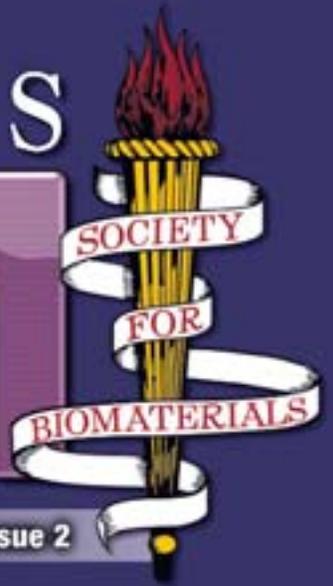


BIOMATERIALS FORUM



Second Quarter 2005 • Volume 27, Issue 2



**Annual Meeting
Program Highlights**



**Broadband CARS
Microscopy**

**Welcome
to Memphis**



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BIOMATERIALS FORUM



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Next Issue Deadline: May 27, 2005

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Coherent Anti-Stokes Raman Scattering (CARS) can be performed at significantly lower light levels than spontaneous Raman scattering, increasing the likelihood that CARS can be applied to live cells without inflicting photodamage. This, in addition to the high spatial resolution inherent in nonlinear optical microscopy, has led CARS microscopy to begin emerging as a powerful, noninvasive technique for biological and materials imaging.



The Society For Biomaterials converges on Memphis, the home of Elvis and world famous Beale Street, from April 27-30 for its 30th annual meeting and exposition. The focus of the 2005 gathering is "New Biomaterials Applications and Technologies to Meet Tomorrow's Clinical Challenges."

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From the Editor

The Society's Annual Meeting



This issue of *Biomaterials Forum* welcomes members and friends of the Society For Biomaterials to the 30th annual meeting and exposition of the Society. For 30 years, this Society has taken the lead in pioneering discoveries to treat patients, assuring training of a new generation of scientists, and leading the advocacy for funding for biomaterials research,

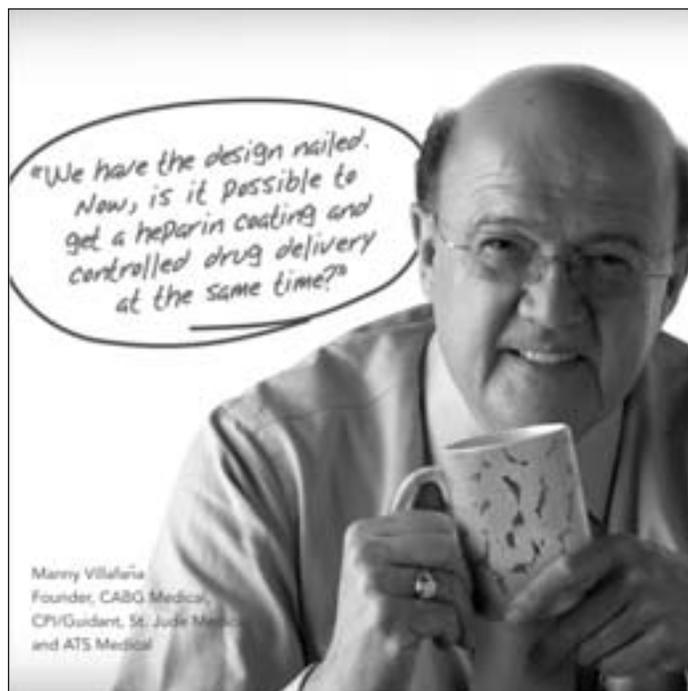
such as the establishment of the National Institute for Biomedical Imaging and Bioengineering at the National Institutes of Health (NIH). Biomaterials is now taught in all bioengineering and biomedical engineering curricula. It has become the focus of many degree programs, such as at Alfred University, Clemson University, Rutgers University, and the University of Washington, to name of few. Numerous academic programs have recently recruited many young faculty members who conduct biomaterials research. During the past 30 years, the Torch has been carried—biomaterials science and engineering have become a “profession.” Indeed, as stated by our incoming president, Michael Sefton, biomaterials is hot!

However, as we are faced with budget reductions in federal funding well below the rate of inflation, many are concerned that NIH will not be able to sustain its current research programs. On February 7, 2005, President Bush proposed to increase NIH's budget by 0.7 percent over the fiscal-year 2005 appropriation. NIH is forecasting an increase in the number of competing research project grants (RPGs) by 247 during fiscal-year 2005, although the total number of RPGs will decline by 402 in fiscal-year 2006. NIH is projecting its success rate to be 22 percent in 2005 and 21 percent in 2006. In 2003, the success rate was 30 percent and in 2004 it was 25 percent (<http://officeofbudget.od.nih.gov/ui/2006Budget.htm>).

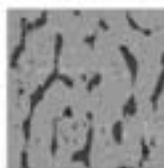
As for other biomedical sciences, the federal budget reductions might contribute to slow down research productivity, new technology discovery, and academic growth in biomaterials in the short term. But, luckily, biomaterials research is privileged with its multidisciplinary and cross-disciplinary approach, allowing many sources of funding to be targeted that will keep the Torch burning.

Biomaterials research productivity and technology discovery are certainly not in jeopardy as demonstrated by the breadth and depth of research highlighted at the 30th annual meeting, a meeting that promises to be highly rewarding from a science and technology perspective, and also very entertaining. We hope that the letters and articles in this issue of *Biomaterials*

Continued on page 3



Manny Villafra
Founder, CABG Medical,
CPVGuidant, St. Jude Medical,
and ATS Medical



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Two Hundred and Two Years Ago



Horizon scanning. Pushing at the frontier. Looking to the long-term. All are often-used phrases to express what curious individuals and societies are doing or, failing that, are itching to do. When I think about frontiers, the examples that quickly come to mind are space exploration, deep sea exploration, and elucidation of the human genome and proteome. But the

example that has not lost its luster over the years is the Lewis and Clark Expedition (1803-1806). Not only because mentioning it allows me to pay homage to then-President Thomas Jefferson, but because the expedition provides a good analogy of the significant results of long-term planning and practical preparation.

I'm going to assume that you know the outline of the story of the Lewis and Clark Expedition. What made it productive and important in the long-term was that there was an amazing amount of preparation (unlike most of the flash-in-the-pan activity of the Gold Rush that came later in the century). Thomas Jefferson was a unique combination; he was highly educated, a dreamer, and absorbed in details. He was the driving force behind the justification, fund-raising, and planning for the expedition. If we were talking about SFB [and we are], Tom would have been the Board of Directors, Council, and management office rolled into one. Until someone like that comes along for SFB, it's critical that you nominate and elect conscientious, talented people to the Board and Council, and that they invite others who are as, or more, skilled to work with them. It takes time, a series of challenges, and mentoring to develop leadership. As members of SFB, each of us has a role in the continuity of effective leadership in the Society.

Re-enter Lewis and Clark and their expedition team. While Jefferson was back in Washington, pacing back and forth, hoping that he had planned for everything, and waiting for the data, the expedition team was having its good days and bad. Bad weather and unexpected terrain meant more time on task, delays, and supply shortages. Unfriendly territory drove the need to form alliances along the way, as well as having to stand and fight once

in awhile. Alliances? Stand and fight? We thought this was the frontier... Well, it's just that Lewis and Clark hadn't been there before; they didn't have the data written down into useful form, yet. And, they were looking at the opportunities with fresh eyes. It is a rare frontier, indeed, that is synthesized entirely from things that didn't previously exist. For instance, have we finished learning from "biomimetics"? Or is it a practical matter of putting a new label on part of it (e.g. nanotechnology), restocking our supply wagon, and moving ahead again?

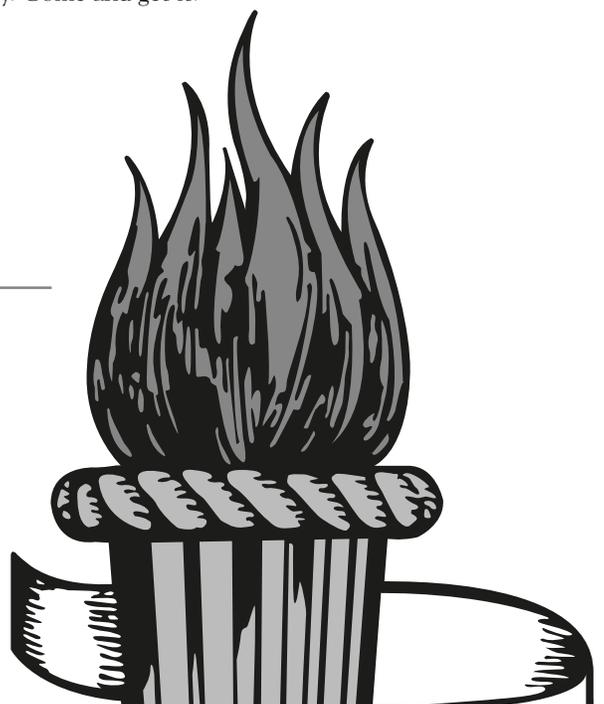
Speaking of restocking, although the Lewis and Clark explorers increasingly relied on resources that they found along the way, the complete loss of a reliable supply line "back home" meant real disaster. If we were talking about SFB [and we are], this means that we cannot afford to lose touch with the knowledge, techniques, and clinical applications that have brought us this far. Besides, things are always changing "back home," too. Often, meaningful ground for exploration is only as far away as the backyard. In science and engineering, the frontier, the "cutting edge," can pop up in the darndest places, where "luck favors the prepared mind." And if I had more time, I would turn to the story of Irving Langmuir (think Benjamin Franklin working in the 20th century).

In closing, thank you for the confidence you have placed in me, the other members of the Board and Council, and the staff during the past year. With the leadership of Michael Sefton in the coming year, please join me as a participant in the discussion and development of a major, new long-term plan for the Society For Biomaterials. Maybe it won't have the lasting impact of that journey that commenced 202 years ago, but it's definitely worth our time and energy to plan and prepare for SFB's future. As I said in an article in this publication many months ago, "It's your Society. Come and get it!"

From the Editor

(Continued from page 2)

Forum will help guide participants in preparing for an unforgettable meeting. The Society's annual meeting remains the ideal platform for team building and collaboration, keys to strengthening research proposals and increasing the likelihood of funding!



Staff Updates from Headquarters

The Torch

By Dan Lemyre,
Assistant Executive Director

Hello from the Society For Biomaterials headquarters! By providing a regular update of staff and membership activities, it is our sincere wish that all of the Society's members stay abreast of current Society activities, and we encourage more members to take an active role in the Society For Biomaterials. This quarter, headquarters staff has been active in their support of the following committee activities:

Awards Ceremonies and Nominations Committee

The 2005 award recipients are listed in this issue of the Forum and staff would like to offer their congratulations to all of this year's award winners! In addition, the election of new society officers is underway. Polls are scheduled to close on March 30, 2005, with the announcement of new officers made at the Society For Biomaterials 30th Annual Meeting in Memphis, Tenn., April 27-30, 2005.

Bylaws Committee

An amendment to the bylaws is being presented for membership approval at the Annual Business Meeting, which will be held in Memphis on Friday, April 29, at 10:30 a.m. Please plan to attend! The bylaws amendment will address a contradiction in the current version of the bylaws concerning editors of the Society For Biomaterials' publications. This contradiction states that editors of the Society's publications are elected in Article VI, Section 1 and appointed in Article VI, Section 5. To correct this contradiction, it is proposed that editors be elected by the Council of the Society as representatives of the Society. Notification of this amendment will be mailed to the voting members of the Society by March 25, 2005.

Education & Professional Development Committee

In addition to ongoing requests for meeting endorsements from other societies, the Education and Professional Development Committee is also on the road toward offering a surgical video library on the Society's Web site. More on this as details unfold!

Finance Committee

With budgeting for 2005 concluded, the Finance Committee will be turning its attention to the long-term financial health of the Society, with proposed revisions to the financial policy that will be presented to Council for discussion.

Long Range Planning Committee

Included in the 2005 budget is a strategic planning initiative that will help ensure the Society's continued success while advancing the Society's mission to provide the leading forum to disseminate knowledge of biomaterials among researchers, educators, and developers of materials and biomedical device technology.

Meeting Committee

Throughout this issue of Biomaterials Forum, you will find event descriptions and information about the Society For Biomaterials' 30th Annual Meeting. The headquarters staff would like to thank the meeting's program chair, Dr. Joel Bumgardner, for his tireless efforts to make this meeting a success.

Membership Committee

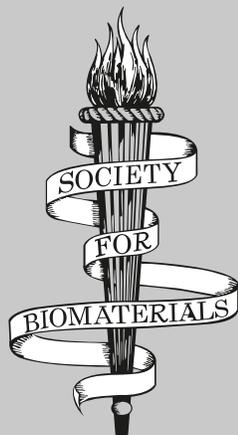
A new online membership application has been completed and the application review process will be significantly streamlined as a result. This will shorten the time it takes to become a member of the Society and also make it easier for members of the Membership Committee to review applications.

Publications Committee

The Publications Committee will be requesting proposals for a new Web site editor in the near future. It is hoped that this new position will improve the content, functionality, and appearance of the Society's Web site. If you know a qualified individual, please refer them to headquarters for an Editor Proposal form.

Continued on page 13

2005 SFB PROGRAM COMMITTEE IS PLEASED TO ANNOUNCE



Cato T. Laurencin, M.D., Ph.D., Lillian T. Pratt Distinguished Professor & Chair,
Department of Orthopaedic Surgery, Professor of Biomedical Engineering, Professor of
Chemical Engineering, The University of Virginia

& Member of the National Academy of Science-Institute of Medicine

AS THE Keynote Speaker FOR THE

30th Annual Meeting & Exposition of the Society For Biomaterials



In a few weeks I will have the honor of stepping into the role of President of the Society For Biomaterials (SFB). I remain somewhat amazed that you have trusted me with this responsibility, especially as I look back on this past year as Anne Meyer's shadow. I have had the opportunity to learn much about the inner workings of the Society and much about Anne. She is really, really well-organized (I guess that's how she has survived working with Bob Baier for so many

years). The Society owes her its gratitude for the incredibly hard work she has done on so many fronts.

Boy, it's a tough act to follow.

One of the things I have learned during the past year is how much SFB relies on a small army of volunteers to do everything from negotiate with Wiley to organize an annual meeting, to make sure we don't breach our bylaws, to devising new ways of drawing members to join. We could never afford to pay people to do this work and perhaps more importantly, we would never want to. One of the challenges facing the Society is to find more opportunities for volunteers to contribute and more ways to harness the energies of our members. The Special Interest Groups are a great vehicle in this context and I don't believe we have ever exploited them properly.

A behind-the-scenes task that Anne has led is the transition to

our "new" management company, Association Headquarters. Our customs and their way of doing things have not always been synchronized and this has led to the not-unexpected communication breakdowns. My sense is that the issues have been identified and I am very impressed with how responsive the senior management at Association Headquarters has been to our concerns. I expect that Anne's focus on this issue will allow the Society to make use of the opportunity afforded by our professional managers.

Biomaterials are hot. Drug-eluting stents, gene delivery, tissue engineering, combination products have led to much interest in biomaterials from surgeons, clinicians, and business folk who might never have given us a passing thought in the past. Now, many societies want to dance with us—co-sponsor symposia, share annual meetings, and do other good things together. We don't have the resources to work with everyone, but then who should we work with? What is our mission and what do we want out of these relationships? There is more and more interest in biomaterials, but this isn't reflected in burgeoning membership rolls. Are we doing something wrong, or better yet, is there something we can do to translate this interest into a positive outcome for the Society? This past year I worked with Jim Burns and the Liaison Committee, and with Tony Mikos and others in the Long Range Planning Committee, on this agenda. The challenge is to adapt to the new landscape yet preserve the core values and interests.

Sounds like we are prepping for a strategic plan. Arrgh!

Say Anne. Want to go for a second term?

Society For Biomaterials Searching for New Executive Director

Steven Echard resigned his position as Executive Director of the Society For Biomaterials to join the American College of Rheumatology. In his Executive Director role, Echard advised and consulted on matters relating to the goals, programs, finances, and operation of the Society, and also saw to the development and implementation of policies and activities authorized by the Board of Directors. He worked in concert with the Board and its committees, and acted as the liaison for members and the public. Association Headquarters has initiated a search for an Executive Director for the Society For

Biomaterials to be appointed before the annual meeting in Memphis. Anne Myer and Michael Sefton are closely involved in the selection process. Dan Lemyre, who has demonstrated consistent commitment to SFB, will remain the Assistant Executive Director.

The Society For Biomaterials thanks Echard for his support to the Society during the past two years.

Welcome to Memphis and the 30th Annual Meeting of the Society For Biomaterials!

The Torch
By Joel D. Bumgardner

I would like to extend a most warm welcome to everyone attending the 2005 annual meeting and exposition of the Society For Biomaterials in Memphis. I would also like to extend a very special thanks to the members of the Program Committee in helping to set the focus and theme for this year's exciting meeting—"New Biomaterials Applications and Technologies to Meet Tomorrow's Clinical Challenges." This theme recognizes the continued evolution and expansion of the Society and its members as leaders in the development of new cutting-edge technologies, materials and devices such as nano-biomaterials, delivery of therapeutics, regenerative medicine, and tissue engineering. This theme is especially relevant to Memphis, with its large medical implant device manufacturing base; clinical, educational and research institutions; and focus on biomedical economic development. Many of the 17 special programs being held during the meeting highlight this evolution and expansion, and include new areas such as surface modification of biosensors/biochips, computational modeling, and engineering of lung, kidney and urological tissues as well as special programs in the business and regulation of biomaterials.

This year we are very excited and honored to have SFB member, Cato T. Laurencin, MD, PhD, from the Department of Orthopaedics at the University of Virginia, and member of the National Academy of Sciences-Institute of Medicine provide the keynote address. In keeping with the general theme of the meeting, Dr. Laurencin's presentation, "Musculoskeletal Tissue Engineering Past, Present, and Future," will trace the evolution of tissue engineering and provide us with a vision of the future that involves molecular biology, stem cells, developmental biology, and nano-biomaterial technology as a paradigm for the treatment of orthopaedic diseases. This presentation is sure to be a particularly insightful address since Dr. Laurencin will be able to provide perspectives from his roles as a researcher, educator and a practicing physician.

Physicians continue to play key roles in highlighting the needs and challenges still facing implant materials and devices. Numerous physicians are providing their clinical perspectives in a variety of programs such as cardiovascular, urological and kidney, lung and liver tissue engineering, to name a few. Student education and professional development continue to be a high priority for the Society and at this meeting with the "Navigating the Biomaterials Career Workshop" and the special symposium on biomaterials instruction.



I would like to note that this is the first meeting for our new headquarters staff at Association Headquarters Inc. I want to personally thank Mr. Anthony Celenza, Senior Meetings Manager, and Mr. Dan Lemyre, Assistant Executive Director, and their staff for their hard work, patience and flexibility in putting the meeting together. With their help, we were able to push back the abstract submission deadline by one month from previous years. This new deadline allowed researchers to include more

data in their abstracts, make their presentations more current, and to enhance the quality and timely exchange and dissemination of new information for the Society's membership and meeting attendees.

And kudos to 19 members of the

meeting's Program Committee (especially Anne Meyer, Lynne Jones, W. John Kao, Warren Haggard, and Karen Burg), the 29 special program and SIG session organizers, and all 185 abstract reviewers for their help and dedication in pulling the program together. With only a few minor hiccups, I am delighted to report that we/you were able to review and score 729 submitted abstracts, organize 682 abstracts into sessions, and send abstract notifications within nine weeks after the deadline for submissions! This effort was a stupendous accomplishment, especially considering that most of these activities occurred during the holiday season with its usual distractions. To quote a famous Memphian, "Thank you, thank you very much!" I offer special thanks also to the Local Arrangements Committee: Jack Parr, Shah Jahan, and Paul Kovacs.

Speaking of distractions, we are lucky to have the world famous "Memphis in May" celebration begin during our meeting. During the April 29-May 1 weekend there will be more than 60 acts featuring blues, jazz, R&B, rock-n-roll, soul, alternative and gospel music. So there is bound to be fun, food and music to appeal to just about anybody!

I believe you will find this year's meeting interesting, educational and of value, and that Memphis has much to offer in the way of biomaterials and entertainment.

So welcome and cheers!

Founders Award

Nicholas Peppas, University of Texas at Austin
Awardee Address: Hydrogels as Biomaterials: Infinite Possibilities in Bionanotechnology, Drug Delivery, Biological Recognition, Tissue Engineering, and Pure Scientific Fun!

Thursday, April 28, 2005

Plenary Session I - Ballroom B • 10:55 a.m. - 11:20 a.m.



C. William Hall Award

Alastair J.T. Clemow, Tanton Technologies
Awardee Address: 25 Years Before the Mast.

Saturday, April 30, 2005

Plenary Session II - Ballroom B • 9:05 a.m. - 9:20 a.m.



Clemson Award for Applied Research

Stephen Badylak, University of Pittsburgh
Awardee Address: A Biologic Scaffold for Tissue Reconstruction: Discovery, Development, and Commercialization.

Thursday, April 28, 2005

Plenary Session I - Ballroom B • 10:30 a.m. - 10:55 a.m.



Clemson Award for Basic Research

Kazunori Kataoka, University of Tokyo
Awardee Address: Smart Polymeric Micelles as Nanocarriers for Gene and Drug Delivery.

Saturday, April 30, 2005

Plenary Session II - Ballroom B • 8:25 a.m. - 8:50 a.m.



Clemson Award for Contributions to the Literature

Christopher Bowman, University of Colorado
Awardee Address: Novel Photopolymerization Strategies for Optimization of Biomaterial Function and Performance

Saturday, April 30, 2005

Plenary Session II - Ballroom B • 8:50 a.m. - 9:15 a.m.



Outstanding Research by a Hospital Intern, Resident or Clinical Fellow Award

Saadq El-Amin, University of Virginia
Awardee Address: Human Osteoblast Cells: Isolation, Characterization, and Growth on Polymers for Musculoskeletal Tissue Engineering

Thursday, April 28, 2005, 6:00 p.m. - 6:45 p.m. &

Friday, April 29, 2005, 11:30 a.m. - 1:00 p.m.

Poster Session I • Poster #342



Technology Innovation and Development Award

Henry Brem, Johns Hopkins
Robert Langer, MIT

Awardee Address: Technology, Innovation and Development of Gliadel for the Treatment of Brain Tumors

Saturday, April 30, 2005

Plenary Session II - Ballroom B • 8:00 a.m. - 8:25 a.m.



Young Investigator Award

Julie Babensee, Georgia Institute of Technology and Emory University

Awardee Address: Dendritic Cells and Biomaterials

Thursday, April 28, 2005

Plenary Session I - Ballroom B • 11:20 a.m. - 11:25 a.m.



Student Awards for Outstanding Research

PhD Category

Elizabeth Christenson, Case Western Reserve University

Awardee Address: Biostability and Macrophage-Mediated Foreign Body Reaction of Silicone-Modified Polyurethanes

Thursday, April 28, 2005 6:00 p.m. - 6:45 p.m. &

Friday, April 29, 2005 11:30 a.m. - 1:00 p.m.

Poster Session I • Poster #344



Heidi Holtorf, Rice University

Awardee Address: Flow Perfusion Culture Induces the Osteoblastic Differentiation of Marrow Stromal Cell-scaffold Constructs in the Absence of Dexamethasone

Thursday, April 28, 2005 6:00 p.m. - 6:45 p.m. &

Friday, April 29, 2005 11:30 a.m. - 1:00 p.m.

Poster Session I • Poster #346



Undergraduate Student Category

Ashley Krout, The University of Toledo

Awardee Address: A Hybrid Coating of Biomimetic Apatite and Osteocalcin

Saturday, April 30, 2005

Concurrent Session VIII: Delivery of Therapeutics from Implant Surfaces II: Bone and Tissue • Ballroom D • 3:30 p.m. - 3:45 p.m.

Matthew MacEwan, Case Western Reserve University

Awardee Address: Monocyte/lymphocyte Interactions and the Foreign Body Response: In Vitro Effects of Biomaterial Surface Chemistry

Friday, April 29, 2005

Concurrent Session V: Immunological Aspects of Regenerative Medicine Symposium

Steamboat Room • 4:30 p.m. - 4:45 p.m.



Masters or Health Science Degree Category

Joanne McBane, University of Ottawa Heart Institute

Awardee Address: Does Protein Kinase C Affect Monocyte-derived Macrophage Mediated Biodegradation of Polycarbonate-based Polyurethanes?

Thursday, April 28, 2005 6:00 p.m. - 6:45 p.m. &

Friday, April 29, 2005 11:30 a.m. - 1:00 p.m.

Poster Session I • Poster #348



30TH ANNUAL MEETING AND EXPOSITION

NEW APPLICATIONS AND CHALLENGES

APRIL 27-30, 2005 • MEMPHIS COOK CONVENTION CENTER • MEMPHIS, TENNESSEE, USA

MEETING OVERVIEW

The meeting has been organized to emphasize the new and expanding clinical applications and challenges of biomaterials as well as highlighting recent advances and the generation of new knowledge in the discipline. Special program topics include the use and immunological consequences of stem and progenitor cells in regenerative medicine, artificial lung and urological biomaterials and tissue engineering, nanotechnology, smart scaffolds, molecular biology techniques and characterizations, materials for biosensors, educational strategies, and regulatory and business operations. Many additional opportunities and programs will be held to address specific developments in topics related to orthopedics, cardiovascular and dental/craniofacial devices, organ/tissue engineering, cells and proteins at surfaces and interfaces, implant pathology, ophthalmology, drug delivery, and surface modifications and interactions.

GENERAL INFORMATION

All sessions of the meeting, including exhibits, posters and oral presentations will take place in the Memphis Cook Convention Center in downtown Memphis, Tennessee.

Located along the Downtown Trolley Line and within walking distance of all of the meeting hotels are attractions and world-famous Beale Street.

There's always something going on in Memphis. Whether you have time to spend a relaxed evening on Beale Street, or just want to take in the view of the mighty Mississippi from your hotel room window. Memphis has just what you're looking for. This year, we are fortunate enough to be in Memphis for the beginning of their annual Memphis in May celebration!

Memphis in May

April 29 - May 1, 2005. To the world, Memphis means great music. Music lovers from around the globe gather at the Beale Street Music Festival to celebrate this vital heritage, this deep river of sound. Three magical days. Four big stages. Thirty-three acres overlooking the Mighty Mississippi, right on the heels of historic Beale Street. More than 60 top artists. Blues, rock, gospel, R&B, alternative, and soul a spine-tingling musical variety guaranteed to shake your soul. With a growing fan base and worldwide media coverage, this stellar event sells out annually (www.memphisinmay.org)!

Transportation to and from the Airports:

The Memphis International airport is located 12 miles from the Convention Center with an approximate taxi fare of \$22 each way.

Dress Code

Business casual is the recommended dress for the meeting.

Weather

The average daytime temperature in Memphis during the meeting dates is 67°F.

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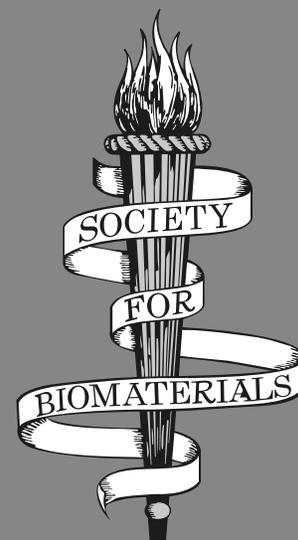
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Asylum Research
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Bioquant Image Analysis Corp.
Boehringer Ingelheim Chemicals Inc.
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2005 SFB ANNUAL MEETING HIGHLIGHTS

Keynote Address

"Musculoskeletal Tissue Engineering Past, Present, & Future"

Cato T. Laurencin, MD, PhD

University Professor

Lillian T. Pratt Distinguished Professor and Chair

Department of Orthopaedic Surgery,

Professor of Biomedical Engineering,

Professor of Chemical Engineering,

The University of Virginia

Member, National Academy of Science -

Institute of Medicine

This address will trace the origins of the field called Tissue Engineering, its evolution and maturity, and provide a glimpse at the future promise it holds in treating orthopaedically related disease as it embraces technologies ranging from molecular biology, to stem cell biology, to nanotechnology to developmental biology. It is my belief that the future will be the combination of biomaterials science and engineering with the technologies mentioned above to create a new science I term Morphoregenerative Engineering.

Symposia

Biomaterials and Nanotechnology

Overview

The objective of this symposium is to examine the impact of biomaterials in nanomedicine. Due to the new NIH roadmap in nanotechnology and nanomedicine, biomaterials scientists are asked to improve the methods of discovery, synthesis and evaluation of new biomaterials. This symposium will concentrate on molecular assemblies and complex polymer structures that exhibit structure, control, recognition and signal transmission of biological properties. The symposium is a direct result of recent directives from NIH.

Invited Speakers: Dr. Jennifer West, Rice University • *"Metal Nanoshells: Diagnostic and Therapeutic Applications of Nanotechnology"*

Dr. Stephanie Lopina, University of Akron • *"PEG-PAMAM Star Polymers for Drug Delivery"*

Chair/co-chair: Nicholas A. Peppas, University of Texas-Austin, Zach Hilt, University of Kentucky

Delivery of Therapeutics from Implant Surfaces

Overview

Surface chemistry alone is often not sufficient to direct the desired biological response to an implanted device. The chances of achieving a successful outcome can be improved by delivery of therapeutics locally from an implant surface. A timely example is the recent success of drug-eluting coatings to reduce the restenosis that occurs after placement of bare metal stents in arteries of the heart. Similarly, antimicrobial compounds on devices such as catheters help prevent infection and reduce the possibility of refractory biofilm formation. Coating strategies for long-term medical implants must accommodate several sometimes conflicting requirements: tenacious adherence to the implant, a reservoir for sufficient amounts of drug, a means for releasing the drug slowly over prolonged periods of time, an outermost coating that can reduce or protect the device against foreign body reaction, and a film chemistry that does not alter the drug itself. Achieving these goals can push the envelope in terms of surface modification techniques and surface characterization methods. This symposium will serve as a forum to present the latest advancements in surface modifications for drug delivery.

Invited speaker: Dr. Klaus Wormuth, Surmodics Corp., Eden Prairie, MN. • *"Surface Characterization of Thin Drug Eluting Coatings on Stents"*

Chair/co-chair: Erika Johnston, Genzyme Corp., Jeffrey Joseph, Thomas Jefferson University, Anna Belu, Medtronic, Liisa Kuhn, University of Connecticut Health Center, Lara Gamble, University of Washington, Hammed Benghuzzi, University of Mississippi Medical Center, Dharendra S. Katti, Indian Institute of Technology - Kanpur

Sponsor: Surface Characterization and Modification & Drug Delivery SIGs

Smart Scaffolds and ECM Analogs for Tissue Engineering

Overview

The symposium aims to discuss the synthesis, manipulation and application of scaffolds that are "smart" and can either respond to physiological stimulus or induce stimulation of useful biological events when implanted (or both things in a synergistic way). This includes the development of an all new generation of scaffolds (porous systems, hydrogels, particles, etc.) that act simultaneously as scaffolds and as carrier (controlled release) system. A few examples are scaffolds that have a capability of releasing in a controllable manner bioactive agents (growth factors, differentiation agents, etc.), that will respond to pH, temperature, enzymatic concentrations or for instances mechanical solicitations. These smart responsive scaffolds can also have the capability of recruiting in vivo useful cells (such as mesenchymal stem cells) and induce/directing their differentiation. Presentations describe the development of scaffolds with such type of characteristics, the tailoring of their properties and/or their biochemical interaction when in contact with cells in-vitro culturing systems (static or dynamic) or when implanted in vivo. In fact, another aspect that the symposium addresses is the use of in-vitro models, such as bioreactors, to study the responsive/inducing properties of the scaffolds when in contact with appropriate cells and correlate those results with appropriate in-vivo animal models.

Invited Speaker: Dr. David J. Mooney, Harvard University • *"Cell Interactive Polymers Guide Tissue Formation"*

Chair/co-chair: Rui L. Reis, University of Minho, Portugal, Laura Suggs, University of Texas at Austin, C. Mauli Agrawal, University of Texas San Antonio

Computational Modeling of Bioresponse to Biomaterials

Overview

The development of modern high-throughput synthesis techniques has resulted in an exponential growth in candidate polymers for biomedical research and clinical applications. Conventional design-of-experiments and other statistics-based techniques are inadequate for identifying promising new biomaterials in vitro, much less in vivo. Computational modeling of bioresponse to biomaterials is an important emerging paradigm for design of biomaterials for biomedical research and clinical applications. It offers the possibility for more efficient identification of high-performance biomaterials for specific biomedical research and clinical applications. The objective of the symposium is to highlight recent advances and new research directions in computational modeling of bioresponse to biomaterials.

Invited Speakers: Dr. Joachim Kohn, Rutgers University • *"Computational Modeling of Bioresponse to Biomaterials - An Overview"*

Dr. Robert Latour, Clemson University • *"Molecular Simulation of Protein-Surface Interactions"*

Chair: Doyle Knight, Rutgers University

Tissue Engineered Product Regulations

Overview

Tissue engineering provides a wide spectrum of possibilities in biomedical applications: from skin and bone regeneration to cardiovascular tissue and even organ repair. Converting the science to a product and bringing that product to market represent different challenges. Regulatory approval for tissue-engineered and combination products is largely new territory. What progress has been made? How is the FDA approval process different from CE mark? Where do we go from here? To answer these and other questions please attend the session on Regulation of Tissue Engineered Combination Products.

Invited Speakers: Dr. David F. Williams, University Birmingham-UK • *"Tissue-Engineering: Promise and Problems"*

Dr. Joyce Frey-Vasconcells, Deputy Director of FDA's Office of Cellular, Tissue and Gene Therapies • *"FDA Regulatory Requirements for Tissue-engineered Combination Products"*

Stephen Rhodes, MS, Deputy Director, Division of General, Restorative, and Neurological Devices, FDA • *"CDRH Perspective on the Regulation of Tissue Engineered Products"*

Dr. Gert Bos, KEMA Medical Inc. • *"CE Mark Requirements for Tissue-engineered Combination Products"*

Dr. David Smith, Pepper Hamilton LLP • *"The Regulation of Tissue-engineered Products; Where Do We Go From Here?"*

Chair/co-chair: Phil Triolo, Phil Triolo and Associates L.C., Karen Masterson, Thoratec Corp.

Sponsor: Biomaterials Availability and Policy SIG

The Influence of Function on Wear Simulation in Artificial Knee Joints

Overview

The international standards for wear simulator testing in the knee have been drafted over the past five years based on a standard walking cycle. During this period researchers have identified that the kinematic conditions in the knee are highly variable and design specific, and the resulting wear is critically dependent on resulting kinematic conditions. Activities with different loading and kinematic conditions can have marked impact on wear. Independently, groups in both academia and industry have been studying a range of different conditions and their impact on wear of the knee. The symposium will bring together leading research groups from industry and academia around the world to present, compare and discuss different approaches and wear simulation studies of artificial knee joints for a range of different conditions, with a view to defining a portfolio of functional simulator conditions to represent different activities in the knee.

Invited Speaker: Dr. Richard D. Komistek, University of Tennessee • *"In Vivo Determination of Kinematics, Forces and Stresses for TKA"*

Chair/co-chair: John Fisher and Jin Zhongmin, University of Leeds-UK

Sponsor: Engineering & Physical Sciences Research Council, United Kingdom, University of Leeds-UK, and EPSRC International Biotribology Network

Stem Cells and Progenitor Cells in Regenerative Medicine

Overview

This is a burgeoning area in the field of regenerative medicine, and the interaction of stem/progenitor cells with biomaterials is crucial to the success of these approaches.

Invited Speaker: Dr. Lola Ried, University of North Carolina-North Carolina State University • *"Hepatic Stem Cells and the Liver's Maturation Lineages"*

Chair/cochair: Karen Burg, Clemson University, Shelly Sakiyama-Elbert, Washington University, St. Louis

Sponsor: Biomaterials-Cell/Organ Therapies SIG

Surface Modification of Biochips and Biosensors

Overview

From genetic screening and glucose monitoring to biodefense awareness and disease diagnosis, societal demands are expanding for compact, rapid, and accurate biological testing. The robustness, sensitivity, and specificity of gene chips and biosensors depend upon the stability and surface density of antibody-, enzyme-, and oligonucleotide-based surface modifications. Furthermore, biochip and sensor designs typically require a non-fouling coating to prevent nonspecific adsorption of biological species in vitro or to minimize and protect against the foreign body response in vivo. The goal of this symposium is to serve as a forum to discuss surface modification applications and techniques that are advancing biological analysis in vivo and in vitro.

Invited speaker: Dr. W. Monty Reichert, Duke University • *"Biocompatibility of In Vivo Biosensors and In Vitro Biochips: Two Different Expectations."*

Chair/co-chairs: Anna Belu, Medtronic, Erika Johnston, Genzyme Corp., Lara Gamble, University of Washington

Sponsor: Surface Characterization and Modification SIG

Immunological Aspects of Regenerative Medicine

Overview

This symposium brings together researchers in inflammatory and immune aspects of biomaterials in medical devices to learn about the significant developments in the basic science of these areas with respect to the development of novel and physiologically integrated novel medical devices (e.g., tissue engineering, natural biomaterials). The objective of the symposium is to highlight recent developments in inflammation, immunology and leukocyte biology in the context of biomaterials that impact the emerging field of regenerative medicine.

Invited Speaker: Dr. Darrell Irvine, Massachusetts Institute of Technology • *"T Cell Motility in a 3D In Vitro Model of Lymphoid Tissue"*

Chair/cochair: Julia Babensee, Georgia Institute of Technology, and W. John Kao, University of Wisconsin

Urological Tissue Engineering

Overview

Traditionally, surgical correction of abnormalities in the lower urinary tract has been performed using autograft, allograft, and xenograft tissues. Although these procedures allow successful reconstruction of the affected organs, there are many complications. The field of Urology has met with some success in tissue engineering for bladder augmentation procedures using biologically-derived and/or synthetic polymer scaffolds to deliver pertinent in-vitro expanded cells to correct surgical defects of the organ. Furthermore, advances are being made in muscle-stem cell based tissue engineering for the treatment of stress urinary incontinence, a major health problem affecting approximately 25 million American women. This is an area of tissue engineering that is extremely important for the American population, yet, has been underrepresented in the field of biomaterials compared to more conventional areas such as cardiovascular and orthopedic applications. The aim of this symposium, therefore, is to introduce the attendees to the current clinical needs as well as the past and latest developments in the urological tissue engineering.

Invited Speaker: Dr. Ron Jankowski, Director of Research and Product Development, Cook MyoSite Inc., Adjunct Assistant Professor, Departments of Bioengineering and Urology, University of Pittsburgh • *"Tissue Engineering to Rebuild the Lower Urinary Tract"*

Chair/co-chair: Jiro Nagatomi and Michael S. Sacks, University of Pittsburgh

Novel Techniques for Biomaterials Instruction

Overview

According to the Whitaker Foundation, there is a large demand and need for highly qualified persons trained in biomaterials science. One way to meet this demand is to increase the interest and subsequent enrollment in biomaterial-related programs. Equally as important is to increase the quality of biomaterials education. That is, due to the diverse nature of our field, techniques to encourage "multidisciplinary" biomaterials education must be stressed. The objective of this symposium is to provide educators ideas to increase interest in and the quality of biomaterials education through novel instructional methods. In doing so, this symposium will highlight alternative, high-quality ways in which concepts in biomaterials can be taught to students. This can include: interactive distance learning, videotapes, Internet courses, seminars, research experiences for undergrads, aspects of entrepreneurship education to disseminate such novel teaching ideals, etc.

Invited Speaker: Dr. Kay C. Dee, Rose-Hulman Institute of Technology • *"Reaching Multiple Learning Styles in the Classroom, With Practical Suggestions for Biomaterials Courses"*

Chair/cochair: Thomas J. Webster, Purdue University, and Lisa Friis, University of Kansas

Sponsor: Biomaterials Education SIG

Artificial Lungs, Livers, and Kidneys: Blood/Material Interactions

Overview

Since the 1970s, cardiothoracic surgeons and engineers have made significant progress in the design of, and animal and clinical trials of, various designs of artificial lungs. The most well-known and in clinical use is "ECMO" (extracorporeal membrane oxygenation), but it is now falling out of favor with clinicians because of recurring problems with over-ventilation, "plasma leakage," and efficacy of gas exchange. These devices now are considered only for short-term use. Longer-term options, including a total liquid ventilator and tissue engineering approaches, are still in the early stages of development and clinical trials. Research, knowledge and experience in blood/biomaterial interactions may provide insights, directions and/or solutions to current challenges and obstacles to clinical success of artificial lungs. The aim of the symposium is to highlight recent research on interactions between synthetic membranes and biological fluids with an emphasis on membrane/blood interactions.

Invited Speaker: Dr. Joseph B. Zwischenberger, University of Texas Medical Branch, Galveston • *"The Artificial Lung: Progress and Prototypes"*

Chair/co-chair: Anne E. Meyer and Robert Baier, University of Buffalo



Allan S. Hoffman Elected Member of the National Academy of Engineering

Allan S. Hoffman, past president of the Society For Biomaterials (1983) and professor of bioengineering and chemical engineering at the University of Washington in Seattle, was recently elected member of the National Academy of Engineering (NAE) for his pioneering work on the medical uses of polymeric materials. NAE has elected 74 new members and 10 foreign associates, bringing the total U.S. membership to 2,195 and the number of foreign associates to 178.

Election to the NAE is among the highest professional distinctions accorded an engineer. Academy membership honors those who have made outstanding contributions to “engineering research, practice, or education, including, where appropriate, significant contributions to the engineering

literature” and to the “pioneering of new and developing fields of technology, making major advancements in traditional fields of engineering, or developing/implementing innovative approaches to engineering education.”

In the past, Dr. Hoffman was recognized by the Society For Biomaterials for his pioneering work and dedication to the field of biomaterials science and engineering by receiving the Clemson Award for contributions to the scientific literature in 1984 and the Founder’s Award in 2000. He is a co-author and co-editor of the new edition of *Biomaterials Science: An Introduction to Materials in Medicine*.

Member-at-Large Antonios Mikos Awarded the Marshall R. Urist Award

On February 22, 2005, at its annual meeting in Washington, D.C., the Orthopaedic Research Society honored Antonios Mikos, Member-at-Large of the Society For Biomaterials, with the prestigious Marshall R. Urist Award. The Marshall R. Urist Award, created in 1996 and sponsored by Osiris Therapeutics Inc., was given to Dr. Mikos for establishing himself as a cutting-edge researcher in tissue regeneration.



Mikos is the John W. Cox Professor in Bioengineering, professor of chemical engineering, and director of the John W. Cox Laboratory for Biomedical Engineering at Rice University. In addition, he also serves as director of Rice’s Center for Excellence in Tissue Engineering.

“This prestigious award reflects the hard work of past and present undergraduate, graduate and postdoctoral research associates in my group over the years,” Mikos said. Over the past 13 years, Mikos’ laboratory has developed extensive expertise in fabricating synthetic materials with tailored chemistries for specific tissue-engineered repair of orthopedic injuries.

Founded in 1954, the 1,700-member Orthopaedic Research Society is dedicated to improving patient care through research and education in orthopedic surgery, musculoskeletal diseases, musculoskeletal injuries and related disciplines.

Congratulations to Dr. Mikos!

A Suggested Change in Abstract Review That Would Improve Quality

The Torch
By Jason Emmanuel

This article is a suggestion for future SFB Program Committees. I encourage all of the SIGs, the 2006 Program Committee, and Council to read this article and discuss it at your upcoming meetings. Please forward your comments to John Kao (Chair, 2006 Program Committee) at wjkao@pharmacy.wisc.edu.

Anne Meyer, President.

Special Interest Groups (SIGs) come in all sizes and this has an effect on the quality of abstracts available to a given SIG's oral and poster presentation sessions. The larger SIGs have larger abstract submission pools. The converse must also be true. As the size of the pool approaches that of the number of presentation slots, reviewers must choose increasingly between filling a slot with a presentation of questionable quality and losing a slot. We would like to request that all abstract submission forms include a first, second and third choice for SIG sessions. After scoring has been completed, a macro in Excel could select out all submissions with a minimum score of 3.5 not assigned to a session and flag them by their second choice. The flagged list would be sent to all reviewers of a given SIG. A new box on the review form would state: The reviewer is satisfied that the quality of this submission pool is sufficient and requires no more abstracts to judge. Reviewers could take the scores of the previous reviewers and merely select abstracts most appropriate for their SIG's session. When the list of abstracts with their review scores is sent to the appropriate SIG officers, it will contain a larger pool with more high-quality presentations.

Staff Updates...

(Continued from page 4)

If you have any questions, require any information, or have suggestions for improved services, please feel free to contact the Society's headquarters office:

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Advances in Tissue Engineering

Rice University

**Center for Excellence in
Tissue Engineering,
Institute of Biosciences and
Bioengineering,
Department of Bioengineering**

Houston, Texas

August 10-13, 2005

Thirteenth annual short course with leading scientists from Rice University, the Texas Medical Center, industry, and other institutions on advances in the science and technology of tissue engineering. Be informed on the latest technology in the world of patient-specific therapeutics, from transplantation of cells and tissues to artificial organs.

For biomaterialists, biomedical engineers, physicians, technical managers, and others involved in research in the areas of:

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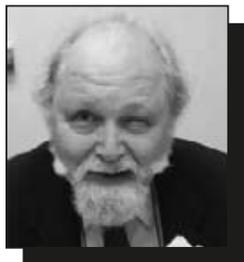
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Katz Named Associate Editor for Biomaterials and Bioengineering for the *Journal of Dental Research*



The Joint Boards of the International and American Associations for Dental Research (IADR/AADR) have named J. Lawrence Katz, PhD, as Associate Editor of the *Journal of Dental Research* (JDR), with primary responsibility for papers in the fields of biomaterials and bioengineering.

Dr. Katz is Distinguished Research Professor of Biomedical Engineering & Oral Biology and Co-Director, UMKC Center for Research on Interfacial Structure & Properties (UMKC-CRISP), at the University of Missouri-Kansas City. He has worked in the field of calcified tissue biomaterials and biomechanics for 40 years and has won many awards for research and academic/educational activities in these sub-areas of biomedical engineering. He has had

considerable experience as both an author and a referee in numerous scholarly publications, and his stated goal is for the *JDR* to become “the primary publishing venue for researchers in dental and craniofacial biomaterials and bioengineering.”

Reacting to his appointment, Dr. Katz said, “I am committed to working with the Editor to ensure the review, acceptance, and publication of manuscripts that represent the application of the most rigorous science in questions relevant to the field of dental and craniofacial biomaterials and bioengineering. I believe that this emphasis is vital to the continued recognition of the *JDR* as the premier publication in this field.”

Editor's note: Dr. Katz served the Society For Biomaterials as president from 1978 to 1979. The Society sincerely congratulates Dr. Katz!

NIST/HHS Join Forces for Medical Innovation

Government News

By Mark Bello, Public and Business Affairs, National Institute of Standards and Technology

The National Institute of Standards and Technology (NIST) has signed a Memorandum of Understanding (MOU) with the Department of Health and Human Services (HHS) to collaborate on programs that facilitate the development and delivery of innovative medical technologies. NIST has been working closely with a variety of HHS agencies, including the National Institutes of Health and the Food and Drug Administration, and the new MOU now provides an umbrella agreement to expand and strengthen those relationships.

NIST and HHS bureaus agreed to collaborate in four main areas: strategic policy and program coordination; streamlining the pathway from discovery to delivery; educational and informational initiatives; and research initiatives.

According to the new agreement, the interface of the physical sciences and life sciences is likely to “spawn the most

revolutionary technological developments.” The MOU “bridges a biological/medical department with one steeped in the physical science and engineering tradition of quantitative measurement.”

Text of the full agreement is available at www.nist.gov/public_affairs/techbeat/mou_hhs_doc.pdf.

The new MOU was released Jan. 13, 2005, in conjunction with the release of a new HHS report, *Moving Medical Innovations Forward*. The report is available at www.hhs.gov/reference/medicalinnovations.shtml.

The Promise of Biomimetic Materials and Nanotechnology in Drug Delivery

Recent advances in the discovery and delivery of drugs to cure chronic diseases have been achieved by the combination of intelligent material design with advances in nanotechnology. In particular, there has been considerable work in preparing **nanostuctured biomaterials** for various applications, such as carriers for controlled and targeted drug delivery, micropatterned devices, and systems for biological recognition, as indicated by Langer and Peppas.¹ Since many drugs act as protagonists or antagonists to different chemicals in the body, a delivery system that can respond to the concentrations of certain molecules in the body is invaluable. For this purpose, intelligent therapeutics or “smart drug delivery” calls for the design of the next generation of responsive devices and materials.

In particular, biomimetic materials, especially polymeric networks, capable of molecular recognition have been prepared by designing interactions between the building blocks of biocompatible networks and the desired specific ligands, and by stabilizing these interactions by a three-dimensional structure.^{2,3} These structures are at the same time flexible enough to allow for diffusion of solvent and ligand into and out of the networks. Synthetic networks that can be designed to recognize and bind biologically significant molecules are of great importance, and influence a number of emerging technologies. These artificial materials can be used as unique systems or be incorporated into existing drug delivery technologies that can aid in the removal or delivery of biomolecules and restore the natural profiles of compounds in the body.

In addition, biomimetic methods are now used to build biohybrid systems or even biomimetic materials (mimicking biological recognition) for drug delivery, drug targeting, and tissue engineering devices.⁴ The synthesis and characterization of biomimetic gels, and molecularly imprinted drug release and protein delivery systems, are a significant focus of recent research. Configurational biomimetic imprinting of an important analyte on an intelligent gel leads to preparation of new biomaterials that not only recognize the analyte but also act therapeutically by locally or systemically releasing an appropriate drug.

The design of a **precise macromolecular chemical architecture** that can recognize target molecules from an ensemble of closely related molecules has a large number of potential applications.⁵ The main thrust of research in this field has included separation processes (chromatography, capillary electrophoresis, solid-phase extraction, membrane separations), immunoassays and antibody mimics, biosensor recognition elements, and catalysis and artificial enzymes. Nanoimprinting creates stereo-specific three-dimensional binding cavities based on the template of interest. Efforts for the imprinting of large molecules and proteins have focused upon two-dimensional surface imprinting, a method of recognition at a surface rather than within a bulk polymer matrix. More recently, by using an epitope approach and imprinting a short peptide chain representing an exposed

fragment of the total protein, three-dimensional imprinting of proteins within a bulk matrix has been successfully prepared.

Additionally, micro- and nano-fabrication techniques have enabled the development of novel drug delivery devices that can improve the therapeutic effect of a drug, such as micro- and nano-scale needles, pumps, valves, and implantable drug delivery devices.

Why do we observe such explosion in the field now?

Electronic devices have now reached a stage of dimensions comparable to those of biological macromolecules. This raises exciting possibilities for combining microelectronics and biotechnology to develop new technologies with unprecedented power and versatility. Thus, in recent years we have seen an explosion in the field of novel microfabricated and nanofabricated devices (e.g. for drug delivery). Such devices seek to develop platforms with well-controlled functions at the micro- or nano-scale, and they include nanoparticulate systems, recognitive molecular systems, biosensing devices, and microfabricated and microelectronic devices.

There are a variety of microelectronic devices that have been studied for controlled drug delivery systems, such as microchips capable of the storage and then delivery of multiple drugs in a controlled manner. Solid-state silicon microchips that can provide controlled release of single or multiple chemical substances on demand have been fabricated and demonstrated.⁶ Microreservoirs that can be filled with chemicals in solid, liquid, or gel form are released individually via electrochemical dissolution of the thin anode membranes covering their opening. The advantages of this microdevice include that it has a simple release mechanism, very accurate dosing, and the ability to have complex release patterns. In addition, multi-pulse drug delivery from a resorbable polymeric microchip device was demonstrated.⁷

Another interesting approach involves the development of microfabricated microneedles. This approach can have a remarkable effect in enhancing the transdermal delivery of drugs without causing significant pain to the patient. The outer 10-20 microns of skin (the stratum corneum) acts as a barrier to the diffusion of the drug molecules. Since the stratum corneum does not have nerves, needles that are long enough and robust enough to penetrate across this layer, but don't penetrate into the deeper skin layers that contain nerves, have the potential to make transdermal delivery a painless and much more viable option.⁸

The development of **nanoparticulate systems** for drug delivery applications has taken a level of sophistication never before seen in the field of drug delivery.⁹ Using intelligent polymers, it is now possible to design new devices for **intelligent therapeutics**. Such systems can be employed for autofeedback drug delivery, whereby

Continued on page 22

Broadband CARS Microscopy for Biomaterials

Feature

By Marcus T. Cicerone and Tak W. Kee,
Polymers Division, National Institute of
Standards and Technology

The task of tracking very complex processes with high spatial resolution, sensitivity, and chemical specificity in living cells is a major challenge in biological microscopy. Chemical specificity is typically achieved through some form of labeling, which has potential to be somewhat invasive. Raman or infrared (IR) microscopy can be utilized to image samples in their natural form using molecular vibrations as a contrast mechanism. The spatial resolution that can be achieved with IR microscopy is insufficient to resolve cellular components. The use of IR microscopy is further limited by interference of water in the vibrational spectra. Spontaneous Raman microscopy can be performed with high spatial resolution, but suffers from low scattering cross-sections, so that high laser power is often required, introducing the possibility of sample photodamage, especially to live cells. Coherent Anti-Stokes Raman Scattering (CARS) can be performed at significantly lower light levels than spontaneous Raman scattering, increasing the likelihood that CARS can be applied to live cells without inflicting photodamage. This, in addition to the high spatial resolution inherent in nonlinear optical microscopy, has led CARS microscopy to begin emerging as a powerful, noninvasive technique for biological and materials imaging. Examples of potential applications for CARS microscopy are noninvasive monitoring of cell metabolic state and detection of cell signaling response to external stimuli.

The initial work on CARS microscopy dates back to 1982, when it was used to resolve detailed structure of onion-skin cells.¹ In 1999, CARS microscopy was used in a collinear geometry and since then significant progress has been made, including imaging of live cells and photoresist materials.² Today, there are two general directions in which CARS microscopy is being taken. One direction involves generation and detection of signal in a narrow spectral band to achieve noninvasive video rate imaging, usually of biological specimens. The other direction is towards hyperspectral imaging. Generation and detection of signal in a broad spectral range provides for high chemical resolving power, but at a slower rate of image acquisition. Until recently, a bandwidth of $\sim 200\text{ cm}^{-1}$ had been achieved and CARS microscopy had been used to image and distinguish two distinct chemical species simultaneously, providing a limited degree of chemical specificity.^{3,4} We recently demonstrated a CARS microscope that exhibited an increased breadth of spectral sensitivity ($\sim 2500\text{ cm}^{-1}$), covering the Raman fingerprint region (800 cm^{-1} to 1800 cm^{-1}) and beyond.⁵ This approach will allow for chemical identification of multiple species, and enables the continuous monitoring of subtle changes in complex systems, such as biological cells.

Figure 1 is ladder diagram that describes the CARS process. CARS microscopy utilizes pulsed laser light of two frequencies to detect molecular vibrations. Pump light, with a frequency of ω_p , is mixed with Stokes light at ω_s in the sample. When the frequency difference ($\omega_p - \omega_s$) is resonant with a vibrational state in the sample, that state gets coherently populated. Population within the vibrational state is further promoted to a virtual state by a second absorption of pump light at ω_p , and relaxation from this final virtual state produces the anti-Stokes light at $2\omega_p - \omega_s$. Because the anti-Stokes light is of shorter wavelength than the pump or Stokes light, CARS avoids the usual problem of

contamination from fluorescence. On the other hand, a nonresonant background, which arises from permutations of the absorption and emission processes depicted in Figure 1, presents a spectral contamination, although of lesser magnitude than is typically observed with fluorescence in spontaneous Raman scattering.

Figure 2a is a CARS spectrum of benzonitrile obtained with a broadband CARS microscope, the details of which we have recently reported.⁵ With this instrument we can acquire spectra in the range of 500 cm^{-1} to 3100 cm^{-1} with good spatial resolution and relatively fast pixilation rates (17 ms signal acquisition). The broadband CARS spectra are generated by using broadband Stokes light, as indicated by the dashed vertical arrows in Figure 1. The instrument utilizes a single 150-fs unamplified Ti:sapphire laser. The laser output was divided into two parts: one was used as pump (ω_p), and another was focused into a tapered silica fiber to generate broadband Stokes light (ω_s). Use of a single laser practically eliminates temporal jitter between pump and Stokes light. The pump and Stokes light, having powers of 13 mW and 10 mW respectively, were combined in a dichroic beamsplitter

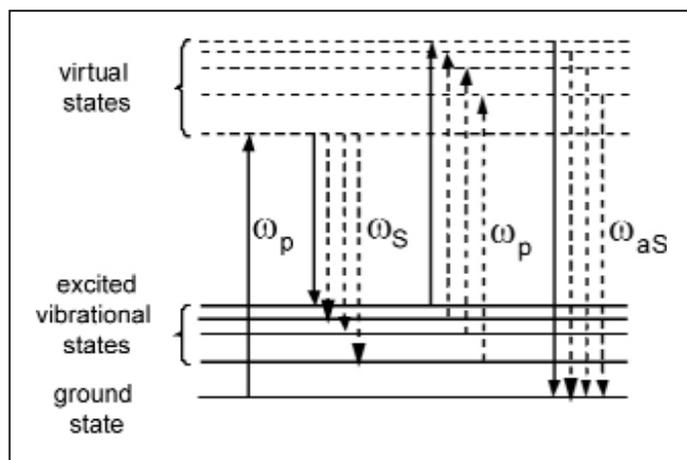


Figure 1. Energy level diagram for single frequency CARS process (solid vertical arrows) and Broadband CARS (solid and dashed vertical arrows).

and directed into a 0.8 NA microscope objective. The sample was scanned with a motorized x-y stage and the broadband CARS signal was collected with a 0.5 NA objective. A charge coupled device (CCD) camera mounted on a spectrograph was used for signal detection after spectral filtering. The stability of the spectrum depends highly on the stability of the broadband Stokes light, which has a noise of below 5 percent within an hour. The dashed line in Figure 2a shows the nonresonant background, which accompanies the resonant CARS signal. In Figure 2b, the normalized CARS spectrum of benzonitrile is presented by taking the ratio between the resonant signal to the nonresonant background. Figure 2c is a spontaneous Raman spectrum of benzonitrile acquired in our instrument at a laser power of 23 mW. To contrast the efficiencies of the two processes, the Raman spectrum required 1,000 ms acquisition time to obtain a similar signal-to-noise ratio to the CARS spectrum taken in 17 ms.

The ability of broadband CARS microscopy to perform chemically sensitive hyperspectral imaging is illustrated in Figure 3a. The sample is a tertiary polymer blend containing equal parts

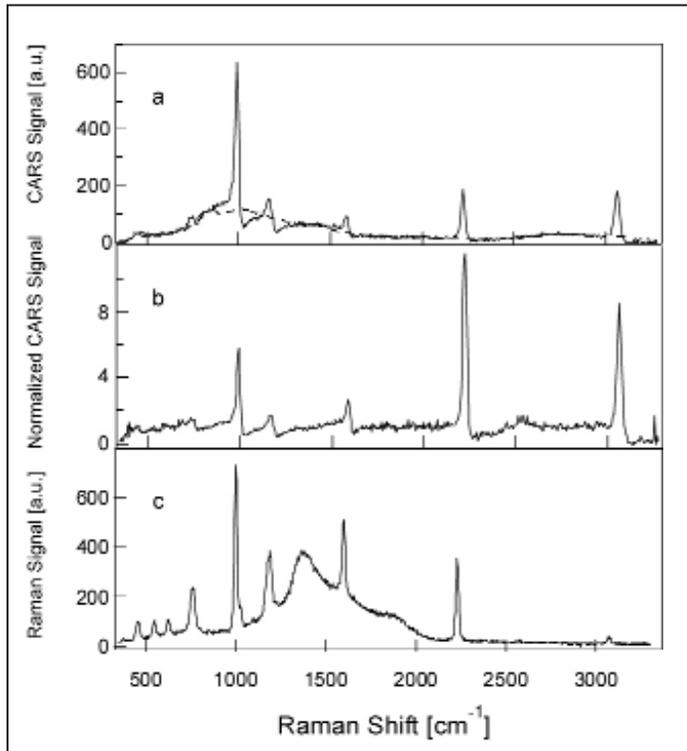


Figure 2. Broadband CARS spectrum of benzonitrile. Panel a: raw CARS spectrum (solid line), and nonresonant background (dashed line). Panel b: ratio of CARS spectrum to nonresonant background (solid line). Panel c: spontaneous Raman spectrum obtained under identical laser flux (23 mW, but all in pump light).

of polystyrene (PS), poly(methyl methacrylate) (PMMA) and poly(ethylene terephthalate) (PET). The pseudo colors red, green and yellow in the image are assigned for PS, PET, and PMMA. The image contains 150 x 150 pixels and the dwell time at each pixel is 17 ms. The CARS spectra for each of the components in the blend are given in Figure 3b. The highlighted regions in the spectra are used to assign the identity of a given pixel. By comparing the spectra, we can assign the polymer identity with a confidence level of 99 percent.

We believe that broadband CARS microscopy has notable potential for developing into a widely used imaging technique. In order for this to happen, two primary challenges must be overcome. These are compensation for axial chromatic aberration (ACA) induced by the focusing objective and minimizing the nonresonant background. A poor spatial overlap between the pump and Stokes light due to ACA of the microscope objective can significantly decrease the signal strength. Sensitivity to ACA is a strong function of numerical aperture. Fortunately, at numerical aperture (NA) = 0.8, the requirement that ACA be less than 1 μm over a spectral range of 800 nm to 1,100 nm is not beyond the specifications of commercially available objectives. Thus we were able to use a commercial 0.8 NA objective in our first study.⁵ Of course, imaging at higher NA is desirable for increased signal and higher spatial resolution, and the ACA issue will have to be resolved. The presence of the nonresonant background is another major challenge in CARS microscopy because it imposes a lower

boundary for detection limit. Reducing or eliminating the nonresonant background is therefore highly desirable. Efforts in addressing these issues are currently underway in our laboratory.

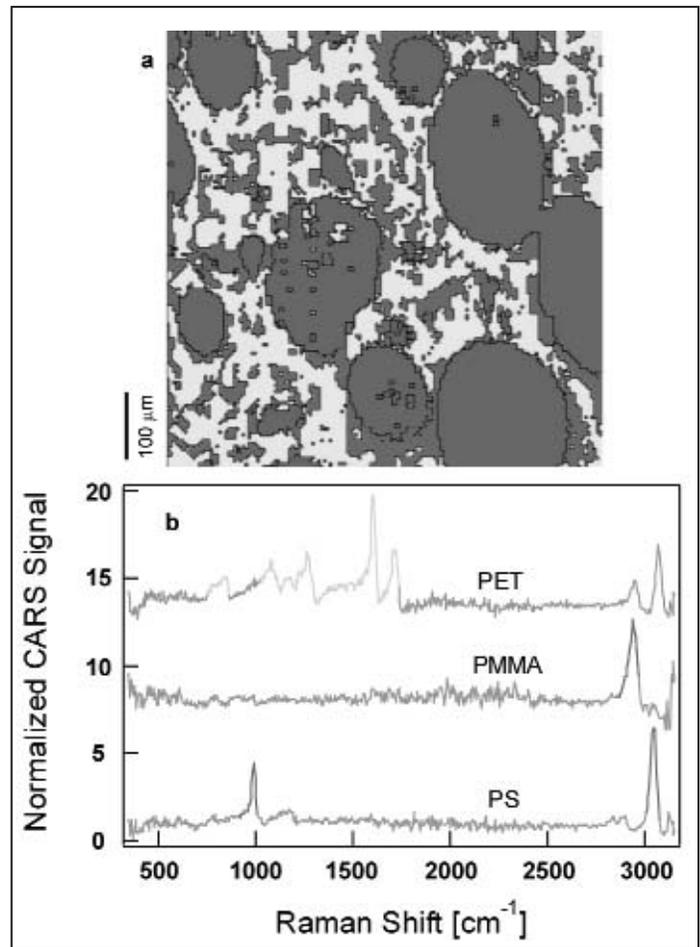


Figure 3. Panel a: broadband CARS micrograph of a phase-separated polymer blend including equal parts of PMMA, PS, and PET. Panel b: reference spectra from each of the individual polymer components (with arbitrary vertical shift for clarity). The highlighted segments indicate spectral regions that were used for identification of spectra from each pixel in Panel a.

We are reasonably confident that these issues will be resolved in the near future and an improved sensitivity and signal-to-noise ratio are within reach.

In the past few years, CARS microscopy has been enjoying increased attention and it is continuously generating strong interests in the field of biological imaging. Most recently, Xie et al. have used narrowband CARS microscopy to monitor lipid droplet trafficking in cells and differentiation of fibroblasts to adipocytes.⁶ The authors show that before fibroblasts fully differentiate into adipocytes by acquiring a large number of lipid droplets in cytoplasm, there exists a period in which almost all the cytoplasmic lipid droplets disappear. This result has never been observed before with other techniques. This work clearly indicates that the noninvasiveness, high sensitivity and selectivity of CARS present the promise of facilitating increased insights into many more biological processes. We are hopeful that the increase in chemical specificity through hyperspectral

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Biomaterials Cell/Organ Therapies Special Interest Group News

Special Interest Group News

By Shelly E. Sakiyama-Elbert

The Biomaterials Cell/Organ Therapies Special Interest Group (SIG) is comprised of approximately 40 members from both industry and academia, including a significant number of student members. The goal of this SIG is to facilitate the education of biomaterials community members with regards to new technological developments that may enhance their research or product development. Towards this goal, the SIG is organizing a tutorial and a symposium at the 2005 annual meeting in Memphis.

The tutorial, "Methods to Characterize Cells in Contact With Materials: Gene Expression and Activation of Cell Signaling Cascades," is chaired by Donald Elbert, from Washington University in St. Louis. The response of cells to materials is dictated by the activation of cell signaling cascades. Characterization of the state of cell signaling cascades relies on a variety of techniques that monitor changes in gene expression, protein phosphorylation, or the presence of GTP on G-proteins. In this tutorial, the application of some of these techniques will be described in detail. For the study of gene expression, the use of quantitative PCR, real-time PCR, and

gene arrays will be discussed. For the study of phosphorylation state or the presence of bound GTP, the use of pull-down assays, immunoprecipitations, gene knockdowns (siRNA and antisense), and chemical inhibitors of specific signaling cascades will be described. Speakers will include Donald Elbert, Shannon Hughes and Shelly Sakiyama-Elbert.

The symposium, "Stem Cells and Progenitor Cells in Regenerative Medicine," is chaired by Shelly Sakiyama-Elbert, from Washington University in St. Louis, and co-chaired by Karen Burg, from Clemson University. This is a burgeoning area in the field of regenerative medicine, and the interaction of stem/progenitor cells with biomaterials is crucial to the success of these approaches. The target audience is researchers with interests in the utility of stem and progenitor cells in regenerative medicine and tissue engineering. The symposium will feature Dr. Lola Reid, from N.C. State University and the University of North Carolina at Chapel Hill, as the invited speaker. Her research focuses on liver stem cell lineage biology and signal transduction mechanisms.

News from the Biomaterials Availability and Policy Special Interest Group

Special Interest Group News

By Karen Masterson

The Biomaterials Availability and Policy Special Interest Group (BASIG) is proud to present two complementary sessions at the 2005 annual meeting in Memphis. These will consist of a panel discussion on biomaterials availability for long-term implants and an invited speaker session addressing the regulatory issues of tissue-engineered combination products. Details of these two sessions are below.

Update on Biomaterials Availability for Long-Term Implants

Panel Discussion, April 28, 2005, from 1:30 p.m. - 3:00 p.m.

It has now been more than six years since the passage on August 13, 1998, of Public Law 105-230, also known as the Biomaterials Access Assurance Act of 1998. Some materials suppliers now allow long-term implant use of their polymers under a variety of restrictions, while others still prohibit their materials from use in long-term implants. Many device and implant manufacturers do not know where they can purchase materials for long-term implants. The objective of the panel discussion is to provide an update on the status of the availability of some biomaterials for long-term implantation. The discussion will address the initial effects of passage of the Biomaterials Access Assurance Act of 1998, the conditions

under which materials are being supplied, and why some materials are still not available.

The panel members for this discussion are:

- Scott Defelice, president, Oxford Performance Products
- Mike Kell, director of sales and marketing-medical, Westlake Plastics
- Brian Jones, chair of Risk Management Committee, Dow Corning
- Bob Ward, president, Polymer Technology Group
- Jennifer Goode, Office of Device Evaluation, CDRH, Food and Drug Administration
- Carl McMillin, consultant, Synthetic Body Parts (Moderator)

Regulation of Tissue-engineered Products Session

April 29, from 8:00 a.m. to 10:00 a.m.

Tissue engineering provides a wide spectrum of possibilities in biomedical applications, from skin and bone regeneration to

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Biomimetic Materials and Design: Biointerfacial Strategies, Tissue Engineering and Targeted Drug Delivery

Book Review

By Liisa Kuhn

Edited by Angela K. Dillow and Anthony M. Lowman.
Copyright 2002, Marcel Dekker Inc., New York, NY, 679 pages.

Description and Commentary

The field of biomaterials has evolved from using already existing polymer and metals, and ceramics, to selecting from a group of application-tailored, novel biomaterials that interact with cells and tissues. Biomimetics, the imitation of aspects of natural materials or processes, has become a fundamental strategy for biomaterials selection and application-tailored synthesis. This approach has led to the development of biomaterials that mimic the extracellular matrix of natural tissues, and have modified surfaces with ligands that interact with cell receptors. They are biointeractive, bioactive, highly biocompatible, and capable of enhancing and directing cell adhesion, cell proliferation and cell differentiation. If you are interested in getting involved in this type of research regarding surface-modified biomaterials for regenerative applications, including tissue engineering and targeted drug delivery, this text is an excellent resource.

There are numerous contributions from heavy hitters in the field: M. Tirrel, K. Healy, D. Grainger, R. Langer, N. Peppas, P. Stayton, A. Hoffman, J. Joseph, and J. West to name a few. The table of contents is included below so you can appreciate the depth to which this subject is discussed. The chapters are written as historical reviews of the progression within the various sub-specialties of biomimetic surface modifications. Refreshingly, the references are thorough and identify the key articles throughout the last nearly 20 years. This text far exceeds anything your graduate student or technical assistant, or a web search, can assemble! For example, there is a summary of 86 different studies indicating how porosity and/or surface ridges affect cell behavior (adhesion, spreading, migration, extracellular matrix production, etc.). If you are a graduate student beginning research in this area, look no further. This is a very thorough and comprehensive review of biointerfacial strategies. There are chapters explaining how the extracellular matrix regulates cell behavior through cell-adhesion-dependent signaling pathways, which set the stage for understanding the impact of biomaterial surface modifications on cellular response. The only downside of this book is that all of the figures are black and white so the striking colors of the fluorescently labeled cells and complicated molecular models are lost. This is probably why the book is reasonably priced.

As Bob Langer puts it on page 278, "The discovery of ligands with exquisite specificity for targets will ultimately become part of the synthetic repertoire for biomaterials." That time is now. Learn about the concepts and capabilities with this comprehensive resource.

Audience

This book is particularly suited for those scientists, from any field, interested in acquiring in-depth information about

biomimetic surface modifications of biomaterials. It could be used as a graduate level textbook for a class on biomimetic materials and design. This book would make an excellent addition to a university library or a corporate library due to the breadth of subject and the rigor with which the subject is reviewed.

Contents

I. Biointerfacial Strategies

1. Use of supported thin films of peptide amphiphiles as model systems of the extracellular matrix to study the effects of structure-function phenomena on cell adhesion
2. Engineering of integrin-specific biomimetic surfaces to control cell adhesion and function
3. Mimetic peptide-modified materials for control of cell differentiation
4. Effects of substratum topography on cell behavior
5. Cytomimetic biomaterials: fabrication, characterization, and applications
6. Micro- and nano-scale organization of proteins modulate cell-extracellular matrix interactions: lessons for the design of biomaterials
7. Cell adhesion-dependent signaling pathways on biomaterials surfaces

II. Tissue Engineering

8. Biomaterials: synthetic and engineering strategies
9. Scaffolds for directing cellular responses and tissue formation
10. Chitosan as a molecular scaffold for biomimetic design of glycopolymer biomaterials
11. "Cell-internalizable" ligand microinterfaces on biomaterials: design of regulatory determinants of cell migration
12. Biomimetic strategies and applications in the nervous system
13. Tissue engineering strategies for axonal regeneration following spinal cord injury

III. Targeted Drug Delivery

14. Micropatterning biomimetic materials for bioadhesion and drug delivery
15. Bioinspired engineering of intelligent drug delivery systems and protein-polymer conjugates
16. Implantable drug delivery devices: design of a biomimetic interfacial drug delivery system
17. Pharmacologically active biomaterials
18. Biomimetic lung surfactant replacements
19. Peptide nucleic acid (PNA) conjugates in biotechnology

Fantastic Voyage: Live Long Enough to Live Forever

Book Review

By Liisa Kuhn

By Ray Kurzweil and Terry Grossman, Copyright 2004, Rodale Books, New York, NY, 452 pages.

Description and Commentary

In *Fantastic Voyage*, inventor and futurist Ray Kurzweil and Terry Grossman, director of a longevity clinic, hypothesize that if many of the products from medical research reach fruition, and the pace of new technology continues at its rapid rate, we may soon live forever. It is an interesting and thought-provoking concept. With our rapidly increasing comprehension of the biochemical processes and pathways of biology, we are quickly gaining knowledge related to biological principles of life. We are beginning to understand aging, not as a single inexorable progression, but as a group of related biological processes. Strategies are emerging, perhaps within your lab, for fully reversing each of these aging processes, and disease processes as well. Many experts, including the authors, believe that within a decade we will be adding more than a year to human life expectancy every year! At that point, with each passing year, your remaining life expectancy will move further into the future. He predicts that radically extending longevity will occur in three steps or bridges. This book is intended to serve as a guide to aggressively apply today's knowledge to live long enough (Bridge One) to take advantage of the full development of the biotechnology revolution (Bridge Two). This in turn will lead to the nanotechnology-artificial intelligence revolution (Bridge Three), which has the potential to allow us to live indefinitely.

While this book review column typically features standard engineering texts, this book was interesting enough to feature within *Biomaterials Forum*. It is an easy and enjoyable read. There are explanations and summaries of most of the recent medical advances, allowing one to view biotechnology from a broad perspective, rather than the narrow one scientists typically utilize within our research. Kurzweil's Web site provides a futurist's portal for those interested in artificial intelligence (www.kurzweilai.net) and descriptions of his other

books, such as the *Age of Spiritual Machines*, and the *Age of Intelligent Machines*. This book is highly recommended by others, such as Dean Ornish, MD, (developer of the Opening Your Heart program), George King, MD, (director of research, Joslin Diabetes Center, Harvard Medical School), and John Gray, PhD (author of *Men are from Mars, Women are from Venus* series of books).

Contents

- Chapter 1. You can live long enough to live forever
- Chapter 2. The bridges to come
- Chapter 3. Our personal journeys
- Chapter 4. Food and water
- Chapter 5. Carbohydrates and the glycemic load
- Chapter 6. Fat and protein
- Chapter 7. You are what you digest
- Chapter 8. Change your weight for life in one day
- Chapter 9. The problem with sugar (and insulin)
- Chapter 10. Ray's personal program
- Chapter 11. The promise of genomics
- Chapter 12. Inflammation - the latest "smoking gun"
- Chapter 13. Methylation - critically important to your health
- Chapter 14. Cleaning up the mess: toxins and detoxification
- Chapter 15. The real cause of heart disease and how to prevent it
- Chapter 16. The prevention and early detection of cancer
- Chapter 17. Terry's personal program
- Chapter 18. Your brain: the power of thinking...and of ideas
- Chapter 19. Hormones of aging, hormones of youth
- Chapter 20. Other hormones of youth: sex hormones
- Chapter 21. Aggressive supplementation
- Chapter 22. Keep moving: the power of exercise
- Chapter 23. Stress and balance

News from the Biomaterials...

(Continued from page 18)

cardiovascular tissue, and even organ repair. Converting the science to a product and bringing that product to market represent different challenges. Regulatory approval for tissue-engineered combination products is largely new territory. What progress has been made? How is the FDA approval process different from CE marking? Where do we go from here? To find answers to these and other questions, attend this BAPSIG-sponsored session.

Invited Presentations

Tissue-Engineering: Promise and Problems, David Williams, PhD, Director, UK Centre for Tissue Engineering

FDA Regulatory Requirements for Tissue-engineered Combination Products, Dr. Joyce Frey-Vasconcells, Deputy Director of FDA's Office of Cellular, Tissue and Gene Therapies (OCTGT)

CDRH Perspective on the Regulation of Tissue-engineered Products, Stephen Rhodes, MS, Deputy Director, Division of General, Restorative, and Neurological Devices, FDA

CE Mark Requirements for Tissue-engineered Combination Products, Gert Bos, PhD, KEMA Medical Inc.

An Overview of Regulatory and Other Factors that Impact the Economic Viability of Tissue-engineered Combination Products, David Smith, JD, of Counsel Pepper Hamilton, LLP, founder and principal, Teregenics, LLC

Session co-chairs are Phil Triolo, president, Phil Triolo and Associates LC, and Karen Masterson, R&D engineer, Thoratec Corp.

Affymetrix Inc., Santa Clara, Calif., and **Karolinska Institutet**, Stockholm, Sweden, announced that they have entered into a strategic alliance designed to improve healthcare by accelerating the translation of basic genetic research into tools for better diagnosis, prognosis, and treatment. During the next five years the projects will include genetic analyses and measurement of gene expression in patients with atherosclerosis, breast cancer, rheumatoid arthritis, asthma and dyslexia. These diseases affect a large number of patients worldwide. Systematic use of the genomic information obtained will enable development of new and better clinical methods and drugs, thereby reducing mortality and improving quality of life for patients suffering from these diseases.

The Karolinska Institutet/Affymetrix Translational medicine research projects will use sufficiently large sample sizes to establish true clinical relevance of both gene expression and DNA sequence variation in key areas of unmet medical needs.

Biacore International AB, Uppsala, Sweden, announced the launch of Biacore® T100, a new generation system for protein interaction analysis. Biacore T100 provides comprehensive information about how proteins interact with other molecules. The unique information generated by Biacore T100 is invaluable for many applications such as elucidation of disease pathways, definition of therapeutic targets, selection of drug candidates, and decisions on the safety of a protein therapeutic. Biacore T100 sets the performance standard for protein interaction analysis. From a single instrument, scientists can determine affinity and rate constants, binding specificity, concentration, and thermodynamic parameters. In this way, applications as time-consuming as antibody characterization, which could take weeks by conventional methods, can be completed in days with Biacore T100. Software wizards assist with the analysis of every interaction parameter, making the system straightforward to use, and suitable for both novice and experienced users.

Dendritic NanoTechnologies Inc. (DNT), Mount Pleasant, Mich., **The Dow Chemical Co.**, and **Starpharma**, Melbourne, Australia, have reached an agreement that provides DNT and Starpharma with ownership or access to the world's broadest patent portfolio in the field of dendrimers, and establishes the companies as leading providers of market-validated nanotechnology with near-term, tangible commercial applications. Under terms of the deal, Dow Chemical will assign its entire intellectual property portfolio and associated royalties in the field of dendrimers (196 patents comprising 41 patent families) to DNT in exchange for a significant equity stake in DNT. Starpharma, which already held a 42 percent interest in DNT, will make an additional cash equity investment in the company in exchange for exclusive rights to DNT and former Dow intellectual property for polyvalent, dendrimer-based pharmaceutical applications.

Dendrimers are a new class of nanostructures with physical properties that make them ideal vehicles for targeting diseases and delivering drugs to fight them. Dendrimer technology was first developed at Dow Chemical. DNT's current product development areas include protein, antibody, and anti-inflammatory drug delivery technologies for the pharmaceutical industry; small-interfering RNA (si-RNA) drug targeting and delivery solutions for the biotech industry; and new diagnostic solutions for enhancing the findings of MRIs. With the assignment of the Dow patent portfolio, DNT will now own the world's broadest intellectual property position in dendrimer science. In January 2004, Starpharma became the first company in the world to initiate human clinical testing of a dendrimer-based pharmaceutical (VivaGel™ for prevention of HIV) under a U.S. FDA Investigational New Drug application. VivaGel was recognized as one of the top five nanotech breakthroughs of 2004 by the Forbes/Wolfe Nanotech Report.

Fertin Pharma, Copenhagen, Denmark, announced that the company will launch a new nicotine gum on the U.S. store brand market in collaboration with Perrigo. Fertin Pharma started shipping nicotine gum to the United States in December 2004. The company has entered into collaboration with Perrigo, America's largest supplier of over-the-counter (non-prescription) pharmaceutical and nutritional products for the store brand and contract manufacturing markets. The new 2-milligram and 4-milligram nicotine gum will be produced in regular, orange and mint flavors and will be Fertin Pharma's first launch in the United States. Perrigo received approval from the U.S. Food and Drug Administration to market the products in October 2004, indicated as an aid to smoking cessation.

New analysis from **Frost & Sullivan**, *U.S. and Asian Markets for Orthopedic Joint Replacement*, analyzes the specific markets in the major Asian countries, namely Australia, China, India, Japan and South Korea. The combined population of these countries is about 2.49 billion. The study reveals that the Asian joint replacement market generated revenues of \$885 million in 2003. During the same period, the U.S. market consumed an estimated \$4.9 billion worth of orthopedic joint replacement implants. Although the United States is the largest market for joint replacements, the Asian market for these implants is growing twice as fast. An aging baby boomer population in the United States as well as in Asia is likely to further propel demand. This trend especially holds true in Asia, as women in this region are more susceptible to osteoarthritis (OA) of the knee than their Caucasian counterparts. Superior technical innovations in this market are also anticipated to boost growth in the near future.

Invitrogen Corp., Carlsbad, Calif., announced it has signed a definitive agreement to acquire privately held molecular separation and purification technology pioneer **Dynal Biotech**, Oslo, Norway, from majority owner Nordic Capital and a co-investor. Dynal is the industry leader in magnetic bead technologies that are used in cell separation and purification, cell stimulation, protein research, nucleic acid research, and microbiology. The acquisition will provide Invitrogen with bead-based isolation technologies that can be leveraged across the company's broad technology portfolio. In addition, Dynal is a major supplier of specialized magnetic particles to major diagnostic product manufacturers for use in high-throughput automated immunoassay and other instrument systems.

Medtronic Inc., Minneapolis, and **Alnylam Pharmaceuticals Inc.**, Cambridge, Mass., a leading RNAi therapeutics company, announced that they will collaborate to pursue potential therapies designed to treat neurodegenerative disorders such as Huntington's, Alzheimer's and Parkinson's disease. The collaboration will focus on developing novel drug-device combinations incorporating RNAi therapeutics. RNAi, or RNA interference, refers to a technique for silencing targeted genes in a cell, inhibiting their ability to produce particular proteins involved in specific diseases. Initial development will focus on delivering RNAi therapeutics to specific areas of the brain using novel infusion systems.

Under terms of the collaboration agreement, after successful completion of an initial joint technology development program and a joint decision to initiate product development, Alnylam would be responsible for the discovery and early development of candidate RNAi therapeutics, and Medtronic would be responsible for late-stage development and commercialization of any drug-device products that result. Medtronic also would adapt or develop medical devices to deliver the candidate RNAi therapeutics to targeted locations in the nervous system.

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Perspectives...

(Continued from page 15)

the hydrogel can be designed to rapidly respond to changes in the external biological conditions. This idea may be used to develop novel insulin delivery systems. Another particularly novel use of these systems is for the release of human calcitonin. The physicochemical understanding of such hydrogels under the conditions of application is neither simple nor well-developed. Considering that all these carriers are ionic hydrogels, and that several ionic and macromolecular components are involved, with associated thermodynamically non-ideal interactions, it is evident that analysis and prediction of the swelling and drug delivery behavior is rather complex. Additionally, new promising methods of delivery of chemotherapeutic agents using nanoscale structures have been recently reported.¹⁰

Particles in the submicron range possess very high surface-to-volume ratios, thus allowing for intimate interaction between the surface of the particles and the gastro-intestinal mucus. Additionally, carriers in the particulate form should be able to diffuse further into the mucus layer enabling them to reach the cells of the epithelial layer. The particle size and surface properties, namely their relative hydrophobicity, are the main factors affecting the particles' effectiveness in prolonging their transit time in the GI tract and protecting the active agents from degradation.

An alternative method of targeting drugs to specific sites is by use of bioadhesive and mucoadhesive nanostructures. Such systems usually consist of hydrogen-bonded structures such as poly(acrylic acid)-based hydrogels, which adhere to the mucosa due to hydrogen bonding and/or polymer chain penetration into the mucosa or tissue. Linear polymeric chains can be added to PAA-based mucoadhesives either as free chains or as tethered structures to serve as mucoadhesion promoters.

These recent developments in the field of drug delivery could not have been predicted 20 years ago when the emphasis of all controlled release work was on the "adjustment" of the drug release rate. These novel drug delivery materials and devices can enable controlled delivery that was previously unattainable, leading to enhanced therapeutic activity of a drug. In the future, biomimetic systems and nanotechnologies are expected to continue to enhance drug delivery methodology as they have been doing in other fields of biomaterials science and engineering.

Dr. Peppas can be reached at Laboratories of Biomaterials, Drug Delivery, Bionanotechnology and Molecular Recognition, Departments of Chemical and Biomedical Engineering and Division of Pharmaceutics, The University of Texas at Austin, Austin, TX, 78712, USA. Dr. Hilt is affiliated with the Departments of Chemical and Materials Engineering, University of Kentucky, Lexington, KY, 40506, USA.

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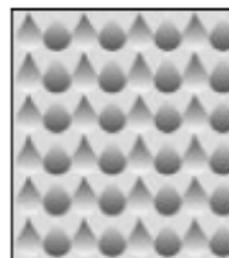
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Biolnk

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Palatin Technologies Inc., Cranbury, N.J., and **King Pharmaceuticals, Inc.**, Bristol, Tenn., announced positive results of a phase 2A pilot clinical study evaluating PT-141 in pre-menopausal women diagnosed with female sexual dysfunction (FSD). Patients in the study receiving PT-141 reported increases in their levels of sexual desire and genital arousal compared to placebo. Additionally, there was a correlation between sexual desire and genital arousal in patients receiving PT-141, an observation that further reinforces the potential importance of these reports. Eighteen women with a diagnosis of FSD were enrolled in this double-blind, randomized, placebo-controlled, single-dose, cross-over clinical study. PT-141 is the first compound in a new drug class known as melanocortin receptor agonists under development to treat sexual dysfunction.

St. Jude Medical Inc., St. Paul, Minn., announced the European market launch of the QuickSite® 1056T bipolar left-heart pacing lead, the world's first cardiac resynchronization therapy (CRT) lead to combine bipolar pacing capability with a composite body for superior handling and a unique S-shaped distal tip for outstanding stability. The lead represents the next advance in the QuickSite family of left-heart leads. Specifically designed for placement in the coronary sinus, the St. Jude Medical QuickSite 1056T bipolar lead enables left-ventricular pacing in cardiac resynchronization therapy applications. At 5.5 French, the lead body is as small in diameter as the previously available QuickSite 1056K unipolar lead.

Broadband...

(Continued from page 17)

imaging with our microscope, in addition to the inherently superb spatial and temporal resolution of CARS, will allow the use of broadband CARS microscopy for noninvasively tracking the temporal and spatial course of cellular events involved in complex biological processes such as differentiation and signal transduction, opening windows to insights on biological processes that were closed, or practically closed heretofore.

References

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www.regenerate-online.com

Controlled Release Society 32nd Annual Meeting & Exposition

June 18-22, 2005
Fontainebleau Hilton
Miami Beach, FL, U.S.A.
www.controlledrelease.org

American Society for Artificial Internal Organs 51st Annual Conference

June 9-11, 2005
The Hilton Washington
Washington, D.C., U.S.A.
www.asaio.com

American Society for Metals, International Materials & Processes for Medical Devices Conference

September 25-28, 2005
David L. Lawrence Convention Center
Pittsburgh, PA, U.S.A.
(440) 338-5151
www.asminternational.org

Biomedical Engineering Society

September 28-October 1, 2005
Hyatt Regency
Baltimore, MD, U.S.A.
www.bme.jhu.edu/BMES2005

Biomedical Imaging Research Opportunities Workshop

March 11-12, 2005
Hyatt Regency Bethesda
Bethesda, MD, U.S.A.
(630) 368-3758
www.birow.org

35th Congress of the International Union of Physiological Sciences

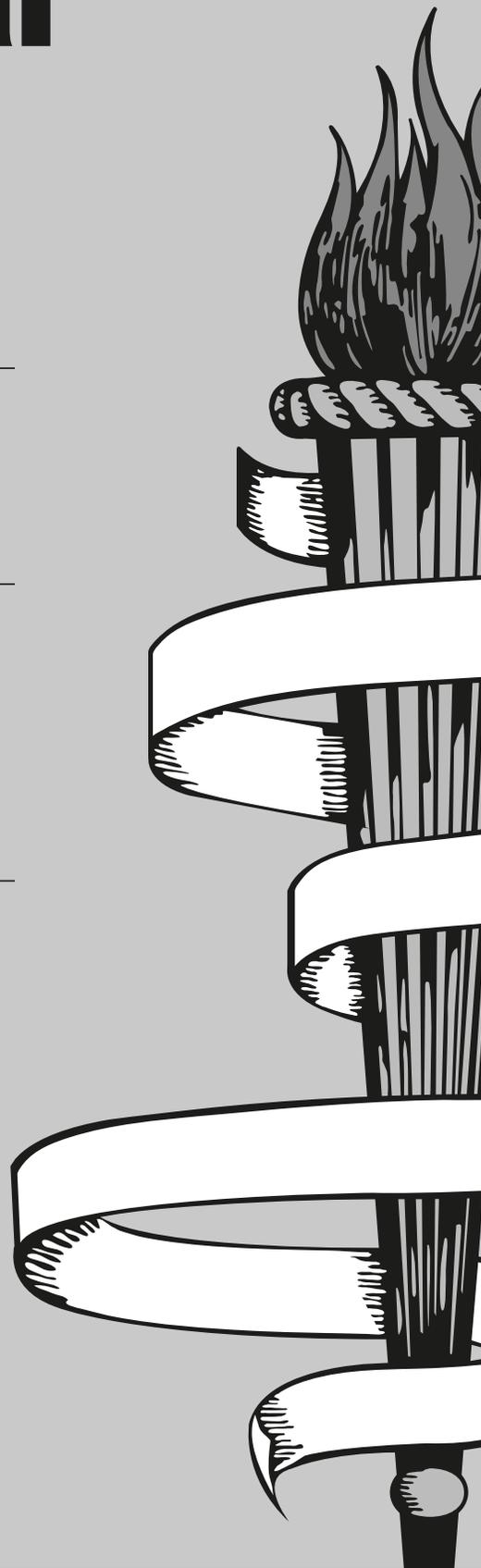
March 31-April 5, 2005
San Diego, CA, U.S.A.
www.iups2005.org

First International Conference on Pediatric Mechanical Circulatory Support Systems and Pediatric Cardiopulmonary Perfusion

May 19-22, 2005
The Hotel Hershey
Hershey, PA, U.S.A.
www.hmc.psu.edu/ce/pediatrics

2005 Summer Bioengineering Conference

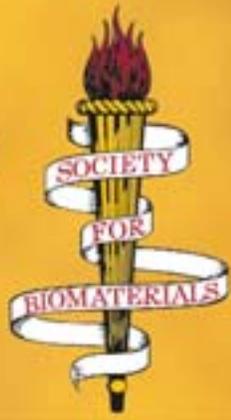
June 22-26, 2005
Vail Cascade Resort & Spa
Vail, CO, U.S.A.
www.asme.org/divisions/bed/events/summer05.html



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