CONCEPT CLEARANCE RECORD
FY 2016 RESEARCH INITIATIVE – NCATS

TITLE: 3-D Bioprinting of Human Live Tissues for Drug Screening

OBJECTIVE(S): To generate architecturally defined human tissues that closely resemble *in vivo* human tissues for drug screening by integrating groundbreaking tissue bioengineering, 3-D printing, cell development, stem cell and disease biology, and noninvasive detection technologies.

DESCRIPTION: Bioprinting of architecturally defined and physiologically relevant human live tissues is emerging as a key enabling technology for drug discovery. 3-D bioprinting of human live tissues has the potential to accelerate the drug discovery process, enabling treatments to be developed faster and at a lower cost by bridging the predictability gap between *in vitro* and *in vivo* assays and positive clinical outcomes. Bioprinting integrates advances in tissue engineering technologies and cell biology with the development of 3-D bioprinters, biocompatible polymers and hydrogels, and noninvasive methods to validate the morphology and function of human tissues. Functional tissues assembled by bioprinting of autologous human cells derived from induced pluripotent stem cells (iPSCs) on biodegradable polymers hold the promise of providing functional and physiologically disease-relevant assay platforms to bridge the gaps between the current simplistic *in vitro* cell assays, non-predictive *in vivo* animal models and human clinical trials by building native tissues derived from human stem cells in which to test small molecules during drug discovery.

This program will create the infrastructure necessary to enable 3-D bioprinting for the fabrication of tissues at NCATS and to establish collaborations with the research community to advance and disseminate its use for drug discovery. The program will include identifying and engaging key engineering and scientific personnel; evaluating and purchasing 3-D bioprinters; developing tissue- and organ-specific cell systems (iPSCs); testing biopolymers, hydrogels and cell-culturing conditions for each tissue developed; and evaluating technologies to characterize the architecture and physiology of the fabricated tissues. Reproducible and robust methodologies will be developed, optimized and validated using the on-going skin and retinal cell systems. Routine printing of live human tissues for drug development applications with well-characterized protocols and procedures developed at the Center will be expanded to additional tissues and organ systems. We also envision a grant mechanism to provide funding to collaborators to help in the morphological and genomic characterization of tissues and protocols for the generation and differentiation of iPSCs to relevant tissue cells.

IMPORTANCE: The major reason for the low success rate in drug development is the lack of efficacy in clinical trials. This failure in the late stages of clinical development is in large part due to the use of simplistic *in vitro* cell assays and non-predictive *in vivo* animal models during the drug discovery and development process. 3-D bioprinting of human live tissues derived from human stem cells is expected to provide data that are more relevant to the whole body response than traditional studies with two-dimensional cell cultures.

HISTORY: Technologies that enable tissue engineering to bridge the gap between *in vitro* and *in vivo* systems have grown rapidly in recent years. However, rapid, scalable and reliable fabrication of architecturally and physiologically defined functional human tissues still remains a challenge that bioprinting promises to address by integrating five recently emerging technologies:

1. 3-D bioprinters are now available with precise XYZ to reproducibly fabricate tissues with defined 3-D geometries.

2. Biomaterials and biocompatible hydrogels are being developed to support the 3-D structures of cell-embedded tissue.
3. Bioreactors are now being designed that enable the delivery of mechanical and chemical cues to the cells seeded in the printed tissue.
4. It is also now possible to obtain autologous cells from patients using human iPSCs.
5. It is now possible to use noninvasive technologies such as high-resolution fluorescence microscopy and histology techniques to quantitatively characterize the morphology and functionality of printed tissues.

Therefore, we believe now is the right time to implement 3-D bioprinting of live human tissues at NCATS to systematically develop robust assays for drug screening of different disease tissues and to disseminate the know-how to the scientific community.

PROJECT/PROGRAM OFFICER:
Samuel G. Michael
Acting Chief Information Officer
Director, Automation and Compound Management
Phone: 301-217-5741
E-mail: michaelsg@mail.nih.gov