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EDITORIAL

Generation of *In vitro* Multicellular Human: A Perspective of the 3D Cell Culturing Approach

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SUMMARY

Organs-on-the-chips are microfluidic channels based micro-engineered systems which are lined by alive human or animal cells to develop integrated micro-organs or *in vitro* multicellular organisms which can be used to understand the efficacy and toxicity of drugs and also are being customized to generate disease models *in vitro*.
Keywords: 3D cell culturing, Organ-on-a-chip, Human-on-a-chip, *In vitro* multicellular organism, Microfluidics

3D cell culturing is an extra cellular matrix (ECM) based artificially-created environment where cells can enhance their interactions in all three dimensions like an *in vivo* environment. This method has achieved much more attention in last few years and technologies such as microfabrication and microfluidics have resulted in the creation of a kind of mechanical living microenvironment where cells can recapitulate to have increased tissue-tissue interactions and can act like a part of living organ. This advanced form of 3D multi-channeled culturing system which is acting like the *in vivo* physiology of tissue in an organ specific context is termed 'organs-on-the-chips' [1]. These organs-on-a-chip (OC) have been created to increase the cellular interactions and to maintain the mechanics and physiology of tissues and organs. These OCs have also been named as *in vitro* multicellular organisms and this achievement was termed as development out of imagination which will abolish the requirements of animals to be used in laboratory and even by developing *in vitro* human will help to test the efficiency of drugs and toxin developed by scientists. The microfluidics used in these organs-on-chips are developed for efficient distribution and transportation of nutrients all over the living organism *in vitro*. These models of living organs are next generation of models to study biological properties, mechanical characteristics and gene and protein expression while working *in vitro* [2].

There are many examples of organs-on-a-chips such as (1) Lung-on-a-chips, (2) Heart-on-a-chip, (3) Kidney-on-a-chip, (4) Artery-on-a-chip, (5) Human-on-a-chip (culturing multiple organs in a single chip) etc. and few of them are explained briefly here.

Lung-on-a-chip: It is a kind of alveolar-capillary interface model *in vitro* on a fabricated microdevice which is designed in such a way that it exhibits the similar structural, functional and mechanical

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characteristics to the human alveolar-capillary interface. In this model, a microfluidic platform has been used to create an air-interface in a dynamic system [3].

Heart-on-a-chip: It is a microfluidic substrate base model which is mimicked for contractility and electrophysiological responses *in vitro*. For this purpose, a hybrid chip containing fabricated microfludic network in silicon elastomer with electrodes (PDMS microchambers) has been built and then aligned with sensors. Single cells (cardiomyocytes) are trapped in the PDMS microchambers via pressure gradients and stimulating electrodes have been used to monitor cardiomyocytes metabolism electrochemically and optically after when they were perfectly maintained in the microchamber [4].

A number of successful reports have been published in last few years and resulted in the generation of lung-on-a-chip, heart-on-a-chip, kidney-on-a-chip, artery-on-a-chip and etc. Now scientists are working on the multiple organ culturing on a single chip terming it human-on-a-chip and reports have been published by MIT and Harvard University in the current years [5, 6]. Organ-on-a-chip is facing currently several challenges in fabrication and microengineering, arising questions on the molecular and supramolecular level of efficiency and attempts are made to generate precise and problem free microchips [7]. Growing trend of microchip technologies has resulted in the generation of devices to integrate multiple organs on a single chip to study the correlation among them taking scientists to develop a body-on-a-chip or human-on-a-chip in future. Number of chips like AngioChip™ have been developed in this regard [8]. Authorities are interested in approving such kind of chips to test drug efficacy or modelling diseases [9]. All these developments are showing the future of translational life science research and development of an *in vitro* human-on-a-chip which would be used to screen drugs *in vitro* and model diseases.

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