Research Activity Report **2013.10.31**

Research title		Development of a Microfluidic Device for Three-Dimensional Cell Culture under Controlled Hypoxic Environment
Visiting researcher	**Name**	Kenichi Funamoto
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	Title	Assistant Professor
Visiting institution		Massachusetts Institute of Technology, USA
Visiting period		February 2011 - January 2012
Host researcher	**Name**	Roger D. Kamm
	Affiliation	Department of Mechanical Engineering, Massachusetts Institute of Technology
	Title	Professor

Summary of Collaborative Research Activities

Hypoxic microenvironment affects cell processes such as viability, migration, proliferation and differentiation both in physiological and pathological *in vivo* tissues. A microfluidic device that enables precise control of oxygen tension around cells was designed for three-dimensional (3D) cell culture (Fig. 1). The device has a central 3D gel region acting as an external cellular matrix, flanked by media channels. On each side, there is a peripheral gas channel through which suitable gas mixture of predefined oxygen concentration is supplied to establish a uniform distribution or a gradient of oxygen tension within the device. The microfluidic device was fabricated by transferring the channel pattern to polydimethylsiloxane (PDMS), and a polycarbonate film with a low oxygen diffusion coefficient was embedded in the device in proximity above the channels to prevent oxygen diffusion from the environment. The effects of various parameters, such as gas and media flow rates, device thickness, and diffusion coefficients of oxygen in the materials were examined by numerical simulations to determine the characteristics of the microfluidic device (Fig. 2). The oxygen tension in the device was then validated experimentally using a ruthenium-coated oxygen-sensing glass cover slip which confirmed the establishment of a low uniform oxygen tension (< 3%) or an oxygen gradient across the gel region (Fig. 3). Finally, migrations of MDA-MB-231 human breast cancer cells were observed under normoxia and hypoxia with the

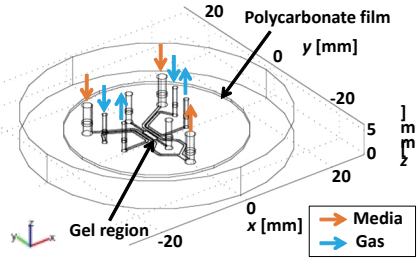

Fig. 1 : Schematic of the microfluidic device

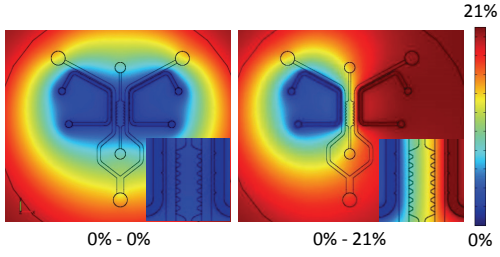

Fig. 2 : Computed oxygen tensions

microfluidic device. The cellular experiment represented an enhanced migration of the breast cancer cells under the hypoxic condition in comparison with the normoxic condition (Fig. 4), implying the utility of the microfluidic device for cellular experiments under hypoxic conditions. The present microfluidic device is a useful tool to investigate cellular processes under controlled hypoxic conditions for various applications, allowing imaging of cells with high-resolution.

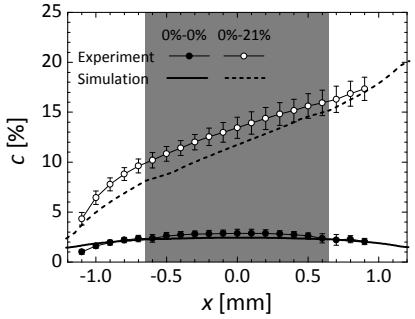

Fig. 3 : Oxygen tension profile across the gel region (gray zone)

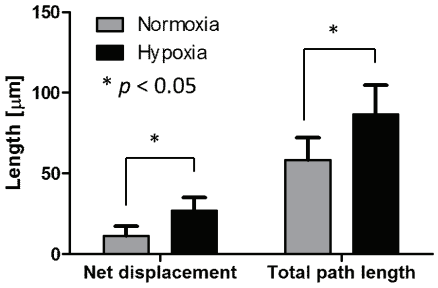

Fig. 4 : Migration of MDA-MB-231 cells for six hours

Publications

1) Journal or conference papers with full paper review

[1] Kenichi Funamoto, Ioannis K. Zervantonakis, Yuchun Liu, Christopher J. Ochs, Choong Kim and Roger D. Kamm: A Novel Microfluidic Platform for High-Resolution Imaging of a Three-Dimensional Cell Culture under a Controlled Hypoxic Environment, *Lab Chip*, Vol. 12, No. 22(2012), pp. 4855-4863.

2) Conference papers or presentation without full paper review

[2] Christopher J. Ochs, Kenichi Funamoto, Roger D. Kamm and Dieter Trau: Oxygen Sensors for Microfluidic 3D Cell Cultures, *EUROPT(R)ODE XI Conference on Optical Chemical Sensors and Biosensors*, (2012), p. 98.

[3] Kenichi Funamoto, Ioannis K. Zervantonakis, Yuchun Liu and Roger D. Kamm: Oxygen Tension Control in a Microfluidic Device for Cell Culture, *Proceedings of the 9th International Conference on Flow Dynamics (ICFD2012)*, (2012), pp. 724-725. (Invited)

[4] Kenichi Funamoto, Ioannis K. Zervantonakis, Yuchun Liu, Christopher J. Ochs and Roger D. Kamm: Computational Simulation to Create Low Oxygen Tension in a Microfluidic Device for Cell Culture, *Proceedings of the 12th International Symposium on Advanced Fluid Information and Transdisciplinary Fluid Integration (AFI/TFI-2012)*, (2012), pp. 88-89.

[5] Shuichiro Fukushima, Reiko Maehara and Kenichi Funamoto: Observation of Hypoxia Cellular Response by Using Microfluidic Devices, *Proceedings of the 12th International Symposium on Advanced Fluid Information and Transdisciplinary Fluid Integration (AFI/TFI-2012)*, (2012), pp. 122-123.

3) Patent, award, press release etc.

Not applicable.