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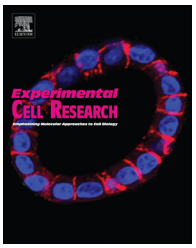

Review Article

Cell culture in autologous fibrin scaffolds for applications in tissue engineering

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ABSTRACT

In tissue engineering techniques, three-dimensional scaffolds are needed to adjust and guide cell growth and to allow tissue regeneration. The scaffold must be biocompatible, biodegradable and must benefit the interactions between cells and biomaterial. Some natural biomaterials such as fibrin provide a structure similar to the native extracellular matrix containing the cells. Fibrin was first used as a sealant based on pools of commercial fibrinogen. However, the high risk of viral transmission of these pools led to the development of techniques of viral inactivation and elimination and the use of autologous fibrins. In recent decades, fibrin has been used as a release system and three-dimensional scaffold for cell culture. Fibrin scaffolds have been widely used for the culture of different types of cells, and have found several applications in tissue engineering. The structure and development of scaffolds is a key point for cell culture because scaffolds of autologous fibrin offer an important alternative due to their low fibrinogen concentrations, which are more suitable for cell growth.

With this review our aim is to follow methods of development, analyze the commercial and autologous fibrins available and assess the possible applications of cell culture in tissue engineering in these three-dimensional structures.

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Introduction

Tissue engineering is an interdisciplinary scientific area that attempts to restore or improve the biological functions of damaged tissues or of tissues that are no longer able to carry out their function. Biomaterials are used as three-dimensional structures that contain cells and biologically active molecules [1]. The scaffold adjusts and guides cell growth and also allows tissue regeneration in a three-dimensional structure [2].

To be feasible, a tissue graft must accomplish two requirements: first, it must allow the development of neovascularization in the area where the avascular matrix has been implanted. This helps to prevent the erosion, infection and necrosis of the graft in which the coordinated and sequential action of certain growth factors will play an important role. Second, grafts must ensure the scarring of the area, thanks to the proliferation and differentiation of the cell component, which helps to regenerate the epithelium [1].

Some authors have considered the possibility of using avascular grafting without the need to add any cell type. In other studies, the existence of epithelial and vascular invasion from the organ towards the graft has been observed [3]. Nevertheless, most studies tend towards the use of different cell types to produce the regeneration of epithelium, ensure the preservation of the capillary network and/or promote graft vascularization [4–7].

In tissue engineering techniques, the cellular component is usually autologous (i.e., from the patient). This is preserved in in vitro culture until it can be introduced into a biocompatible three-dimensional scaffold, together with new biologically active substances that will promote angiogenesis and cell proliferation. The resulting tissue graft is preserved under adequate culture conditions until in vivo implantation is carried out (Fig. 1).

In short, thanks to the techniques of tissue engineering three important components have become available for obtaining a feasible graft: the biomaterial that will act as scaffold, the cell component and inducer substances. Below we describe and review the biomaterials most widely used for the development of scaffolds in cell culture.

Biomaterials as scaffolds

The ideal scaffold must be developed using biocompatible materials with surface properties that will benefit cell adhesion, proliferation and differentiation [6] and will not produce inflammatory reactions after implantation [2].

Depending on their origin, biomaterials can be classified as natural and synthetic. The first group generally includes proteins and polysaccharides (collagen, fibrin, alginate, hyaluronic acid, etc.), whereas the second one is composed of metallic, ceramic or polymeric materials, such as polyglycolic acid (PGA) and polylactic acid (PLA). All of them have been used to manufacture scaffolds in tissue engineering [6–8]. A comparison of natural and synthethic materials is given in Table 1 [6–18].

Natural biomaterials mimic the structure and composition of the native extracellular matrix. Their stimulating effects allow the inclusion of growth factors and other proteins able to boost cellular functions. However, they deteriorate easily and can transfer pathogens, and their variability depends on the structure of the original natural polymer [10].

Certain natural polymers such as collagen have been used for different purposes in soft tissue engineering, for example in skin.

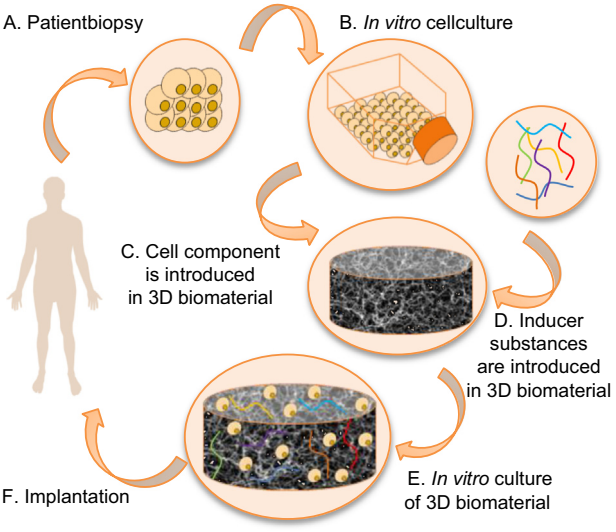

Fig. 1 – Outline of the process of techniques of autologous tissue engineering. A patient biopsy is obtained (A) to extract the cell component. This is seeded in an in vitro culture (B), after which the cell component (C) is introduced with inducer substances (D) in a biomaterial or scaffold and is cultured (E) until it is implanted in vivo (F).