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**Corresponding Author:** Kunyoo Shin

**Authors:** Kunyoo Shin<sup>1,\*</sup>

**Institution:** <sup>1</sup>School of Biological Sciences, Seoul National University, Seoul 08826, Korea,

**Title:** Stem cells, Organoids and Their Applications for Human Diseases

Kunyoo Shin, Associated Professor

School of Biological Sciences, Seoul National University, Seoul 08826, Korea

E-mail: [kunyoos@snu.ac.kr](mailto:kunyoos@snu.ac.kr)

Studying human biology has been challenging with conventional animal models or two-dimensional (2-D) cultured cell lines. Recent advances in stem cell biology have made it possible to culture stem cells in vitro, leading to the establishment of in vitro three-dimensional (3D) organ-like structures known as organoids. Organoids are self-organizing 3D miniature tissues, that mimic the tissue architecture and functionality of in vivo counterparts. Currently, organoids can be established for multiple tissues such as intestine, brain, kidney, prostate, pancreas, liver, bladder, heart, and retina, either from pluripotent stem cells (PSCs), including embryonic stem cells (ESCs) and induced pluripotent stem cells (iPSCs), or adult stem cells (AdSCs). In addition to normal organoids, patient-derived tumor organoids have been established from various human tumors such as pancreatic, colorectal, breast, liver, prostate, and bladder tumors. Also, bioengineering technologies including biomaterial and scaffold fabrication, bioprinting, and microfluidics have been recently applied to create more mature and complex organoids and miniature tissues in vitro. Incorporating recently advanced computational analyses including multi-omics profiling and bioinformatics, further facilitated the process of using human organoids as a novel platform for human disease modeling, drug screening to identify potential targets and novel therapeutics, and the development of precision medicine and regenerative therapies.

In the current issue of BMB reports, six review articles covering stem cells and organoids in multiple tissues and their applications are invited. The first review by Dr. Sekyu Choi and colleagues summarizes the current status of adult stem cell biology, focusing on hair follicle stem cells (HFSC) and their aging. They discuss intrinsic and extrinsic mechanisms that can induce HFSC aging and the association of HFSC aging, with hair loss and hair follicle regeneration. The second review by Dr. Jongman Yoo and colleagues provides a general review for organoids and discusses the current status of organoid-based regenerative therapies, providing multiple cases on how organoids are used for regenerative medicine in various diseases, which could be applied in future clinical trials. Dr. Hyung-Sik Kim and colleagues review the technology for a microbial co-culture system with intestinal organoids

for modeling host-microbiome interactions, which provides an excellent platform to better understand the nature of host-microbe crosstalk in diverse contexts, such as tissue homeostasis and disease. Regarding human organoids derived from various human tumors, Dr. Minyong Kang and colleagues summarize the advances of patient-derived tumor organoids over conventional cell lines and animal models, especially focusing on prostate cancer and kidney cancer. In particular, this review covers the establishment of tumor organoids from prostate cancer and kidney cancer, and their applications including drug screening and genomic analysis. The applications of bioengineering technologies to stem cell biology and organoid research are covered by the review from Dr. Seung-Woo Cho and colleagues, in which they describe the 3D engineered human tissue models for disease modeling, focusing on cardiac tissues and heart disorders. The authors summarize the cell types required for the fabrication of cardiac tissues and diverse 3D human cardiac tissue models, and further discuss the modeling of various heart diseases. Lastly, Dr. Sanguk Kim and colleagues describe many advances in organoid models and how computational methods can be used for analyzing the experimental results using organoids. The authors also introduce several bioinformatical tools used in organoid analyses including genomic analysis, transcriptomic profiling, and multi-omics analysis.

In conclusion, stem-cell derived organoids have been established for various human tissues, and are currently used for many aspects of human biology such as understanding the basic principle of stem cell biology, investigating the mechanisms of host-pathogen interactions, modeling human diseases, and developing the novel therapeutic options for the regenerative medicine. Patient-derived organoid models, including tumor organoids, also allow to address many aspects of cancer biology, and provide a valuable platform for drug screening and precision medicine. Also, 3D bioengineering technology and computational biology have been applied to the organoid research, and have advanced the field of stem cell and organoid biology by increasing structural complexity, cellular diversity, and tissue maturity of human organoids, as well as by facilitating the use of organoid technology in the development of new drugs and regenerative medicine.