CIBiS Center for International Research on Integrative Biomedical Systems

MATSUNAGA LAB.

BIO ARCHITECTURE LABORATORY

[It's a Small World —Cells as Tissue Design Tools—]

Center for International Research on Integrative Biomedical Systems

Tissue Engineering, Organ-on-a-chip

Department of Bioengineering

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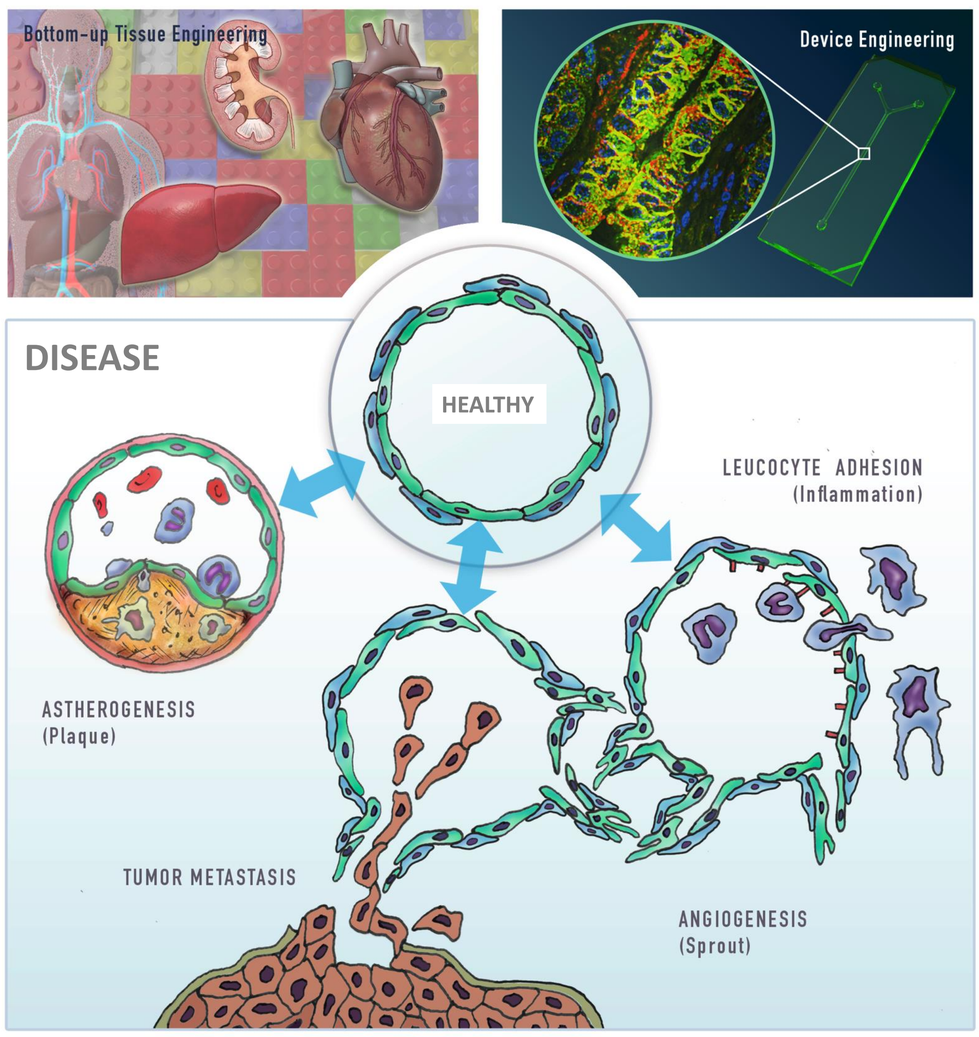
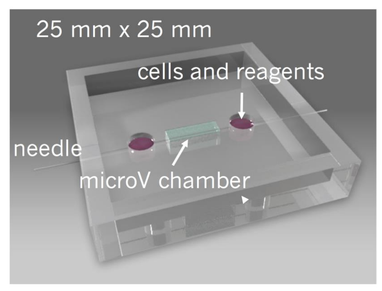
Overview

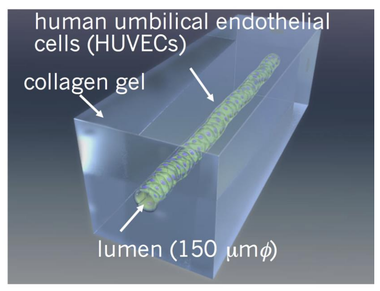
Matsunaga lab has been focusing on bottom-up tissue engineering by unifying biomaterial synthesis, microfabrication and cell biology. Our goal is to develop controllable *in vitro* tissue models enable to "visualize" the microenvironment of tissues from healthy to disease state at the cellular and tissue level.
This approach serves a powerful tool for mechanistic understanding of disease and drug discovery.

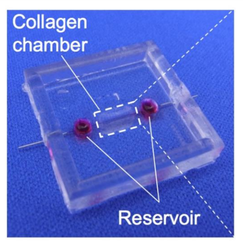


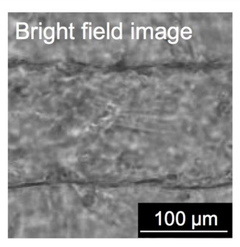
3D microvessel model

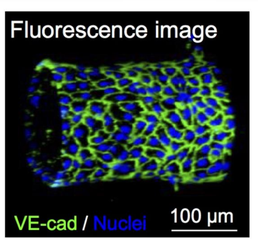
***In vitro* microvessel engineering has long been one of the biggest challenges for tissue engineering and vascular-related biological study. Both stable microvessel formation with continuous lumen structure and post perfusion system is important for fabricating functional tissues mimicking physiological behavior. We have designed collagen gel-based microchannel to accumulate cells and developed *in vitro* 3D microvessel model that allows: (i) rapid formation of stable microvessels, (ii) simple and non-invasive observation, and (iii) scalability (i.e. co-culture, perfusion etc.).**



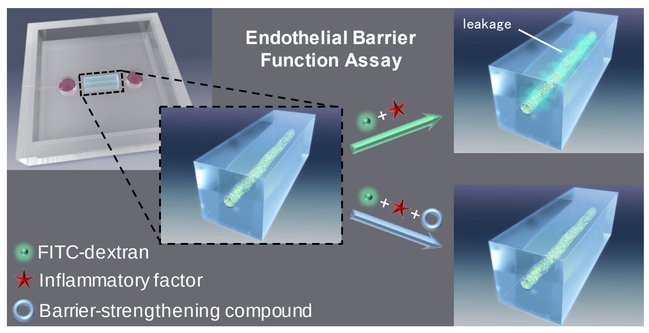




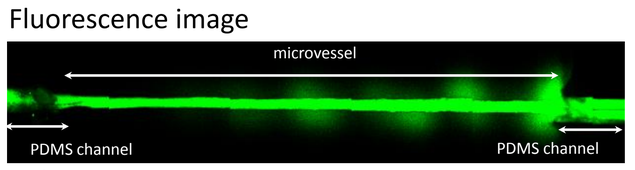




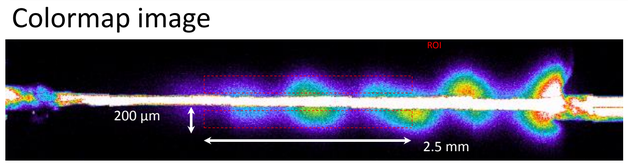
Vascular permeability assay



Fluorescence image



Colormap image



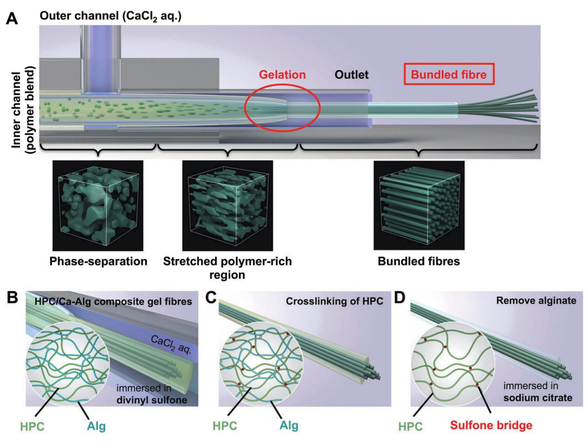
J. Pauty, R. Usuba *et al.*, *Nanotheranostics*, 1, 103-113 (2017).

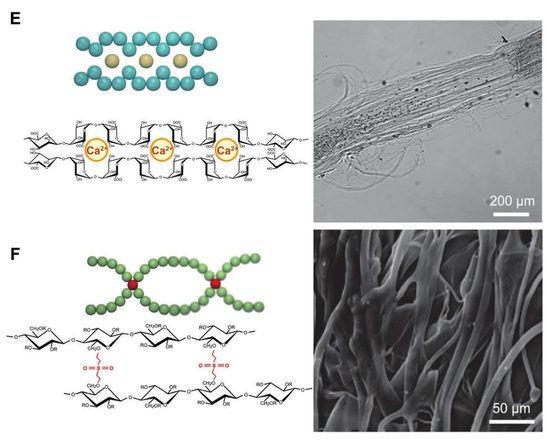
Vascular barrier is an important function of the endothelium and its dysfunction is involved in several diseases. The barrier function of the endothelial cell monolayer is governed by cell-cell, cell-extracellular matrix (cell-ECM) contacts, and inflammatory factors such as thrombin, histamine or vascular endothelial growth factor.

We have developed an *in vitro* 3D microvessel model in which we can manipulate the endothelial barrier function and permeability. This system could be used to screen for compounds modulating the barrier function of endothelial cells, as well as investigating mechanistic aspects of barrier dysfunction.

Bundled gel as cell scaffold

Bundles of thin, multiply parallel fibers are widely seen in nature such as plant xylems, human protein assemblies and muscle/nerve tissues. Because of their hierarchical structure, they have superior toughness and strength relative to single fibers, and have been a key research focus in artificial tissue engineering. We have developed a new method to prepare biomimetic bundle-structured gel fibers using a microfluidic device and rapid cross-linking of a phase-separated polymer blend solution. The bundled gels have a feature of tunable surface topology and mechanical stiffness, and allow guiding cell orientation. These properties can be applicable for the cell culture scaffold, especially for muscle/nerve tissue regeneration.

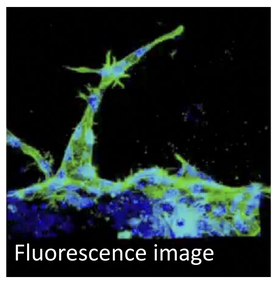


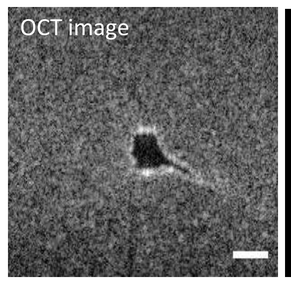


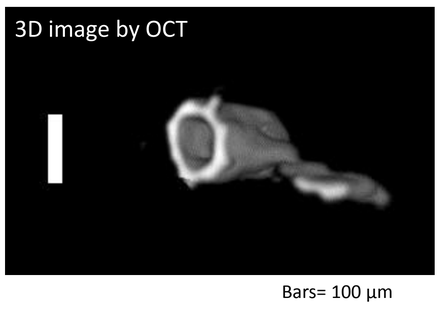
Y.J. Kim and Y. Takahashi *et al.*, *J. Mater. Chem. B*, 3, 8154-8161 (2015), Y.J. Kim *et al.*, *Biomater. Sci.*, 4, 1197-1201 (2016).

3D imaging of angiogenesis

Angiogenesis is a sequential process that develops new vasculature from existing blood vessels. Found throughout the body, it is relevant in a number of physiological events and diseases, such as wound healing and tumor progression. Numerous studies have investigated angiogenesis, however, the mechanism still remains unclear because microscopic observation of angiogenesis is challenging in spatial-temporal resolution. To meet this problem, we developed 3D *in vitro* microvessel for physiologically relevant angiogenesis model and utilized "stage-top type" of optical coherence tomography (OCT) for non-invasive imaging of angiogenic process in live.







Bars= 100 μm

H. Takahashi *et al.*, *Sci. Rep.*, 7, 42426 (2017).