Organs-on-Chips

Technology Summary

Pharmaceutical companies rely on the use of expensive, time-consuming, and controversial animal testing to validate their test compounds and drugs, but these studies often fail to predict results obtained in human clinical trials and in patients. Scientists have worked for years to create alternatives to animal testing, but with little success. The team at the Wyss Institute have used microfabrication techniques first developed for the computer microchip industry to engineer functional human organs-on-chips that provide a novel alternative to conventional cell culture and animal models for drug discovery development applications, as well as for testing of chemicals, toxins, and cosmetics.

The paradigm-shifting paper in Science 2010, entitled “Reconstituting Organ-Level Lung Functions on-a-Chip”, received world-wide attention and has garnered the interest from multiple leading pharmaceutical companies as well as funding from the U.S. Food and Drug Administration. The Lung-on-a-Chip combines modern tissue engineering with cultured human cells to mimic the structure and functions of a living, breathing human lung on a clear, flexible microchip. The chip contains parallel microfluidic channels separated by a porous membrane with human lung air sac cells on one side and human lung capillary cells on the other. Air is flowed over the top and the lower side is exposed to flowing nutrient medium containing human white blood cells while cyclical stretching forces are applied to both cell layers to mimic physiological breathing motions. This simple microdevice recapitulates human lung responses to infection, inflammation, environmental toxins, and drugs delivered to the blood side of the chip or by aerosol to the air-side. The chip also has been modified to model complex human diseases, such as chemotherapy-induced pulmonary edema, furthermore, predictions obtained using the lung chip have been confirmed in animal models.

The Wyss team also recently developed a human gut-on-a-chip inhabited by bacteria (mimicking the environment of the intestine) that experiences intestinal peristalsis-like motions and flow. The team is now extending this approach to develop a growing pipeline of Organ Chips (e.g., beating Heart-on-a-chip, metabolic Liver-on-a-Chip, peristaltic Gut-on-a-Chip, regenerative bone marrow-on-a-chip) and to link them together to predict the responses of a multi-organ system. An automated instrument for multi-organ integration and analysis of clinically relevant read-outs that can be extrapolated to predict human responses is also currently under development.

Market Opportunity

The current model for drug discovery and development is ineffective, and in recent years, increased financial stress, dwindling pipelines, and persistent failures in the clinic have created a critical need for better and more
predictive research tools for drug discovery applications. Socio-economic pressures, ethical concerns and new regulatory requirements are also driving the need to find replacements for animal models.

Despite significant reductions in R&D investments, the pharmaceutical industry has seen a strong shift towards cell-based in vitro assays with $2.6 billion spent in 2009 and an 18% growth in 2010 alone. This market is expected to continue to rapidly expand over the next decade. *(Visiongain Report: Cell-Based Assay - World Market Prospects 2011-2026)*. However, conventional in vitro models are seldom being used to drive key decisions during the drug discovery and development process because these models fail to maintain cell function, do not exhibit organ-level functions, lack predictive value, and hence, they are not meeting the needs of the industry.

Organs-on-Chips containing functional human cells organized within physiological microenvironments offer new and promising capabilities for the pharmaceutical and biotechnology industries. The technology is designed to generate high impact, human relevant, predictive data during critical stages of the drug discovery process that will help drive key decisions and prioritize drug candidates for clinical development. This is not intended to be a high throughput platform but rather a high content high impact, and hence, high value technology. Organs-on-Chips also offer the opportunity to engineer human disease models to help elucidate disease mechanisms and to identify and validate novel drug targets. In addition, this technology offers the opportunity to identify novel human biomarkers of efficacy and safety that can be used from preclinical research to clinical applications. This technology has the potential to utterly transform the way in which we do drug discovery and development by providing more predictive tools that can be applied across the entire process from early discovery, target identification, and target validation, to lead optimization, in addition to providing tools to better design regulatory studies and clinical trials.

The Organs-on-Chips technology has a broad market opportunity that reaches beyond the pharmaceutical industry to include the chemical and nanotechnology industries (safety testing, risk assessment); cosmetics industry (toxicity and efficacy testing); animal health industry (efficacy models and safety testing); government agencies such as EPA (environmental toxicity testing and risk assessment), the FDA (advancing regulatory sciences); defense (rapid testing of efficacy and safety for biological, chemical and radiation countermeasures); armed forces (field applications for assessing exposure); as well as stem cell companies and regenerative medicine companies seeking to address shortfall in cell functions and utility of conventional culture systems. Establishment of an in-house integrated human organ chip platform will also likely lead to identification of new drug targets, and thus possibly result in the discovery of proprietary novel therapeutics or re-purposing of existing drugs.

**Intellectual Property**

The Wyss Institute holds a strong intellectual property (IP) portfolio on the organs-chip technology with multiple US/International patents filed.

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