Organoids: ready for the revolution?

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Organoids are a diverse set of 3D in vitro model systems which can recapitulate to a remarkable extent the structure and function of developing and adult organs and tissues. This technology enables us to mimic cellular and molecular features of distinct organ systems and tissue contexts in mice and humans with great detail. Organoids have helped us study various aspects of mouse and human development and physiology. They have further been established to serve as disease models when derived from human patients and have contributed significantly to biomedical research enabling, e.g., banking of patient materials, screening for novel drugs and therapeutic targets, and development of long-sought diagnostic tools and approaches. Organoid technology has also contributed to the advancement of basic science, including animal research where organoids have been derived from various farm, companion, and exotic animals. All in all, organoids are undoubtedly a disruptive and ground-breaking technological achievement in today's arena of life science research. Interestingly, despite its many promises, it has not been fully adopted to the many challenges of the biomedical research field. Moreover, mimicking human organs such as the brain or certain aspects of human embryos has raised various ethical concerns among the public as well as the scientific community. In this special issue, we have tried to cover the major

relevant aspects related to this emerging field of research, not only highlighting the frontier areas of organoid technology but also discussing pressing ethical and societal issues. To provide a perspective on the future of the field, we also interviewed one of the pioneers of organoid technology, Dr. Hans Clevers [1].

Biomedical research in the first two decades of the twenty-first century was significantly impacted by two novel technologies—induced pluripotent stem cells and CRISPR genome engineering. These two Nobel prize-winning technologies have dramatically changed the landscape and speed of biomedical research. Mankind has obtained the ability to read and easily edit genomes of plants and animals, including that of our own, while we also became able to derive, manipulate, and analyze pluripotent stem cells and their derivatives from every individual, representing an unprecedented opportunity and momentum for the advancement of medical science and clinical research in the history of our species. In spite of all its scientific and technological advances, our civilization has also immensely affected the environment, influencing the fate and future of all species on this planet including our own. So far, members of other species, i.e., model organisms, have been utilized for studying various aspects of development and disease and had in the most cases to be sacrificed in large numbers while striving to gain novel insights into our own biology and pathology. Now, stem cell biologists have managed to create organoid technology, which can potentially replace or at least reduce the use of animals, while enabling us to study human biology directly, utilizing human materials and establishing human-specific models of development and disease. This revolutionary technology has hence the capacity to transform the entire field of biomedical research, but even after a decade of progress, it is surprisingly still not widely used and not fully available in many laboratories around the globe. Besides the prowess and promise of organoid technology to advance basic and medical research, it has also begun to challenge our traditional views and thoughts on human consciousness and life, necessitating ethical, philosophical, and societal discussions and debates.

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In this special issue, we have introduced different organoid model systems and highlighted their applications and impacts on basic life science and medical research. Organoids can be derived either directly from tissue-resident adult stem cells and developmental progenitors or from embryonic and induced pluripotent stem cells via stepwise in vitro differentiation. Dr. Anne Grapin-Botton and Dr. Jason Spence, together with their respective colleagues, introduce pluripotent stem cell-derived endodermal organoids and focus on organoid model systems capable of reconstituting distinct aspects of human endodermal organ formation [2, 3]. Dr. Ryuji Morizane and his colleagues give an overview on the latest developments on kidney organoids, while Dr. In-Hyun Park and colleagues focus on human brain organoid technology [4, 5]. All of these review articles highlight how pluripotent stem cell-derived organoids can be used to study defined aspects of mouse and human embryonic development.

Dr. Kai Kretzschmar, Dr. Sina Bartfeld, Dr. Margherita Turco, and colleagues cover in this special issue cancer organoids, organoids of the gastrointestinal tract, and organoids of the reproductive tract, respectively [6–8]. Such organoids can be directly isolated and grown from either cancer tissues or adult and fetal tissue-resident stem and progenitor cells. Cancer organoids allow in this context to preserve cancer patient materials as live biobanks, while also providing novel powerful experimental platforms for cancer research. Dr. Bon-Kyoung Koo and colleagues focus on the latest developments in the field of genetic engineering of organoid culture systems [9].

Lastly, Dr. Ali Brivanlou and colleagues discuss the latest developments in the field of human embryo model systems and embryoid research, focusing on the potential philosophical, ethical, and regulatory challenges these and similar organoid-based model systems may pose for the present and future of this rapidly growing field of research [10].

We are hopeful and believe that this special issue will guide other colleagues outside the field to embrace and utilize this new technology and may encourage them to take part in this imminent revolution sweeping the fields of biomedical research and life sciences.

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