Preface: The Clinical Imperative for Regenerative Medicine

A critical need exists in clinical medicine for effective methods to regenerate tissues. Many of the world's leading killers, including coronary artery disease, stroke, emphysema, diabetes, cancer, and traumatic injuries, could be alleviated by regenerative medicine. For example, novel methods for pancreatic islet regeneration can address diabetes; autologous cells for heart muscle regeneration can address coronary artery disease; and nerve regeneration technologies can be utilized to treat stroke. Effective materials for tissue regeneration will, therefore, find applications in practically every clinical discipline. Regenerative medicine has the potential to improve patient outcomes, lower the incidence of complications, and reduce hospital stays. Such technologies will enable cost-effective treatments, and lessen morbidity and mortality.

The ultimate goal of tissue engineering is to regenerate tissues that restore normal physiological function. A general strategy of tissue engineering is to replace lost tissues or organs with polymeric scaffolds that contain specialized populations of viable cells. Within a tissue engineered construct, a three-dimensional polymer scaffold provides support and structure, while living cells contribute biological functionality. The scaffold may take the form of a mesh, patch, or foam, and it may incorporate mechanical or chemical cellular signals to stimulate the expansion of desirable cell populations. Once implanted, the tissue-engineered construct guides the growth and development of new tissue; the polymer scaffold degrades away to be replaced by healthy functioning tissue. An optimal biomaterial for tissue regeneration enhances cell attachment, proliferation, and differentiation. To initiate tissue renewal, the biomaterial must integrate with the host tissue and promote in vivo revascularization to ensure adequate oxygen supply. The biomaterial must also exhibit mechanical properties that are compatible with native tissue. At the same time, the implanted biomaterial must safely degrade at a rate similar to that of the new tissue formation, such that the biomaterial is eventually removed from the body by natural metabolic processes. Ultimately, any biomaterial platform for regenerative medicine must provide clinical benefit for patients.

This book will describe the latest methods for regulating the biological and chemical composition of engineered biomaterials, as well as techniques for modulating mechanical properties of engineered constructs. The book will delineate methods for guiding the host response to implantable materials, and explain the use of biologically inspired materials for optimal biological functionality and compatibility. The book will culminate in a discussion of the clinical applications of regenerative medicine.

The first section of this book details methods for optimizing cellular populations and cellular behavior. Michael King and Srinivas Narasipura of Cornell University discuss biomaterial surfaces for capture and purification of hematopoietic stem cells and progenitor cells. Such methods can be utilized to provide cell sources for tissue engineering; these surfaces could also be incorporated into tissue-engineered scaffolds, to attract desirable native cell populations and promote engraftment. Cynthia Reinhart-King and colleagues of Cornell University then review cellular mechanics, specifically the role of the extracellular matrix in tuning cellular properties and tissue formation. These insights are useful for enhancing cellular migration and proliferation within engineered constructs and may be utilized to promote tissue integration of engineered matrices. The next section of this book covers another essential component of tissue engineering, the delivery of oxygen to nascent constructs. Susan Roberts and Whitney Stoppel of the University of Massachusetts-Amherst review methods for ensuring adequate oxygen transport within engrafted tissues.

The book then turns to the mechanical structure of the polymer scaffold, and discusses strategies for controlling the mechanical properties of biomaterials. Santanu Kundu of NIST and Edwin Chan of the University of Massachusetts-Amherst explain the adhesion behavior of soft materials, including elastomers and hydrogels. Incorporation of patterned surfaces and other topological features can enhance the adhesive performance of biomaterials. Proceeding on this theme, Gregory Tew and Surita Bhatia of the University of Massachusetts-Amherst summarize efforts to regulate structural and mechanical properties of novel hydrogels. The self-assembly, cross-linking, and stiffness of hydrogels are critical structural characteristics which can be modulated. This approach enables adaptation of biomaterials for a wide variety of implantation sites and a wide variety of applications in regenerative medicine.

The book continues with a detailed discussion of biocompatibility and host–biomaterial interactions. Anjelica Gonzalez-Simon of Yale University and Omolola Eniola-Adefeso of the University of Michigan delineate the host response to biomaterials. The host reaction is an essential consideration for any tissue-engineered construct. Thomas Dziubla and Paritosh Wattamwar build on this subject and describe a novel biomaterial platform which incorporates antioxidants to minimize inflammation and maximize wound healing. Such an antioxidant-conjugated scaffold may add therapeutic functionality to implantable biomaterials.

Because implanted biomaterials must be biocompatible with natural tissues, some of the most effective biomaterials are those inspired by natural structures. The book thus progresses with a section on biologically inspired materials for tissue engineering. Jeffrey Karp, Woo Kyung Cho, Robert Langer and colleagues at Harvard-MIT describe their invention of tape-based adhesives for regenerative medicine.

These biomaterials are nanotopographically patterned to mimic the adhesive footpad of the gecko. Kristi Kiick and Christopher McGann of the University of Delaware discuss their innovation of hydrogels functionalized with the natural polysaccharide heparin. Such hydrogels may assemble through protein–polysaccharide interactions, and the inclusion of heparin can impart anti-thrombogenic activity to scaffolds for tissue regeneration.

The real value of tissue-engineered scaffolds lies in their clinical utility. This book concludes with a significant section on the design of biomaterials for specific clinical applications. Xinqiao Jia and colleagues of the University of Delaware detail their efforts to create biomimetic matrices for vocal fold repair and regeneration. These matrices recapitulate the features of the vocal fold lamina propria; the scaffolds encourage the attachment and proliferation of vocal fold cells, as well as the production of an extracellular matrix that resembles native tissue. Millicent Sullivan and Kory Blocker of the University of Delaware review methods of nonviral gene delivery for tissue regeneration. This work enables spatial and temporal control of gene delivery and has specific applications for promoting angiogenesis. Finally, Yunzhi Yang and Sungwoo Kim of the University of Texas Health Science Center describe their progress in chitosan-based systems for applications in chemotherapy, wound healing, and regenerative medicine.

Together, the innovations of these investigators demonstrate the versatility and the potential of engineered biomaterials for regenerative medicine. Fundamental advances in cellular mechanics, intracellular and extracellular signaling, host–cell interactions, polymer chemistry, and materials science have been applied to create biomaterials with novel design and functionality. These visionary approaches to tissue engineering will, in turn, enable breakthroughs in clinical medicine, enhancing the human body's capability to regenerate and repair itself.

Cambridge, MA, USA Sujata K. Bhatia

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