# Chapter 1
# Introduction

**Elzbieta Jastrzebska and Zbigniew Brzozka**

Microfluidics is a quite mature technology, but its medical applications for disease diagnosis and personal therapy studies are still insufficient. The usage of the microsystems for such applications should be supported by elaboration of new diagnostic methods/models because the currently applied ones exhibit many drawbacks. One of the biggest disadvantages of in vitro tests on cell cultures is an oversimplified model, i.e., a cell monolayer. Moreover, the existing protocols for in vitro tests consist of many steps, from preparation of biological material for the assay to the final determination, and are time-consuming. Standard methods require the application of the advanced, expensive instruments, and large amounts of expensive reagents. An application of the microanalytical devices for this purpose seems to be a promising approach/solution to all mentioned problems, and it can increase the experimental throughput.

The development of the microdevices allows for research carried out with three-dimensional (3D) biological model, for example, multicellular spheroids. The 3D arrangement is the factor that affects the cellular phenotype in vivo, including cellular interactions with other cell types, other systemic factors, and extracellular matrix. In situation when there are no other cells, which they could interact with or communicate, cells cultured in vitro do not behave in the same way as components of organs. In a cell monolayer, there is a lack of essential interactions present in vivo, i.e., 3D structure, direct cell-to-cell junctions, or paracrine signaling, which cause the inability of referring results obtained to the drug effect on living organism. Experiments performed on 3D biological model would be more reliable and more similar to the in vivo conditions than those carried out with cells culture in a form of monolayer.

E. Jastrzebska · Z. Brzozka (✉)
The Chair of Medical Biotechnology, Faculty of Chemistry,
Warsaw University of Technology, Warsaw, Poland
e-mail: brzozka@ch.pw.edu.pl



Z. Brzozka and E. Jastrzebska (eds.), *Cardiac Cell Culture Technologies*,
https://doi.org/10.1007/978-3-319-70685-6_1

The main factors that stimulated the rapid development of the *Lab-on-a-Chip* devices are the economic considerations (reducing the costs of analysis, reagent consumption) and the requirements of the new areas as diagnostics in the patient's home, DNA analysis, rapid screening tests. A close cooperation between interdisciplinary research groups from many areas is essential to develop new microtechnologies, which could be useful in medical diagnostics, clinical chemistry, pharmacology, proteomics, metabolomics, biology, tissue engineering, etc. Miniaturization of the diagnostic tools and devices allows, among other things, the transfer of the complex analysis performed in clinical laboratories to non-laboratory environment. It promotes the introduction and dissemination of the concept of *Point-of-care*. One of the most prominent research fields in modern science is research work concerning the application of the integrated systems *Lab-on-a-Chip* in cell and tissue culture and engineering.

*Organ-on-a-chip* systems, which simulate organ functions, are increasingly developed. Such microfluidic systems are used to investigate cell-cell and cell-extracellular matrix (ECM) interactions as well as to perform cytotoxicity assays of various drugs. Lab-on-a-Chip systems for mimicking of organs such as: liver, skin, lung, kidneys, or breast are presented in the literature. The microsystems used to simulate the vascular system and heart tissue functions (*Heart-on-a-chip* systems) are also fabricated. They play an increasingly important role in biomedical sciences. It results from the fact that cardiovascular diseases (CVDs) are the most frequent causes of death over the world. There are many types of treatments and therapies of heart diseases. However, development of new methods for the improvement of heart functions is still needed. In vivo-like cardiac models created in *Heart-on-a-chip* systems can be used to develop new cardio-therapies. Two approaches of *Heart-on-a-chip* systems are proposed: the microsystems, which mimic a beating heart tissue and the microsystems, which mimic a whole vascular system. The developed microsystems can be used for investigation of cardiac cell processes as well as the elaboration of new therapies for heart failure. The usage of the microsystems for cardiac cell engineering have many benefits resulted from miniaturization, e.g., similar microstructure dimensions to cell dimensions, a laminar flow, high surface-to-volume (SAV) ratio, and effective culture volume (ECV). However, it should be underlined that conditions, which are specific for heart cells can be created in microscale. Features such as: dynamic condition, electrical field, stretching, hydrogels, and nanofibrous are used to mimic a native myocardium. Additionally, heart cell culture in the microsystems is often used to simulate heart diseases and investigate heart regeneration using stem cells (SCs).

Technology of *Lab-on-a-Chip* is an object of interest to companies in the following areas: laboratory diagnostics, pharmaceuticals, biotechnology, nanotechnology, medical devices, biocompatible polymer materials, bioinformatics, and genetic testing. It will also be the object of interest of the companies engaged in programs to discover and develop new drugs and biomarkers, microarray manufacturers and equipment *Lab-on-a-Chip*, antibodies, enzymes and primers, research teams in the following areas: bioinformatics and cancers and clinical practitioners.