BIOMATERIALS
FORUM
SOCIETY FOR BIOMATERIALS
Third Quarter 2006 • Volume 28, Issue 3

Combinatorial Biomaterials: Opportunities Beyond Synthesis

Histotechnology and the Biomaterials Connection

Call for Nominations

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BIOMATERIALS FORUM

The official news magazine of the **SOCIETY FOR BIOMATERIALS** • Volume 28, Issue 3

Special Interest Group Reporters

BIOMATERIALS FORUM

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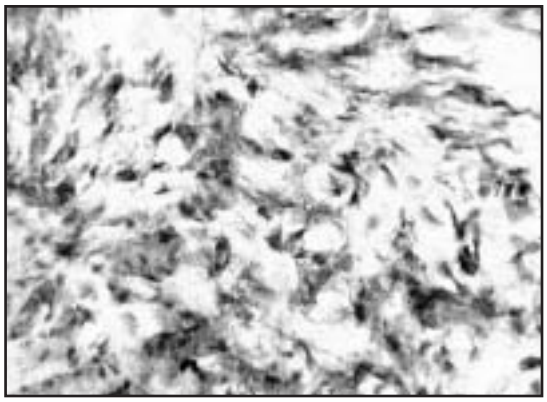
Features



The membrane surrounding a failed acetabular component demonstrates a significant level of TNF-alpha being released. *(Photo courtesy of Dr. Lynne Jones, Johns Hopkins University School of Medicine).*

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From the Editor

The Torch
By Karen J.L. Burg

This issue includes news of the recently announced National Science Foundation reorganization, geared toward "enhancing agility within disciplines, broadening multidisciplinary research, and enabling discovery at the emerging frontiers of engineering." Although foreign to many in other disciplines, words such as "multidisciplinary," "agility," and "discovery" are quite familiar in the world of biomaterials engineering. Indeed, collaboration is as natural to the biomaterialist as....orange is to the Clemson Tiger! We, as biomaterialists, have an opportunity to lead the charge by demonstrating our innovative approaches and expertise at team play. The world may be flatter than before due in large part to the internet, as Thomas Friedman suggests, but the reality still is that it is the interpersonal connections and diversity of perspective that make us strong.

Jim Collins, in his book *Good to Great*, suggests that a successful organization has a hedgehog concept, or an effort-driving concept based on a defining talent or passion. The reference to a hedgehog is derived from the image of an animal that is singularly focused on the simple and the essential, namely, searching for food, while always at the ready to quickly roll into a prickly ball if danger lurks. No matter how complicated or clever the approach of predators, the hedgehog's response is the same and consistently successful. That is, the hedgehog knows its objective (it must find food) and knows its limitations (it moves slowly) and talents (it can form a prickly ball instantaneously). Perhaps our SFB hedgehog concept is our ability to cross disciplines and to nimbly maneuver from concept and theory to clinical reality.

It may be, however, that we pay more attention to the culminating images of engineered beating hearts and we forget that our ability to bridge concept to reality (our hedgehog concept) relies on our talents and passion for team play, iterative process, and the endless development of seemingly mundane, yet crucial, techniques and methods (i.e., 90 percent perspiration and 10 percent inspiration). Where would we be, for example, without the development of gene identification tools and assays? Think of how many individuals contributed to the development of this vast toolkit during the course of many years. What would we really understand about cell-material interactions without the ability to repeatedly assess this interface through advanced imaging or histological techniques? Methods development, though generally not considered high profile or glamorous, is undoubtedly an important key to technology translation and our hedgehog concept.

This issue of the *Forum* includes a contribution from Vincent Della Speranza, President of the National Society for Histotechnology (NSH). The NSH is dedicated to histological methods development and dissemination. Several of our members have collaborated with this Society to better serve the biomedical community. Mr. Della Speranza's remarks remind us of our SFB hedgehog concept and should lead us each to consider our personal hedgehog concepts in a new context. So, what is your passion/talent and how will you apply it to make SFB a better Society?

Karen J.L. Burg
Hunter Endowed Chair & Professor of Bioengineering

From the President

The Torch
By C. Mauli Agrawal

After spending a year watching Michael Sefton do all the hard work, it is now my turn to do the heavy lifting as the President of our Society. I am enthusiastic about the coming year and the issues we must address. I must admit that I have a wonderful team to work with, both at the Board and Council levels. With the help of these folks and our management team from Association Headquarters, I am sure we will have a very productive year.

Our organization stands at a crossroads. If we desire to flourish and continue representing the field of biomaterials to the world, we must reassess who we are and who we want to be within the milieu of a rapidly changing world. Michael Sefton recognized this need and called for a strategic planning retreat last year. Based on this retreat, several task forces were formed and are now finalizing their reports on topics such as the annual meeting, fund raising, governance and branding. These reports will form the basis of more discussion and then some strategic moves later this year.

In his book *The World is Flat*, Thomas Friedman describes how the business world has changed and has evolved from a command and control, or silo strategy, to a connect and collaborate paradigm. Those of us in academics and research have seen similar changes — successful grant applications are usually no longer solo efforts but collaborative in nature. It is time to ponder how to use the connect-and-collaborate strategy to further the cause of biomaterials. A logical step would be to partner with some other professional scientific organizations to reach a broader audience and cover a wider field. This is one area on which I intend to spend significant time this year.

I think discussions about the future direction of our Society should be taking place not only at the administrative levels but also in the offices and labs where our members work. Make sure your ideas and thoughts percolate up to your representatives in the SIGs, on the various committees, and on the Board/Council. The future of the Society For Biomaterials is ours to make. I look forward to hearing from you.

Staff Updates from Headquarters

By Dan Lemyre,
Assistant Executive Director

Throughout the second quarter of 2006, headquarters staff has been busy preparing for the Annual Meeting, the Annual Business Meeting, and most recently working with the Council on the implementation of new committees and endeavors for the coming year.

The following is an update on staff activities undertaken to support the various committees, Council and Board, and some important notices to members. The list of 2006-07 committees, chair persons and goals for the year can be found on the SFB website at www.biomaterials.org/Welcome/welvl.htm.

Awards Ceremonies and Nominations Committee – Members are strongly encouraged to consider names of qualified colleagues to serve as SFB President-Elect, Member-At-Large, and Secretary-Treasurer-Elect. A description of each position may be found in the SFB bylaws, published online at www.biomaterials.org/Welcome/welbylaw.htm. Officer nominations are due September 8, 2006, and the nominations website is open as of July 10, 2006.

Each year the SFB honors the achievements of members through a variety of awards such as the Clemson Awards, the Founders Award, the C. William Hall Award, the Young Investigator Award, the Technology Innovation and Development Award and Outstanding Research Awards. What a great opportunity to see one of your colleagues receive recognition for a job well done. For more information about the awards, and to view a list of the 2006 winners, visit the SFB website at www.biomaterials.org/Awards/award_06.htm. Nominations may be submitted online; the nomination submission page of the SFB website is live as of July 10, 2006. The award nominations deadline is September 15, 2006.

Education and Professional Development Committee – The committee successfully implemented the Student Travel Achievement Recognitions (S.T.A.R.s) in conjunction with the Special Interest Groups. Awardees were recognized at the Annual Meeting in Pittsburgh. The committee continues to receive requests from numerous organizations seeking endorsement of their meetings. As a result of the recent activity, the committee is considering other ways in which SFB can obtain additional recognition of its endorsement of other Society meetings.

The National Student Section held a very successful career fair at the recent Annual Meeting. More than 40 students participated in the event, which featured eight companies offering a variety of positions. A similar event is already being planned for next year's Annual Meeting!

Finance Committee – The audit of the 2005 financials has been completed and the final draft will be reviewed shortly by the Board. As a result of recommendations of the committee, the SFB Board has formed an Audit Committee, the purpose of which will be to (1) select the audit firm for the annual audit and recommend to the Board for approval; (2) review the annual audit report with the accounting firm; and (3) review the Society's accounting policies.

Long Range Planning Committee – Work continues with the Strategic Planning Task Forces, whose recommendations for strategic priorities of the Society are forthcoming.

Meetings Committee – The committee has recommended, and the Council has approved, the selection of San Antonio as the location of first choice for the 2009 Annual Meeting. The committee continues to consider options and formats for a fall event in the year 2008.

Membership Committee – To date, there are 1,209 members, 247 of whom are new to the Society. Fifty-five percent of the current membership has opted for the new electronic subscription option for JBMR. The Membership Committee is continuing in its endeavors to streamline the membership application process, increase member numbers, and develop meaningful services and benefits for members.

Program Committee – Congratulations to John Kao, chair of the 2006 Program Committee, for a most successful meeting in Pittsburgh. Unfortunately, John was unable to attend the program, but was happy to remain at home to prepare for a new addition to his family! Please join us in congratulating him! The 2007 Program Committee is already busy making plans for next year's meeting scheduled for April 18-21, 2007, in Chicago. While the call for proposals deadline has passed, members can look for the call for abstracts in the near future, with a deadline for submission of abstracts slated for mid-October.

Publications Committee – SFB website editor Tom Webster has been busy developing the forthcoming Biomaterials Education Classroom that will feature a "Biomaterial of the Week." In addition, thanks go to Jeff Karp of MIT for his efforts in developing the new Surgical Video Library. Look also for the new Special Interest Group web pages featuring bulletin boards and other areas of interest to enable ongoing interaction with peers in your specialty throughout the year.

Special Interest Groups – SIG officer elections were held in May. The final results are on (page 5). The officers of all the SIGs met while in Pittsburgh attending the Annual Meeting. Much of the discussion centered on select preliminary recommendations of the SIG task force for structural changes, as well as ways to improve the involvement of SIGs in the development of the program content of the Annual Meeting. SIG Representative Andrés Garcia will use the feedback from these discussions to further refine the task force recommendations, and to work with the 2007 Program Committee on SIG participation in the planning for next year's meeting.

If you are interested in knowing more about a particular issue or committee activity, please contact the SFB headquarters office:

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Engineering Education Goes Liberal and Beyond

The Torch

By Guigen Zhang, University and Research Institution News Contributing Editor

Engineering is a practical art learned from scientific knowledge, mathematical logic and applied experience to innovate under constrains. Engineering innovations are successful solutions for problems that lead directly or indirectly to improvements in our quality of life. In a report by the National Academy of Engineering (NAE), "The Engineer of 2020: Visions of Engineering in the New Century," innovation is identified as the key task for the U.S. to maintain its economic leadership, and engineering is essential to this task. The NAE and other leading organizations of industry and academia have been envisioning new ways to revamp engineering education. A converging vision is that future engineers must be creative, innovative, life-long learners, effective communicators in technical and non-technical forums and competitive in a global environment.

It is a daunting challenge for the engineering profession and engineering education to remain relevant to a changing world. Future engineers will have to wrestle with problems that today are rooted in physical sciences, biological sciences, environmental sciences, arts and social sciences, in addition to engineering problems. To alter the way engineering is taught and the way engineering is perceived, and to connect it to real world application, Harvard University announced a proposal to create the School of Engineering and Applied Sciences. This new school will reside within the Faculty of Arts and Sciences and will not have traditional academic departments. Harvard is taking a cross-disciplinary approach to structure its engineering education with more broad connections with liberal arts.

Harvard is not alone. In 2001, the University of Georgia (UGA) established the Faculty of Engineering with a view "not to pursue a 'boilerplate' model with pigeonholed departments, but rather an evolutionary approach which is primarily driven by and focused on meeting societal needs." The UGA approach allows the Faculty of Engineering to provide engineering students liberal learning experiences that prepare them for careers devoted to the integration of discoveries from multiple disciplines and to find creative solutions at the interface of disciplines.

During the past several decades, the Society For Biomaterials (SFB) has played a leading role in promoting the education of bioengineers with multidisciplinary scientific knowledge and experience, and these bioengineers have made significant contributions in improving our quality of life. But what should the SFB do to remain relevant in educating bioengineers of the future?

Jim Anderson Receives Chugai Mentoring Award

The Torch

From Press Release

The Society For Biomaterials congratulates Dr. James M. Anderson, Professor of Pathology, Macromolecular Science and Biomedical Engineering at Case Western Reserve University, who received the 2006 Chugai Mentoring Award from the American Society for Investigative Pathology (ASIP). This award, funded by Chugai Pharma USA LLC, is presented to a member of ASIP with a distinguished career dedicated to mentoring and education, and who is still productive at the time of the award.

Dr. Anderson is best known nationally and internationally for his contributions to the basic and applied science of biodegradable polymers and the interaction of polymeric and other biomaterial in medical devices and implants with blood and other tissues. Dr. Anderson has offered an unusually interdisciplinary environment in which he has fostered the development of his medical students and served as a research advisor and mentor. The impact and significance of Dr. Anderson's scholarly activities have been widely recognized.

Funding for his research includes an NIH MERIT Award (1993-2003) that focused on developing a better mechanistic understanding of the cell and molecular biology of inflammatory cells, including macrophages and foreign body giant cells, adherent to biomaterials. He has been recognized nationally and internationally for his contributions to the understanding of tissue/materials and blood/materials interactions. His numerous awards include the Excellence in Surface Science Award, Surfaces in Biomaterial Foundation; Founders Awards from both the Society For Biomaterials and the Controlled Release Society; and the Japanese Society for Biomaterials Award for Distinguished Service in Advancement of Biomaterial Science.

Since 1988, he has served as Editor-in-Chief of the *Journal of Biomedical Materials Research*, a leading journal in its field. Dr. Anderson has served in the regulatory aspects of product development that has aided companies in their interactions with the Food and Drug Administration in an effort to make worthwhile products available to the public more quickly.

Dr. Anderson received his BS from Wisconsin State University and his PhD from Oregon State University. After receiving his MD from Case Western Reserve University in 1976, he pursued clinical training at the University Hospitals and became a member of the faculty at Case Western Reserve, attaining the rank of Professor in 1984. Dr. Anderson received the Chugai Mentoring Award at ASIP's Annual Meeting in San Francisco on April 3.

Attention Biomaterial Educators!!!

By Thomas J. Webster, Web Editor

Have you seen the Society For Biomaterials website (www.biomaterials.org/) lately? The site contains many new features that can be used in your biomaterials class.

For example, every week, a new biomaterial is highlighted on the web in a feature called "Biomaterial of the Week." A picture is shown and various facts about how that particular biomaterial is being used today are given. What a great way to point your students to the web to complete a weekly assignment or have a weekly in-class discussion about a biomaterial! You could start every class with what every student likes: a quiz on key facts about the "Biomaterial of the Week" that appears on the Society's web page!

"The site contains many new features that can be used in your biomaterials class."

Plus, this will help educate your students about the Society For Biomaterials and possibly encourage them to complete biomaterials research and attend the Annual Meeting.

"Biomaterial of the Week" is not the only excellent resource for biomaterial educators. Don't forget about the Surgical Video Library, which contains video and explanations of numerous implant procedures. What a great way to incorporate these surgeries into your classroom and have students use this knowledge in a term project. Please send any other ideas on how we can create a website that best suits your needs as a biomaterial educator to thomas_webster@brown.edu. This is only the start, so keep on checking the web!

Society For Biomaterials • 2006-2007 SIG Officers

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Engineering Directorate Reorganizing

Effective October 1, 2006, the Engineering Directorate (ENG) of the National Science Foundation (NSF) will put in place a new organizational structure to further enhance agility within disciplines, broaden multidisciplinary research, and enable discovery at the emerging frontiers of engineering.

ENG investments in engineering research and education build and strengthen the nation's capacity to lead the world in innovation. This capacity will continue to grow as ENG and NSF push the frontier with the creation of new knowledge and disruptive technologies that have the potential to secure our nation and enhance our quality of life. These investments include such emerging technologies as bioengineering, cyberinfrastructure, manufacturing innovation, metabolic engineering, molecular electronics, nanotechnology, photonics, and sensors and sensor systems.

The new structure, which merges many of the current divisions' existing disciplines under broader themes and clusters, will help ensure that ENG continues to support cutting-edge engineering research and education, while addressing the emerging and perennial needs of the nation. For more than a decade and a half, the current structure for ENG has effectively met these goals by 1) serving the nation's community of engineers, and 2) supporting the most outstanding proposals from all fields of engineering.

During that time, ENG has helped catalyze advances in emerging fields, while a new era of international competition and global innovation has evolved. These conditions compelled ENG to reassess how to best position itself to respond proactively to new challenges both domestically and abroad.

ENG's new structure is an outgrowth of these conditions and assessments. It was developed through thorough strategic planning, self-examination, and community feedback. The result is a directorate better able to support the future of research, education, and innovation.

The following outcomes are anticipated through the reorganized directorate:

- Leadership at the frontiers of engineering discovery, innovation, and education
- Enhanced flexibility for change
- Enhanced interdisciplinary research
- Greater opportunities for exploring new areas not yet recognized to their full potential
- Greater ability to integrate research across priority areas
- Enhanced synergy between education and basic research
- Programs that facilitate the continuum from discovery through innovation

Included in this vision is the ability to support broad, foundation-wide investments in a number of areas, including NSF's multidisciplinary priority areas and the Administration's interagency R&D priorities. The Engineering Directorate will also utilize this new structure to further advance the frontier in the key priority areas for ENG and NSF. The new structure will entail consolidating ENG's five current disciplinary divisions into three, and establishing three crosscutting units.

Specific outcomes of the reorganization can be found on the NSF website at www.nsf.gov/publications/pub_summ.jsp?ods_key=nsf06033.

Call For Nominations

The Society For Biomaterials is soliciting nominations for the 2007 Awards listed below and for the following Board of Directors positions:

President-Elect
Secretary/Treasurer-Elect
Member-At-Large

2007 Awards

Founders Award • C. William Hall Award • Clemson Award for Applied Research • Clemson Award for Basic Research Clemson Award for Contributions to Literature • Technology Innovation and Development Award • Young Investigator Award Student Award for Outstanding Research • Outstanding Research by a Hospital Intern, Resident, or Clinical Fellow Award

To nominate a colleague, or yourself, for an award or position on the SFB Board of Directors, please visit the SFB website at www.biomaterials.org.

By Jack E. Lemons, Professor and Director of Laboratory of Surgical Implant Research, University of Alabama-Birmingham

Biomaterials: Experience and Opinions from Participation

Experiences at the initial meetings of the founders group and others at Clemson University (1969 and early 1970s), the establishment of SFB in San Antonio (1974) and subsequent annual meetings have established the fundamental importance of multidisciplinary information exchange about biomaterials. The progression from idea-to-laboratory, testing-to-clinical, trial-to-routine use for surgical implant devices of synthetic biomaterial origin has been based on, in part, learning curves at several levels. Many have said, "Why can't others obtain the same excellent results as the inventor-developer-user?" The message is "we learn from the experience gained during the process," from benchside to bedside. Unique problem-solving is required at all levels in order to achieve success (i.e. longevity of the application).

"I believe the SFB is in a position to provide the information needed for our future and improvements through information exchange."

The SFB has evolved significantly during the decades and we appreciate the importance and future of tissue engineered medical products and regenerative medicine—this is our "future." Interestingly, simple assessments of population demographics, the scientific needs of fully understanding emerging biological regeneration in the presence of biodegradable delivery systems and active biological factors, and the anticipated societal demands of the "baby boomers" related to aesthetical and functional quality of life are important considerations. These considerations cause me to suggest that the next 20 years will probably continue to be an era of synthetic origin biomaterials and devices. This opinion is based on the results of multiple NIH and professional society peer reviewed consensus conferences, where decades of clinical outcomes experience(s) have been presented. Many clinical conditions of aging, disease and trauma are appropriately treated with devices constructed from metallic, polymeric and ceramic biomaterials. Most available surgical treatments and devices provide opportunities for rapid recovery, relatively normal anatomical dimensions, and pain-free function.

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Combinatorial Biomaterials: Opportunities Beyond Synthesis

Submitted by Joy Dunkers, Government News Contributing Editor

Written by Matthew L. Becker, Nathan D. Gallant and Eric J. Amis, Polymers Division, National Institute of Standards and Technology, Gaithersburg, MD 20899, USA

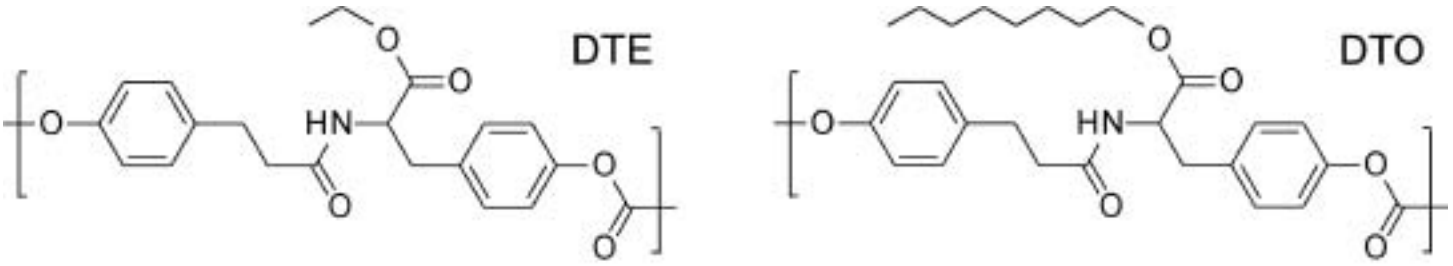

Figure 1. Synthetic scheme and chemical structure of desaminotyrosyl–tyrosine alkyl esters and the resulting polycarbonates. The pendent R groups of the polycarbonates reported in this article consist of ethyl and octyl esters, respectively. The corresponding polymers are referred to as poly(DTE carbonate) and poly(DTO carbonate).

Material surface properties influence cell behavior and are a critical parameter in the design of tissue engineered medical products (TEMPs). Surface-mediated interactions dominate the early response of cells to polymeric biomaterials by influencing protein adsorption, cell adhesion and spreading, and extracellular matrix production.[1-5] Identifying and outlining a framework of how these responses are interrelated for materials optimization is a resource-intensive process out of reach for all but the largest institutional efforts. Establishing this framework for a class of biomaterials is a measurement-intensive regimen that can involve several approaches.

Sample Composition		Glass Transition	Contact Angle	Surface Roughness RMS (nm)	
DTE	DTO	Temperature (°C)	Water (°)	Annealed	Unannealed
100	0	88.2 ± 0.7	71.6 ± 0.6	2.08 ± 1.49	2.20 ± 2.65
70	30	85.2 ± 0.4	83.3 ± 1.2	91.1 ± 0.9	58.77 ± 7.19	5.77 ± 3.94
50	50	85.8 ± 0.7	84.0 ± 0.6	89.1 ± 1.0	66.58 ± 4.32	4.71 ± 3.89
30	70	86.6 ± 0.5	81.5 ± 0.7	92.7 ± 2.2	45.94 ± 10.45	5.26 ± 2.40
0	100	32.8 ± 1.6	91.4 ± 1.0	2.40 ± 1.20	3.67 ± 1.39

Table 1. Measured Physical Properties of DTE/DTO Homopolymers and Blends.

One approach to optimize biomaterial response is an iterative synthesis-characterization approach of a single polymer composition or architecture. The New Jersey Center for Biomaterials, directed by Professor Joachim Kohn, has driven the development of advanced experimental and computational methods in combinatorial chemistry, materials science, bio-interfacial science and computational modeling for the purposes of application specific material development. The goal of the Integrated Technologies Resource for Polymeric Biomaterials (RESBIO) has been to accelerate the discovery of new polymeric biomaterials with the ultimate goal of facilitating the development of advanced biomaterials-based therapies in regenerative medicine and drug delivery. During the last 10 years, Professor Kohn's group has developed a library of tyrosine-derived polycarbonates and polyarylates for use in tissue engineering and drug delivery applications that has been remarkably successful clinically.[6-10] These materials share a structurally identical backbone with a rich chemical and structural diversity in the pendant ester substituent groups. These small differences affect significantly the mechanical properties, degradation rates, and cellular responses of the respective polymers. The current library has almost 10,000 different members with slight structural and chemical variations.

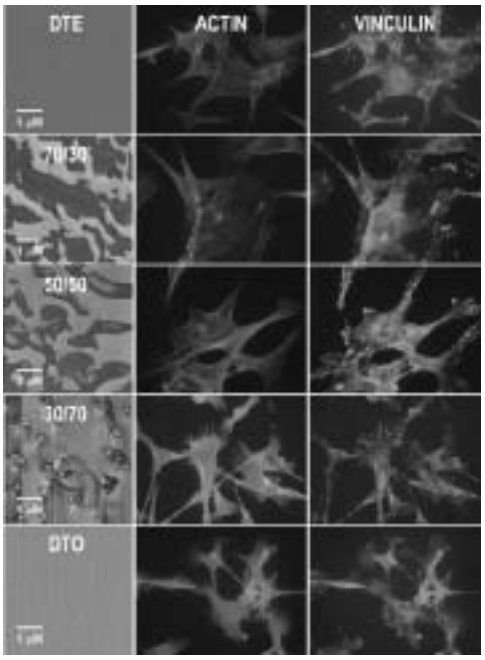

Figure 2. From top to bottom are five 5 mm _ 5 mm AFM images in which the amount of DTO is increasing. The discrete DTE/DTO blends form phase-separated domains under the prescribed annealing conditions. Immuno-fluorescent staining for actin and vinculin of MC3T3-E1 osteoblasts showing the cytoskeleton and focal adhesion contact formation 16 h after seeding on each of the respective homopolymers and blends.

However, there are opportunities for materials optimization outside of continually synthesizing new materials. Synthetic polymers have unique processing characteristics that include composition-dependent phase behavior, thermal history, and molecular mass and mass distribution effects. Polymer blending introduces several variables that increase significantly the physical parameter space, including temperature, film thickness, and the chemical nature of both the boundaries and individual polymers. All of the aforementioned properties influence the extent of phase separation. Typically, the desired result is a new material that possesses a "synergistic"

improvement in properties that are preferred over those of the individual components.

An interesting approach to materials optimization is to develop methods for the fabrication of continuous variable gradient libraries using mixtures of individual polymers. Recently, the authors and others have placed increased emphasis on developing combinatorial and continuous variable gradient sample fabrication methods that aid in reducing the bio-complexity and identifying these interactions.[11-20] The continuous variable approach has been particularly useful when trying to optimize two-component blends. Combinatorial and gradient methods offer the ability to change multiple variables simultaneously and to examine the synergistic effects of various properties and are thus ideal for mapping cell response to surface properties. Using precisely fabricated and characterized gradients, one reduces the complexity of the overall system and is able to distinguish subtle differences over small spatial increments among closely related specimens. The use of continuous variable gradient methods further increases the possibility for the identification of compositions and processing conditions that would have otherwise been missed in discrete spot arrays. This approach coupled with detailed surface characterization affords the opportunity to extract and identify the important surface mediated interactions influencing observed cellular responses.

Current efforts in the development of gradient methods for biomaterials optimization are based on a recently published study on a small series of structurally related tyrosine derived polycarbonates. Briefly, two-dimensional thin films consisting of homopolymer and discrete compositional blends of tyrosine-derived polycarbonates were prepared and the surfaces were characterized in an effort to elucidate the nature of the corresponding cell responses *in vitro*. The authors demonstrated that composition-dependent phase separation in a series of discrete blend tyrosine-derived polycarbonates influenced the acute inflammatory response and extracellular matrix production.[21]

Atomic force microscopy (AFM) micrographs indicated that 16 h at 105 °C was required to complete the annealing process. The AFM images of the DTE and DTO homopolymers in Figure 2 depict smooth and featureless surface morphologies. However, two distinct phases that correspond predominately to DTE and DTO are seen in each of the blends. In the 70/30 (by mass) DTE/DTO blend, a two-phase bicontinuous network was observed while the 50/50 and 30/70 blends exhibit isolated domains of various size. The darker phase features in Figure 2 decrease qualitatively with increasing DTO content.

MC3T3-E1 osteoblasts adhered to this series of polymer blends and were stained using immuno-fluorescent techniques. Texas red-conjugated phalloidin was used to stabilize and stain the fibrillar actin and fluorescently-labeled secondary antibody to an anti-vinculin primary antibody was used to look at the vinculin distribution to examine if gross changes were occurring in the cytoskeleton, cell spreading or in the focal adhesion contacts (Figure 2). Upon close examination of the vinculin staining (focal contact assemblies), there are distinct differences in the amount of cell spreading and the shape and extension of the lamellapodia. The reduced spreading and large lamellapodia protrusions of the MC3T3-E1 cells on DTO are readily apparent in comparison to those imaged on the tissue culture polystyrene (TCPS) and DTE homopolymer. These lamellar extensions increase in the blend samples with increasing DTO content. Also, the cells appear to spread less with increasing DTO content as seen in the distribution of the fibrillar actin.

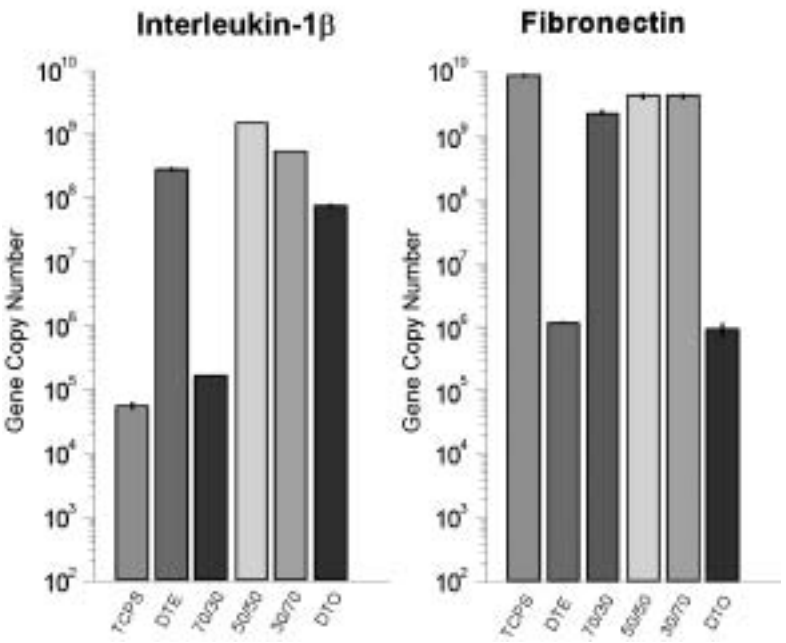

Figure 3. Gene copy numbers of interleukin-1b and fibronectin after 24 h of surface exposure on the respective homopolymers and blends for MC3T3 E1 bone osteoblasts. Error bars are representative of one standard deviation from the mean of triplicate samples harvested from a single population of cells and are the estimate of the standard uncertainties.

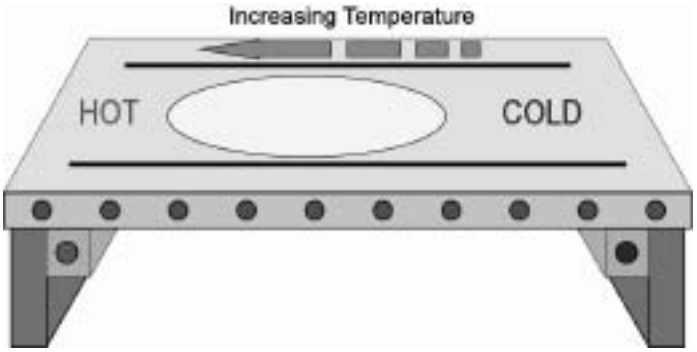

Figure 4. The gradient hot-stage shown above consists of an aluminum (Al) sample plate. Two adjustable Al blocks, with machined heating/cooling channels, are attached to the bottom of the plate. The block channels hold cylindrical heating cartridges or accommodate plumbing for fluid-mediated cooling. The range and slope of the temperature gradient are tailored through the respective block temperatures and their distance apart.

Genetic expression profiles of interleukin-1ß (IL-1ß and fibronectin (FN) in MC3T3-E1 osteoblasts were measured using real-time reverse transcriptase polymerase chain reaction (RT-PCR) and the results are depicted in Figure 3. The osteoblasts demonstrated significant changes in IL-1ß mRNA levels on the blends relative to the homopolymers, but the exhibited trends measured in these experiments were very different. The homopolymers DTE and DTO demonstrated ≈5.1×10^3-fold and 1.4×10^3-fold increases in cytokine induction in relationship to TCPS control levels. The gene copy numbers

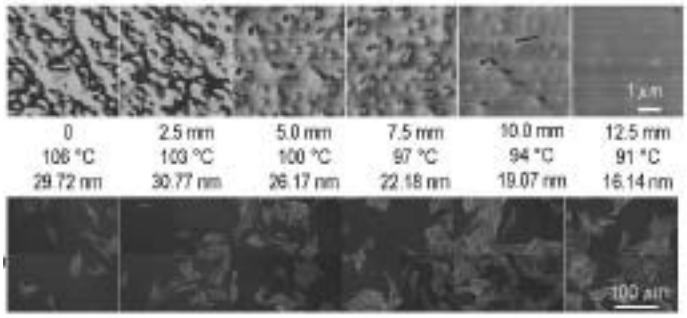

Figure 5. Shown above are a series of six 5 mm _ 5 mm AFM phase images from a discrete 30/70 DTE/DTO blend film annealed on a variable temperature hot stage for 16 h and the corresponding immuno-fluorescently labeled cells. The spatial arrangement on the surface of the film with the corresponding annealing temperatures and the measured root-mean-square (RMS) roughness data are shown.

produced by each of the homopolymers and the blend samples were expected to exhibit similar expression levels. The 50/50 and 30/70 (DTE/DTO) blends measured ≈$2.7x10^4$ fold and $1.0x10^4$ fold increases over control levels. However, the 70/30 DTE/DTO blend only registered a 2.9 fold increase over TCPS at the 24 h time point. The underlying physico-chemical parameter causing the significant and reproducible decrease in IL-1ß gene expression is unknown at this point and is currently being investigated further.

The osteoblast mRNA expression levels of FN on the homopolymer samples were $4.8x10^3$-fold and $9.6x10^3$-fold lower than the TCPS population. However, the osteoblast levels of FN on the blend samples were comparable to TCPS levels. These findings provided data that was complementary, meaning, the DTE/DTO polymer blends stimulated the up-regulation of FN relative to each of the homopolymers singly in both cell types. We have demonstrated that bovine serum albumin (BSA), the predominate protein in cell culture media, adsorbs preferentially to DTO which is more hydrophobic than DTE. These differences were the underlying contributors to compositionally dependant gene expression behavior of FN and IL-1ß. These interesting data on a subset of structurally related materials within a much larger materials library led us to believe that further manipulation of composition and phase profiles could lead to additional materials enhancement.

These measurements were made in a phase equilibrium state. Non-equilibrium phase separation exposes various amounts of the respective materials to the surfaces. In addition, the domain sizes and amount of interface between the domains changes significantly during the process. The rate of phase-separation is temperature dependent. In order to measure and optimize further the nature of these expression profiles, we have utilized a temperature gradient heat stage (Figure 4) to fabricate a discrete composition substrate possessing a linear phase separation gradient over a small distance. This strategy affords the opportunity to measure precisely and map the physico-chemical nature of the changing surface. The properties of the spatially controlled surface can be correlated easily to the cell behavior captured via cell staining and automated fluorescence microscopy.

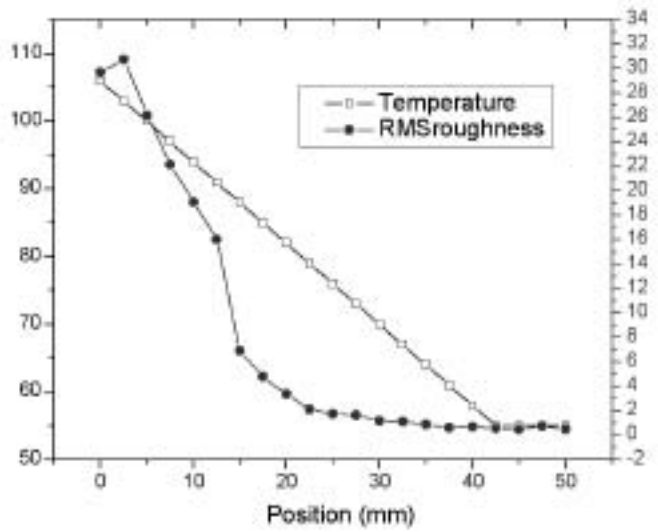

Figure 6. A plot of temperature and RMS roughness vs. position shows both the linearity of the temperature gradient and the distinct drop in RMS roughness that occurs near 90 °C which happens to be the glass transition temperature of DTE (91 °C).

In this instance, the temperature settings in each of the aluminum blocks were 110 °C on the hot end and 0 °C on the cold end, maintained with a recirculation bath, spaced 50 mm apart. These settings created a stable and linear temperature range from 105 °C to 55 °C over 40 mm. Both the temperatures and the distance between the aluminum blocks can be controlled to adjust the range and slope of the gradient. It also allows for rapid iterative changes to the system to refine a range for the purposes of optimization.

AFM micrographs were taken every 2.5 mm on a continuous film that was annealed with decreasing temperature (105 ° to 91 °C) from left to right (Figure 5) that influenced the rate of phase-separation. As seen in the picture and noted in the RMS roughness data, the images exhibiting large areas of phase separation are very rough as opposed to the unannealed film and the roughness progressively decreases with decreasing temperature (distance).

The fluorescent images on the bottom of Figure 5 depict the cellular behavior on the sections corresponding to the AFM images above. Immuno-fluorescent staining for actin (red) and vinculin (green) of MC3T3-E1 osteoblasts shows the cytoskeleton and focal adhesion contact formation 16 h after seeding on the gradients. Qualitatively, the cell number, area, and aspect ratio all vary considerably with the respective physical properties at each position on the gradient. Quantitative evaluation of each of these cellular metrics on a number of discrete composition and homopolymer annealing gradients is continuing.

Figure 7. Shown above are a series of twelve 5 mm _ 5 mm AFM phase images from a compositional gradient of DTE/DTO blend film fully annealed for 16 h.

Similarly, Figure 7 shows our preliminary efforts at composition optimization with this same DTE/DTO pair using the method first described by Meredith et. al.[17] and later by Simon et al.[18] Additional work on developing advanced algorithms to collect cell data and statistical methods for normalizing cell population distributions for further bio-analysis of closely related materials is ongoing.

Summary

Optimization of multi-component polymer blends for use in biomaterials applications is difficult due to phase behavior, thermal history, and variable surface interactions with serum proteins. Herein the authors demonstrate a versatile tool for precisely fabricating discrete thin-film blends possessing a gradient in phase separation using a variable temperature heat stage. It is particularly useful in combination with cell studies where multiple substrates are needed with tight spatial tolerances for physical parameters among samples for both comparison and cell statistics. The characterization results described herein demonstrate the precise fabrication required for sample-to-sample comparison. Preliminary cell analyses suggest strongly that the small physico-chemical variations beyond composition have significant biological implications. These results highlight the need for new methods and combinatorial approaches to polymeric formulations in biomaterial applications.

Acknowledgements

The authors benefit greatly from an existing relationship with the NIST Combinatorial Methods Center within the Polymers Division. The authors thank Drs. Michael Fasolka, Christopher M. Stafford, Thomas H. Epps III and the rest of staff at the NIST Combinatorial Methods Center for many valuable discussions. A NIST/NRC postdoctoral fellowship (NDG) is gratefully acknowledged. The authors are fortunate to be part of a highly productive and interactive collaboration with the New Jersey Center for Biomaterials and Professor Joachim Kohn. His efforts are supported by NIH NIBIB (Grant No. EB001046 RESBIO - Integrated Technologies Resource for Polymeric Biomaterials). The authors are affiliated with the Biomaterials Group in the Polymers Division, National Institute of Standards and Technology in Gaithersburg, Md.

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† Certain commercial materials and equipment are identified in this paper in order to specify adequately the experimental procedure. In no case does such identification imply recommendation by the National Institute of Standards and Technology nor does it imply that the material or equipment identified is necessarily the best available for this purpose.

Histotechnology and the Biomaterials Connection

By Vincent Della Speranza, President, National Society for Histotechnology, Guest Contributor

While perusing back issues of *Biomaterials Forum* during a recent visit to the Society For Biomaterials website, it occurred to me that the work of many of your organization's members must rely heavily on histology laboratory support to assess human tissue reactions to implanted biomaterials. In this vein, I am grateful for the opportunity to introduce our organization to you as I believe a collaborative relationship would be mutually beneficial to our respective members.

The National Society for Histotechnology (NSH) represents laboratory professionals from around the globe whose work involves the preservation, preparation and tinctorial or immunohistochemical staining of human and animal tissues for microscopic examination. While many use their talents in clinical laboratories, histotechnologists are also hard at work in research, pharmaceutical, industrial, forensic, veterinary and marine laboratories as well. It is entirely probable that those of you in biomaterials science have relied upon the expertise of histotechnologists in your work.

The NSH offers a number of publications and other resources to those in histotechnology practice. *The Journal of Histotechnology* (JOH) publishes original articles dealing with vertebrate histology or cytology, histochemistry, immunohistochemistry, marine histology, nuclear histology, veterinary histology, fluorescence and electron microscopy, molecular biology as well as clinical case studies. A special issue each year provides an in-depth discussion of a specific area of interest. The 2005 special issue included numerous topics in molecular histopathology and the 2006 special issue, edited by SFB member Lynne Jones, will highlight biomedical devices and biomaterials. Of special interest to SFB members may be our Immunohistochemistry (IHC) Resource Group and Hard Tissue Network. The IHC resource group maintains a tissue control bank and can provide resources and support for those conducting immunohistochemistry. Individuals participating in our Hard Tissue Network include those having special expertise working with decalcified or undecalcified bone.

The NSH conducts a large annual symposium drawing 1,500 attendees from around the globe that offers more than 100 half- or full-day workshops and seminars during a five-day period. This conference offers an opportunity to network face-to-face with thought leaders in the various sub-disciplines of histotechnology. The NSH Symposium will be held this year in Phoenix from September 8-13, 2006. We sincerely hope you will be in attendance!

If you believe that we can be of assistance to you in your work, I hope you will visit our website at www.nsh.org or contact me directly at dellav@musc.edu.

Scaffolding in Tissue Engineering

Book Review

By Liisa Kuhn, Assistant Professor, University of Connecticut Health Center, Center for Biomaterials

Ed. by Peter X. Ma and Jennifer Elisseeff • Copyright 2006, CRC Press, Boca Raton, FL. 638 pages.

Description

Finally in one place, everything you wanted to know about scaffolds, and I'm not kidding. As the field of regenerative medicine or tissue engineering has evolved, so has the complexity and diversity of the biomaterials that are used as extracellular matrix replacements for cell implantation. This current, comprehensive text covers all of the types of biomaterials that have been, and are currently, used for scaffolds. Importantly, it spans materials chemistry, scaffold fabrication technologies, structural and functional materials modifications, and tissue engineering applications. The depth of each contributed article is impressive and leaves the reader feeling educated, rather than vaguely aware of some new concepts. Since so many types of biomaterials are included, and each author points out the strengths of their approach and the weakness of the others, a thorough read of this book provides a balanced view of the available options for scaffolding materials. The editors have compiled 38 chapters written by the names you've come to know and respect in the field. The field of tissue engineering is multi-disciplinary and the book reflects this through the inclusion of not only materials science, but also important biological concepts governing the observed cellular responses to the materials. This is a "must-have" book if you are interested in scaffolding in tissue engineering.

Audience

This book is an excellent review and reference book for academic and corporate researchers of any specialty working in the field of tissue engineering. It could be used as a textbook for advanced undergraduate and graduate students, but would require additional, basic, supplemental material. This book would make a valuable addition to university libraries, particularly biomedical engineering or materials science department libraries.

Contents

National Student Chapter News

Chapter News

By Dina M. Basalyga, President of SFB National Student Chapter

I hope everyone had a positive experience at the Pittsburgh meeting and were able to take advantage of the many exciting events. Conferences are such a wonderful opportunity to network and meet new people, and it makes it easier to do so at organized student events. For those of you that could not attend the career fair, I would like to give a brief update on its success.

The following companies were there: Integra Life Sciences, WL Gore, Baxter Biosurgery, Genzyme, Cook, Wright Medical, PolyMed Inc., and Boston Scientific. The representatives from these companies were from Research & Development; therefore, they were able to answer specific questions about their daily tasks as well as their division. I thank everyone who came to this event and made it a success. There is always room to grow and there are many things that can be improved next year. I welcome any feedback or comments.

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continued from page 7

Clearly, we will evolve to routine and large-number applications within regenerative medicine; however, if prior experience is an indicator, this process will take many years to mature.

This realization was "emphasized" for me at the 2006 SFB meeting in Pittsburgh. The current and past presidents organized sessions on "the future and what we have learned from our mistakes." The presenters in one session changed the word "mistakes" to "experiences" and I learned several new aspects of biomaterials and applications from the session presenters (and other talks/presentations/posters). During my talk, as I looked out over the audience, I realized how many in the room were now benefiting from implanted devices. In this regard, my theme during the past decade has been "we can further improve existing systems to enhance some clinical outcomes?"

Returning to a historical perspective, I believe the SFB is in a position to provide the information needed for our future and for improvements through information exchange. We should continue to emphasize biomaterial, biomechanical and biological properties of classes of devices utilizing key identifiers of "what is the limitation and what might be done, conservatively, to improve or replace for longevity?" Once again, we could bring the various investigators into a single room and include younger and older investigators in a presentation-open discussion format. I believe this activity, if included in the annual SFB and perhaps set into the SIG agendas, could enhance opportunities for all, especially the individuals approaching treatment(s) (i.e., my group – the seniors) to maintain life and quality of life. I have attended every Clemson and SFB meeting thus far, and hope my health and professional interactions will allow me to continue to benefit educationally, professionally and personally from every meeting. As Bill Hall said, "the second half-century of life should be the best."

BioInk

Steve T. Lin, Industrial News Contributing Editor
From Press Releases

Abiomed (Danvers, Mass.) reported that the FDA has granted approval for it to begin a pilot clinical trial immediately in the United States for the Impella 2.5 minimally invasive ventricular assist device (VAD). The indication for use is support during high-risk angioplasty for up to five days as a left ventricular assist device. The company said the approval is conditioned upon the company's submission of additional information to the agency during the next 45 days. High-risk angioplasty is defined as patients undergoing angioplasty on an unprotected left main coronary artery lesion, or the last patent coronary conduit, and poor cardiac function

Agilent Technologies Inc. (Palo Alto, Calif.) introduced an innovative technology that fractionates proteins and peptides with unprecedented simplicity and resolution. Co-developed with DiagnoSwiss S.A., the Agilent 3100 Offgel Fractionator enables scientists to identify more proteins, peptides and potential biomarkers by liquid chromatography/mass spectrometry (LC/MS). Biological samples such as blood plasma and cells typically contain tens of thousands of proteins over a wide range of concentrations. This high complexity makes it difficult to identify low-abundance proteins that play important roles in normal biological processes and disease. The Offgel Fractionator improves researchers' ability to identify low-abundance proteins and peptides by reducing sample complexity and greatly increasing the sensitivity of LC/MS analysis.

Researchers from **BioSurface Engineering Technologies Inc.** (College Park, Md.) and the U.S. Department of Energy's Brookhaven National Laboratory (BNL) have developed a synthetic peptide that mimics the effects of a tissue growth factor known as fibroblast growth factor, or FGF. FGFs are a family of proteins in the human body responsible for the proliferation, repair, and differentiation of cells in many tissues. BioSET has an exclusive license to develop and market these bioactive analogs. The researchers designed the peptide to target the FGF-2 receptor molecules that occur on the surface of cells. The peptide, called F2A4-K-NS, is one of a series of synthetic analogs of naturally-occurring growth factors being developed at BioSET, and is the first of several that completely mimic the action of the parental molecule. The new analogs developed at Brookhaven are proteins that are easier to produce than natural growth factors or growth factors derived by recombinant techniques. BioSET has taken an exclusive license to Brookhaven's bioactive analogs and improved techniques for making the analogs. Several of these bioactive analogs are currently in testing.

Cordis Endovascular, division of Cordis Corp. (Warren, N.J.), announced the nationwide introduction of two breakthrough devices: Frontrunner® XP CTO and Outback® LTD™ Re-Entry Catheters to treat artery blockages in the lower leg, a common finding in patients with diabetes and peripheral vascular disease. Both devices facilitate the placement of a guidewire in minimally invasive procedures such as angioplasty and stenting of chronic total occlusions (CTO). A CTO is a complete or nearly complete blockage of an artery that can lead to surgery or lower leg amputation. Previously, many patients with CTOs did not have access to less-invasive procedures, like angioplasty or stenting, to open blockages. To treat CTOs with less-invasive methods, a doctor must first cross through the blockage. The Frontrunner XP CTO and Outback LTD Re-Entry Catheters allow physicians to break through complete blockages allowing treatment with stents or balloons. By using these catheters, patients may avoid having to undergo difficult surgeries or even amputations. More than 20 million Americans who suffer from diabetes are at risk of amputation of a lower limb. About 9 million people in the U.S. have peripheral vascular disease, only 725,000 people are diagnosed annually and less than half receive either surgical or endovascular treatment.

Gyrus ACMI (Maple Grove, Minn.) announced a development partnership with Intuitive Surgical Inc. (Sunnyvale, Calif.). The agreement enables Intuitive Surgical to license Gyrus ACMI's proprietary PK™ technology for development of the Intuitive Endowrist® PK Dissecting Forceps to be used with the da Vinci® Surgical System. The Endowrist PK Dissecting Forceps will provide da Vinci Surgical System users greater tissue management capabilities utilizing the unique traits of PK Technology for a variety of robotically assisted surgical procedures. The da Vinci Surgical System is used in several major institutions worldwide in advanced or complex surgical procedures. As a result of this collaboration surgeons will be able to achieve a similar tissue effect in both robotics and manual laparoscopic surgery.

IBM announced it has collaborated with **St. Jude Medical Inc.** (St Paul, Minn.) to produce the St. Jude Medical Merlin™ Patient Care System, a portable system that programs St. Jude Medical's implantable cardioverter defibrillators (ICDs) and pacemakers. IBM provided resources, industry experience, and consulting to St. Jude Medical's team in the development effort of this state-of-the-art system designed to help physicians conduct tests, analyze therapeutic and diagnostic data, and program implanted devices more efficiently. The Merlin Patient Care System received approval from the U.S. Food and Drug Administration (FDA) in April, following a development effort where St. Jude Medical consulted with the engineers of IBM's recently formed Technology Collaboration Solutions unit.

Nanogen Inc. (San Diego, Calif.), developer of advanced diagnostic products, has announced a collaboration agreement with Oy Jurilab Ltd., the Finnish genomics company. The collaboration is designed to identify and validate new prognostic markers for type II diabetes, one of the leading causes of death in the United States. Complications arising from diabetes include heart disease, stroke, blindness, kidney disease, and nervous system damage, and constitute a tremendous economic burden on healthcare systems. Global incidence of diabetes has been on the rise, in both developed and developing countries, and is projected to reach 220 million by 2010. Jurilab has access to genetic screening of an isolated population in East Finland, which is derived from one of the most genetically homogeneous populations available. Estimated at approximately 20 generations old, it is about half the age of other populations employed in screening programs. Fewer generations result in less genetic variation, and statistically significant data can be derived from relatively small sample groups, reducing research time and costs.

Community Calendar

World Congress on Medical Physics and Biomedical Engineering 2006
August 27-September 1, 2006
International Union for Physical and Engineering Sciences in Medicine
Seoul, Korea

The 32nd Annual National Society for Histotechnology Symposium/Convention: Rising to Greater Heights
September 8-13, 2006
Phoenix Convention Center
Phoenix, AZ
www.nsh.org

5th International Conference on Inorganic Materials
September 23-26, 2006
Cankarjev Dom Cultural and Congress Centre
Ljubljana, Slovenia
www.im-conference.elsevier.com

ESF-EMBO Symposium on Stem Cells in Tissue Engineering - Isolation, Culture, Characterization and Applications
October 28 - November 2, 2006
Hotel Eden Roc
Sant Feliu de Guixols, Spain
www.esf.org/conferences/lc06213

The 8th New Jersey Symposium on Biomaterials Science
November 8-10, 2006
Hyatt Regency Hotel
New Brunswick, NJ
www.njbiomaterials.org

5th Asian-Australian Conference on Composite Materials
November 27-30, 2006
Harbour Plaza Hong Kong Hotel Conference Centre
Hong Kong
www.me.ust.hk

OARSI 2006 World Congress on Osteoarthritis
December 7-10, 2006
Hilton-Prague
Prague, Czech Republic
www.oarsi.org

Society For Biomaterials 2007 Annual Meeting and Exposition
April 18-21, 2007
Chicago, IL
www.biomaterials.org


SOCIETY FOR BIOMATERIALS 2007 ANNUAL MEETING
CALL FOR ABSTRACTS
CHICAGO
SOCIETY FOR BIOMATERIALS
April 18-21, 2007
Chicago, Illinois
Abstract Deadline: November 1, 2006
The abstract submission website will be available from www.biomaterials.org by September 1, 2006. Abstracts must be completed by November 1, 2006 to be considered for the meeting. Please visit the SFB website or contact SFB headquarters at info@biomaterials.org for more information about the 2007 Annual Meeting.

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