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Editor's Spotlight/Take 5

Editor's Spotlight/Take 5: Nano-ceramic Composite Scaffolds for Bioreactor-based Bone Engineering

Seth S. Leopold MD

Most of the content we publish comes under the "Clinical Orthopaedics" banner. Yet, our journal's name consists of four essential words, not two. The article from Dr. Cato Laurencin's (Fig. 1) award-winning laboratory is a sterling example of the "Related Research" side of our journal that clinical orthopaedists should not ignore.

The problem is, many of us will get halfway through the title and consider the work beyond our grasp. Do not get discouraged — this material is both approachable and important. Some background here, as well as in the *Take 5* interview that follows, may help those who are unfamiliar.

Broadly speaking, Dr. Laurencin's team is engineering biologically active polymeric/ceramic scaffolds (matrices populated with different kinds of cells, including stem cells) that share properties of bone. These amped-up scaffolds may promote bone regeneration because they are seeded with bone-producing cells throughout the entire scaffold, not just on the surface, which is typically what occurs with static cell culture approaches. The hope is that such scaffolds may be suitable for applications that call for augmented bone healing. Think bone defects, nonunions, and perhaps some tumor indications.

We are doing well so far, but that title is still intimidating — Bioreactor? A bioreactor is nothing more than a vessel that contains cells or organisms, and provides an environment conducive to the cells' survival, allowing us to harness their natural processes, whether biological, chemical, or both. If you have ever enjoyed a cold beer or a nice Pinot Grigio on a hot summer day, you have benefited from the work product of a bioreactor: Fermentation. Like the fermentation vessels used in breweries, the conditions and "ingredients" used in Dr. Laurencin's bioreactors need to be tightly controlled, but they can be varied to generate desired effects. A key benefit of the bioreactor approach is that it "kickstarts" the cellularization of a scaffold prior to implantation.

In previous work [1], the authors created three-dimensional (3-D) structures called porous, 3-D poly D, L-lactide-co-glycolide (PLAGA) scaffolds. The authors seeded PLAGA scaffolds with stem cells that were conducive to alkaline phosphatase secretion and calcium deposition. In this report, the authors set out to determine whether adding nano-hydroxyapatite (n-HA) would weaken the scaffolds (bad) or improve the output of the system (ie, mineralization, which

Note from the Editor-in-Chief:
In "Editor's Spotlight," *one of our editors provides brief commentary on a paper we believe is especially important and worthy of general interest. Following the explanation of our choice, we present* "Take Five," *in which the editor goes behind the discovery with a one-on-one interview with an author of the article featured in* "Editor's Spotlight."
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S. S. Leopold MD (✉)
Clinical Orthopaedics and Related Research, 1600 Spruce Street, Philadelphia, PA 19013, USA
e-mail: sleopold@clinOrthop.org

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would be good), when the structures were placed in a bone-generating bioreactor. In short, Dr. Laurencin and his colleagues found that adding n-HA did not weaken the PLAGA scaffolds. In fact, the addition to the scaffolds increased production of osteogenic markers, as well as more mineral deposition. The researchers found that human mesenchymal stem cells populated the hydroxyapatite-coated scaffolds uniformly — all promising findings.

This is not easy reading, but I encourage you to take in the interview with Dr. Laurencin. Discover what ignited his interest in this important area. Then read some "related research" on bioreactors and bone regeneration. Enjoy the other side.

Take 5 Interview with Dr. Laurencin

Senior author: Nano-ceramic Composite Scaffolds for Bioreactor-based Bone Engineering [DOI: 10.1007/s11999-013-2859-0]

Seth S. Leopold MD: *Let us start with the big picture. You are an orthopaedic surgeon who has made a career in, and won awards for, your research in nanoscience, for which I congratulate you. Yet, I would venture to say that many surgeons have never heard the term, at least not in the context of our specialty. How would you introduce the broad topic to someone unfamiliar to it? Why should the practicing surgeon at least be peripherally familiar with the subject?*

Fig. 1 Dr. Cato Laurencin is the senior author of Nano-ceramic Composite Scaffolds for Bioreactor-based Bone Engineering.

Cato Laurencin MD, PhD: I think the first big reference to nanotechnology came in 1959 with Richard Feynman's talk at an American Physical Society meeting. The talk, entitled "There's Plenty of Room at the Bottom," is great and widely available. It gives a summary of what the field could become. My coauthors and I [4] wrote the paper, "Nanotechnology and Orthopedics: A Personal Perspective," which introduced the importance of nanotechnology in the field to orthopaedic surgery, and might be of interest to someone approaching the field. Nanotechnolgy has huge implications for addressing the behavior of musculoskeletal implants and (as discussed in the current paper) in creating systems for regenerating bone and other musculoskeletal tissues. Its importance is being increasingly recognized. Practicing surgeons should be familiar with the discipline.

Dr. Leopold: *What originally sparked your interest in orthopaedic nanoscience research? How would you recommend a curious reader go about learning more about this exciting and fast-moving discipline?*

Dr. Laurencin: While a professor at Drexel University, I started collaborating with engineers who experimented with nanofibers for textile purposes. They appeared to have structures resembling collagen and I started working in collaboration with them to create biomimetic implants. Our paper was the seminal contribution in the field on biomedical purposes of nanofibers. Literally, there are thousands of papers in the area published annually. In collaboration with my colleague Dr. Lakshmi Nair [2], we published a comprehensive book on nanotechnology and musculoskeletal regeneration entitled, "Nanotechnology and Tissue Engineering: The Scaffold." We discussed ways in which nanomaterials interact with cells, a basic principle of the field, and outlined contemporary applications of nanomaterials, as well as future directions.

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Dr. Leopold: *Please share with our readers the major threads going on around the world in orthopaedic nanoscience research. Whose works are you most interested in now, what are they studying, and how might the results of those works affect practice?*

Dr. Laurencin: I love the work of, Dhiru Katti, Sangamesh Kumbar, Rocky Tuan, Tom Webster, and of course Robert Langer and Nicholas Peppas to name a few. They are demonstrating how modulation of cells and biological factors can take place using nanobased materials. They are developing new nanobased materials; their work is cutting edge. I admire Sam Stupp's work using platforms of self-assembling molecules, mostly based on peptide amphiphiles that are employed for regeneration. Finally, Chad Mirkin's work in nano-scale manufacturing, and his innovative broad based studies involving nanomaterials in medicine deserve special mention.

Dr. Leopold: *Your study involves a model that uses a bioreactor; the broad goals of this model involve the topic of bone regeneration. But I think many readers will find this kind of study — which incorporates a healthy dose of engineering along with cell biology into its nanoscience — somewhat intimidating. The very concept of bioreactors will be unfamiliar to most orthopaedic readers. What background can you offer the "nanoscience novice" so (s)he can approach and enjoy reading a study like yours?*

Dr. Laurencin: I think it is important to place everything in a big picture perspective. I recently discussed the fact that a new field is emerging that I call "Regenerative Engineering." This new field is the integration of traditional work in tissue engineering with new developments in materials science (especially nanoscience), stem cell science, and developmental biology. I was fortunate to recently have the concept presented in the journal, *Science-Translational Medicine* [3]. It discussed in a big picture way how these technologies operate. Dr. Yusuf Khan and I completed an instructional text focusing on making the language easy to read with the hope that engineers and physicians alike can benefit from it. It provides great background for the new field and how nanotechnology will play a big role.

Dr. Leopold: *How do you see your work transitioning from the lab to clinical practice, and when might we expect to see clinical trials using bone-regenerating bioreactors like those you are studying?*

Dr. Laurencin: Sir William Osler once said, "He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all." I think it is important for physician-scientists to drive research to clinical application, and I am hopeful we can begin bring these concepts to the benefit of patients in the next few years.

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