

Human-on-a-Chip Technologies as the Next Generation Drug Screening Platforms

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Understanding tissue function and the physiology of complex living organs and the impact of pharmaceuticals both in effectiveness and safety are significant challenges. Organs are composed of multiple types of interdependent tissues in a dynamic microenvironment that includes biochemical transportation, signaling networks, and biomechanics. However, most studies to discover and screen drugs rely heavily on analysis of cells and tissues grown on 2-D static culture models with further *in vivo* testing in animal models. Though useful in terms of accessibility, 2-D models rarely mimic the *in vivo* microenvironment and, therefore, are not the best approach to provide sufficient biological knowledge to evaluate drugs for organ-specific physiology. Animal studies are normally expensive and involve ethical issues. A number of drug candidates fail in animal/preclinical trials due to toxicity and are withdrawn because of adverse drug effects. Accurate prediction of drug behavior in human specific biology is the key factor to find better models to test drugs.

3D cell culture models that mimic *in vivo* scaffold microenvironments with Extracellular Matrix (ECM) coating, fluidic mass transportation, differentiable cell/tissue functions, multiple cell seeding, and specific-organ function are often termed organ-on-chip technologies [1,2]. These techniques hold great promise as better models in studying the effectiveness of drugs and their metabolism. 3D culture models can represent better *in vivo* environments than classic 2D cell/tissue culture models in terms of oxygen and nutrient transport, flow-induced shear stress, mechanical strain/stress, ECMs structure, cell-to-cell communication, intracellular signaling network, tissue to tissue interaction, differentiation, and specific organ function. Maturation of organ-on-chip technology will eventually reduce the need for animal studies and will help expedite new drug discovery. Furthermore, association of successful 3D cultures will result in human on-chip studies and may prove to be the ultimate model for testing pharmaceuticals and for the development of patient specific therapeutics.

With the advance of nanomedicine technology, scientists face a new realm in biotherapeutics and drug development that includes vaccines, antibodies, gene therapies and nanoparticles such as liposomes,

polymeric micelles, nanoparticles, dendrimers, and nanocrystals for drug delivery and contrast agents. The large numbers of biotherapeutics and drugs that have been developed during the last decade tax the current system for preclinical tests to screen and optimize the concentration. The need for streamlined systems that mimic human function is further necessitated. Organs-on-chips that can mimic the *in vivo* environment can be a cost-effective way to study the toxicity and biocompatibility for specific organ function. Furthermore, organs-on-chips can also be used to mimic disease models. The effectiveness of drugs and efficiency for targeting drugs to a specific location can be evaluated.

Some organs, for example, liver, lung, and kidney, have been designed as chips but many challenges still remain [1-3]. 3D organ models are still in the initial stages of realizing human organ function by combining all *in vivo* physiological environments. Furthermore, diseases-on-chips studies are still far away from the goal in which drug response can be predicted much less to customize medicine for patients. However, the potential of 3D cell culture and human-on-chip pursuits to better and more rapidly determine the efficacy and safety of pharmaceuticals and nanomedicine applications with a reduction in the use of animal models is foreseeable. The near future will see great advances in the area of human-on-a-chip technologies.

Acknowledgment

This research was partially supported by BAA11-001 Long Range Board Agency for Navy and Marine Corps Science and Technology Program, Engineering Research Center for Revolutionizing Metallic Biomaterials (NSF-0812348) from National Science Foundation, and the Korean Small and Medium Business Administration (Project no.00042172-1).

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Received April 17, 2012; Accepted April 18, 2012; Published April 20, 2012

Citation: Yun Y, Lee S, Collins B, Gomez FA, Sankar J (2012) Human-on-a-Chip Technologies as the Next Generation Drug Screening Platforms. J Nanomedic Biotherapeu Discover 2:e113. doi:10.4172/2155-983X.1000e113

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