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Organ–on–Chip: Emerging Trends in Biomedical Engineering

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Abstract:*The study of an organ – On – Chip (OC) is a multi channel 3-D micro-fluidic cell culture chip which stimulates the mechanism, and physiological response activities of entire organ system in a human body. The convergence and development of this matter in to an electronic device/ chip is a matter of significant biomedical engineering research. The convergence of lab – on- chip (LOCs) and cell biology has permitted to the study of human physiology and introducing a novel model study of in –vitro multi cellular human organism. The Organ – on – chip is small micro-fluidic devices with hollow channels lined by living human cells. They have several properties to make them more realistic models of human organ system of lab grown cells. In organ – on – chips, the human cells are cultured with hollow channels through nutrient liquid flows. This technology allows researchers to alter the mix of chemical compounds that the cells encounter, as well as fluid shear forces that can influence the cell activities. A lab on a chip is a device that integrates one or several laboratory functions on a single chip that deals with handling particles n hollow micro-fluidic channels. The advantage in handling particles at such a small scale include lowering fluid volume at a low cost and less waste and increase portability of the devices, increasing control due to quicker thermo-chemical reactions and decreasing fabrication cost. The development of 3-D cell culture system are more successful due to the flexibility of the ECm gels accommodate shape change and cell to cell function i.e. cell binding and also include tissues – to-tissue interfaces e.g., epithelium and vascular endothelium, chemical gradient and mechanical active micro environments. Presently, researchers are working on a building of a multichannel- 3- D micro fluidic cell culture system in which 3-D cellular aggregate re cultured to mimic multiple organs in the body. The goal of the development of human tissue chip " Organ – On – Chip" is that stimulate the structure and function of human organ e.g., liver, lungs, kidney, heart etc. This approach to be more effective to cure such tissues rapidly and cost effective than those currently available to test drug candidates and also predicts their safety measures.*

Keywords:*Biomedical, electronic, organ-on-chip, nephron, physiology*

I. Introduction

In an ancient period of life, the drug development and the treatment procedure of any type of disease or metabolic problem was a major task. Slowly slowly (chronically) the development of any type of drug(may be synthesized or herbal formulation) were depend on the animal models, in vivo data obtained authentically that would predict the human pharmacokinetic response as well as physiological changes. These data were only few certain animal system. However, these experiments are lengthy, expensive, cost effective and even few may be controversial. It was more often subjected/ to chemical/ mechanical techniques that simulate the human injuries. [1]. The animal models are offer very limited control value to harvest specific information.

Therefore a mimicking human physiological response (MHPR) in an in-vitro model needs to more affordable and to offer the cellular level control in biological experiment, biometric micro fluidic system could replace the animal model testing. The development of MEMS – based biochip electronically in biomedical engineering, reproduce a complex organ – level of pathological/ physiological responses could revolutionize many engineering field including toxicology, as well as pharmaceuticals/cosmetic developmental process that rely on animals testing and clinical trial. [2-3].

Recently, physiological/ meta-biological based perfusion in – vitro system have been developed to provide a cell culture system which are closely related to in- vivo model assay. It is based on multi-compartmental perfuse system and provide us a remarkable interest in pharmacology as well as toxicology by electronic engineering techniques. Its aim to provide an authentic cell culture process/ techniques close to the in – vivo situation to reproduce more reliably in vivo mechanisms i.e. absorption, distribution, metabolism and elimination (ADME).

Efforts made towards the development of micro- fabricated cell culture that aim to develop a models that replicate the aspect of human bodies as closely as possible and give an example which demonstrate the potential use in drug development. Multi compartment based devices are physical representation of physiological based pharmacokinetic (PBPK) model which represent the mass infrastructure of compound in compartmental model of mammalian body which may contribute the drug development in nature.

The development of multi compartment micro fluidic devices in a laboratory integrates several laboratory functions as a single chip. The advantage of such a small scale device include lowering fluid volume i.e. lowering reagent cost, less waste and increasing portability of the devices and also increasing process control due to quicker thermo- chemical reaction. The laboratory development device is a chip develops on cell culture process for an organ/ tissue activities similar to the human body also called Organ – On – Chip (OC).

Organ – on – Chip (OC) are small hollow channels lined by living human cells. These cells are cultured with in hollow channels through nutrient fluid. Moreover, these cells are arranged in devices to mimic key structural features of the internal matters architecturally of the organs. Such mechanical forces provide cues that are critical for cellular function e.g., the contraction of the gut wall as wave like during peristalsis turn out to be crucial for intestinal functions. As together with, these properties of organs on chip allow researchers to analyze dynamic interaction between cells and drug can normally measured in living animals.

II. Work Done

A gut on a chip developed by Ingber's teams enables cultured human intestinal cells to regenerates into a specialized tissue that looked and functioned like human small intestine. In the device, the cultured cells are stretched and release to mimic the forces they had experience over the tissue as it does in the human gut.

Later on, Ingber Kim and their colleagues at Wyss Institute first reported the gut on a chip in 2011, that the devices life like condition. In this device the cells are spontaneously arranged themselves into finger like projections called with normally present s in living intestine which produce mucus and increase of cytochrom p450 can enzyme that break down as drugs.

Later, on Kevin Kit Parker and his team worker developed a device i.e heart -on –a-chip which is very useful to estimate the toxicity of drug to the heart .it excreta enzymes critical to transmitting the electrical signals that central the heartbeat similarly .in this devices, the cells line up in parallel as in the wall of a real heart and co-ordinate their efforts to beat as one.

Similarly ,the different scientist at Wyss Institute models Ingber, Kyung-Jin-Jang develop the kidney as Kidney-on-a-chip in which cell grew from a portion of a healthy human kidney called proximal tubule on a porous membrane in a device as similar structure seen in living kidneys including with hair like projection i.e., cilia.This work organ-on-a chip as done by Inber' and Parker ,was funded by Wyss Institute for Biologically Inspired Engineering at Haward University, the Defence Advanced Research project Agency, National Institute of Health, National of Environmental health etc.

A reported design of a heart as-a-chip claims to have built an efficient means of measuring structure & functional relationship in constructs that replicate the hierarchical tissue structure of laminar cardiac muscles [4]. This chip determine the alignment of myocytes in the contractile apparatus made of cardiac tissue and gene expression profile which contribute the force to produced in cardiac contractility. A micro fluid disease has already contribution to in vitro experiment on cardiomyocytes, which generate the electrical impulses and central the heart rate [5]. This chip (heart –on-a-chip) is a biohybrid; an engineering anisotropic ventricular myocardium is an elastromeric thin film. The design process of this micro fluidic chip entails first covering the edges of a glass surface with any protective film such as to contour the substrate desire shape.

In this chip, researchers have developed a co-relation between tissue stress and the radius of curvature of the muscular thin film (MTF) strips during the contractile cycles, validating the demonstrated chip as a heart –on-a –chip. i.e a platform for quantification of stress, electrophysiology and cellular structure [4-6].

Generally, in human beings heart problem a survey report of 2003 from National Health Nutrition examine a major non diabetic person ,CV D are often cause due the structural &functional changes in small blood vessels [7]. In this regard a chip & devices has developed for artery function –on-a-chip) to screens for a drug development trial based. Held a comprehensive understanding of the Underlying mechanism behind Pathological change in small arteries and develop better treatment strategies. Devices could potentially help in the assessment of a patient's micro vascular status in a clinical medicine [8].

The artery –on-a-chip is designed for reversible implantation of the sample. The device contains a micro channel network, an artery loading area and separate artery inspection area. The micro channel area used for loadings the artery segment, and also used as a perfusion channel to replicate the process of nutritive delivery of arterial blood to capillary bed in the biological tissue [9]. As another pair of micro channel serves to fix the two ends of the arterial segment and last pair of micro channels used to provide super fusion. However, in order to maintain the metabolic and physiological activities, a thermo electric heater and thermo resistor are connected to the chips which maintain the physiological temperatures at the artery in this design.

Similarly, a chip was developed for nephron – on- chip. This research is striving to bring transportability, wear ability and implantation capability through micro fluidic miniaturization and nanotechnology [10]. The nephron is the functional unite of the kidney and composed of organ – on- chip claims a bio artificial device that replicates the function of nephron, glomerulus, proximal tubules and loop of Henle. In this process, each part of the device has unique design. The device is design for the entering blood sample and

glomerulus section of the nephron, the membrane allow certain blood particles through its wall of capillary cells, composed by the endothelium, basement membrane and epithelial podocytes. The fluid that is filtered from capillary blood into Bowman's space i.e. primary urine. And in tubules section some substances added to the filtrate as part of urine formation. At last this device developed is just function similar to kidney as focus to recapitulate the real physiology in 3D. This study demonstrates the beneficial potential to mimic renal physiology for regenerative medicine and drug screening.

III. Conclusion

The goal into develop of human on chip i.e. organ on chip (OC) that stimulate the structure and function of human organs such as heart, kidney, liver and lungs. Researchers/scientist could then use this organ chip i.e., tissue (cell culture device in vitro) to test drug/compounds in vitro and predict their safety before next step of human drug studies. This approach is more rapid economic that those currently available. The OC may after more accurate predictions if the side effects of potential therapeutic agents because they contain human cells. These bioengineering devices as design 3-dimensional (3D) cellular micro system will produce relevant physiological function and will reflect the complexity and diversity of living organs including genetic difference and disease complexity and also pharmological responses.

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