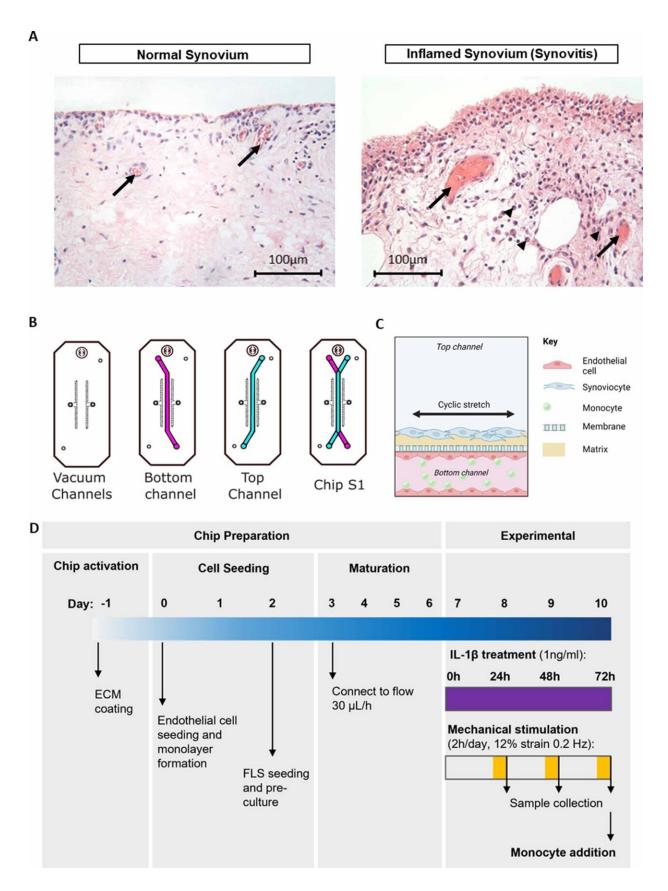


New organ-on-a-chip model of human synovium could accelerate development of treatments for arthritis

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Developing an organ-on-a-chip model of vascularised synovium. (A) Representative histological images of normal synovium (left) and inflamed (highgrade synovitis) synovium (right) as determined by the Krenn synovitis score [20], with associated blood vessels (arrows). The inflamed synovium demonstrates intimal layer thickening, increased stromal cellularity and the presence of macrophages (arrow heads) in proximity to blood vessels, suggesting increased monocyte extravasation. (B) Schematic of the Chip S1[®] from Emulate Inc., comprising two overlapping channels separated by a permeable membrane. Top channel (blue) is 1 mm in height, bottom channel (pink) is 0.2 mm in height. The channels are flanked by two vacuum channels which are used to apply cyclic tensile strain to the co-culture region. (C) Schematic (created using Biorender.com) illustrating the final synovium-on-a-chip model with human fibroblast-like synoviocytes (hFLSs) cultured in the top channel, human umbilical vein endothelial cells (HUVECs) cultured in the bottom channel in coculture with THP-1 monocytes added under flow. (D) Schematic highlighting the key steps for chip preparation and subsequent experimentation whereby chips are subjected to interleukin -1β (IL -1β) stimulation in the presence of mechanical stimulation (2 h, 12% at 0.2 Hz). Credit: *Biomedical Materials* (2023). DOI: 10.1088/1748-605X/acf976

Researchers at Queen Mary University of London have developed a new organ-on-a-chip model of the human synovium, a membrane-like tissue that lines the joints. The <u>model</u>, published in the journal *Biomedical Materials*, could help researchers to better understand the mechanisms of arthritis and to develop new treatments for this group of debilitating diseases.

In the UK, more than 10 million people live with a form of arthritis, which affects the joints and can cause pain, stiffness, and swelling. There is currently no cure for arthritis and the search for new therapeutics is limited by a lack of accurate models.



The new synovium-on-a-chip model is a three-dimensional microfluidic device that contains human synovial cells and blood vessel cells. The device is subjected to <u>mechanical loading</u>, which mimics the forces applied to the synovium during joint movement.

The developed synovium-on-a-chip model was able to mimic the behavior of native human synovium, producing key synovial fluid components and responding to inflammation. This suggests that the new platform has immense potential to help researchers understand disease mechanisms and identify and test new therapies for arthritic diseases.

"Our model is the first human, vascularized, synovium-on-a-chip model with applied mechanical loading and successfully replicates a number of key features of native synovium biology," said Dr. Timothy Hopkins, Versus Arthritis Foundation Fellow, joint lead author of the study. "The model was developed upon a commercially available platform (Emulate Inc.), that allows for widespread adoption without the need for specialist knowledge of chip fabrication.

"The vascularized synovium-on-a-chip can act as a foundational model for academic research, with which fundamental questions can be addressed, and complexity (further cell and tissue types) can be added. In addition, we envisage that our model could eventually form part of the drug discovery pipeline in an industrial setting. Some of these conversations have already commenced."

The researchers are currently using the synovium-on-a-chip model to study the disease mechanisms of arthritis and to develop stratified and personalized organ-on-a-chip models of human synovium and associated tissues.

"We believe that our synovium-on-a-chip model, and related models of human joints currently under development in our lab, have the potential



to transform pre-clinical testing, streamlining delivery of new therapeutics for treatment of <u>arthritis</u>," Prof. Martin Knight, Professor of Mechanobiology said. "We are excited to share this model with the <u>scientific community</u> and to work with industry partners to bring new treatments to patients as quickly as possible."

More information: Clare L Thompson et al, Human vascularised synovium-on-a-chip: a mechanically stimulated, microfluidic model to investigate synovial inflammation and monocyte recruitment, *Biomedical Materials* (2023). DOI: 10.1088/1748-605X/acf976

Provided by Queen Mary, University of London

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