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Implications of Three Dimensional Cell Culture in Drug Discovery

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Abstract

According to its numerous advantages in delivering more physiologically appropriate information and more predictive data for in vivo studies, three-dimensional (3D) cell culture techniques have attracted growing interest in drug development and tissue engineering. In this study, the differences between two-dimensional (2D) monolayer culture and three-dimensional (3D) cell culture methods, with a particular emphasis on cell growth conditions, cell proliferation, population, and gene and protein expression patterns.

Keywords: Three-dimensional; Cell culture techniques; Cell proliferation; Gene.

Introduction

Cell-based assays have been a key component of the drug discovery process because they offer a quick, easy, and affordable method to replace expensive and time-consuming large-scale animal testing. Since findings are dependent on cellular reactions to medications, chemicals, and environmental stimuli, the crucial component of this approach is the main element-cultured cells. Most cell-based tests performed to date employ conventional two-dimensional (2D) monolayer cells maintained on flat, inflexible surfaces. Although the traditional 2D cell culture approach has been shown to be useful for cell-based investigations, its limitations are now more well understood. Because the majority of cells in the *in vivo* environment are encircled by Extracellular Matrix (ECM) and other cells in a three-dimensional (3D) manner, 2D cell culture does not sufficiently account for the 3D environment of cells. As a result, 2D cell culture experiments can yield inaccurate and imprecise information about *in vivo* reactions. Currently, the typical process for screening compounds in drug development begins with 2D cell culture-based studies, followed by tests using animal models, and finally, clinical trials [1]. Only 10% of the molecules make it through clinical development successfully. Many pharmaceuticals fall short in clinical trials, notably in phase III, the most expensive stage of clinical research, usually because they don't work or have severe side effects.

Relating 3D cell culture characteristics to the traditional 2D cell culture

In 2D and 3D cultures, growth conditions, cell shape, and population Cells adhere to and develop on a flat surface in conventional 2D monolayer culture. In a monolayer environment, the growth medium may provide uniform amounts of nutrients and growth agents to all of the cells. Necrotic cells are often unattached from the surfaces of the monolayer and are easily eliminated during medium changes; therefore the monolayer is mostly made up of proliferating cells. In 2D culture, cells are often flatter and more spread out than they would be *in vivo*. The aberrant cell shape in 2D culture affects a wide range of physiological functions, including gene and protein expression, cell proliferation, differentiation, and death [2].

As a conclusion, because this model does not sufficiently simulate the *in vivo* milieu, 2D-cultured cells might not behave as they would in the body. Technologies that imitate the topographical characteristics of the ECM, such as nano-patterning, have been researched to enhance cellular behaviour and function in 2D cell culture. The question of whether or whether these modifications to cell function more closely resemble *in vivo* behaviours is currently being researched. The most popular *in vitro* testing system for drug screening is still the conventional 2D cell culture.

Drug discovery using 3D cell cultures

It has been demonstrated that cellular responses to pharmacological treatments in 3D cultures are more comparable to what takes on *in vivo* than in 2D cultures. Studies have shown that cells cultivated in 3D models are more resistant to anticancer medications than cells cultivated in 2D cultures [3]. For instance, paclitaxel therapy reduced ovarian cancer cell survival and proliferation in 3D cultures by 40% or 60% in 3D cell spheroids, but the same treatment resulted in 80% lower cell viability in the 2D cell monolayer. Limited diffusion through the spheroid and hypoxia, which has been demonstrated to activate genes important in cell survival and drug sensitivity, can also be blamed for the enhanced drug resistance in 3D culture. The same chemo resistance that was acquired in 3D spheroids is shown in living things. The stromal cells also had a role in the medication resistance of cancer cells, according to a study that used multicellular 3D growth of liver tumour cells as an *in vitro* model to evaluate anticancer medicines.

By directly adhering to the surface of a biotic or abiotic substrate or by trapping in a biocompatible biopolymer, cells produced in 3D culture can be integrated into a biosensor. The choice of substrate is determined by the cell type and the intended function of the sensor; silicon, glass, or plastic surfaces are typically used in biosensors. The use of luminescent and fluorescent analytical methods is constrained by silicon's lack of optical transparency while having desirable electrical and mechanical characteristics [4].

Commercial wafers come in a broad range of compositions and sizes, and glass provides optical transparency, making it simple to

choose a substrate and observe cellular responses visually using fluorescent reporters and high-resolution imaging equipment. The auto fluorescence of plastics, despite their low cost, and their propensity to absorb water and other solvents might distort the fluorescence signals from the sensor element.

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Conclusion

The advantages of 3D cell culture models over conventional 2D monolayer cultures, including superior cell-cell and cell-ECM interactions as well as cell populations and architectures that closely mirror *in vivo* architecture, are becoming more and clearer. Many different 3D cell culture systems have been developed over the course of the last few years as experimental tools for various types of study. Without a doubt, 3D culture techniques, which connect conventional 2D monolayer cell culture to animal models, show considerable potential for applications in drug discovery, cancer cell biology, stem cell research, and many other cell-based studies and devices.

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