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Stem Cell Research 2019: Stem cell based human on a chip models for drug efficacy safety and precision medicine_ John W Rumsey_ Hesperos, Inc., USA

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The utilization of humanon- a-chip (HoaC) systems for compound efficacy and safety testing which could ultimately lead to precision, personalized medicine is a topic that has recently received much attention. Of critical importance to the development of these systems is the incorporation of organ modules derived from human stem cells. Stem cells provide an inexhaustible source of cells that can be differentiated in multiple lineages with induced pluripotent stem cells (iPSCs) serving as the benchmark for personalized medicine. Key characteristics needed for these systems are the ability for organ-to-organ communication in a serum-free recirculating medium, and incorporation of induced pluripotent stem cells that allow for understanding individuals' genetic variation and for construction of systems using diseased patients' cells. Additionally, real-time monitoring of organ health and physiology using noninvasive, functional readouts is a desirable system characteristic for repeat dose or chronic drug treatment programs. Currently, these are only possible using animal models or human clinical trials. Hesperos has constructed stem cell-based, human body-on-a-chip systems demonstrating physiological responses to compounds in configurations of up to five organs. System configurations have included stem cell-derived cardiomyocytes, skeletal muscle myotubes, brain micro vascular endothelial cells, motoneurons, sensory neurons and cortical neurons. Acute and chronic compound testing in our HoaC systems (>28days) has generated responses similar to those seen in clinical data or reports in the literature.

Mechanistic studies, on the other hand, aimed to recreate the clinical image of human DM in animal models. A translation to human biology is, however, often inadequate due to significant differences between animal and human physiology, including the regulation of species-specific glucose. Thus, there is an urgent need to develop advanced human in vitro models with the potential to identify new treatment options for DM. This review provides an overview of technological advances in DM-relevant stem cell research and their integration into microphysiological environments provided by organ-to-chip technology.

Organ-on-a-chip (OOC) is a burgeoning technology with the potential to revolutionize disease modeling, drug discovery and toxicological research by enhancing the relevance of crop-based models while reducing costly animal studies. While OOC models may incorporate a variety of tissue sources, the most robust and relevant OOC models in the future will include stem cells. In this review, we will highlight the benefits of stem cells as a tissue source while taking into account current limitations to their full and effective implementation in OOC models.

This different rate of lung development results in a greater degree of branching and complexity of human distal lung structures, including respiratory bronchioles, alveolator ducts and associated alveoli [9]. The cell composition also differs between the mouse and the human lung. For example, in the airways of mice, mucus-producing cup cells are rare and secretive club cells (formerly called Clara cells) are abundant, while the opposite applies to human airways [10]. In addition, many genetic mutations induce different respiratory symptoms, if any, in mice compared to humans [11]. Although rodents remain the primary animal model for preclinical studies, other non-rodent species such as guinea pigs, dogs, sheep, pigs and non-human primates that more closely mimic human pulmonary physiology are also used in preclinical studies.

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