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Biocompatibility Pathways in Tissue-Engineering Templates

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ABSTRACT
Tissue engineering, which involves the creation of new tissue by the deliberate and controlled stimulation of selected target cells through a systematic combination of molecular and mechanical signals, usually involves the assistance of biomaterials-based structures to deliver these signals and to give shape to the resulting tissue mass. The specifications for these structures, which used to be described as scaffolds but are now more correctly termed templates, have rarely been defined, mainly because this is difficult to do. Primarily, however, these specifications must relate to the need to develop the right microenvironment for the cells to create new tissue and to the need for the interactions between the cells and the template material to be consistent with the demands of the new viable tissues. These features are encompassed by the phenomena that are collectively called biocompatibility. However, the theories and putative mechanisms of conventional biocompatibility (mostly conceived through experiences with implantable medical devices) are inadequate to describe phenomena in tissue-engineering processes. The present author has recently redefined biocompatibility in terms of specific materials- and biology-based pathways; this opinion paper places tissue-engineering biocompatibility mechanisms in the context of these pathways.

1. Introduction: The nature of tissue-engineering templates

Regenerative medicine involves therapies to treat disease and injury through the regeneration of functional tissues or organs. This may be conceptually achieved in one of three ways. The first method, usually called cell therapy, involves the use of groups of cells, derived from the patient or elsewhere, which can be injected or placed at the site of disease or injury in the expectation that they will facilitate the spontaneous regeneration of tissue. The second method involves gene therapy, in which specific genes are inserted into specific cells in order to correct deficiencies in those cells. The third method is that of tissue engineering, "the creation of new tissue … by the deliberate and controlled stimulation of selected target cells, through a systematic combination of molecular and mechanical signals" [1]. Although cell and gene therapies do not normally involve biomaterials, these are usually required for tissue-engineering processes; new tissue generated in this way usually requires form and structure, and injected cells are unlikely to provide this by themselves without the assistance of biomaterials. Moreover, molecular signals are not easy to deliver with the appropriate spatial and temporal characteristics; a biomaterial that contains and delivers such signals to the required cells would be very beneficial. Also, mechanical signals may be equally difficult to deliver without the sustained effects of a biomaterial support [2].

It has been common practice to describe the material constructs used in tissue engineering as scaffolds. Conventional scaffolds tend to comprise discrete porous constructs, usually of polymers or ceramics, in which appropriate cells infiltrate the pores and are intended to express new tissue within these spaces as the biomaterial degrades and resorbs at the same time. Such constructs have usually been produced by three-dimensional (3D) techniques such as solid free-form fabrication, electrospinning, and solvent casting with porogen leaching. However, a scaffold is required to provide an environment, or