Gene-Modified Tissue-Engineered Skin: The Next Generation of Skin Substitutes

Stelios T. Andreadis

Bioengineering Laboratory, Department of Chemical & Biological Engineering, University at Buffalo, The State University of New York (SUNY), Amherst, NY 14260, USA
sandread@eng.buffalo.edu

Abstract  Tissue engineering combines the principles of cell biology, engineering and materials science to develop three-dimensional tissues to replace or restore tissue function. Tissue engineered skin is one of most advanced tissue constructs, yet it lacks several important functions including those provided by hair follicles, sebaceous glands, sweat glands and dendritic cells. Although the complexity of skin may be difficult to recapitulate entirely, new or improved functions can be provided by genetic modification of the cells that make up the tissues. Gene therapy can also be used in wound healing to promote tissue regeneration or prevent healing abnormalities such as formation of scars.
and keloids. Finally, gene-enhanced skin substitutes have great potential as cell-based devices to deliver therapeutics locally or systemically. Although significant progress has been made in the development of gene transfer technologies, several challenges have to be met before clinical application of genetically modified skin tissue. Engineering challenges include methods for improved efficiency and targeted gene delivery; efficient gene transfer to the stem cells that constantly regenerate the dynamic epidermal tissue; and development of novel biomaterials for controlled gene delivery. In addition, advances in regulatable vectors to achieve spatially and temporally controlled gene expression by physiological or exogenous signals may facilitate pharmacological administration of therapeutics through genetically engineered skin. Gene modified skin substitutes are also employed as biological models to understand tissue development or disease progression in a realistic three-dimensional context. In summary, gene therapy has the potential to generate the next generation of skin substitutes with enhanced capacity for treatment of burns, chronic wounds and even systemic diseases.

1 Introduction

Tissue Engineering applies the principles and methods of engineering and the life sciences toward the development of tissue substitutes to restore, maintain or improve tissue function [18, 71, 97]. The field of tissue engineering is motivated by the tremendous need for transplantation of human tissue. In particular, the large number of patients with severe burns (13,000 per year, with 1000 of these involving more than 60% of the body surface), diabetic ulcers (about 600,000 per year), venous ulcers (∼1 million per year) and pressure sores (about 2 million per year), creates a pressing need for artificial skin substitutes [117]. In addition to providing an alternative to autologous transplantation, engineered tissues have great potential as realistic biological models to obtain fundamental understanding of the structure-function relationships under normal and disease conditions and as toxicological models to facilitate drug development and testing.

To engineer tissues in the laboratory, cells must grow on three-dimensional scaffolds that provide the right geometric configuration, mechanical support and bioactive signals that promote tissue growth and differentiation. The cells may come from the patient (autologous), another individual (allogeneic) or a different species (xenogeneic). Cell sourcing may be overcome by use of adult or embryonic stem cells that have the capacity for self-renewal and can differentiate into multiple cell types, thus providing an unlimited supply of cells for tissue and cellular therapies. Application of stem cells in tissue engineering requires control of their differentiation into specific cell types, which in turn depends on fundamental understanding of the factors that affect stem cell self-renewal and lineage commitment [162, 173].