

# Developing complex hydrogel microcapsules for high throughput, confined tissue culture: small packages, big potential

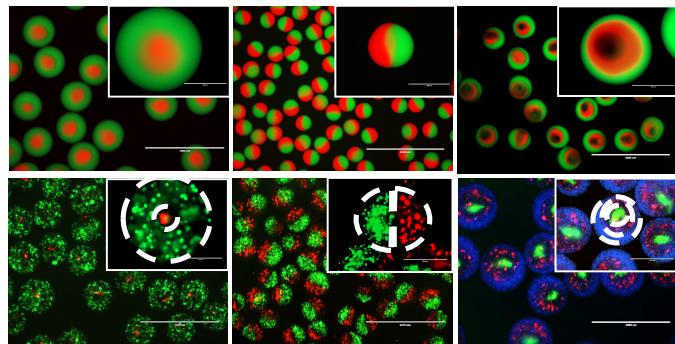
Yen-Chun Lu<sup>\*1</sup>, Wei Song<sup>1</sup>, Duo An<sup>1</sup>, Beum Jun Kim<sup>1</sup>, Robert Schwartz<sup>2</sup>, Mingming Wu<sup>1</sup>, Minglin Ma<sup>1</sup>; Cornell University

<sup>1</sup>Department of Biological and Environmental Engineering

<sup>2</sup>Weill Medical College of Cornell University

\*: Presenter, e-mail [y12347@cornell.edu](mailto:y12347@cornell.edu)

Cell encapsulation in hydrogel microparticles has been investigated for decades in various bioengineering applications including tissue engineering, and cell therapy. However, most of the time, the cells are encapsulated randomly in whatever material that forms the microparticles, most commonly alginate. The lack of control over the spatial organizations of the cells and the extracellular environment within the microparticles significantly limits for advanced applications. Here we report a novel, multi-fluidic cell microencapsulation approach where 1 or more types of cells are encapsulated in pre-assigned compartments in the microparticles with controlled extracellular matrix. These microparticles can be produced with controllable and nearly monodispersed sizes at rates of over 10,000 microparticles per min and therefore provide a promising platform for high throughput applications. We demonstrated the utilization of these extracellular matrix-supported microparticles for 3D culturing of cells that typically require specific microenvironment to survive such as human umbilical vein endothelial cells (HUVECs) and small intestine stem cells. By taking advantage of the confinement effect, we also showed robust and scalable productions of size-controlled multicellular microtissues. Lastly, to demonstrate the broad applications of these microparticles, we performed proof-of-concept studies on three different co-culture systems including cell segregations under 3D confined space, the supporting role of stromal cells in hepatocyte functions and the paracrine cell signaling in aggregation of endothelial cells, all in a high throughput manner.



Uniform size and shape compartmentalized microparticles can be produced in high production rate with tunable ECM supporting for various 3D cell culture applications.