Novel Microfluidic Models of Atherosclerosis and Atherothrombosis

Fahima Akther,^{1,2} *Dimple Thomas*,^{1,3} *Huong D.N. Tran*,^{1,2} *Shebbrin Moonshi*,¹ *Yuao Wu*,¹ *Jun Zhang*,¹ *Nam-Trung Nguyen*,^{1,3} *Hang T. Ta*,^{1,2,3*}

¹Queensland Micro- and Nanotechnology Centre, Griffith University, Nathan, Queensland 4111, AUSTRALIA

² Australian Institute for Bioengineering and Nanotechnology, University of Queensland, St Lucia, Queensland 4072, AUSTRALIA

³ School of Environment and Science, Griffith University, Nathan, Queensland 4111, AUSTRALIA * Presenting and Corresponding Author: <u>h.ta@griffith.edu.au</u>

Abstract

Atherosclerosis is an inflammatory disorder of blood vessels that is a major cause of death worldwide. Atherothrombosis, an atherosclerotic plaque disruption condition with superimposed thrombosis, is the underlining cause of cardiovascular episodes. Monocyte recruitment and transmigration are crucial in atherosclerotic plaque development. The multi-disease complexities aggravate the situation and continue to be a constant concern for understanding atherosclerosis plaque development. We have developed 3D models mimicking the development of atherosclerosis and thrombosis under static condition in 96-well plate¹ and also under flow condition in microfluidic devices^{2,3,4}. We have demonstrated that these models could be employed to study disease development, to test efficacy of drugs and nanomedicine, and to evaluate thrombosis risk and treatment strategies.

References

[1] F. Akther, D. Sajin, S. S. Moonshi, Y. Wu, K. Vazquez-Prada, H. T. Ta. Modelling Foam Cell Formation in A Hydrogel-Based 3D-Intimal Model: A Study of The Role of Multi-Diseases During Early Atherosclerosis. *Advanced Biology*, 8 (2024), 2300463.

[2] F. Akther, J. Zhang, H. D.N. Tran, H. Fallahi, H. Adelnia, H.P. Phan, N.T. Nguyen, H. T. Ta. Atherothrombosis-on-chip: a site-specific microfluidic model for thrombus formation and drug discovery. *Advanced Biology*, 6 (2022), 2101316.

[3] F. Akther, H. Fallahi, J. Zhang, N.T. Nguyen, H. T. Ta*. Evaluating thrombosis risk and patient-specific treatment strategy using an atherothrombosis-on-chip model. *Lab on a Chip*, 24 (2024), 2927-2943.

[4] F. Akther, D. Sajin, S. S. Moonshi, J. Pickett, Y. Wu, J. Zhang, N-T. Nguyn, H. T. Ta*. An intimal-lumen model in a microfluidic device: potential platform for atherosclerosis-related studies. *Lab on a Chip*, 25 (2025), 354-369.



Figure 1. A microfluidic site-specific atherothrombosis-on-chip model. **A)** Illustration of an atherosclerotic artery with a ruptured plaque, exposing plaque components to the circulation and causing thrombosis. **B)** Illustration of a proposed in vitro site-specific atherothrombosis model, exposing extracellular components to the circulation and developing thrombosis at that site. **C)** A schematic diagram of the model. The widths of the main channel and the supporting channel are 200 and 100 µm, respectively. Both channels are interconnected by a 400 µm long porous region. The height of both channels is 50 µm. Each channel has an inlet and an outlet. Devices with different stenosis are fabricated by reducing the width or increasing the blockage height a at the porous connecting region. The blockage heights of 0, 50, and 100 µm correspond to 0%, 25%, and 50% stenosis. **D)** A photograph of the microfluidic atherothrombosis-on-chip device for site-specific atherothrombosis formation. The red dye was used to highlight the microfluidic channels and a ruled was placed to represent the relative size of the device. **E)** Schematic diagram of the supporting channel. 1) The first syringe pump was connected to the inlet 2) of the main channel for infusing phosphate-buffered saline (PBS) (red). 3) A tygon tube was attached to the outlet of the main channel for the waste removal. 4) The second syringe pump was connected to the outlet of the supporting channel for the waste removal.