

Body on Chip-A Distant Dream or an Emerging Reality?



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Opinion

We are currently facing a global health challenge regarding the way we discover and develop new drugs. Small biotech companies, as well as large pharmaceutical corporations, spend increasingly more money on the classical route of drug development, and it fails more often than it succeeds. Consequently, some diseases are not being treated and patients who are in dire need of new therapies are not receiving them. The classic tools available for testing whether a drug will work efficiently and safely or fail before we reach advanced stages of human clinical trials and spend millions of dollars, do not predict in a robust way. The realization that our bodily cells are dynamic organisms under constant mechanical stress and movement emphasizes the notion, although not new, that cell cultures in 2D Petri dishes for cancer research do not fully reflect their *in-vivo* microenvironment [1-3]. In addition, current drug research still depends largely on time-consuming and costly animal studies that often fail to predict human trial efficacy and toxicity [4]; and that raise ethical questions regarding the sacrifice of experimental animals. These issues pose major challenges to the development of experimental research using the *in-vitro* model. An emerging field, with high potential, which could bridge the abovementioned gaps, is microfluidics technology-organ-on-a-chip. Microfluidics technology enables the manipulation of fluid flow at the microscopic scale. The capability to use small volumes of samples and reagents flowing through specially designed micro-channels embedded into a chip provides a new and improved platform for wide areas of research, ranging from physics, through chemistry and biology [5,6].

To achieve a reliable tool that will demonstrate the complexity of the *in vivo* microenvironment, living organs or cancerous biopsies, we need a system that will replicate the main key functions of living organs. Organ-on-a-chip are micro-engineered devices that biomimic the smallest unit that represents the function, biochemistry and the mechanical cell strain of various living organs: the lungs, liver, and brain; and even tumors are represented on a

chip [7-11]. This microchip provides a powerful scientific tool for simulating and advancing research in a 3D way, improving tissue spatial organization and enhancing cell to cell and cell to matrix interactions under a continuous flow. The chips are prepared under a meticulous manufacturing process with special materials and polymer mixtures, usually from polydimethylsiloxane (PDMS) [12]. Other bio-engineered microstructures are incorporated, thus enabling expansion and contraction of the chips such that cells experience a dynamic environment, both with other cell types and mechanically, similar to their being in the human body [13]. The design of a versatile multi-organ chip could facilitate the investigation and monitoring of potential side effects, and the testing of various drug concentrations, not only on the specific target cells but also on other cells incorporated in the tissue parenchyma. Furthermore, industries such as chemicals and cosmetics are facing similar challenges in trying to develop improved *in vitro* methods for more predictive clinical outcomes, on one hand; and powerful technology for achieving complex encapsulations and precision particle morphologies, on the other hand [14-16]. Alongside the remarkable technological leverage and advantages of a well-mimicked environment and acceleration of research, the use of microfluidic devices is not without limitations. It requires particular equipment that is mostly not portable and calibration of the flow system. In addition, optimization of a chip with a specific design requires special training and a long fabrication process. Further, the devices may clog, either by unstable movements of the worktop platform or by various debris; and requires specialized cleaning procedures to overcome such.

Research in microfluidics technology has grown exponentially over the past decade. Although well studied, technologies for organ-on-a-chip have yet to be comprehensively adapted by the pharmaceutical industry; and most preclinical analyses and experimental data prior to scaling up is still mostly performed using classical techniques. One of the aspects to be considered is how or

whether the regulation authorities should confirm microfluidic testing as a component of the pre-clinical data that pharmaceutical companies are obligated to report. We trust that in the present golden technological era, new upcoming innovative technologies, such as the revolution of 3D-printing, will minimize barriers of manufacturing and costs, and will enable a simple, improved and automated process for microfluidic device fabrication, characterized by higher resolution and an improved throughput process [17-19]. A tumor on a chip is no longer a distant dream. Indeed, several research centers around the globe have acquired “plug and play” microfluidic kits that enable acceleration of their research and more efficient testing of their pipeline molecules for new cancer treatments. The benefit is especially high when the components of the tumor niche are incorporated along with cancer cells [2,20]. Overall, a miniature bio-engineered chip can contribute to the understanding and exploration of drug effects, disease-causing pathogens and other potentially harmful materials, on the human body. The expected outcome is sophisticated physiologically-relevant *in-vitro* assays, in which drug molecules can be tested faster thus reducing unnecessary preclinical animal testing and potentially minimizing failures in clinical investigations. In the long run, besides preclinical testing, organ-on-a-chip technology could help break the glass ceiling of personalized medicine [21-23], by enabling researchers to individualize medical treatments using patients' own cells.

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