Tissue Eng Regen Med (2020) 17(6):729–730
https://doi.org/10.1007/s13770-020-00315-y

Online ISSN 2212-5469

PREFACE

Applications of Organoids for Tissue Engineering and Regenerative Medicine

James J. Yoo[1] · Chong-Su Cho[2] · Inho Jo[3]

Accepted: 24 September 2020 / Published online: 12 November 2020

Organoids are miniaturized, self-organized three-dimensional tissue units that mimic the spatial, chemical, structural, and physiological elements of *in vivo* tissue environments [1]. Research involving organoids is currently one of the hottest and rapidly expanding areas due to its potential and practical uses, from basic science to clinical applications, such as drug screening and toxicology, tumor models for cancer diagnosis, and models for human development and diseases [2–6].

This special issue brings together leading experts in the field to define this growing area. The intent of this special issue is to provide essential information and insights on how tissue and organ-specific organoids are developed and used in biomedical applications for tissue regeneration. The articles provide an update of the current and trending research that may give readers new perspectives and creative ideas for further development. This special issue consists of one original and five review articles covering platform technologies and tissue applications in the liver, brain, ovary, skeletal muscle, and tumor microenvironment (TME) such as breast cancer.

Liver tissue organoid that possesses biological and physiological functions is one of the most studied models. Lee et al. [7] highlight the development of various liver model systems and discuss the dire need to overcome the current limitations before advancing to translational applications. The authors emphasize that three-dimensional biomimetic liver models may hold great promise for biomedical applications. Another area that is actively studied recently is research using brain organoids, ranging from development processes to applications in neurological diseases. In this issue, Jeong et al. [8] cover platform technologies used to develop human brain organoids and discuss the importance of disease modeling for various pharmacological and tissue applications. In the subsequent article, Kondash et al. [9] developed human skeletal muscles composed of myobundles and tested for the metabolic function. These human myobundles serve as a useful platform for developing a human *in vitro* model of normal and diseased muscle. In their study, the authors evaluated glucose uptake and insulin responsiveness in human tissue-engineered skeletal muscle myobundles. This study showed that the model of human myobundles recapitulated key features of *in vivo* insulin sensitivity and exhibited relevant drug-mediated perturbations in contractile function and glucose metabolism.

Another research area gaining increasing attention is generating TME, an ecosystem that surrounds a tumor. The TME consists of many tissue components, including cells, extracellular matrix, vasculature, and growth factors. Tumor behavior is believed to be dependent on the interactions of the TME and cancer cells. In this special issue, Devarasetty et al. [10] present an overview of the developed TME models and point out the essential components comprising the TME. They also discuss how the TME models are applied across various cancer types to provide a foundation for future research into the TME. Using the TME models, Mertz et al. [11] examined the recent studies involving the breast tumor. Adipocytes are a cell type increasingly recognized to have complex functions in

✉ James J. Yoo
jyoo@wakehealth.edu

[1] Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, NC 27157, USA

[2] Research Institute of Agriculture and Life Sciences, Seoul National University, Seoul 08826, Republic of Korea

[3] Department of Molecular Medicine, Ewha Womans University Medical College, Seoul 07804, Republic of Korea

breast cancer. This article reviewed both two-dimensional and three-dimensional models of adipocytes in the breast TME and discussed how these models are related to breast tumor progression. Many technologies have been developed to facilitate the use of organoids for different applications. Microfluidic systems have emerged as a powerful tool that can closely replicate the *in vivo* physiological conditions of organ systems. In this issue, Sequeira et al. [12] examined how microfluidic systems can be used to study the ovarian follicle development and applied to improve the outcomes of assisted reproductive technologies (ART). The authors believe that microfluidic systems will likely play a role in revolutionizing fundamental reproductive physiology/toxicology research and clinically applicable ART.

This special issue presents perspectives on the development and application of tissue-specific organoids and how these miniature organs could provide benefits to patients and human health. Furthermore, recapitulating the TME allows for an enhanced understanding of tumor behavior and progression. Technologies, such as microfluidic systems, help provide an environment closely mimics the *in vivo* physiological conditions. It is believed that this special issue could serve as a useful resource for researchers and students who are interested in developing organoids for basic science and application studies.

Acknowledgements The editors would like to sincerely thank all the invited authors, reviewers, and editorial team at Tissue Engineering and Regenerative Medicine (TERM) for making this special issue possible. A special thanks to the Managing Editor, Ms. Jung Hyun Ahn, who has patiently provided guidance from the start to the completion of this special issue.

References

1. Schutgens F, Clevers H. Human organoids: tools for understanding biology and treating diseases. Annu Rev Pathol. 2020;15:211–34.
2. Xu H, Lyu X, Yi M, Zhao W, Song Y, Wu K. Organoid technology and applications in cancer research. J Hematol Oncol. 2018;11:116.
3. Clevers H. Modeling development and disease with organoids. Cell. 2016;165:1586–97.
4. Kaushik G, Ponnusamy MP, Batra SK. Concise review: durrent status of three-dimensional organoids as preclinical models. Stem Cells. 2018;36:1329–40.
5. Rossi G, Manfrin A, Lutolf MP. Progress and potential in organoid research. Nat Rev Genet. 2018;19:671–87.
6. Artegiani B, Clevers H. Use and application of 3D-organoid technology. Hum Mol Genet. 2018;27:R99-107.
7. Lee SW, Jung DJ, Jeong GS. Gaining new biological and therapeutic applications into the liver with 3D in vitro liver models. Tissue Eng Regen Med. 2020. https://doi.org/10.1007/s13770-020-00245-9.
8. Jeong HJ, Jimenez Z, Mukhambetiyar K, Seo M, Choi JW, Park TE. Engineering human brain organoids: from basic research to tissue regeneration. Tissue Eng Regen Med. 2020. https://doi.org/10.1007/s13770-020-00250-y.
9. Kondash ME, Ananthakumar A, Khodabukus A, Bursac N, Truskey GA. Glucose uptake and insulin response in tissue-engineered human skeletal muscle. Tissue Eng Regen Med. 2020. https://doi.org/10.1007/s13770-020-00242-y.
10. Devarasetty M, Forsythe SD, Shelkey E, Soker S. In vitro modeling of the tumor microenvironment in tumor organoids. Tissue Eng Regen Med. 2020. https://doi.org/10.1007/s13770-020-00258-4.
11. Mertz D, Sentosa J, Luker G, Takayama S. Studying adipose tissue in the breast tumor microenvironment in vitro: progress and opportunities. Tissue Eng Regen Med. 2020. https://doi.org/10.1007/s13770-020-00299-9.
12. Sequeira RC, Criswell T, Atala A, Yoo JJ. Microfluidic systems for assisted reproductive technologies: advantages and potential applications. Tissue EngRegen Med. 2020. https://doi.org/10.1007/s13770-020-00311-2.