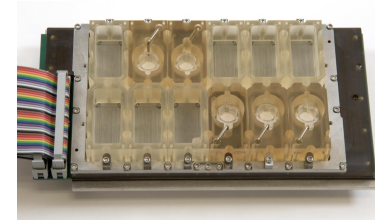
Cell
monolayer



organoids



2 cell
interaction



Multi-tissue
interaction

Physiological Relevance

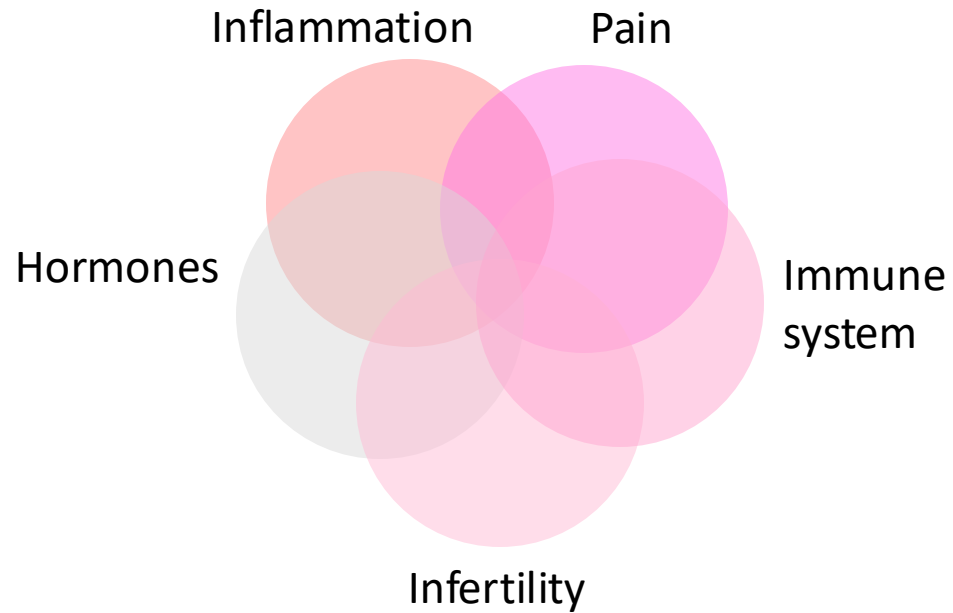


Experimental Tractability



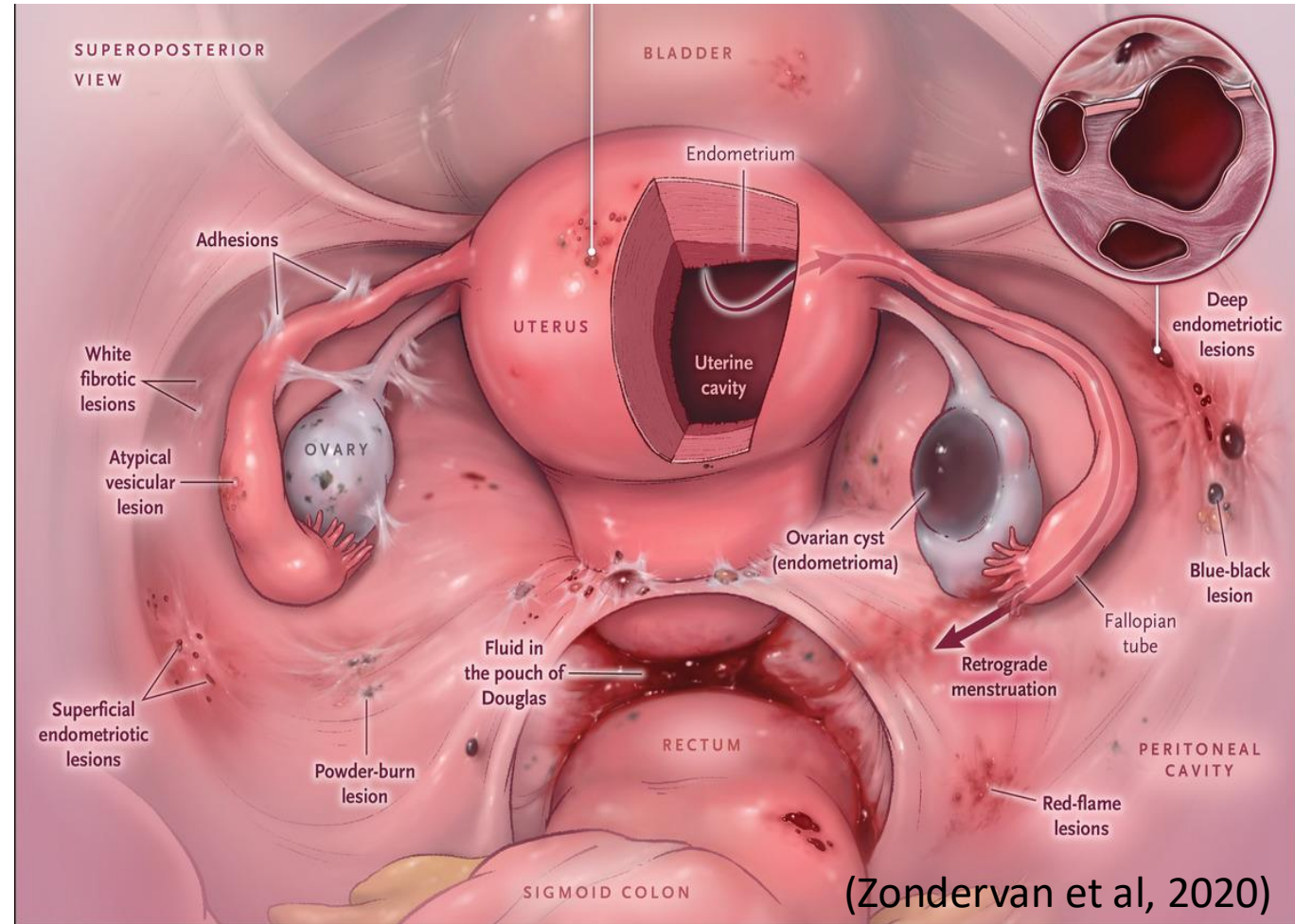
Modeling
Endometriosis
using induced
pluripotent
stem cells

Endometriosis



- Ectopic presence of endometrial-like tissue
- Affects ~10% of women

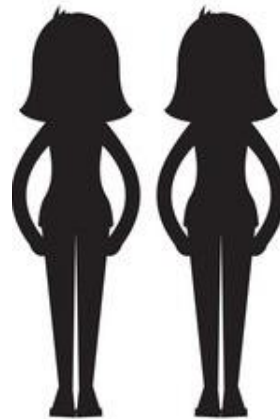
~ 200 million women worldwide



Genetics of Endometriosis

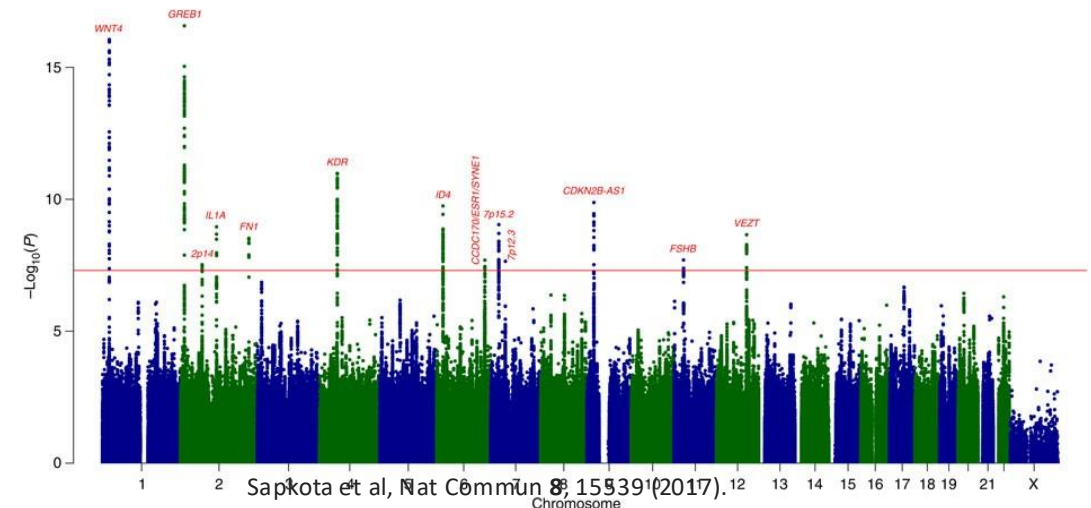
Twin studies

- have estimated the heritability of endometriosis at approximately 50%.

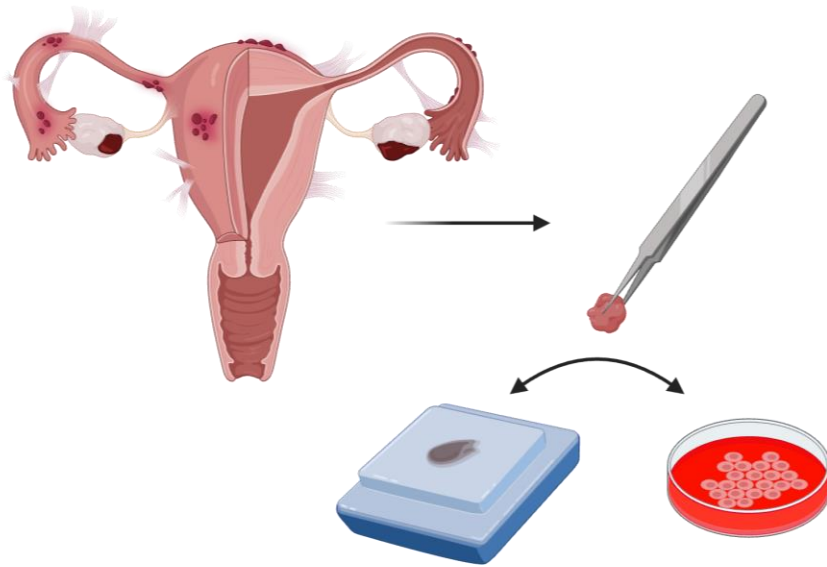


Genome Wide Association Studies (GWAS)

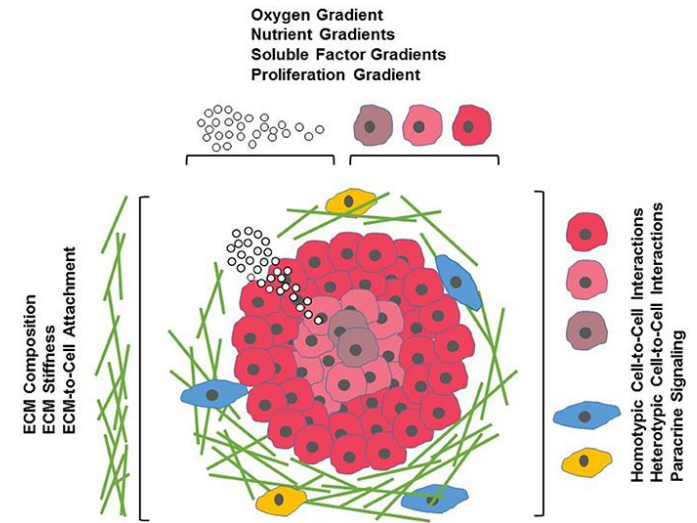
- 10 GWAS studies (European and Japanese) showed 18 genome wide significant loci identified, 14 of which were robustly replicated
- **A key challenge** - how does genome-wide significant loci contribute to the pathogenesis of endometriosis



Challenges in Research of Endometriosis

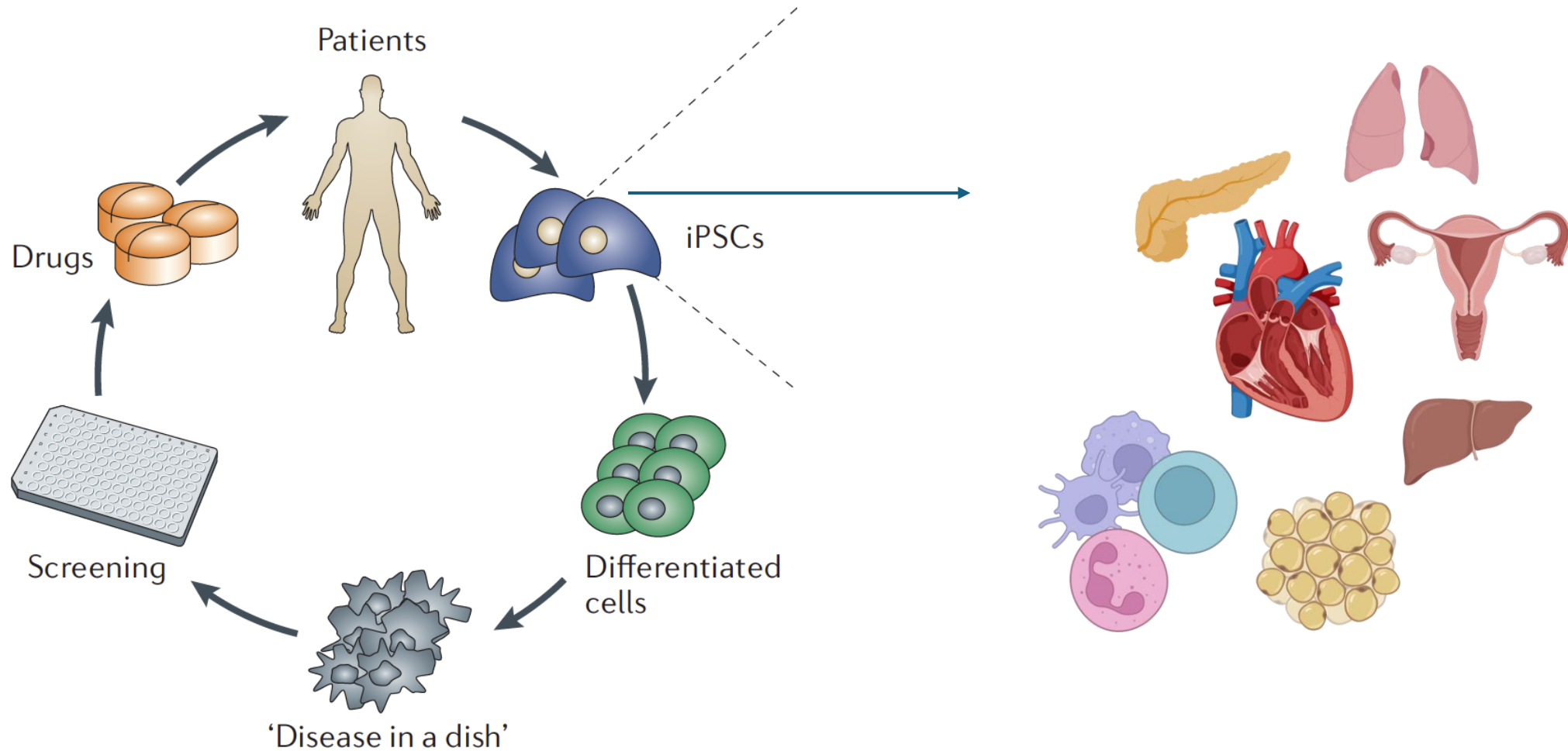


Low Tissue Availability and Yield

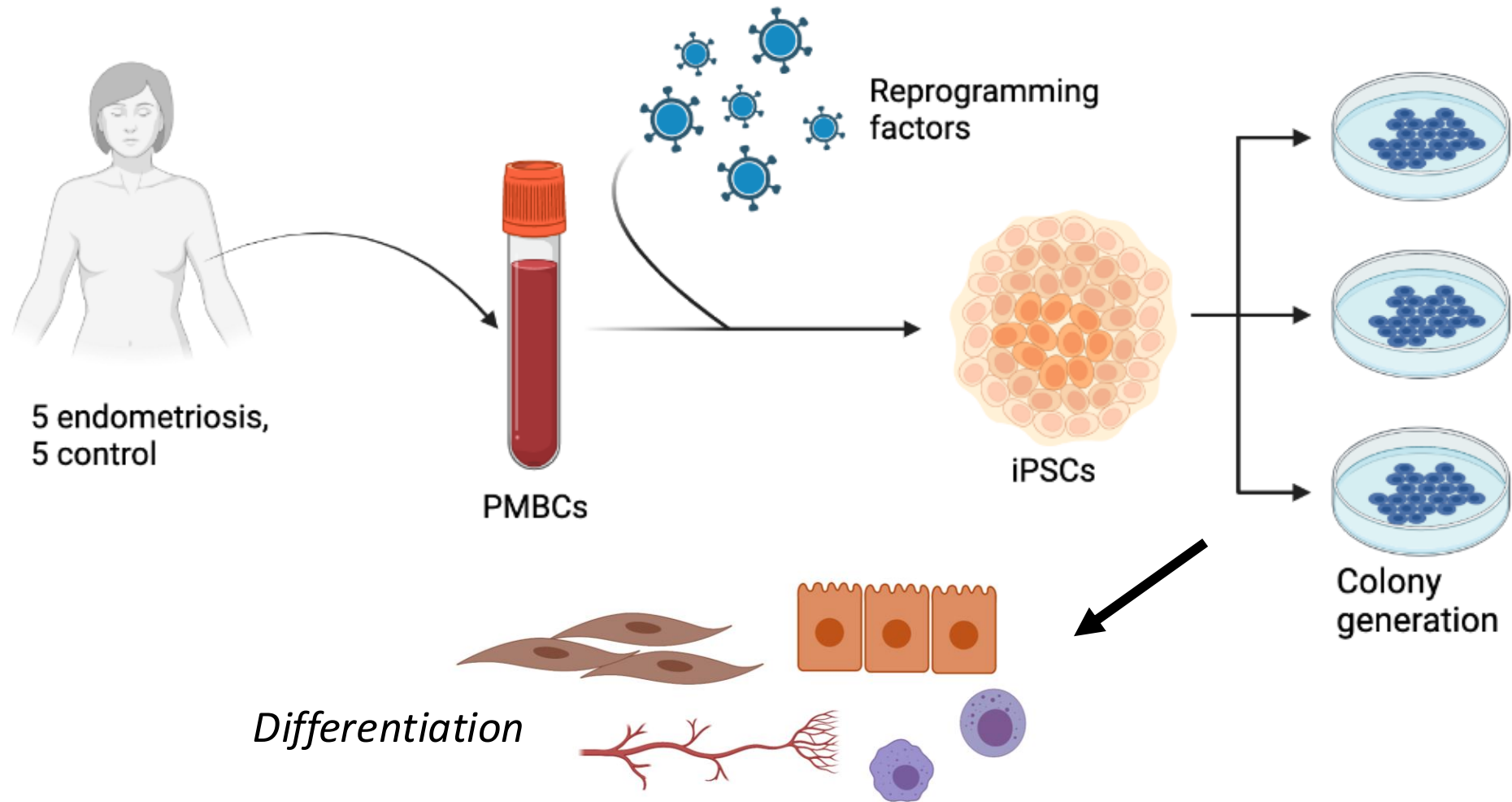


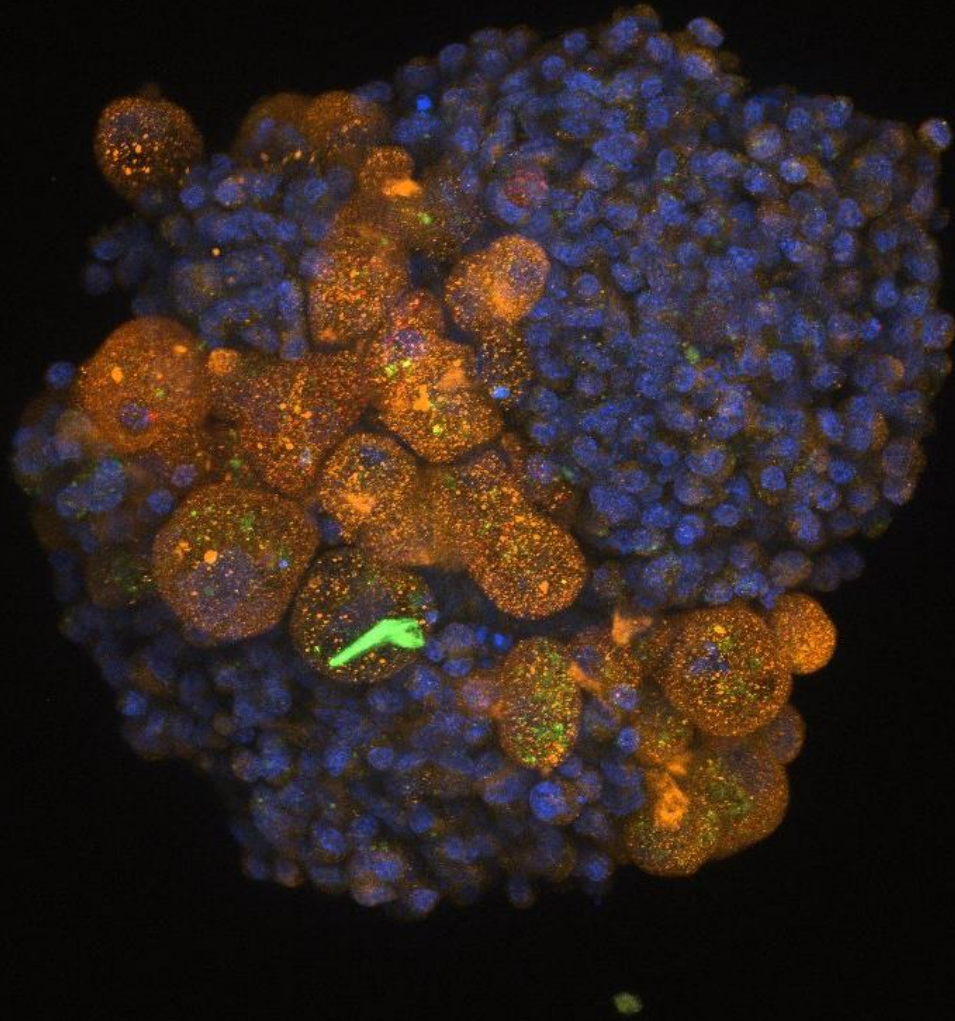
Missing other important cell types

Induced pluripotent stem cells — Opportunities for disease modelling



Endometriosis Patient-derived iPSCs

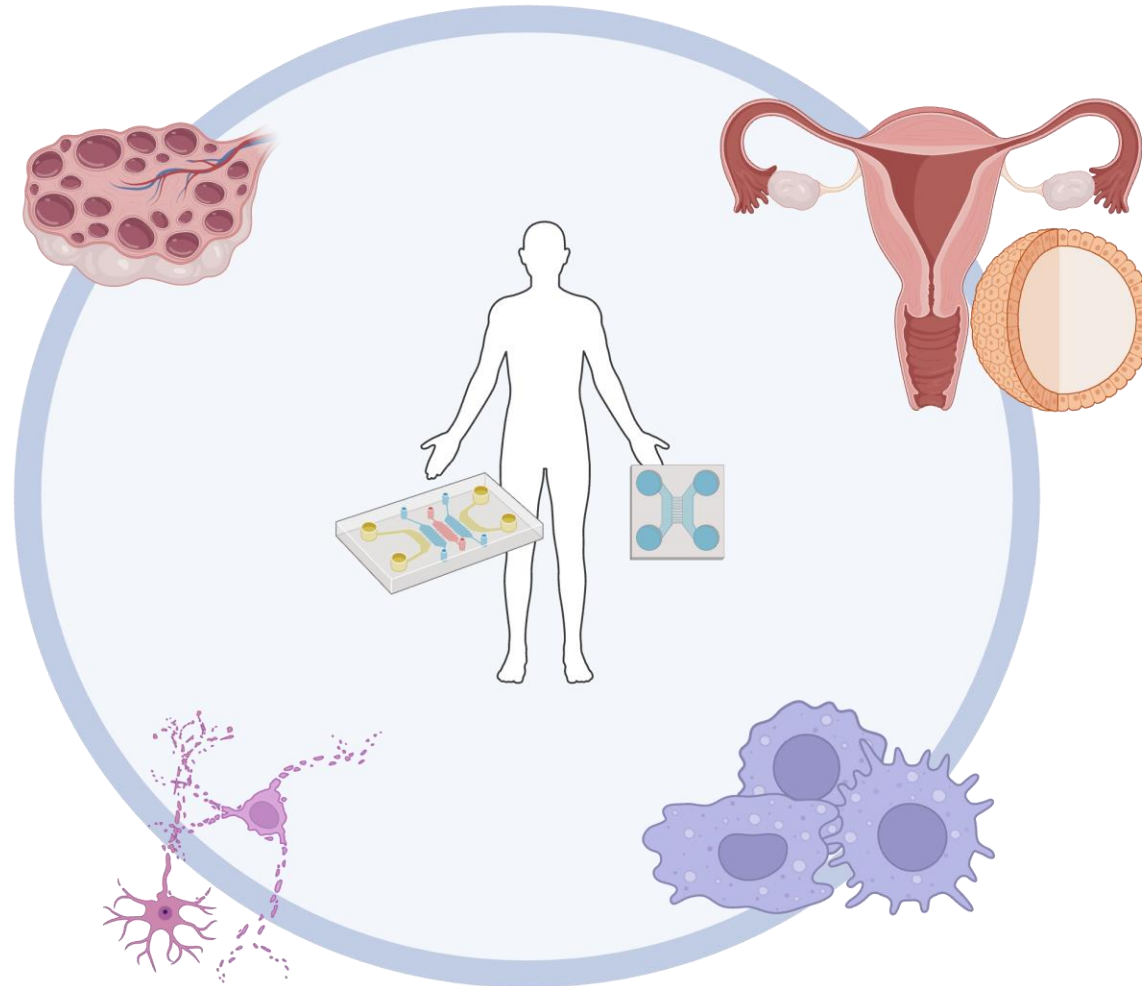




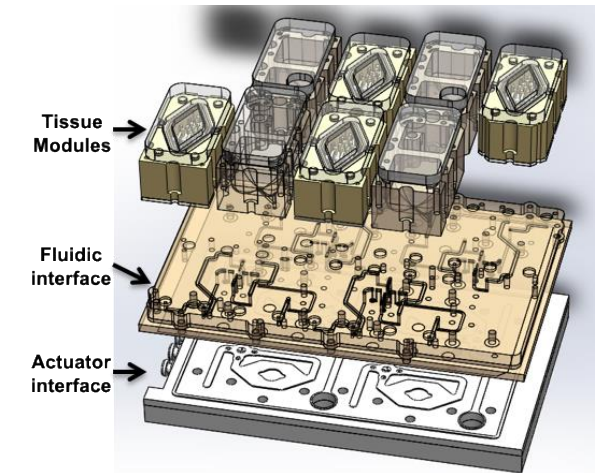
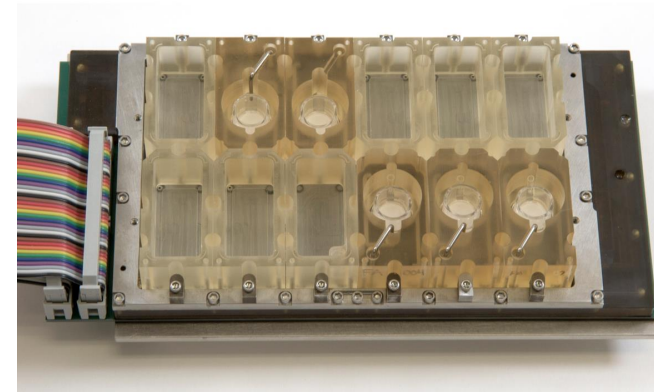
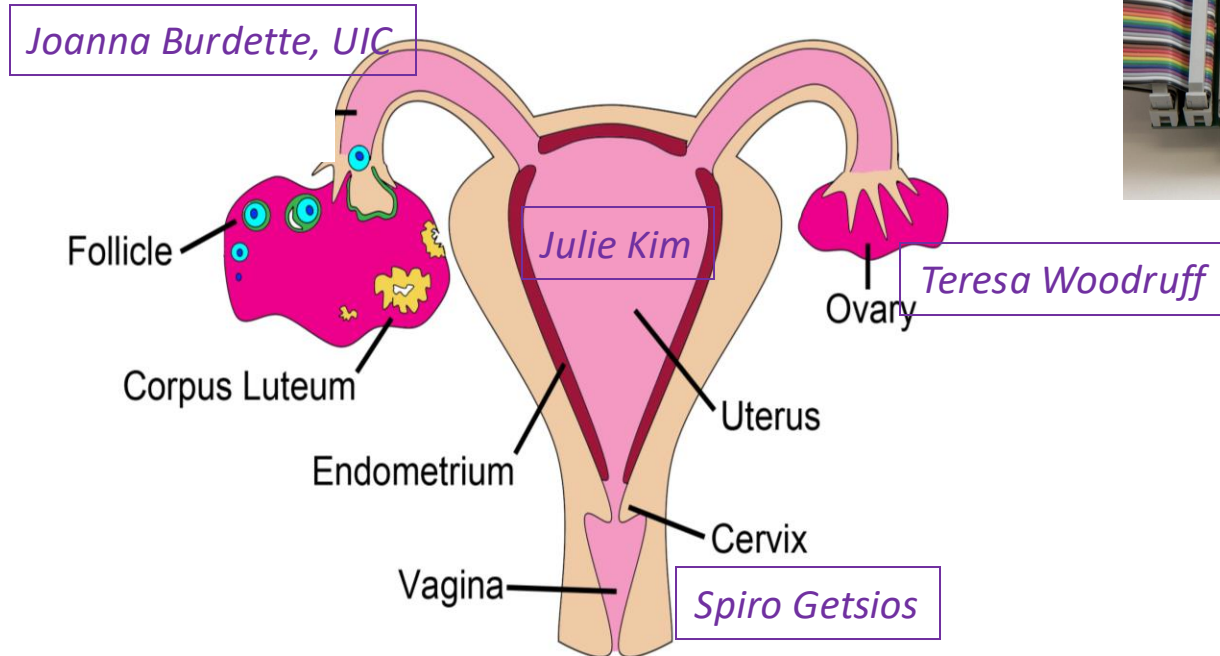
Ongoing studies

- Validation of gene expression differences between Endometriosis and Control endometrial stromal cells
- Differentiation to Endometrial Epithelial cells
- Differentiation to macrophages
- Multi-organ interactive cultures

Multi-organ system to study Endometriosis and test compounds



EVATAR: The Mother of Microphysiological Systems



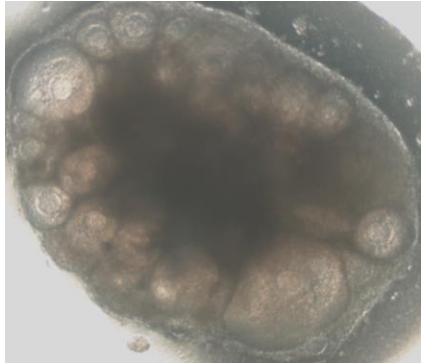
- **Materials:** can be sterilized, non-toxic to cells/follicles, do not bind hormones;
- **Pumping pattern:** computer program controlled.

*Jeffrey T. Borenstein
Jonathan R. Coppeta
Brett C. Isenberg*

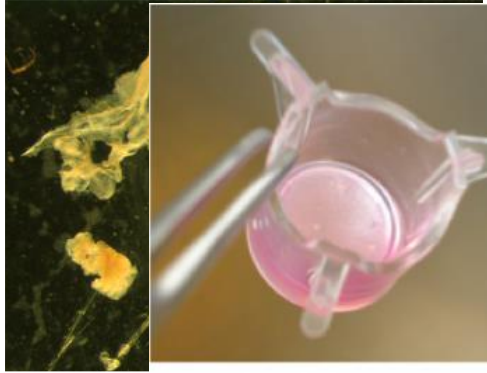


EVATAR – Multi-organ Female Reproductive Tract

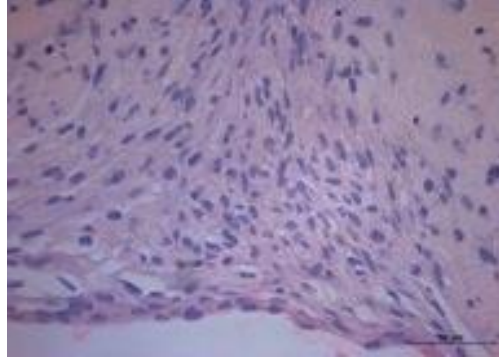
Mouse ovary



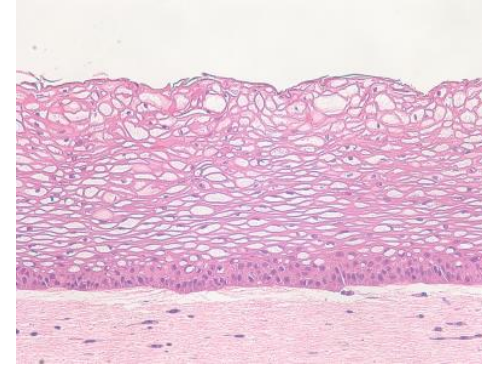
Human Fallopian tissue



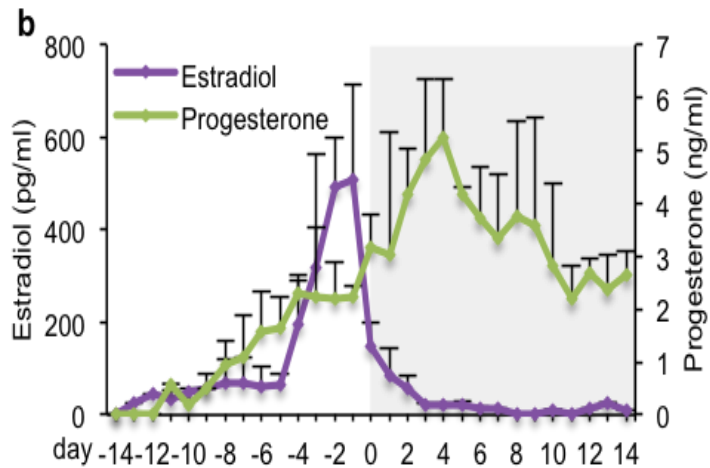
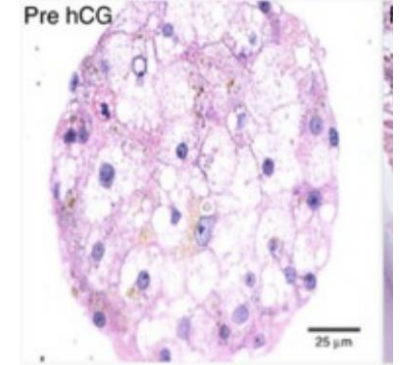
Human Recellularized Endometrium



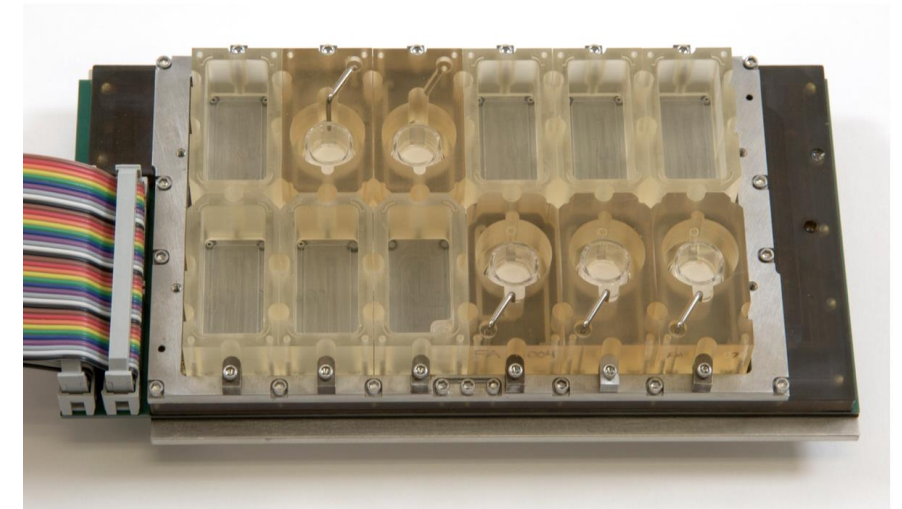
Engineered Human Ectocervix



Human liver microtissues



- One media
- Tissue longevity over 28 days
- Functional response to hormones





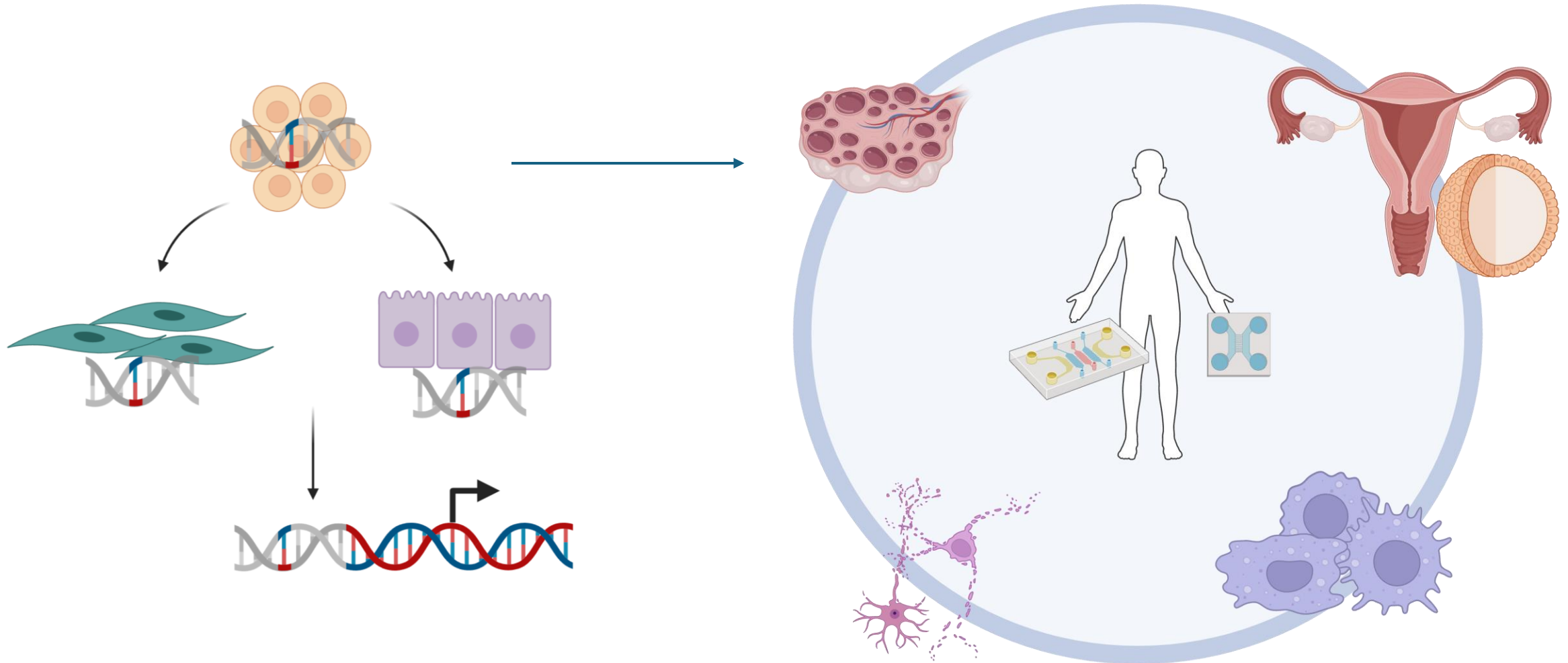
Lattice

(Video credit © Sam Palahnuk)

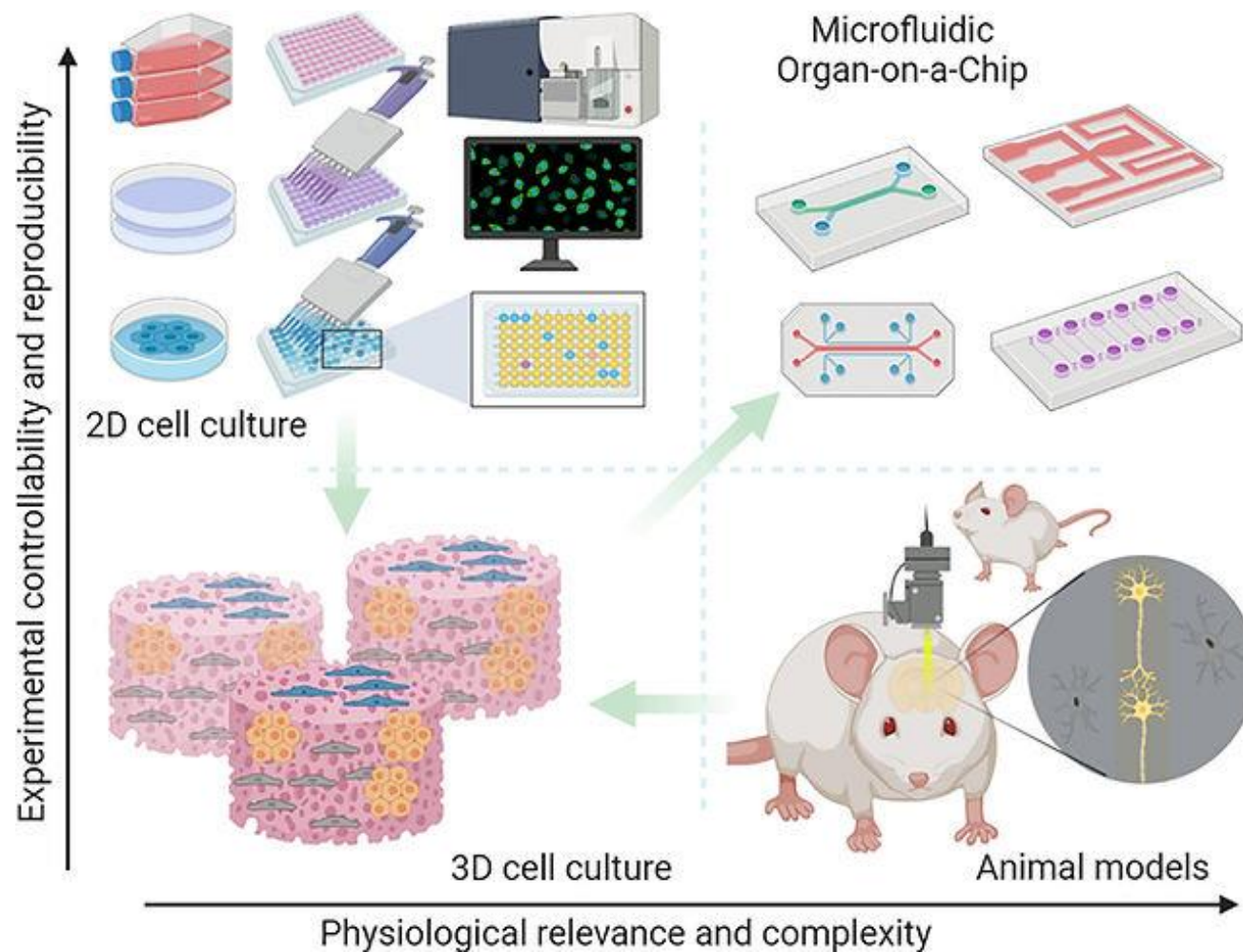
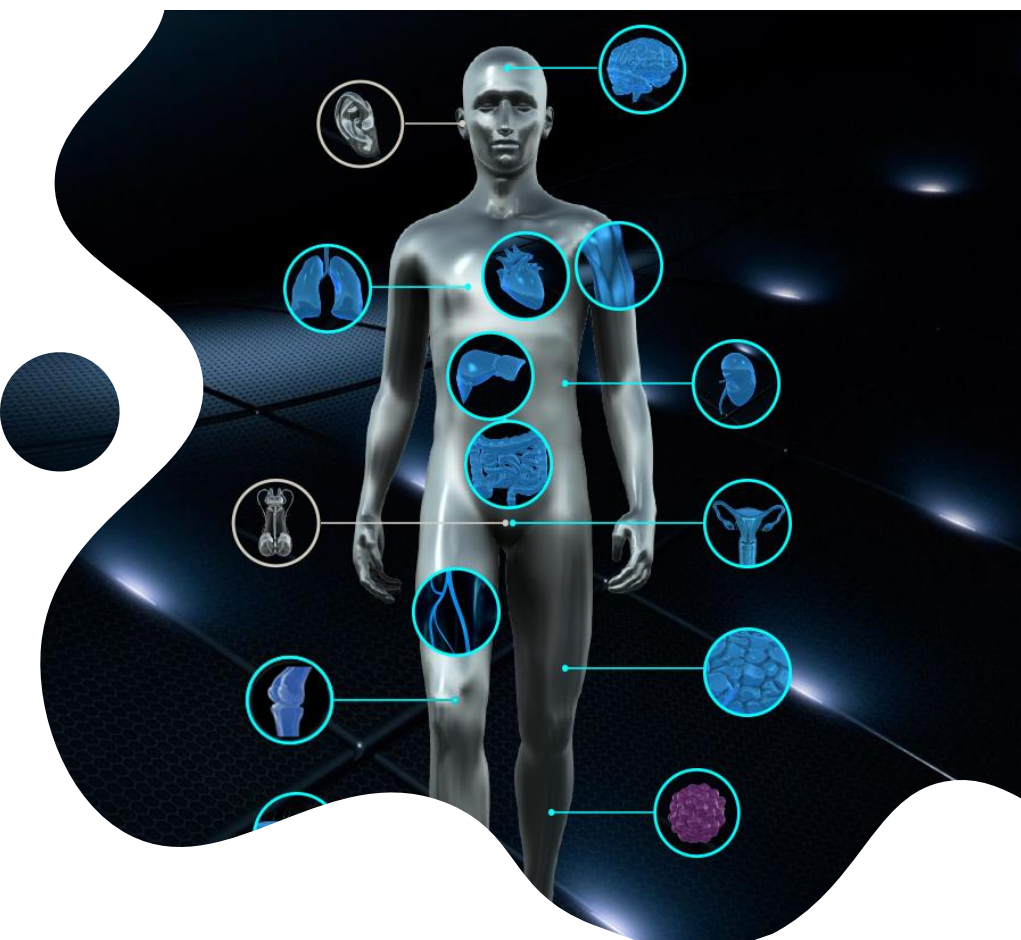
Biomedical Visualization program at University
of Illinois Chicago

Campo et al, Lab on a Chip, 2023

Multi-organ system to study endometriosis and test compounds in a personalized manner using iPSC derived tissues



Tools and Models for Drug Testing



Ma et al, Trends Pharmacol Sci. 2021

Acknowledgements



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