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Tissue engineering in oral and maxillofacial reconstruction

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Abstract

The artificial generation of tissues, organs, or even more complex living organisms was throughout the history of mankind a matter of myth and dream. During the last decades this vision became feasible and has been recently introduced in clinical medicine. The interest and attention that this rapidly developing area has received are based on the vision that the growing understanding of tissue healing and the achievements of biotechnology will be of profound therapeutic relevance. Clinically, reconstructive surgery has arrived at a standard of care that allows for repair and restoration of the vast majority of tissues/organs with established techniques. The real challenge of tissue engineering in clinical treatment is the reduction of surgical morbidity by the application of biological signals or bio-artificial components cultivated from the patient's own cells, that can replace the lost body part or accomplish its repair without the need for autogenous tissue transfer. Initially, activities in this area were mainly focused on cell-based approaches aiming at the generation of tissue-like constructs by combining ex vivo expanded cell populations with various types of scaffolds. Today, the field of tissue engineering has expanded tremendously, in that not only cells and scaffolds but also growth factors, controlled release carriers, engineering of biomaterials and many other areas of basic and applied research are considered to be part of the field of tissue engineering.

Keywords: Tissue engineering; Mesenchymal stem cells; Gene therapy; Maxillofacial reconstruction; Bone morphogenic proteins

1. Introduction

The artificial generation of tissues, organs, or even more complex living organisms was throughout the history of mankind a matter of myth and dream. During the last decades this vision became feasible and has been recently introduced in clinical medicine. Old stories from the Greek mythology e.g., the generation of Prometheus may be considered as early reports representing the idea of regeneration of living creatures from living or nonliving specimens/organs. Later on, as science and medicine progressed, a multitude of stories, reports, paintings, and films dealt with the idea that humans could create life by modern "scientific" measures. A prominent newer example in literature and film is the story of Frankenstein, written by Mary Shelley in (1818), describing the vitalization of a creature, reassembled from different body parts [1].

The term "tissue engineering" was up to the mid 1980's loosely applied in the literature in cases of surgical manipulation of tissues and organs or in a

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broader sense when prosthetic devices or biomaterials were used. The term "tissue engineering" as it is nowadays used was introduced in medicine in 1987. A key point in tissue engineering was given by the close cooperation between Dr. Joseph Vacanti from Boston Children's Hospital and Dr. Robert Langer from M.I.T, whose article in "Science", describes the new technology, and can be referenced as the beginning of this new biomedical discipline [1].

The interest and attention that this rapidly developing area has received are based on the vision that the growing understanding of tissue healing and the achievements of biotechnology will be of profound therapeutic relevance. In clinical reality, reconstructive surgery has arrived at a standard of care that allows for repair and restoration of the vast majority of patients with established techniques; the challenge of tissue engineering in clinical treatment is the reduction of surgical morbidity by the application of biological signals or bio-artificial components cultivated from the patient's own cells, that can replace the lost body part or accomplish its repair without the need for autogenous tissue transfer [2].

The term "tissue engineering" was initially defined by the attendees of the first NSF (National Science Foundation) sponsored meeting in 1988 as "application of the principles and methods of engineering and life sciences toward fundamental understanding of structure–function relationship in normal and pathological mammalian tissues and the development of biological substitutes for the repair or regeneration of tissue or organ function." In 1993, Langer and Vacanti [3] summarized the early developments in this field and defined tissue engineering as "an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain or improve tissue or organ function."

James Alexander Thomson (born December, 1958) is an American developmental biologist best known for deriving the first human embryonic stem cell (SC) line in 1998 and for deriving human induced pluripotent stem (iPS) cells in 2007. Human embryonic stem cells have the ability to divide unlimitedly while maintaining the potential to differentiate into different types of body cells. This remarkable potential makes them useful for basic research on the function of the human body, for drug discovery and testing, and as a source of cells and tissues for transplantation medicine [4,5].

The basic premise of regenerative medicine or tissue engineering is that a practitioner could provide a new construct to replace lost tissue whether that tissue be bone, skin, mucosa, tendon, cartilage, heart muscle, liver, entire solid organs, or composite tissues. Various terms have been used to describe activities involved in repairing and regenerating tissues, wholly or partly by using cells, proteins, matrices, signaling molecules or other strategies. "Regenerative medicine", "reparative medicine", and "tissue engineering" have been used, somewhat interchangeably, to describe these activities over the past several decades [6].

2. Basic principles of regenerative medicine

To regenerate new tissues within a specific environment, 3 basic tools are required: the cells, a scaffold, and the signaling molecules. Regeneration of tissues is a complex and highly orchestrated process that, nevertheless, proceeds along a rather uniform pathway including the three well known steps of inflammation, proliferation, and remodeling. During this process biological signals accomplish the increase in cell numbers that fill the defect or cover the wound. At the same time, specialization of the newly formed tissue-occurs through morphogenic signals which induce the tissue specific differentiation [3].

Most of the biological signals that increase both proliferation and induce differentiation of cells are conveyed by polypeptide growth factors. These growth factors are supplied by either local cells or by circulating cells and blood components such as macrophages and platelets. Moreover, growth factors originate from the extracellular matrix (ECM) where they are stored and released during tissue remodeling and repair. During this process, the extracellular matrix serves an additional purpose by providing a three-dimensional scaffold for the migration of cells and their arrangement in a tissue-specific manner. In this way, cells, signaling molecules, and the ECM are closely linked and form the basis of tissue homeostasis and regeneration in vivo [3].

When these three components are transferred to the in vitro environment of tissue-engineered constructs, the extracellular matrix is replaced by synthetic or natural scaffolds which are used to accommodate and arrange the cells in a three-dimensional fashion. The triad of cells, signals, and scaffolds thus makes up the "classic" tissue engineering triad (Fig. 1) [3].

However, beyond these three components, angiogenesis and vascularization play an important role in cellular behavior and tissue repair, not only because blood supply is necessary for cell survival and development, but also because vessels provide a reservoir of undifferentiated perivascular cells that are recruited during tissue repair [2].