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SCAFFOLDS FOR TISSUE ENGINEERING – INTRODUCTION

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Abstract: For the past 40 years we have developed a variety of techniques to create scaffolds. Raw materials, mostly polymers, are processed and shaped into different structures depending on various applications in tissue engineering. One of the main obstacles to the correct creation of fully functional tissue substitution is the complexity of the design as well as the manufacturing process itself. The biomaterial scaffold must be designed to perform the function of the native tissue extracellular matrix and still maintain its bioactivity during interaction with patient´s body. In this paper we describe the use of scaffolds in tissue engineering in general.

1 Introduction

Every day, thousands of surgical procedures are performed to replace or repair tissue that has been damaged by illness or injury. An evolving area of tissue engeneering focuses on the regeneration of dameged tissue. Detached cells from the body which we associate with porous supporting – scaffolds act as a template for tissue regeneration and lead to the growth of new tissue. Tissue engineering (TE) was first defined in 1988 during the workshop National Science Foundation as an application of the principles and methods of engineering and natural sciences, which lead to an understanding of the structural and functional relationships in physiological as well as pathology altered mammalian tissue and to the development of biological substitutes so as to restore, maintain or improve function [1].

Disease, injury or trauma can lead to damage and degradation of tissue in the human body, requiring treatment for repair, replacement or regeneration. Treatment usually focuses on tissue transplantation from one site to another in one patient (autograft) or from one person to the other (allograft). While such treatment is revolutionary and life-saving, there are fundamental problems with both techniques [1].

While such treatment is revolutionary and life-saving, there are fundamental problems with both techniques. Autographs are expensive, painful, limited by anatomy, and associated with donor disease due to infection or hematoma. Similarly, it is also true for allografts and transplant because of the potential risks of rejection of the transplant by the patient's immune system and the possibility of introducing an infection or donor disease to the patient. The field of tissue engineering focuses on the regeneration of damaged tissues rather than replacing them, the development of biological replacements for recovery, preservation or improvement of tissue function [1-4].

The field of tissue engineering is a multidisciplinary area that draws on the knowledge of clinical medicine, engineering, material science, genetics and related disciplines, as well as natural sciences and engineering. This area is largely based on the use of 3D porous scaffolds to provide a suitable environment for the regeneration of tissues and organs. In essence, these scaffolds act as a template for tissue formation and are usually deployed by cells and growth factors, or are subjected to biophysical stimulus in the form of a bioreactor, device or system that applies various types of mechanical or chemical stimulation of cells [1, 5, 6]. These cell-based scaffolds are either cultured for *in vitro* tissue synthesis, which are then implanted directly into the damaged site or implanted directly into the site of *in vivo* damage where the regeneration of tissues or organs is stimulated by the body's own system [7]. This combination of cells, scaffolds and signals is often referred to as the "triple or trio of tissue engineering" (Figure 1). The term scaffolds refers to a 3D material before it was embedded with cells (*in vitro* or *in vivo*) [1, 8].

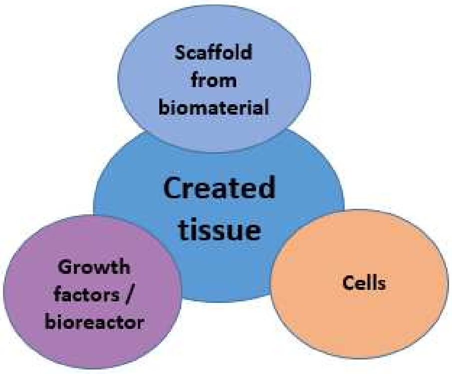

Figure 1 "Trio of tissue engineering" [1, 9]

1.1 Scaffolds and cells

In order to allow cellular morphogenesis associated with living tissue functionality, cell support is necessary to support the cells in their physical 3D support structure. Without adequate 3D support, cell formation can be achieved in only one layer of tissue. Cells without 3D support will not begin to create multiple layers in 3D space in the form of tissue. This phenomenon is known as " contact inhibition ", characterized by the limitations in the design of complex tissue structures of the 2D supports such as for exaple the tissues from the culture flask. Therefore, cells are seeded and cultured in 3D porous structures known as scaffolds to improve tissue regeneration. Scaffold works as a temporary extracellular matrix (ECM), which is intended for the arrangement of cells in 3D architecture and to provide incentives necessary to produce the desired tissue. The resulting substitute of living tissue is composed of two basic parts: living cells and a suitable material that is able to temporarily function as the ECM [10, 11]. The cells may be isolated from the patient's body and then grown on the scaffold *ex vivo* prior to implantation or received *in situ* from the healthy tissue surrounding the site of implantation. The most commonly studied cells in connection with scaffolds are mesenchymal stem cells [12, 13]. Scaffolds should be able to support cells with respect to structural integrity, provide them with sites for adhesion and allow cell morphogenesis and migration, which are key factors in the tissue regeneration process (Figure 2).

One of the main obstacles that prevent proper creation of a fully functional replacement tissue is the complexity of the design and actual production biomaterial scaffold to perform the function of native tissue ECM and still maintain their bioactivity during the interaction with the patient's body. This bioactivity includes the support of the cell remodeling process taking place within scaffolding and the synchronization of remodeling with the ongoing process od tissue repair. Such synchronization should optimally lead to a complete replacement of implanted scaffold that has been created by living tissue, with a consequent degradation of temporary scaffolding. The main focus of tissue engineering is the creation of scaffolds to provide adequate 3D space for the remodeling of natural tissue, leading to complete replacement of functional living tissue.

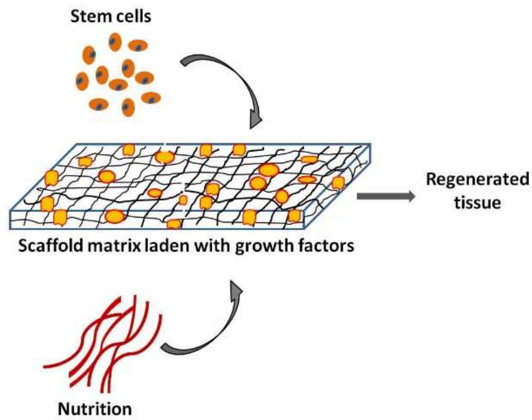

Figure 2: Demonstration of seeding of cells to scaffold [14]

The development of such a complex and sophisticated scaffolding is necessary to apply multidisciplinary scientific platform, which includes the fields of cell biology, developmental biology, biomaterial engineering and advanced manufacturing technology [15, 16].

From the point of view of scaffolding, many studies are focused on supporting tissues such as bones, cartilage, tendons. Bones are among the most intensively studied biological tissues in terms of mechanical properties.

There are three important areas where it is important to know the mechanical properties of tissues:

1. Basic modelling of biological tissues.

Advanced material models are needed to describe the mechanical response of biological tissues to multi-axis load. This mechanical response is partly due to the heterogeneity of mechanical properties, anisotropy, time-dependent mechanical behavior, the presence of several phases (liquid, solid, etc.) and the adaptation of the mechanical properties to the mechanical load. It is important in the development of mathematical models of tissues [17].

2. Regeneration of tissues

Regeneration of damaged tissue by TE and regenerative medicine is an important approach in biomedical engineering. It is necessary to ensure the correct environment for tissue regeneration including the media (i.e. scaffolds, gels, etc.), which are mechanically strong to support the regeneration process. At the same time scaffolds should not be too rigid, because they can otherwise prevent regeneration of the tissue. The question arises, what is the optimal range of mechanical properties of scaffolds and gels? One possibility is to characterize the native tissue and thus get a preview of the expected range of mechanical properties of the scaffold. The properties of native tissue are in many cases the best starting point. Moreover, the mechanical properties of biological tissue could be used to diagnose disorders and diseases that are manifested precisely in relation to changes in the mechanical properties of tissue (Figure 3) [18].

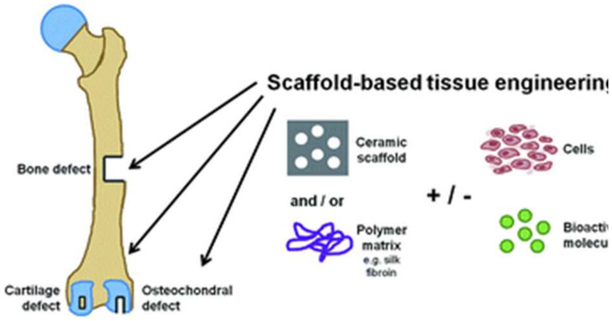

Figure 3: A schematic representation of the use of scaffolds for tissue engineering [19]

3. Tissue damage and trauma

Mechanical stress combined with tissue disease could lead to tissue damage. It is not only the non-physiological stress that occurs in traumatic events but also the physiological load of tissues if chronic damage is present such as for example osteoporosis in bone tissue. We should know what level of load, bones with osteoporosis still tolerate, without the risk of fracture. Similarly, in the study of osteoarthritis it is important to compare changes in mechanical properties of cartilage. We know that changes in the cartilage is one of the first indicators of the onset of osteoarthritis [20, 21].

2 Conclusion

Creating a scaffold with the required properties such as mechanical strength and chemical properties of surface controls tissue regeneration. These properties can be modified and adapted by a suitable choice of material, scaffold´s components and, in particular, by the manufacturing technique itself.

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