Tissue-engineered 3D human model of peritoneal endometriosis using self-assembling peptide hydrogel composites

Raul Silva[1], Debbie Fischer[2], Kay Marshall[2], Julie Gough[3], Alberto Saiani[4], Aline Miller[4] and Sarah Herrick[1]

1 - Blond McIndoe Laboratories, Division of Cell Matrix Biology & Regenerative Medicine, School of Biological Sciences, Faculty of Biology, Medicine and Health, University of Manchester; 2 - Division of Pharmacy & Optometry, School of Health Sciences, Faculty of Biology, Medicine and Health, University of Manchester;
3 - Department of Materials & Henry Royce Institute, School of Natural Sciences, Faculty of Science & Engineering, University of Manchester; 4 - Manchester Institute of Biotechnology, Department of Chemical Engineering, School of Engineering, Faculty of Science & Engineering, University of Manchester

1. What is Endometriosis?

Endometriosis is a chronic, oestrogen-dependent condition characterised by the presence of endometrial-like tissue outside the uterine cavity, commonly on the peritoneum and ovaries. It is associated with pelvic pain, fatigue, and infertility. Despite its high prevalence, disease mechanisms remain poorly understood, and diagnosis and treatment remain challenging

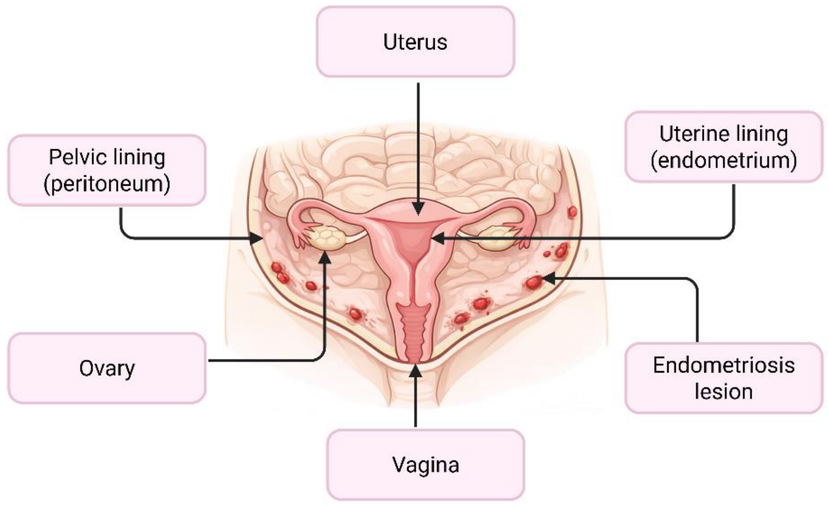


Figure 1. Simplified anatomy of the female reproductive system showing where endometriosis lesions can form on the pelvic lining (created with BioRender and Copilot).

2. How do endometriosis lesions form?

Endometriosis is thought to arise, in part, through retrograde menstruation, where menstrual tissue flows through the fallopian tubes into the peritoneal cavity. These endometrial fragments reach the peritoneal lining, attach to the mesothelial cell layer, and begin to invade the underlying tissue. Over time, this contributes to the development of early endometriosis lesions.

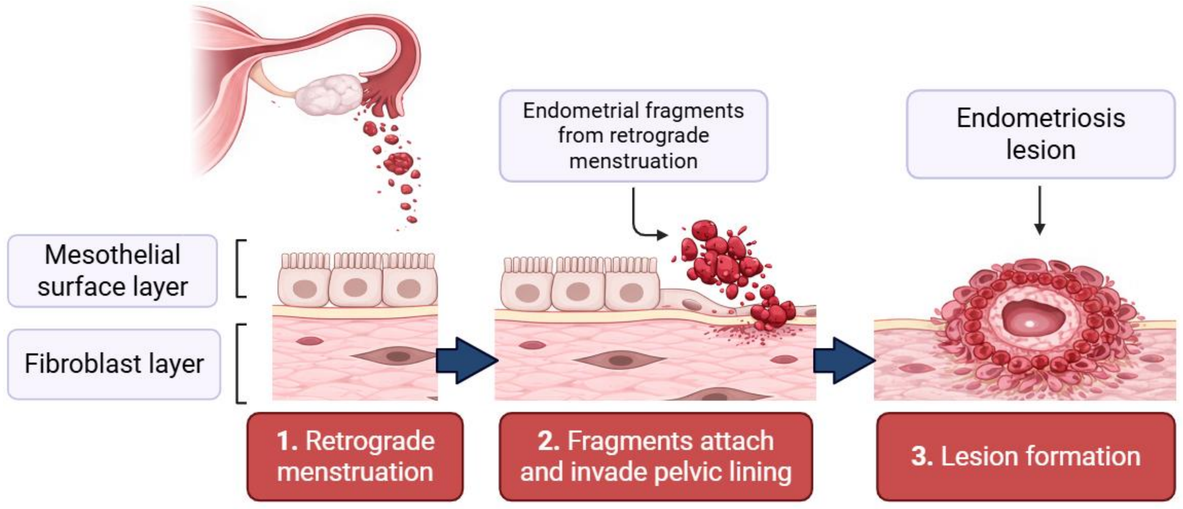


Figure 2. Proposed early stages of endometriosis lesion formation: endometrial fragments from retrograde menstruation attach to the pelvic lining, disrupt the mesothelial surface, and invade the underlying tissue (created with BioRender and Copilot).

3. Current gaps in endometriosis research

- Current models fail to recapitulate the earliest stages of lesion formation
- Most models do not include the pelvic lining where endometriosis commonly forms
- 2D systems do not recreate the 3D tissue environment
- Animal-derived matrices are variable and not fully defined
- There is a need for more reproducible, human-relevant models

4. Building a cultured 3D human model of endometriosis

We have created a human 3D tissue model that mimics lesions forming on the pelvic lining, where endometriosis commonly forms. This model combines human support cells within an engineered 3D gel and a surface mesothelial layer that recreates the lining of the peritoneum.

Source of cells used to build the model

We used patient-derived tissues and cells to recreate key parts of the endometriosis microenvironment, including mesothelial cells, fibroblasts, endometrial epithelial organoids, and stromal cells. Ethical approval and patient consent gained in collaboration with our clinical colleagues.

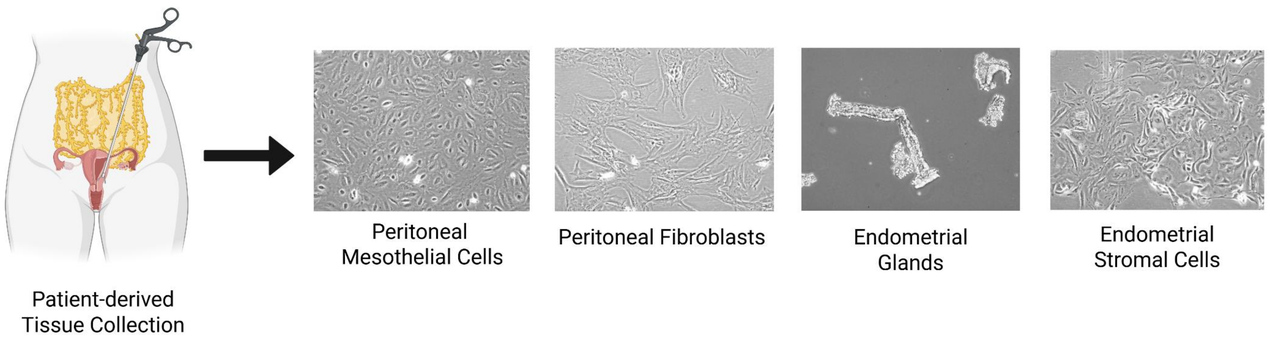


Figure 3. Source of cells used to build the 3D endometriosis model. Patient-derived tissue samples were processed to isolate key cellular components, including peritoneal mesothelial cells, fibroblasts, endometrial glands (epithelial cells), and endometrial stromal cells.

Building the peritoneal tissue component

A composite hydrogel of self-assembling peptides (SAPH) and collagen I, containing fibroblasts, was combined with a mesothelial surface layer to mimic the pelvic lining.

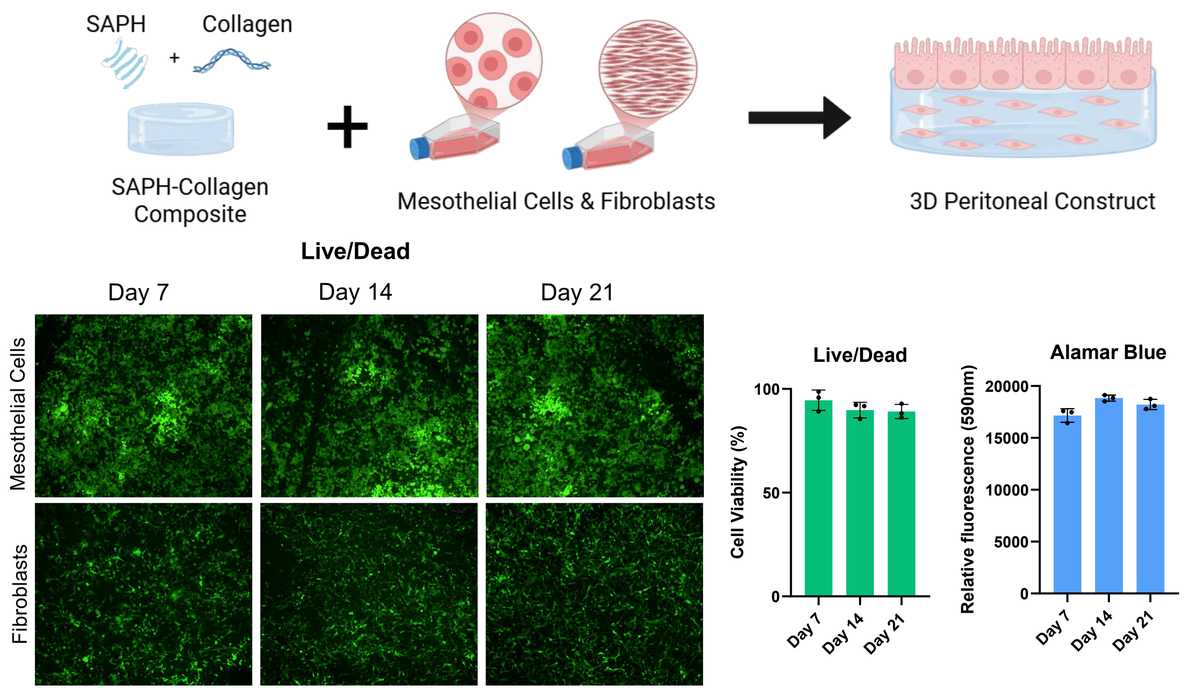


Figure 4. Development and validation of a 3D peritoneal construct. SAPH–collagen I composite hydrogels with mesothelial cells and fibroblasts form a layered model. Live/Dead imaging and Alamar Blue quantitative assays confirm sustained viability and metabolic activity.

Building the endometrial tissue component

Patient-derived endometrial gland organoids were combined with stromal cells to create more representative endometrial lesions after being introduced into the model.

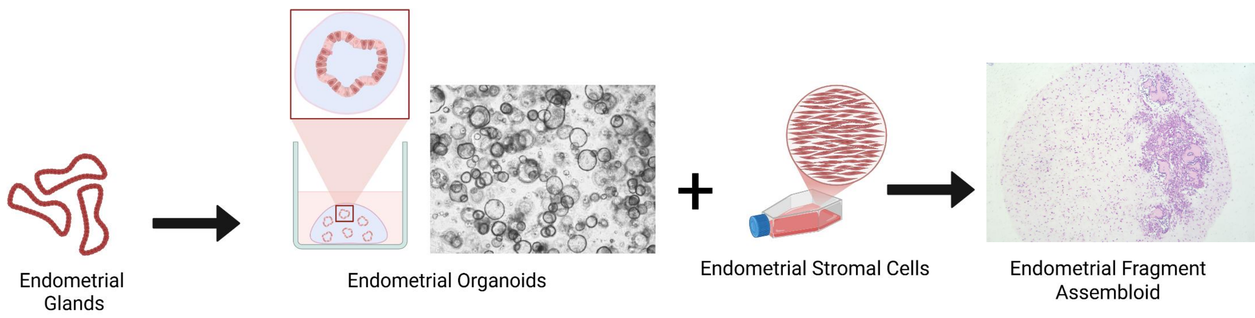


Figure 5. Endometrial assembloids from patient-derived cells. Endometrial epithelial organoids and stromal cells were combined to form multicellular fragments mimicking shed endometrial tissue.

Assembling the human 3D endometriosis model

The endometrial fragment was placed onto the engineered peritoneal construct, allowing us to study how patient-derived endometrial fragments interact with the pelvic lining in a human-relevant 3D environment

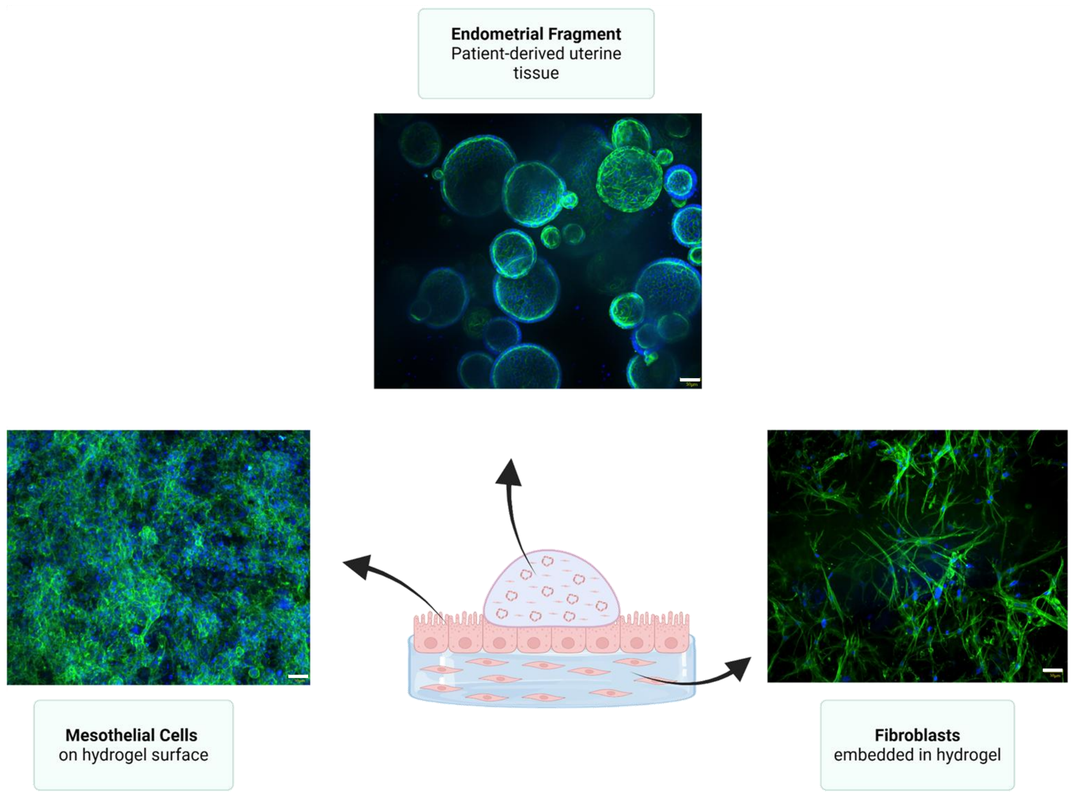


Figure 6 Integrated 3D model of early endometriosis lesion formation. Endometrial fragments positioned on a mesothelial layer and fibroblast-rich composite hydrogel, capturing key features of the peritoneal microenvironment. Representative images show phalloidin (F-actin) and DAPI staining of cellular organisation (scale bars: 50 μm)

5. Future development of model

We have developed a human-relevant 3D model of peritoneal endometriosis that recapitulates key features of the peritoneal microenvironment. Built from patient-derived cells within a defined synthetic matrix, this platform provides a foundation for studying peritoneal–endometrial cell interactions and advancing mechanistic and translational research to further understanding of endometriosis, with future development towards a fully animal-free system.

TERMIS EU-Chapter 2026 PALMA DE MALLORCA 21-24 APRIL / SPAIN

Email: raul.silva@postgrad.manchester.ac.uk **LinkedIn:**

In partnership with

Acknowledgements: The authors would like to thank the EPSRC-funded Centre for Doctoral Training in Advanced Biomedical Materials (grant reference EP/S022201/1) for funding this work, and the patients and clinical colleagues at the Northern Care Alliance Endometriosis Centre, Royal Oldham Hospital, for their support and contribution to this research.