Stem Cell Rev and Rep (2017) 13:319–320
DOI 10.1007/s12015-017-9744-2

Special Issue: Organs-on-Chips & 3D–Bioprinting Technologies for Personalized Medicine

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Published online: 24 May 2017

Micro-physiological systems (MPSs) aim to model various diseases, different stages of disease development, immunogenicity, toxicity, while also allowing researchers to develop accurate ADME profiles for the development of safe and effective drug candidates prior to clinical evaluation.

Animal models are among the standard methods for drug development in biotechnology and pharmaceutical industries. Thus, fundamental biological research attributes for the highest number of laboratory animal use worldwide. On the other hand, accumulating evidence shows that the animal studies often misrepresent the human physiology. Low success rates of candidate drug testing in clinical trials prompt for more accurate and reproducible methods for avoiding candidate attrition in the late phases. Moreover, market withdrawals are expensive, time-consuming and on some instances, related to mortalities. Including the drug failures, new successful drugs cost in the range of billion dollars. A more precise, physiologically relevant testing mechanism can decrease the overall losses due to early identification of negative attributes.

Emulation of the human physiological properties undertakes the in-vitro implementation of biological situations, functions and disease processes. Organs-on-chips emulate cell-matrix or cell-cell interactions, signaling and three-dimensional (3D) architecture of human organs. These systems mimic the micro-architecture of tissues and organs by recapitulating the individual characteristics of tissue identity and function. Hence, pathophysiological conditions emulated in the chip setting can provide unprecedented insight on both the intricate nature of diseases and their treatments.

Organ-on-a-chip systems emulate human biology at the smallest scale by using dynamic fluid flow to produce nutrition, oxygenation with tissue-specific environmental cues and molecular gradients. With microfluidic systems, environmental physical factors such as pH, temperature, oxygen concentration and humidity are controllable. Several tissue-specific cues such as, air, cerebral fluid or blood flow, physical pressure, shear stress, peristaltic movements or strains can be simulated. Tissue–specific electro-mechano-biochemical signals can be emulated by using miniaturized actuators. Moreover, the response from "micro-tissue constructs" is traceable in real-time. These tunable systems will eventually allow for the development of reproducible, high-throughput results.

This special issue of *Stem Cell Reviews and Reports* brings together some of the prominent teams furthering the field of organ-on-chip technologies. Review papers discuss an array of model systems ranging from cancer screening, liver, heart, cornea, skin, bone, gut and neurological models for healthy and diseased organs. Park et al. bring together the advancements and shortcomings of in-vitro and ex-vivo models for the gastrointestinal system [1]. These systems elucidate the host-gut microbiome crosstalk in health and disease conditions. Conant et al. review the advances and challenges in heart-on-a-chip models, presenting perspective on tools for assessing drug-induced cardiotoxicity and discuss ways of realizing the full potential of these systems [2]. Carvalho et al. delve on 3D drug screening approaches involving bioengineered tumors for the treatment of cancer types, complementing the NCI60 panel through tissue engineering [3]. Relating to the same area, Khazali et al. discuss human micrometastases investigating all-human 3D ex-vivo liver-on-a-chip system [4], while also examining the aspects of human

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liver modeling. Haring et al. review the novel design methodologies and manufacturing processes of human microphysiological neural systems that model neurological diseases, disorders and injuries [5]. Their work underlines the emerging revolutionary aspect of brain and neural MPSs for the field of personalized medicine. Arrigoni et al.'s work covers the 3D bioprinting approach for the development of personalized bone grafts and manufacturing of bone-on-a-chip systems for personalized treatments [6]. Van den Broek et al. discuss state-of-the-art of in-vitro skin models, remarking the potential use of induced pluripotent stem cells for the generation of skin-on-a-chip technologies for developing physiologically relevant healthy and diseased skin models [7]. Lastly Prina et al. explore the innovations in the use of 3D–microfabricated scaffolds and microfluidic devices [8]. The work mentions the advancements in 3D–microfabrication technique, while also addressing clinical application of corneal substitutes and corneal models for in-vitro evaluations.

As the guest editor of the special issue entitled "*Organs-on-Chips & 3D-Bioprinting Technologies for Personalized Medicine*", I thank the contributors for their valuable time and for submitting such review papers of high quality. I deeply appreciate the supports of Dr. Kursad Turksen, the former Editor in Chief, and Dr. Mariusz Z. Ratajczak, the current Editor in Chief for their continuing efforts for the realization of this much-needed special issue.

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