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Corrected: Publisher Correction

ORGANS-ON-A-CHIP

Eternal blood vessels

Many haematological and inflammatory diseases are characterized by endothelial-barrier dysfunction, a condition that is difficult to study in vitro. Now, writing in *Nature Biomedical Engineering*, Wilbur Lam and colleagues report a 'microvasculature-on-a-chip' device, which combines a hydrogel-based microfluidic device with human endothelial cells (ECs), mimicking in vivo conditions, to enable the study of such diseases.

Severe diseases such as sickle cell disease and malaria are characterized by a disruption in endothelial-barrier function. This loss of barrier function is a major part of the inflammatory aspects of these diseases. The in vitro model developed by Lam and colleagues can be used to study this phenomenon. "Our microvasculature-on-a-chip system allows for the first time long-term culture of ECs at reproducible microvascular size scales under well-controlled flow conditions," says Lam.

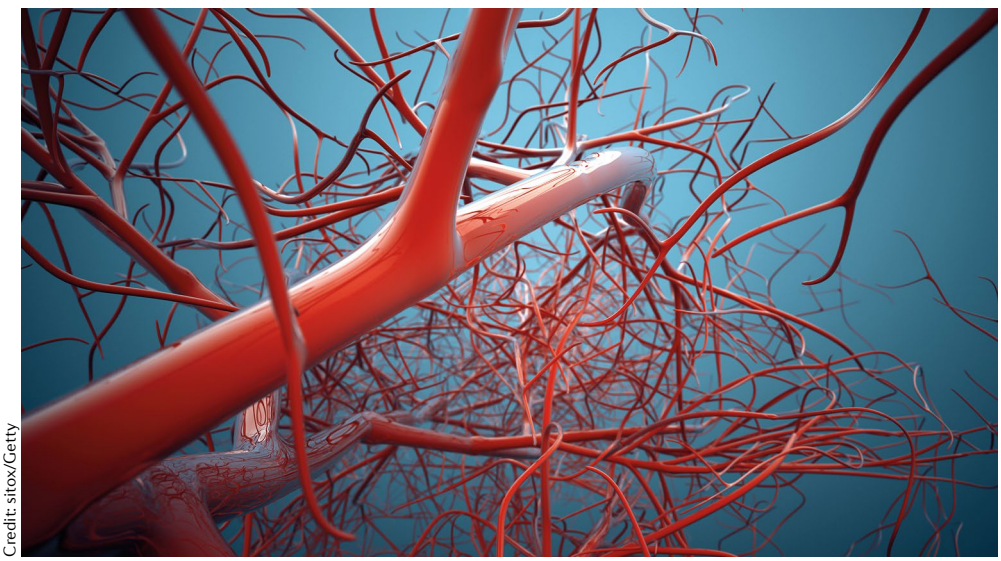
Using an agarose–gelatin interpenetrating polymer network (IPN) hydrogel, the researchers designed a microfluidic device that mimics the in vivo properties of blood vessels in terms of diameter of post-capillary venules, stiffness of the blood vessel intima and self-healing properties of the endothelial barrier. Photolithography was applied to create a silicon mould of branching microchannels of physiologically relevant size, which were transferred to the IPN hydrogel; each hydrogel layer was then crosslinked by carbodiimide. Human ECs can be cultured within this IPN hydrogel network under physiologically relevant conditions.

This modelled endothelium self-deposits basement membrane proteins and allows for real-time, high-resolution and long-term visualization of vaso-occlusion, an obstruction of the vasculature characteristic of sickle cell disease. Previous in vitro microvasculature models have struggled to maintain the relevant in vivo conditions long term; for example, the use of solid polymeric materials does not allow for tuning of the stiffness to match that of the blood vessel intima. "Because the biochemical and biophysical properties of our device accurately mimic in vivo conditions, ECs and their function can be maintained in our system for very long periods of time — we have cultured them for almost up to 2 months now," says Lam.

Long-term EC culture enables the study of not only acute events such as microvascular occlusion and thrombosis, but also of their recovery. "Our system can be applied to any disease in which there is some pathologic interaction between blood and the vessel wall," comments Lam. "As such, we are interested in studying clotting and bleeding diseases as well as rare diseases that affect the microvasculature. Most importantly, we can study diseases long-term, which has not been feasible thus far." The researchers used the device to demonstrate that sickle cell disease or malaria-infected red blood cells cause microchannel occlusion and increased endothelial permeability.

Lam and colleagues now hope to soon be able to use patient-specific ECs and blood for personalized medicine applications to study how potential therapies may affect individual patients and to tailor their treatments accordingly.

Jordan Hindson



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