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Editorial

New Biomaterials as Scaffolds for Tissue Engineering

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Tissue engineers attempt to harness the body's natural ability to repair and regenerate damaged tissue through the application of biological, chemical, and engineering principles. This strategy can potentially provide improved clinical options by supplying the appropriate biological and mechanical properties at the time of reconstruction without the limitations associated with current surgical techniques. The traditional tissue engineering paradigm combines isolated cells with appropriate bioactive agents in a biomaterial scaffold. Scaffolds are seeded with primary cells or multipotent stem cells prior to implantation in order to establish new centers for tissue formation. Alternatively, acellular scaffolds are implanted incorporating biological cues to induce tissue ingrowth after implantation. The biomaterial scaffold serves to sustain functionality during regeneration and as a template for the cellular interactions necessary for tissue repair. Consequently, the advancement of tissue engineering strategies is strongly dependent on the development of biomaterials that meet the rigorous design criteria of regenerative medicine.

This theme issue focuses on the development of new biomaterials as scaffolds for tissue engineering. There are 6 articles in this issue representing several of the key biomaterial research fronts in regenerative medicine. These articles highlight research from the development of new biodegradable polymers to strategies that enhance tissue integration and vascularization of tissue engineering constructs. Specifically, the first two articles focus on the development of new biodegradable polymers. One limitation of current hydrolytically degradable polymers based upon an ester moiety is the release of acidic degradation products and lack of cellular control of degradation. A significant portion of biomaterial research is focused on the development of new synthetic polymers that overcome these challenges. The following articles serve as a selection of representative strategies. The first article by Falco *et al*. reviews a novel class of biomaterials based upon a cyclic acetal unit that does not produce the inflammatory acidic biproducts of polyesters. In contrast, Guan *et al*. details a biomimetic approach to biodegradable polyurethanes that introduces enzyme-labile peptides into the polymer structure. The next two articles focus on the development of degradable and elastomeric polymers with properties appropriate for mechanically active tissue engineering. Current regenerative strategies are limited by poor understanding of the complex feedback mechanisms relating mechanical load, tissue organization and scaffold degradation. Thus, the development of new biomaterials that can be used to elucidate these feedback mechanisms is a key area of research. Bryant *et al*. describes the development of synthetic hydrogels with controlled macroscopic properties and biological functionalities. These materials are utilized as tools to elucidate the role of gel structure and chemistry in regulating biomechanical cues in cartilage tissue engineering. New biomaterials that can be tailored to meet the rigorous design criteria elucidated in these studies are also needed. Hafeman *et al*. describes biodegradable polyurethanes for ligament scaffolds synthesized from triisocyanates that exhibit tunable and superior mechanical properties. The advantages of these materials are detailed and include injectability, biocompatibility and tunable degradation. The last two articles deal with enhancing tissue integration of the construct and improving angiogenesis during tissue repair. Tissue integration is of great importance in the translation of tissue engineering strategies to the clinic. Physicochemical and biochemical coating techniques to enhance bone regeneration at the interface of titanium implant materials are reviewed by de Jonge *et al*. In addition to integration with existing tissue, injury sites require a dense capillary network during repair to deliver oxygen and nutrients. Patel *et al*. describes novel composite scaffolds of gelatin microparticles within a porous polymer scaffold that achieves controlled delivery of vascular endothelial growth factor, a potent angiogenic growth factor.

There has been significant progress in the field of tissue engineering in recent years, particularly in scaffold design. We hope that the present theme issue reflects these advances and will serve the scientific community in the continued develop-

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ment of tissue engineering strategies. The guest editors would like to extend our sincerest gratitude to the contributors of this issue for providing extensive and comprehensive reviews of key research in this arena.

GUEST EDITORS

Elizabeth Cosgriff-Hernandez is an Assistant Professor in Biomedical Engineering at Texas A&M University. She received her B.S. in Biomedical Engineering and Ph.D. in Macromolecular Science and Engineering from Case Western Reserve University. She was a postdoctoral fellow at Rice University prior to joining the TAMU faculty in 2007. Dr. Cosgriff-Hernandez's current research interests are focused on musculoskeletal tissue engineering and include biomaterial synthesis, structure–property relationships, cell–material interactions, and biodegradation characterization. Specifically, novel block copolymer systems are under investigation as polymeric scaffolds for tendon and ligament tissue engineering. Complementary experiments that generate quantitative models of tissue remodeling are being utilized to improve the design of new biomaterials and guide tissue regeneration strategies.

Antonios G. Mikos is the J.W. Cox Professor of Bioengineering and Professor of Chemical and Biomolecular Engineering at Rice University. He received his Dipl.Eng. (1983) from the Aristotle University of Thessaloniki, Greece, and his Ph.D. (1988) in Chemical Engineering from Purdue University. He was a postdoctoral researcher at the Massachusetts Institute of Technology and the Harvard Medical School before joining the Rice Faculty in 1992. His research focuses on the synthesis, processing, and evaluation of new biomaterials for use as scaffolds for tissue engineering, as carriers for controlled drug delivery, and as non-viral vectors for gene therapy. He is the author of over 350 publications and 23 patents. He is the editor of 10 books and the author of one textbook (Biomaterials: The Intersection of Biology and Materials Science, Pearson Prentice Hall, 2008). Mikos is a Fellow of the International Union of Societies for Biomaterials Science and Engineering and a Fellow of the American Institute for Medical and Biological Engineering. He has been recognized by various awards including the *Alpha Chi Sigma Award for Chemical Engineering Research* of the American Institute of Chemical Engineers, the *Robert A. Pritzker Distinguished Lecturer Award* of the Biomedical Engineering Society, the *Edith and Peter O'Donnell Award in Engineering* of The Academy of Medicine, Engineering and Science of Texas, the *Marshall R. Urist Award for Excellence in Tissue Regeneration Research* of the Orthopaedic Research Society, and the *Clemson Award for Contributions to the Literature* of the Society for Biomaterials. Mikos is president elect of the North American Tissue Engineering and Regenerative Medicine International Society. He is also a founding editor of the journal *Tissue Engineering* and the organizer of the continuing education course *Advances in Tissue Engineering* offered annually at Rice University since 1993.

What Do You Think Holds the Key to Your Success as Biomaterial Scientists?

We believe that an innate satisfaction in discovery and problem solving keeps the work fun and perseverance overcomes roadblocks along the way. The addition of excellent mentors, collaborators and students throughout your career provide the means to tackle the complex and truly interesting research problems. Finally, the knowledge that the principle purpose of your research is to help people continues to motivate and inspire medical research to greater heights.

What Do You Consider to be Your Key Research Accomplishments?

As academics, our first product is the training of the next generation of researchers. Therefore, our key accomplishments continue to be our students. On the research side, we both believe that the creation of novel classes of biomaterials by integrating engineering, biology and materials science principles has been our key research accomplishment. These materials have enabled the exploration of numerous fundamental studies in drug delivery and tissue engineering.

What Was The Turning Point in Your Career?

Mikos: I was very fortunate to start my career in a very stimulating and interdisciplinary environment at Rice University. This has provided numerous opportunities over the years that have shaped my career.

Cosgriff-Hernandez: My first turning point was going to my first research conference and seeing the interdisciplinary nature of biomedical research. The way that researchers took knowledge from several different disciplines and applied it in new ways to help people sparked my interest. I was, and continue to be, fascinated by the complexity of the human body and the ingenuity of medical research. The second shift was in graduate school when I decided to pursue an academic career as opposed to a career in the biomedical industry. Academic research is used to advance medicine *and* serve as a training ground for future researchers. This seemed the ideal place for me to give back to the community that had nurtured my passion for research.

Who Are The Individuals Who Most Influenced Your Research Career?

Mikos: There have been numerous mentors and collaborators that have had great influence on my career, but three in particular stand out. First, my graduate advisor and long-time friend Nicholas Peppas of the University of Texas at Austin provided exceptional training in research and biomaterial science. Next, I had the opportunity to work in the emerging field of tissue engineering with my postdoctoral mentors, Robert Langer of MIT and Joseph Vacanti of Harvard Medical School.

Cosgriff-Hernandez: My father, Chris Christenson, who always encouraged me to ask 'why?' and then expected me to search out my own answers. My graduate advisors, Anne Hiltner and James Anderson of Case Western Reserve University, who showed me the opportunities available to a researcher at the interface of medicine and material science and gave me the tools necessary to succeed. Finally, Tony Mikos of Rice University provided an opportunity to pursue biomaterial science in the emerging field of tissue engineering.

What Is Your Philosophy of Educating Graduate Students?

We both believe that the Socratic method of challenging graduate students to ask questions is at the core of training independent scientists. An innate curiosity is certainly necessary to drive researchers to want to know 'why.' However, this curiosity must then be trained by teaching students what questions to ask to unravel complex problems and how to find solutions through experimental design. In addition to teaching critical research skills, graduate school needs to also impart the ability to communicate ideas and research findings. Without effective written and oral communication skills, a scientist is without a voice and the impact of the research is significantly reduced.

Biomaterial Scientists Are Faced With The Dilemma of Having to Publish in Biomedical or Basic Science Journals. Does It Mean Cutting Edge Science Will Not Likely be Featured in the Pharmaceutical Research?

A large portion of biomaterial research in tissue engineering is focused on the delivery of bioactive agents to improve cellular recruitment and differentiation, tissue integration and neovascularization. Therefore, Pharmaceutical Research will continue to be an excellent forum for publication of biomaterial research in these areas.

What Are The Challenges Facing the Biomaterial Sciences?

Biomaterial scientists are challenged to understand and modulate the interactions of biomaterials with biological systems in order to achieve effective tissue repair or restore function. The development of new biomaterials with designer physical, chemical, and biological properties for specific performance requirements can be utilized to address both of these requirements.

What Are The Challenges for the Use of New Biomaterials for Tissue Engineering and How Can Be Overcome?

Tissue remodeling is an inherently dynamic process. Predicting and monitoring the progression of these remodeling processes in a tissue engineering construct continues to be challenging. Non-invasive imaging of the construct would provide an invaluable tool for assessing function over time. This may be accomplished by integrating diagnostic elements within the structure of the construct in combination with new imaging technologies.

What Is The Key to Developing Successful Collaborative Relationships?

The advantage of successful collaborative relationships is that the strengths of each person complement and build upon each other to create a greater whole. In addition, the weaknesses are offset by the strengths of the other partner. Therefore, a successful collaborative relationship requires an understanding and appreciation of the strengths and weaknesses of each partner.

What Is The Place for Collaboration With Industry in Academia?

Collaborations with industry are an integral part of any research effort. These partnerships enable academic researchers to better understand modern clinical and technological needs. In addition, collaborations with the biotechnology industry facilitate the translation of research discoveries from the benchtop to the bedside.