Micro/Nano Engineering for 3D Tumor Models and Tumor Calcification: From Biomimetic Cancer Models to a New Therapeutic Concept

マイクロ・ナノ工学が切り拓く 3 次元腫瘍モデルとがん石灰化研究
— 生体模倣から新たながん治療コンセプトへ —

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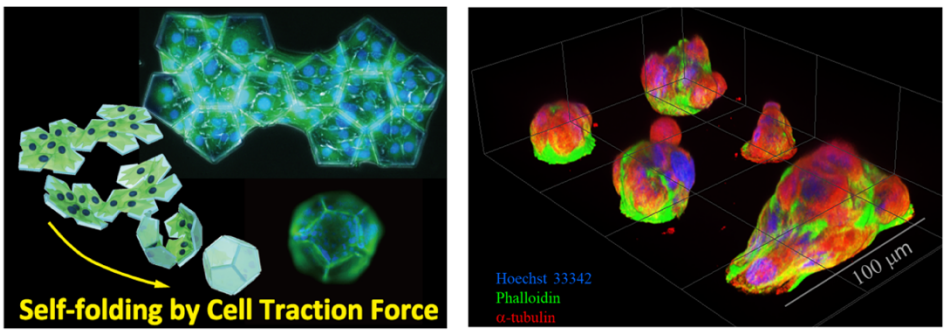
Three-dimensional (3D) cell culture has become an indispensable platform for studying cell biology, cancer progression, drug discovery, tissue engineering, and regenerative medicine. In this seminar, I will introduce our micro/nanoengineering approaches for constructing biomimetic 3D tissues and discuss their application to understanding tumor biology and developing future therapeutic strategies.

First, we developed a self-folding technique, termed “cell origami”, that exploits cell traction forces (CTFs) to transform two-dimensional microfabricated plates into 3D cell-laden microstructures. Unlike conventional microfabrication approaches requiring external actuation, cell origami utilizes intrinsic cellular forces to achieve spontaneous folding, enabling the rapid fabrication of diverse 3D tissue architectures by simply designing the geometry of microplates and hinges.

Second, we established a micro/nanopatterned culture platform that enables cancer cells to spontaneously organize into 3D microtumors exhibiting cell-in-cell (entosis-like) structures, closely resembling invasive tumor lesions observed in pathological tissues. The platform allows real-time observation of tumor morphogenesis and reveals distinct growth and invasive behaviors depending on cancer malignancy, providing a powerful in vitro model for cancer research and drug screening.

Finally, I will present our recent discovery that these engineered pancreatic tumor tissues undergo localized tumor calcification. Live-cell imaging revealed that dead-cell debris generated within the tumors accumulates on the tumor surface, where phospholipid-rich membrane fragments serve as nucleation sites for calcium crystal formation. This biomimetic tumor-on-a-chip platform provides a unique opportunity to investigate the mechanisms of pathological calcification and may open a new therapeutic concept of "turning tumors into stone" by promoting tumor-specific calcification.



3D cell culture systems using Origami folding technique (left) and a micro/nano pattern plate (right)

References

1. K.Kuribayashi-Shigetomi, et al, PLOS ONE, 7(12), e51085 (2012)
2. Q. He, et al, Scientific Reports 8(1) 4556 (2018)