

LETTER TO THE EDITOR

Lo and Behold, the Lab-Grown Organs Have Arrived!

Jaesang Kim

Department of Life Science, Ewha Womans University, Seoul, Korea

Model organisms have played essential roles in biological studies over the centuries. Typically fast-growing in laboratory settings and fertile with numerous offsprings, various model species including *C. elegans*, *D. melanogaster* and *M. musculus* have provided the *in vivo* contexts for making novel observations and testing emerging hypotheses. One important goal of such research efforts has been and will be extrapolating the knowledge to human species. Using model organisms has been without question a successful approach to this end as much of the molecular mechanisms associated with development, metabolism and pathogenesis are conserved across metazoan species.

Still, there are clear limitations. Biological processes such as brain development in humans are not properly or adequately modelled by other organisms. Some diseases including the currently rampant COVID-19 also have yet to be matched with a suitable model organism that mimics the pathogenesis in infected patients. Drug efficacy and side effects are also often human-specific, and new drugs ultimately need to be tested using human subjects.

Organoid, a 3D *in vitro* cellular complex, represents a potential solution to at least some of these problems. Organoids are generated mostly from pluripotent stem cells and adult stem cells and often closely simulate real organs in terms of development, cellular composition, or-

gan-wide structure and perhaps most importantly physiological processes. Organoids of brain, intestine, lung, liver and numerous other organs are routinely generated now and used for purposes ranging from basic research to drug screening.

The current field of organoid research can be regarded as an offshoot of stem cell research. In fact, it is the series of advances made in human embryonic stem cells and adult stem cells (which of course owes much to the fore-running advances in murine counterparts for the rapid progress) that made the organoid field so 'hot' and accessible. The advent of induced pluripotent stem cells and supporting technological advances such as clonal culture and CRISPR/Cas9-based genetic manipulation now herald a new way of undertaking biological research and applying the outcomes.

This issue of International Journal of Stem Cells is a collection of review articles, technical reports and an original research article on organoids. It is a special issue reporting up-to-date information, discussing troublesome issues and looking ahead for future directions. Kim et al.'s report perhaps is a surprising opener in that rather than discussing historical aspects of organoid biology, the article deals with its most avant-garde utilization, research on COVID-19 (1). This is followed by three neurobiology articles also dealing with highly timely topics: 1) generation of glial cells by direct conversion by Yun et al. (2); 2) induction of region-specific brain organoids by Susaimanickam et al. (3); 3) maturation of organoids with proper connectivity by Jang et al. (4). Next article by Heo et al. describes latest information on the extracellular matrix, a key player in differentiation and expansion of organoids (5). The last review article by Park and Koh introduces a new player in the field, the microbiome, well known for the major role in intestinal development (6). The sole research article of this issue touches on the most pressing issue of the field, assembling cells of different

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Correspondence to **Jaesang Kim**

Department of Life Science, Ewha Womans University, 52 Ewha-yeodae-gil, Seodaemun-gu, Seoul 03760, Korea

Tel: +82-2-3277-3414, Fax: +82-2-3277-3760

E-mail: jkim1964@ewha.ac.kr

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lineages for better simulation of *in vivo* organs. Kook et al. present their data on generation of cortical brain organoid with vascularization (7). Two technical reports that follow also serve good purposes for researchers. The simple and easy-to-follow description for generation of cerebral organoids by Hong et al. should be an excellent introduction for new investigators in this field (8). Detailed yet again easy-to-follow presentation by Kwon et al. on a robust and reliable culture method of intestinal spheroids describes a new scalable source for intestinal stem cell and organoid research (9).

Last but not least, the editors should be praised for their great effort in putting together a series of excellent articles containing latest information and tackling timely issues. I hope that the readers concur with me and more importantly of course enjoy this special issue.

Keywords: Orgnoid, Special issue, Stem cell, CRISPR/Cas9

Potential Conflict of Interest

The authors have no conflicting financial interest.

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