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The Role of Bioreactors in Synthetic Biology

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Introduction

Bioreactors are devices that allow biological and/or biochemical activities to take place under highly monitored and regulated environmental and operational conditions. Bioreactors' high level of repeatability, control, and automation for specific experimental bioprocesses has been critical for their transfer to large-scale applications. Bioreactors are commonly used in industrial fermentation, wastewater treatment, food processing, pharmaceutical manufacture, and recombinant protein synthesis. Tissue engineering is described as the use of engineering and life science ideas and methodologies to build biological replacements that restore, maintain, or improve tissue function. 3D tissue constructions are created in one of the most common methods by combining cells with porous scaffolds, which serve as a template for tissue formation and degradation [1-3].

About the Study

In vitro culture of 3D cell-scaffold constructs under conditions that support efficient cell nutrition, possibly in combination with the application of mechanical forces to direct cellular activity and phenotype, is a critical step toward the development of functional grafts for the treatment of lost or damaged body parts. *In vitro* generation of functioning 3D tissues does not necessarily result in grafts; it can also result in non-implantable structures that can be employed as external organ support devices when a suitable donor is unavailable. Engineered tissues might also serve as dependable model systems, allowing for a better understanding of structure–function correlations in normal and diseased circumstances, as well as potential commercial uses in molecular therapies.

Because of the physicochemical requirements of large cell-masses, the generation of 3D tissues *ex vivo* not only necessitates the development of new biological models rather than those already established for traditional monolayer or micromass cell cultures, but it also poses new technical challenges. We examine the function of bioreactors in processes such as cell seeding of porous scaffolds, feeding of cells in the resultant constructions, and mechanical stimulation of emerging tissues in *ex vivo* creation of 3D tissues based on cells and scaffolds. The management of environmental conditions and the automation of bioprocesses that bioreactors may provide will be given special attention.

These features are essential not only for controlled fundamental studies of 3D tissue development but also to reduce manufacturing costs of engineered tissues and facilitate their broad clinical use. Cell seeding of scaffolds – that is, the dissemination of isolated cells within a scaffold – is the first step in establishing a 3D culture, and might play a crucial role in determining the progression of tissue formation. Seeding cells into scaffolds at high densities has been associated with enhanced tissue formation in 3D constructs, including higher rates of cartilage matrix production, increased bone mineralization, and enhanced cardiac tissue structure.

In order to build autologous grafts for therapeutic applications with high initial cell densities while restricting sample size and/or cell proliferation, the cells must be seeded as efficiently as feasible. Furthermore, the initial distribution of cells inside the scaffold after seeding has been linked to the distribution of tissue created later within engineered constructions, implying that uniform cell seeding might lay the groundwork for uniform tissue production. Even with a modest 3D scaffold, however, distributing a high density of cells effectively and evenly throughout the scaffold volume can be a substantial difficulty. Although the most frequent seeding approach is static loading of cells onto a scaffold, multiple studies have observed poor seeding efficiency and non-uniform cell distributions inside the scaffold.

When poly non-woven meshes were seeded in stirred-flask bioreactors, they produced much greater efficiencies and uniformities. Convection moves the cells into the scaffolds by mixing the dilute cell solution around stationary scaffolds dangling from the flask's mouth. Seeding in stirred flask bioreactors, on the other hand, can result in low seeding efficiency and non-uniform distributions of cells, with a larger density of cells along the scaffold surface, perhaps due to inadequate convection of cells into the inner area of the scaffolds. Using the idea of convective transport for scaffold seeding, researchers used a multi-pass filtration seeding approach to flow a cell solution directly through the pores of 3D scaffolds, producing more evenly populated scaffolds than static seeding.

In comparison to static seeding or the stirred-flask bioreactor, direct perfusion was introduced into an automated bioreactor for 3D-scaffold seeding, which resulted in greater seeding efficiencies and more uniform cell distributions. Using this simple principle and a simple built bioreactor, a variety of scaffolds may be successfully and reproducibly seeded in an automated and controlled manner. Furthermore, perfusion seeding may be easily incorporated into a perfusion bioreactor system that can do both scaffold seeding and subsequent construct culture [4,5].

Conclusion

These seeding and culturing bioreactors were originally developed for the engineering of vascular grafts, but they have lately been used to the engineering of cartilage and cardiac tissues, as well as the maintenance of hepatocyte activity within 3D scaffolds. These methods not only speed up the engineering process, but they also lower the dangers of handling and moving constructions across different bioreactors.

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