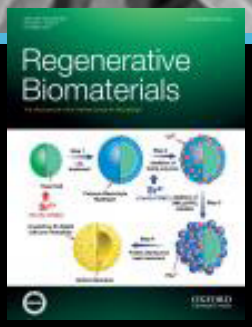
HIGHLIGHTS OF THE LATEST BIOMATERIALS RESEARCH FROM NATURE MEDICINE
HIGHLIGHTS FROM THE ORTHOPEDIC BIOMATERIALS SIG

BIOMATERIALS FORUM

OFFICIAL NEWSLETTER OF THE SOCIETY FOR BIOMATERIALS

Fourth Quarter 2016 • Volume 38, Issue 4



Introducing **REGENERATIVE BIOMATERIALS**, a biomaterials/regenerative medicine journal published by Oxford University Press with Prof. Xingdong Zhang, President of the International Union of Societies of Biomaterials Science and Engineering, as its Editor-in-Chief.

ALSO INSIDE

Biomaterials Forum, the official news magazine of the Society For Biomaterials, is published quarterly to serve the biomaterials community. Society members receive Biomaterials Forum as a benefit of membership. Non-members may subscribe to the magazine at the annual rate of $48. For subscription information or membership inquiries, contact the Membership Department at the Society office (email: info@biomaterials.org) or visit the Society's Website, biomaterials.org.

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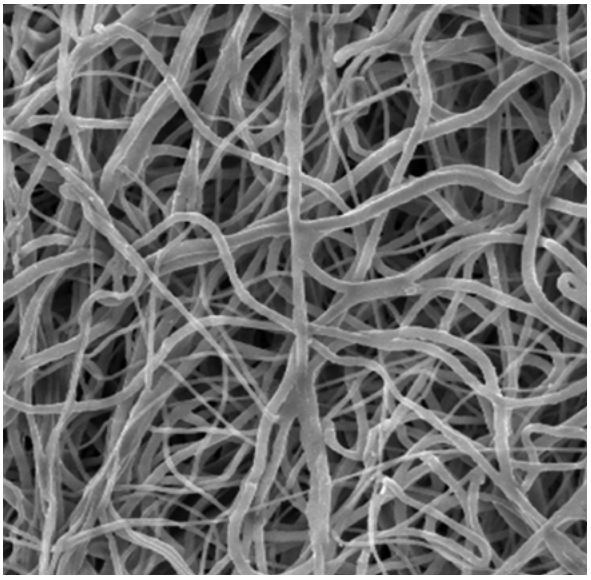
BIOMATERIALS
FORUM

The official news magazine of the **SOCIETY FOR BIOMATERIALS** • Volume 38, Issue 4

Special Interest Group Reporters



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On the cover: The cover image, provided by Haripriya Ramesh of Prof. Martin W. King's Medical Textile Laboratory in the College of Textiles at the North Carolina State University, shows the electrospun fibers of polycaprolactone after the treatment with sodium hydroxide and sputter-coated with gold. The image was captured by a VEGA3 TESCAN under a 10kV accelerating voltage.

WHAT IS REGULARTORY SCIENCE?

Guigen Zhang

In his 2013 book, *The Cure in the Code – How 20th Century Law is Undermining 21st Century Medicine,* Peter Huber (a senior fellow at the Manhattan Institute) highlighted the outdated practices the US Food and Drug Administration (FDA) uses in its regulatory approval processes. His observations were echoed by many in the biomedical community, as well as those within the FDA. Indeed, the FDA's desire to change and improve is evident in its emphasis in recent years on calling for advancing the regulatory science and innovation. As argued by Janet Woodcock (Director of CDER of FDA) and colleagues in a 2015 article that the agency lacks "all the requisite expertise, resources to address…key barriers to biomarker development. …While the ultimate decisions…rest with the FDA, the process could be accelerated if diverse experts and stakeholders came together to identify and prioritize needs, gather relevant scientific information, and develop community consensus in an open and transparent process."

The National Academies of Science, Engineering, and Medicine (NASEM) Forum on Drug Discovery, Development and Translation, together with the Burroughs Wellcome Fund, held a workshop Oct. 20-21, 2015, to facilitate dialogue among stakeholders about the current state and scope of regulatory science and opportunities to address barriers. As evident in the forum's report, the workshop yielded many mixed views and suggestions without clear consensus on how to overcome the challenges.

So, what is regulatory science? According to the FDA, regulatory science is the science of developing tools, standards, and approaches to assess the safety, effectiveness, quality, toxicity, public health impact and/or performance of FDA-regulated products.

Is it all? If regulatory science is about developing tools, standards and approaches, will a tool, standard or approach developed based on incomplete scientific premises help improve the regulatory processes and pathways? It would be a fair statement to make that every time an approval decision made by the FDA on a therapeutic product should have been based on the best science available at that movement. Yet, there are often FDA recalls for products that do not perform the ways as scientifically anticipated. What does this suggest?

To me, it suggests that the challenges in advancing regulatory science are far more serious than most of us would think. Aside from developing relevant tools, standards and approaches, regulatory science should be regarded as the science of the highest level—the science of making right regulatory decisions that will not only assure public safety but also promote innovation. In my opinion, to truly advance regulatory science we must first break away from the ways we have done science in the past (or maybe in the recent past; see Bob Baier's Historical Flashback piece).

To facilitate that, I have planned the panel session "Convergence for Advancing Regulatory Science" during the 2017 IBE Annual Conference in Salt Lake City, Utah, March 29-31, 2017 (more information in the Member News section) to engage the audience to brainstorm the meaning, needs, ethics and challenges of regulatory science, and identify best practices for pursuing convergence to advance regulatory science and innovation. I am hopeful that through such efforts, real-world validated successes like the pyrolytic-carbon based artificial heart valves (as reflected in Prof. Bob Baier's Historical Flashback piece) can be supported, realized and repeated for the advancement of regulatory science.

In closing, let me briefly mention what we have prepared for you in this issue. In the Letter from the President, Liisa Kuhn shares with us her personal experiences with standards development and invites your participation in the process. In the News and Updates section, you will catch up with Member News, the Staff Update and student activities. In the SIG section we have updates from the Orthopedic Biomaterials SIG and highlights of a recent work published in *Nature Medicine* called "Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats." In a new column called Meet the Rising Stars, you will find an interview with SFB 2016 Young Investigator Awardee, Fan Yang, that shares her insights on how to thrive in today's academic environment. In our regular columns, you will find latest industry news from Steve Lin, government news from Carl Simon, educational news from Yusuf Khan and a book review from Lynne Jones. Also new to this issue, you will find a brief introduction to the ASTM F04 committee from its staff manager Kate Chalfin. Finally, I want to bring your attention to the Historical Flashback column, in which Bob E. Baier, SFB 1992 President, shares with us a memory on the accidental innovation of the pyrolytic carbon as a blood compatible biomaterial.

With my best wishes,

Guigen Zhang
Executive Editor, Biomaterials Forum

SOCIETY FOR BIOMATERIALS: A GLOBAL COMMUNITY IMPACTING HUMAN HEALTH

Liisa Kuhn

I think many biomaterials scientists share a fundamental desire to enhance human health and quality of life. We chose the field of biomaterials because it gives us a direct opportunity to participate in improving medical products and technology. Those of you who work in industry or are clinicians can directly fulfill that desire of enhancing human health through your day-to-day work on, or with, clinically used medical products and patients. For those of us in academia, our research is not typically a direct path that leads to an impact on clinical practice. With each passing year, I appreciate even more how difficult it is to take an idea from bench to bedside.

As a faculty member who worked in industry prior to taking a university position, I had the opportunity to start writing medical product standards through participation in the American Society of Testing and Materials (ASTM) while I worked for a company. I have continued ever since. Standards are used in a number of ways, but in large part to set a bar for product quality and to help facilitate regulatory approval. Industry participants are kept balanced at an equal number with academics/clinicians/regulatory agencies that typically do not have a conflict of interest with the technology. Each company is allowed a single vote to restrict possible attempts to push through standards that impede another company's products from gaining regulatory approval or market share. I'm writing about ASTM in this letter in part to let you know that there is a shortage of academic researchers in ASTM at this time. For example, the subcommittee that I chair, F04.42 (Biomaterials and Biomolecules), needs about five new members to allow participation of more companies that are eager to join and help with standards writing to accelerate product approval. They are currently on a waiting list. As an SFB member, you have the expertise to contribute to biomaterials standards writing within ASTM immediately, either virtually or through attendance at the biannual meetings. Membership is inexpensive ($75) and comes with a free full volume of medical product standards of your choice and will:

- Help streamline your academic or corporate research
- Increase your global visibility,
- Help move new technologies, such as regenerative medicine/tissue engineering strategies, into patients faster
- Allow basic scientists to gain an understanding of what quality measures are required for a safe and successful medical product
- Allow industry/consultants to gain an understanding of the competition and new technologies that may impact future medical product design

Bottom line: Standards writing is rewarding work that provides a direct opportunity to participate in improving medical products and technology that I believe is a dream of all of ours. Since there is a significant need to have equal representation, I hope that the academics, consultants and clinicians reading this letter will consider participating in standards writing that is often the domain of industry. I believe SFB is a global community with preeminent knowledge of biomaterials, interactions of cells with biomaterials and host response to biomaterials. I would like to increase the transfer of that knowledge to standards writing activities to help achieve our Society's mission of enhancing human health and quality of life. Please consider participating.

In support of this mission, the 2017 annual meeting will feature "standard methods" workshops, tracks and lectures that share know-how and may be the basis for future medical product standards. Evolving regulatory requirements will be explained. You can learn more about specific subcommittee activities by reading the article in this issue from the ASTM F04 staff manager or going to www.astm.org or contacting me directly. The next ASTM working meeting will occur after the SFB 2017 annual meeting, so there's time to plan for your future involvement.

All the best,

Liisa Kuhn

Liisa Kuhn
SFB President

Surprising Blood Compatibility of Pyrolytic Carbon

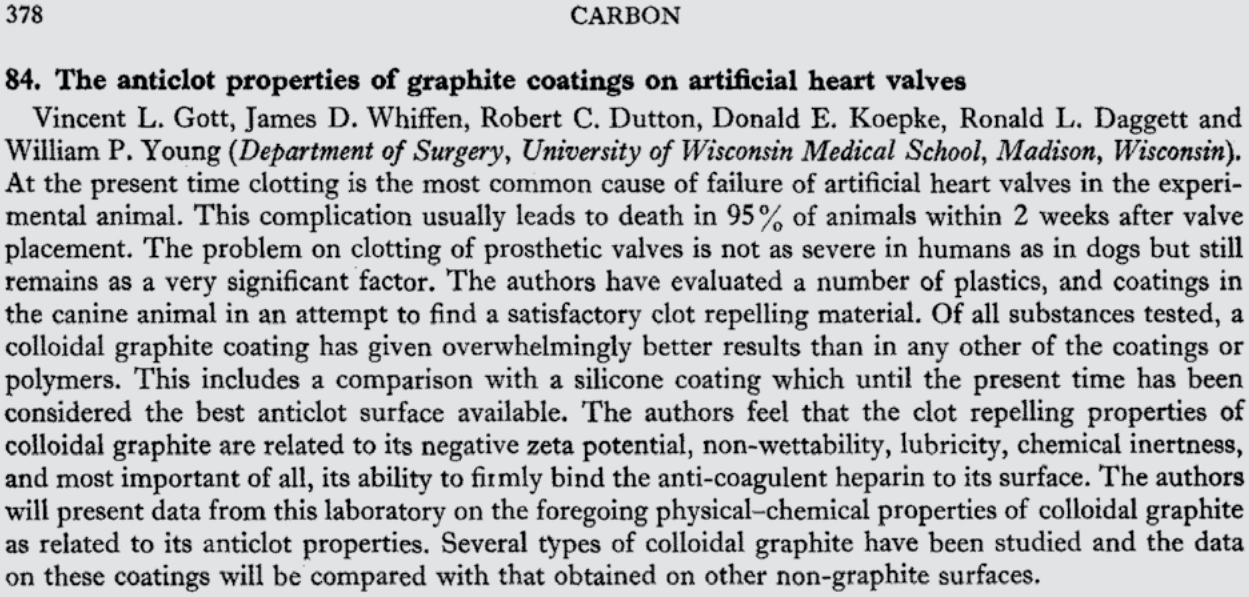
A MEMORY FROM PAST-PRESIDENT R.E. BAIER, PhD, PE, 1992 SFB PRESIDENT

It was in late 1967, early 1968, that a strange finding emerged from the pioneering "Gott Ring" studies in canine vena cavae being done at Johns Hopkins Hospital in Baltimore, Maryland. Classical inorganic materials scientist, Dr. Jack Bokros, of San Diego's General Atomic Corp., had become "accidentally" a co-worker of Dr. Vincent Gott through Bill Ellis. Ellis had read an abstract in *Carbon* by Gott et al: "The Anticlot Properties of Graphite Coatings on Artificial Heart Valves" (Fig.1),[1] and informed Bokros that colloidal graphite (carbon) coatings were being used as a base for blood anti-coagulant on Dr. Gott's short-ring implants, to good effect. Ellis was a bit offended by the choice of a commercial product, which was much less pure than what had recently been developed at General Atomic (Pyrolytic Carbon, PyC), and so samples of the newly developed PyC at General Atomic Corp. were sent to Dr. Gott as "positive" (clot-provoking) controls. I was one of the "boys in the back room," providing surface analyses of all proposed new blood-contact materials, and from early measurements predicted securely—with Dr. Gott—that these PyC rings would immediately cause both thrombosis and coagulation of slow-flowing dog blood. Wrong, again.

We were all surprised when the naked PyC rings stayed clean for two hours (most everything else had clotted solid by then), and then were amazed when the dogs were brought back after two weeks "at the farm!"

The rings were still clean, clearly violating all that we had considered ample predictive data to the contrary. Carrying the tests further, I was able to show that the PyC material uniquely bound one of the blood's proteins in a configuration that expressed an outermost critical surface tension in a zone previously identified as triggering the least thrombosis and coagulation. It was in that zone, and specifically for the PyC, that surgeon Eugene Bernstein and PhD (later MD and SFB President) Fred Schoen had shown that such PyC leaflets on a pioneering centrifugal blood pump least distorted attached blood platelets and, thus, did not trigger viscous metamorphosis and thrombus growth. Our colleague, Dr. Emery Nyilas, then working at AVCO-Everett Corporation near Boston, showed that the heat of adsorption was minimal during key blood protein trials (carried out in the middle of the night to avoid traffic vibrations) by micro-calorimetry. Drs. Andrade and Kim subsequently showed that the mode of protein adsorption and not the quantity of protein adsorbed on foreign surfaces was a key, consistent with Nyilas' micro-calorimetric studies. PyC adsorbed a layer of blood proteins rapidly without the expected denaturing of proteins on blood contacting surfaces that generally triggered the clotting cascade. Many others joined in, General Atomic became Gulf General Atomic, which spun-off CarboMedics and went on to inspire Medical Carbon Research Institute. A large fraction of the world's synthetic heart valves have since been

Figure 1.



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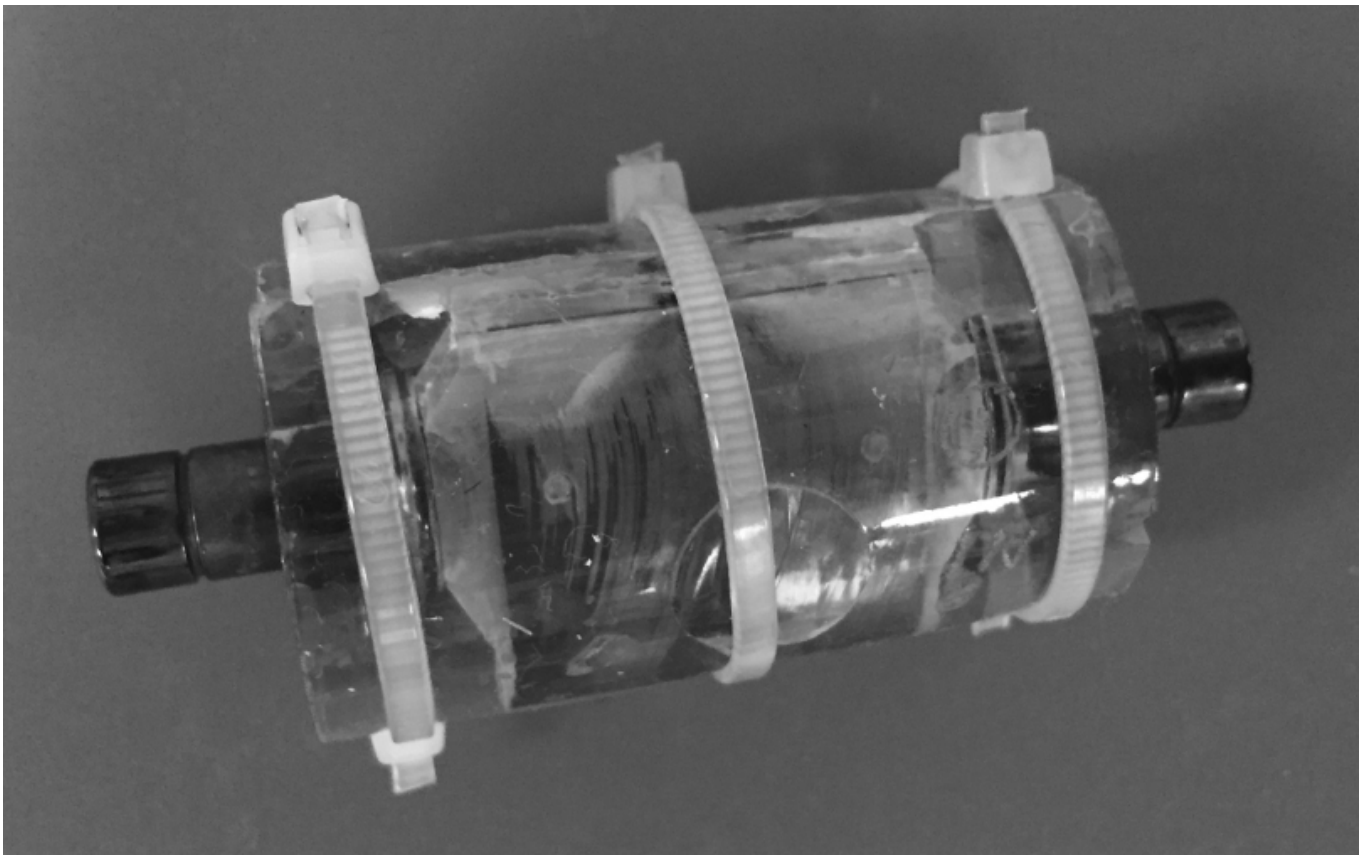
84. The anticlot properties of graphite coatings on artificial heart valves

Vincent L. Gott, James D. Whiffen, Robert C. Dutton, Donald E. Koepke, Ronald L. Daggett and William P. Young (*Department of Surgery, University of Wisconsin Medical School, Madison, Wisconsin*). At the present time clotting is the most common cause of failure of artificial heart valves in the experimental animal. This complication usually leads to death in 95% of animals within 2 weeks after valve placement. The problem on clotting of prosthetic valves is not as severe in humans as in dogs but still remains as a very significant factor. The authors have evaluated a number of plastics, and coatings in the canine animal in an attempt to find a satisfactory clot repelling material. Of all substances tested, a colloidal graphite coating has given overwhelmingly better results than in any other of the coatings or polymers. This includes a comparison with a silicone coating which until the present time has been considered the best anticlot surface available. The authors feel that the clot repelling properties of colloidal graphite are related to its negative zeta potential, non-wettability, lubricity, chemical inertness, and most important of all, its ability to firmly bind the anti-coagulent heparin to its surface. The authors will present data from this laboratory on the foregoing physical–chemical properties of colloidal graphite as related to its anticlot properties. Several types of colloidal graphite have been studied and the data on these coatings will be compared with that obtained on other non-graphite surfaces.

The abstract that led to the "accidental" innovation.

Figure 2.



An in vivo flow cell made of pyrolytic carbon, post-canine implantation.

rendered from those pioneering contributions between academia and industry. The recently announced sale of St. Jude Medical to Abbott Laboratories for $25 billion is–in my view—predominantly owing to the initial success of St. Jude with these PyC heart valves, and subsequent copying of the technology. Figure 2 is a contemporary photo of a PyC "flow cell" that had been implanted in a 27kg dog by Dr. Gott to establish the details of thromboresistance now shown in over 15 million successful valve implants.

Can this happen again, today? NO! At the recommendations of our academicians, NHLBI of NIH ceased allowing industrial participation in the federal biomaterials research effort by canceling the contract funding option from their portfolios years ago. The NIH funding for such efforts is almost as dim for practicing clinicians, as conflict-of-interest concerns have interceded to separate the inventors from their inventions—making sure they receive neither credit nor cash for their inspired hard work and practical observations. Our journals have protected us from debate and controversy, and also suppressed invention. I invite readers to seek old volumes of *Transactions of the American Society for Artificial Internal Organs,* the society from which the Society For Biomaterials spun off, to experience the debates and controversies leading to these older successes that we all now claim.

REFERENCE

1. Gott V, Whiffen JD, Dutton RC, et al. The anticlot properties of graphite coatings on artificial heart valves. *Carbon.* 1964;1(3):378.

Staff Update

BY DEB DUPNIK, ASSISTANT EXECUTIVE DIRECTOR

Hello from Society For Biomaterials headquarters! The Society's Board of Directors and governing Council will be meeting in November at SFB headquarters in Mount Laurel, New Jersey. They will be reviewing the 2017 budget and continuing their work on the strategic plan for the society. The following is a brief rundown on some of the things being done on behalf of the membership.

AWARDS, CEREMONIES AND NOMINATIONS

CHAIR ANTONIOS G. MIKOS, PhD

The Awards, Ceremonies and Nominations Committee has received a total of 40 award nominations and six nominations for the three open officer positions. There were 14 Clemson nominations, eight Student nominations for Outstanding Research and six Young Investigator nominations. The full slate of officers and awards were presented to Council for approval on November 10, 2016. After Council's ratification to the proposed slate, award winners and officer candidates were announced in November. Thank you to all those who made nominations, and please start thinking about possible nominations for next year!

BYLAWS

CHAIR BENJAMIN G. KESELOWSKY, PhD

The Bylaws Committee will be reviewing the bylaws and discussing possible amendments. Based on last year's recommendations, Council asked the committee to affect three changes to the SFB bylaws.

1. Rename the Devices and Materials Committee. Council members considered the new name "Industrial Liaison Committee," but were in agreement that the word "Liaison" might need to be replaced as there was concern that members would confuse it with the Liaison Committee.
2. Eliminate the Long Range Planning Committee and add the duties of this committee to the Council to be coordinated by the President-Elect.
3. Eliminate the Meetings Committee and add the duties of this committee to those assumed by Board.

DEVICES AND MATERIALS COMMITTEE

CHAIR SPIRO J. MEGREMIS, PhD

The committee is actively supporting the third SFB Business Plan Competition, which was developed by the Biomaterials and Medical Products Commercialization SIG, and is working to develop and evaluate other opportunities for industry members in Minneapolis, including a possible site visit/facility tour.

EDUCATION & PROFESSIONAL DEVELOPMENT

CHAIR ELIZABETH COSGRIFF-HERNANDEZ, PhD

The E&PD Committee is soliciting applications for the 2017 C. William Hall Scholarship. This award honors the memory of the Society's first president, Dr. C. William Hall. Any undergraduate students interested in attending the annual meeting of The Society For Biomaterials in Minneapolis, Minnesota, April 5–8, 2017 should apply for the 2017 C. William Hall Scholarship. The scholarship covers the entire expense of the event. For more information, visit **biomaterials.org/students/c-william-hall-scholarship.**

Cato T. Laurencin Travel Fellowship: Named in honor of a distinguished member of the SFB, the Cato T. Laurencin, Travel Fellowship will support under-represented minorities in the field of biomaterials by providing an undergraduate student resources to attend the 2017 annual meeting of the, and a complimentary membership in the Society. The goal of this initiative is to stimulate/encourage recipients to pursue a career in biomaterials. For more information about the Cato T. Laurencin, MD, PhD Travel Fellowship or an application, visit **biomaterials.org/awards/cato-laurencin-travel-fellowship.**

Biomaterials Day: The committee received nine grant applications for the 2017 Biomaterials Day program and is in the process of reviewing these.

FINANCE

CHAIR SHELLY SAKIYAMA-ELBERT, PhD

Development of the 2017 budget is underway and is being prepared to deliver a modest net income. This may mean nominal increases in dues and/or registration rates, and/or a reduction or cessation of some programs. Reserves remain healthy, and the 2017 budget was reviewed by the Board of Directors Nov. 10.

LIAISON

CHAIR TIM TOPOLESKI, PhD

Satellite meetings for 2016 were organized to provide additional opportunities for members and to liaise with other societies in a WBC year. The liaison committee will request feedback from each of the satellite symposium organizers including the number of people who attended, and will investigate opportunities for further outreach.

LONG RANGE PLANNING

CHAIR DAVID KOHN, PhD*

The Long Range Planning Committee is charged with increasing membership, especially from industry and clinical sectors; furthering international collaborations; increasing the visibility of SFB through public relations

efforts; governmental/policy issues; and potential collaborations with other organizations. SFB continues to engage the public relations firm of Schneider Associates to:

1. Build awareness for and advance the brand image of the SFB through a combination of earned and owned media
2. Promote the work of individual SFB members in order to help them gain exposure for their work and provide additional value in their membership
3. Increase visibility for the SFB among key audiences including stakeholders, members of the biomaterials community and members of the broader science community

MEETINGS

CHAIR LIISA KUHN, PhD*

Plans are well underway for the annual meeting in Minneapolis, April 5-8, 2017. Abstracts were solicited with an extended Nov. 14, 2016 deadline. In recognition of the fact that speakers from industry need to protect their intellectual property, it is understood that some technical details cannot be disclosed. SFB is introducing "Biomaterials Technology in Industry" sessions that will relax some of the typically rigorous scientific requirements for these specific sessions.

For the first time, in addition to the awards addresses and the keynote, SFB will host four additional 30-minute plenary lectures.

Six pre-meeting workshops are being scheduled for Wednesday, April 5, 2017 in the morning.

*** Note:** The Long Range Planning and Meetings Committees responsibilities are being transferred to the Board of Directors. A Bylaws change in 2017 is expected to codify this operational shift.

MEMBERSHIP

CHAIR LIJIE GRACE ZHANG, PhD

The committee is working to develop strategies to increase membership, especially in industry and clinical sectors.

PRESIDENT'S ADVISORY

CHAIR THOMAS WEBSTER, PhD

The committee will review the code of ethics for SFB and advise the council about any matter requested by the president. The committee will work with the education committee to put together a panel on ethics for 2017.

PROGRAM

CO-CHAIRS REBECCA CARRIER and SUPING LYU

The theme for the 2017 annual meeting is Where Materials Become Medicine, and with Minneapolis in the heart of Medical Alley, that may be truer for this meeting than anywhere else in the world. In keeping with that theme, the Program Committee is developing a program that focuses on biomaterial research specifically oriented to clinical application with commercial impact. Major themes will include: 3D printing, cells, drug delivery, immune response, regulatory/standardization issues and translation.

The Society's annual meeting focuses on fostering development of new implantable materials spanning both devices and biologics for improvement of the human condition. The meeting program will include the latest innovations in materials science, molecular and cell biology and engineering, new opportunities and mechanisms for translation of these findings to new or improved medical treatments or diagnostics. The meeting format will include symposia, general sessions, workshops, panel discussions and tutorials, covering all aspects of basic, applied and translational biomaterials science.

The 2017 Program Committee received 88 ideas for sessions at the 2017 meeting in Minneapolis. From that, a total of 74 proposals were requested. The program will also feature two competitions for students: the Business Plan Competition and the Education Competition. The Committee will meet to finalize the 2017 program in January 2017. Please visit the meeting website at **2017.biomaterials.org** for the most up-to-date information about the 2017 meeting.

PUBLICATIONS

CHAIR SACHIN S. MAMIDWAR, MBBS, MS

The Publications Committee continues its work with the bi-weekly e-newsletter, *Biomaterials Bulletin*. In addition, the committee will be working to expand services available on the website, and will look to maintain SFB's partnership with Wiley in the publication of the *Journal of Biomedical Materials Research.*

NATIONAL STUDENT CHAPTERS

PRESIDENT CHRISTOPHER J. GEHRMANN

The national student section officers are making efforts this year to help improve the value of membership through increasing volunteering, networking and training

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

SOCIETY FOR BIOMATERIALS
1120 Route 73, Suite 200
Mount Laurel, NJ 08054
Phone: 856-439-0826
Fax: 856-439-0525
info@biomaterials.org
biomaterials.org

ANDRÉS J. GARCIA

I am honored to serve as your 2016-2017 Member-at-Large representative. As Member-at-Large, I serve as YOUR representative on both the Board of Directors and the council of SFB. I will also serve as your representative on other committees (e.g., Long Range Planning Committee) so that members have a clear voice for direction of SFB. I plan to focus my efforts on three areas: (1) be a voice for all the members, (2) foster scientific excellence and a nurturing environment, and (3) expand the impact of SFB. I encourage all members to send me your ideas and feedback about SFB (andres.garcia@me.gatech.edu). With your help, we can continue to improve SFB and increase the value for all members. I also write this column highlighting member news and accomplishments.

The fourth Hoffman Family Symposium (HFS) was held in Taipei, Taiwan in September, 2016. There were over 100 attendees from around the world, including many colleagues and former students of **Allan Hoffman** (University of Washington). This year's conference on Biomaterials and Biointerfaces was held at National Taiwan University (NTU) in Taipei, and chaired by Prof. Wei Bor Tsai, a former class student of Allan's. The three earlier HFSs were held in Japan twice and Korea. Another HFS is planned for Shanghai in 2017.

Warren Haggard, Professor and Associate Dean of Research and Graduate Studies for the Herff College of Engineering at the University of Memphis, was honored as Herff Chair of Excellence in Biomedical Engineering at UoM football game.

Michael Sefton (University of Toronto) was awarded the Terumo Global Science Prize from the Terumo Foundation for Life Sciences and Arts. This prize is awarded to outstanding researchers who have demonstrated unique, internationally renowned achievements in research, made significant contributions to the field of regenerative medicine particularly through novel biomaterials discovery, and continued to work in the frontline of research.

Guigen Zhang, Professor and Associate Chair of Bioengineering at Clemson University, will organize a panel discussion/workshop session themed "Convergence for Advancing Regulatory Science" during the 2017 IBE Annual Conference, over which he will preside as the IBE President of 2017, in Salt Lake City, Utah, March 29-31, 2017. This session, endorsed by the SFB and IBE and sponsored by the Burroughs Wellcome Fund and Clemson Bioengineering, includes an invited panel of distinguished, influential scientists, engineers, regulators and think-tank members who will engage the audience to brainstorm the meaning, needs, ethics and challenges of regulatory science and identify best practices to advance regulatory science and innovation through convergence of disciplines. Please join the panel and contribute to this important science that affects all aspects of life. The panelists include Dr. Peter Huber, a senior fellow at the Manhattan Institute; Dr. David Grainger, distinguished professor and chair of bioengineering at the University of Utah; Dr. Guru Madhavan, a senior policy advisor at the National Academy of Sciences; Dr. Nigel Walker, deputy director of science at the National Toxicology Program at NIEHS and NIH; and Dr. Frank Weichold, director of critical path and regulatory science initiatives at the FDA.

Amol Janorkar, Associate Professor in Biomedical Materials Science at the University of Mississippi Medical Center, received an R01 grant titled "3-D Models of Adipose Pathophysiology." The main goals of this grant are to develop in vitro models of adipose tissue that allow a superior hypertrophic growth of adipocytes and facilitate investigation of metabolic stresses and signaling mechanisms during pathological culturing conditions mimicking those of progressing obesity.

New Optional Publication for SFB Members: SFB members will have an option to subscribe to *Biomedical Materials - Materials for Tissue Engineering and Regenerative Medicine* when they join/renew for 2017 at an additional cost of $110. The publication features original research findings that contribute to our knowledge about the composition, properties and performance of materials for tissue engineering and regenerative medicine. Additional information can be found at iopscience.iop.org/journal/1748-605X.

If you have news that you would like to share with your fellow members, please send it to Prof. Andrés Garcia.

PREPARING FOR GRADUATION: DAY ONE OR THE HOME STRETCH

BY CHRISTOPHER GEHRMANN, STUDENT NEWS EDITOR

As we reach the end of the Fall semester, our student chapter is revisiting the importance of emphasizing professional development. For some, this time involves finishing their first semester of college or graduate school, while for others it represents a frantic race to the finish line as they prepare to graduate. Regardless of your time left, it is always important to keep in mind that preparing for life after the degree is key in successfully landing the right job. When it comes to networking, student chapters can provide resources and opportunities by establishing connections with their communities. In the case of institutions isolated from sufficient representation of these fields, fellow SFB student chapters can create joint opportunities, which promote the unity of our chapters. To help discover these opportunities, we have compiled a few examples to help student chapters identify future events.

For academia careers, students are well positioned within their university and can find opportunities by exploring their own department. Student chapters can initiate this networking by holding student chapter meetings to introduce faculty and provide opportunities to ask questions. By helping inform our members about academia and explaining the rigors of such a career, the SFB also provides great opportunities for connecting with other institutions through several means. The most easily utilized resource is simply our large, diverse and widespread group of members where contact information can be accessed from our website. Also, SFB provides various in-person networking events throughout the country through multiple, localized mini conferences called Biomaterials Days. These events facilitate multi-institutional collaborative events drawing together both students and faculty into a single location. These events are more accessible for members than our national conference, and provide a similar benefit on a smaller scale. However, our national conference should not be undervalued; this year's conference, especially, provides unique benefits for multiple fields of interest. These conferences congregate a large number of our members, faculty and students alongside many attendees from institutions outside of the U.S. At our national conference students will have the opportunity to meet with an enormous group of professionals capable of guiding our members seeking a career in academia.

Some of our chapters are located near medical device companies, and inviting local professionals to meetings or scheduling tours of the facilities can be very useful in helping students discover opportunities. These events can also help provide exposure to our members during their job search. For institutions not located in an industry hub, joint Biomaterials Day events can offer similar experiences. This past year has highlighted the ability of Biomaterials Day events to draw not only multiple institutions but even industry partners looking for quality students to hire. We are excited to see this type of benefit become available to our students and we hope to continue sponsoring and encouraging these great events. Our national conference also draws many companies that come to showcase products and find prospective applicants. Our Spring 2017 national conference will have a particularly strong industry presence with local Minneapolis-based companies such as Medtronic and Boston Scientific in attendance, which we hope to capitalize on for our students.

Finally, we wish to open a conversation regarding an often encouraged but rarely pursued career path: entrepreneurship. Biomedical engineering is a field that has a tremendous potential to create innovative companies, and, as such, attracts investment from across the country. Memphis, alone, has seen several of our students become founders who continue to grow successfully funded companies. Spurring on these opportunities are local business development organizations, which are often scouting for talent year-round. These companies are eager to help develop technologies from universities and work primarily with students who are integral to the development of the technology. These organizations are great for finding networking events throughout the city, and can help provide connections for various sponsorships. Again, Biomaterials Day events are great opportunities to bring these types of organizations to students and have already shown great success at events this past year.

Overall we see that utilization of local resources by student chapters helps provide amazing career development for our members, including job opportunities. Our goals as the student section of the SFB include "[aiding] the efficacy of students seeking research, education and professional development opportunities." We hope to encourage the promotion of these types of events at each chapter, between many institutions as Biomaterials Day conferences, and as a whole during the SFB's annual conference. With so many opportunities for involvement in the SFB, we hope to maintain a great value for student membership year after year.

Meet the Rising Stars

AN INTERVIEW WITH SFB'S 2016 YOUNG INVESTIGATOR AWARD WINNER

Notes from the Editor: *In my first "Letter from the Editor" I mentioned my plans to use the Forum to periodically introduce the rising stars of the SFB. I thus very much welcome any suggestions and nominations you may have for the individuals whose story you would like us to feature in future issues.*

Here is ***an interview with SFB's 2016 Young Investigator Award winner - Fan Yang****, Assistant Professor in the Departments of Orthopaedic Surgery and Bioengineering, at Stanford University. Dr. Yang's research seeks to understand how microenvironmental cues regulate stem cell fate, and to develop novel biomaterials and cell-based therapeutics for tissue regeneration, with special focus on treating musculoskeletal diseases, cardiovascular diseases and cancer. Prior to joining Stanford, Dr. Yang received her PhD in biomedical engineering from Prof. Jennifer Elisseeff's lab at Johns Hopkins University, and then completed a postdoctoral fellowship in the laboratory of Prof. Robert Langer at MIT.*

Among the most recent awards that Dr. Yang received in recognition of her innovation are the 2011 Technology Review TR35 Global list, NSF CAREER Award, the NIH R01 award, California Institute of Regenerative Medicine Tools and Technologies Development Award, Young Investigator Award from Alliance for Cancer and Gene Therapy, National Scientist Development Award from American Heart Association, Rising Star award from BMES-CMBE, Mission for Learning Faculty Scholar Award in Pediatric Translational Medicine, Donald E. and Delia B. Baxter Faculty Scholar Award, the McCormick Faculty Award, Stanford Asian American Faculty Award, the 3M Non-tenured Faculty Award, the Basil O'Connor Starter Scholar Research Award, Biomaterials Science Lectureship Award and the SFB Young Investigator Award.

GZ: First of all, I want to congratulate you again for receiving the SFB Young Investigator Award in May 2016, as well as many other awards. I would like to start by asking: when did you become interested in biomaterials research?

FY: Thank you and it's an honor to be the recipient of such a prestigious award. I was first exposed to biomaterials research in 2001 when I started out as a rotation PhD student in Prof. Jennifer Elisseeff's lab at the Johns Hopkins University. I was fascinated by the exciting prospect of repairing/regenerating human tissues using biomaterials and cell-based approaches. This sounded like a much more attractive option than metal or plastic- based medical devices/prosthetics. What was particularly attractive to me was how biomaterials could serve as a powerful tool to integrate the fields of biology and medicine, and offer solutions for tissue repair in a way that current medicine cannot achieve.

GZ: Would you give some brief highlights of your research work? What impact you would like to make in terms of helping people and improving quality of life?

FY: A bioengineer by training, I work at the interface of materials science, biology, engineering and medicine. I am

Figure 1.

Fan Yang (front row in blue with her son Eric standing behind) with her students and postdocs in a lab outing.

particularly interested in developing biomaterials as an artificial cell niche with independently tunable niche cues to elucidate the mechanisms of how matrix cues drive normal tissue development or diseases progression. Such knowledge can enable us to improve the quality of life by developing novel biomaterials that can enhance cell survival, engraftment and differentiation *in situ* to improve tissue regeneration that cannot be removed using current approaches.

GZ: How big is your research group? What can you share with our readers about the ways you run your group and motivate the students and/or postdocs, the challenges and the rewards?

FY: My research group is composed of about 12-15 members (Fig. 1) with postdoctoral fellows and PhD students from diverse backgrounds including bioengineering, materials science & engineering, chemical engineering, mechanical engineering, stem cell biology and medicine. Their diverse backgrounds provides a great niche for fostering creativity and innovation. Research is a journey of discovering unknowns and is filled with unexpected challenges. To make the process fun and productive, I try to foster a supportive and collaborative lab culture. As such, each student/fellow not only gets feedback from me, but also peer mentoring. We always have active and dynamic discussions in our weekly lab meetings and subgroup meetings, and this brainstorming process is very rewarding as it helps everyone grow together in a synergistic manner. I am very grateful that we have a wonderful group of talented people in our lab who not only help each other with research challenges, but are also a source of support and encouragement as we face inevitable challenges.

GZ: You are very successful in securing research funding from highly competitive sources such as the NSF and NIH. In your opinion, what are the keys to such successes?

FY: For lab PIs, getting continuous funding is one of the most important responsibilities and also the toughest job. Funding for a lab is like the fuel for a car, without which no car can run. I started actively engaging in grant writing when I was a graduate student and a postdoc, and I would encourage junior fellows/students to volunteer to help with writing fellowships/grants. If you want to learn how to drive, the only way to do it is to take driving lessons and learn from experience. Grant writing is still an ongoing learning experience for me. Most of my grants involve clinician scientists as collaborators, who are the end-users of the technologies that we develop. I make a concerted effort to seek their feedback early during the proposal development phase. Their clinical expertise is very helpful and offers complementary perspectives to help me define the right problems that are not only innovative but also clinically impactful.

Figure 2.

Fan and her son, Eric, enjoy the nature during a weekend hiking near Stanford University.

GZ: What can you share with our readers in terms of the DO and DON'T in research program development, proposal writing, etc.?

FY: All roads can lead to Rome, and I don't think there is only one way to get there. From my own experience, I think it is important to follow your passion, stay positive and be patient. Things often take longer than you expect, and that is normal. In today's tough funding environment, rejection is common and that can discourage the more junior faculty, especially after they have invested so much time and energy on something they are so passionate about. It is OK to feel down for a bit, but don't let it bother you for too long. Take the constructive comments and move on. Keep trying, learn from each experience and stay resilient! Believe in yourself and a great idea will be funded, sooner or later!

GZ: To date, you have published about 70 papers and received some 20 grants as PI or co-I. What percentage of your time is spent on writing papers and/or proposals?

FY: I don't keep track of time on that, but it is a lot for sure. It is a dynamic process and I prioritize my time differently depending on the funding cycles and needs of the lab.

GZ: A successful young researcher often gives people the impression that work is all of your life. You seem to be doing extremely well balancing work and life, as both an accomplished researcher and a mother of a young son. How do you do it? Can you share with our readers something about your son and your family life?

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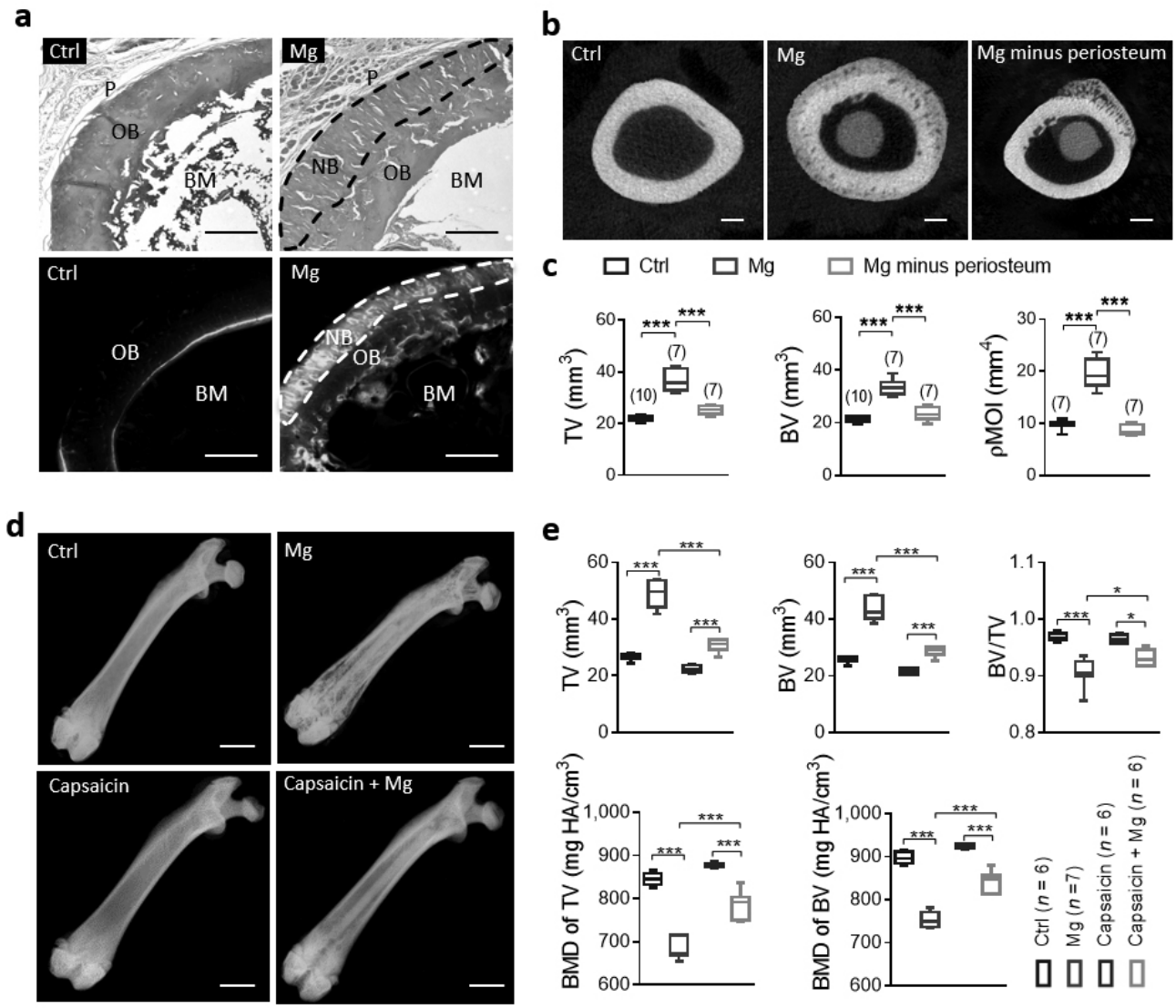
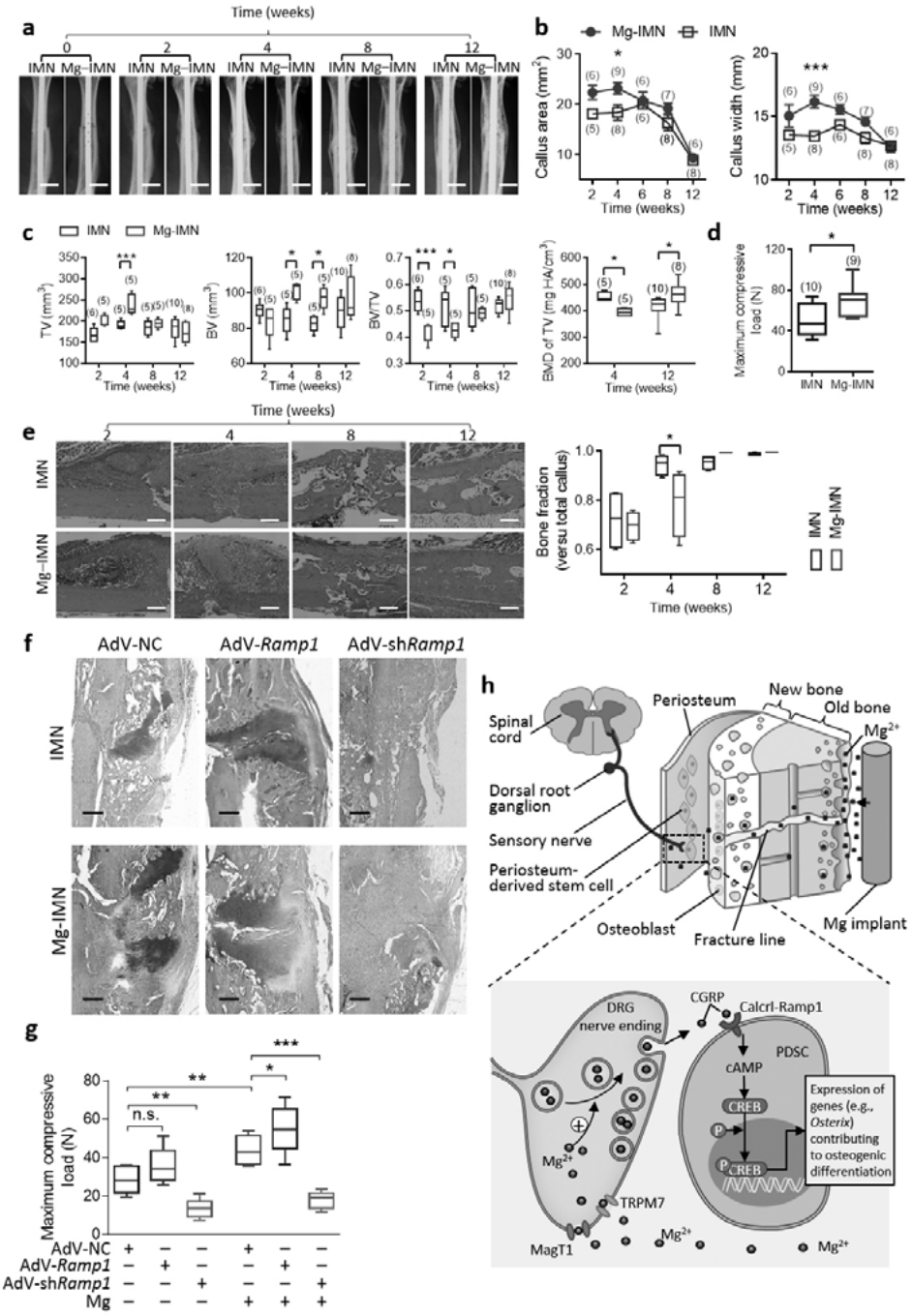
Highlights of the Latest Biomaterials Research from Nature Medicine

Topic

Zhang Y, Xu J, Ruan YC, et al. Implant-derived magnesium induces local neuronal production of CGRP to improve bone-fracture healing in rats. Nat Med. 2016;22:1160-1169.

In this recent publication in *Nature Medicine,* the group used non-fractured femur model to confirm the osteogenic effect of magnesium. They surgically implanted either a 99.99%-pure magnesium or a stainless steel rod (as a control) into the medullary cavity of the femur in rats. Hematoxylin and eosin staining and calcein labeling showed a substantially larger amount of new bone was formed at the peripheral cortex in magnesium-implanted femora (Figure 1a). Higher total bone tissue volume (TV), high-density bone volume (BV) and ρ-moment of inertia (ρMOI) were found in magnesium-implanted femora, as compared to that in the controls (Figure 1b,c). However, no new bone was formed at regions where the periosteum was surgically removed, but only found at peripheral cortex that contained residual periosteum (Figure 1b,c). They destroyed the sensory nerves by injecting high-dose capsaicin into the dorsal spine in rats. Consequently, the degree of magnesium-induced new bone formation was significantly lower as compared to the group without capsaicin treatment (Figure 1d,e). Immunofluorescence staining showed abundant CGRP in peripheral cortical bone received magnesium-implantation, whereas in controls only scattered CGRP labeling was found. ELISA analysis showed that CGRP expression in bone tissues was higher after magnesium-implantation, which peaked at day four with a value eight-fold higher than the controls. In addition, at week two post-surgery, substantially greater CGRP was also found in L4 dorsal root ganglion in magnesium-implanted rats as compared to the controls. *Calcrl* (calcitonin receptor–like receptor) or *Ramp1*





(receptor activity-modifying protein 1, the direct binding site for CGRP) overexpression further enhanced, whereas *Calcrl* or *Ramp1* knockdown attenuated magnesium-induced new bone formation.

By using FM1-43 to label the synaptic vesicles in DRG neurons under a live-cell confocal system, they found that Mg2+ induces movement and aggregation of these vesicles toward neuronal terminals. Addition of $MgCl_2$ (10 mM) into the Mg^{2+}-free bath induced a significant increase in $[Mg^{2+}]i$, indicating Mg^{2+} entry into DRG neurons, which was significantly inhibited by nitrendipine (inhibiting MagT1) or 2-APB (inhibiting TRPM7), but not by ruthenium red (inhibiting TRPM6), indicating that the elevation of extracellular Mg^{2+} induced MagT1- and TRPM7-dependent Mg^{2+} entry.

Western blot results showed that treatment with CGRP (10–10 M, 72 hours) resulted in higher phosphorylated CREB (pCREB) and Osterix in PDSCs, which was blunted by *Calcrl* knockdown. The CGRP-induced osteogenic differentiation of PDSCs was promoted by *Calcrl* overexpression and diminished by *Calcrl* knockdown. Interestingly, treating the PDSCs with Mg^{2+}-conditioned neuronal culture medium facilitated their osteogenic differentiation, and this facilitation of differentiation was inhibited in *Calcrl* knockdown cells.

To translate the osteogenic effect of magnesium for orthopedic application, however, their pilot study showed pure magnesium pin alone failed to fix femoral fracture due to the fast loss of mechanical strength, they then tested the ability of the magnesium-containing intramedullary nail (Mg-IMN) system (by inserting a magnesium rod into a hallow IMN made of stainless steel with drilled holes, to heal fractured femurs in OVX rats. They confirmed the release of magnesium from the Mg-IMN was comparable to pure magnesium pin in vitro. Using the μX-ray fluorescence, they also found the diffusion of magnesium from the endosteum toward the periosteum. Given the suggested involvement of the periosteum in magnesium's beneficial effects on fracture healing, they used a closed femora fracture model in which the periosteum remained intact during bone injury. X-ray analysis showed that at week four post-implantation, the width and area of callus in the Mg-IMN-implanted group were significantly

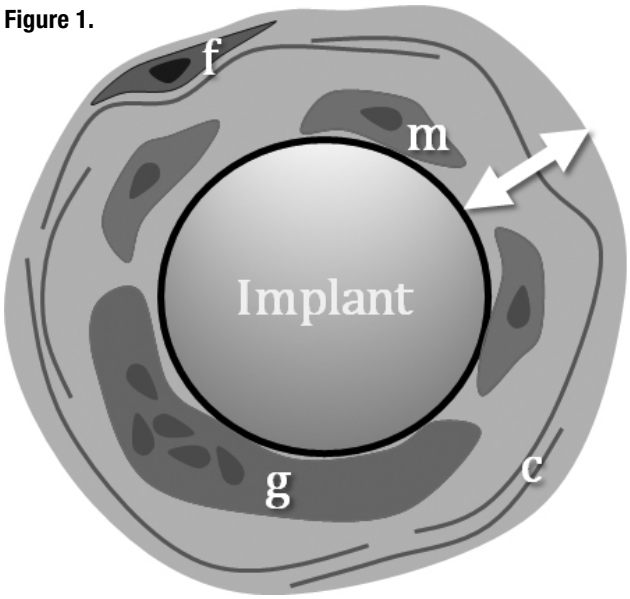
(continued on page 21)

45S5 BIOGLASS® FOR INHIBITION OF FOREIGN-BODY CAPSULE FORMATION AND INTEGRATION TO NATIVE TISSUES PART 2: BIOLOGICAL STRUCTURE GROWTH

BY ROCHE C. DE GUZMAN, PhD, ASSISTANT PROFESSOR, DEPARTMENT OF ENGINEERING, HOFSTRA UNIVERSITY

The formation of a fibrous capsule structure is one of the foreign-body responses to implanted biomaterials.[1,2] Orthopaedic devices, particularly those used as "permanent," such as metallic pins, screws, rods and plates trigger a fibrous encapsulation response[3] to potentially isolate the non-self and bulky solid object from the rest of the organism's biological system. The sequential events leading to this fibrous layer formation are generally characterized as: a) protein binding to the biomaterial surface through adsorption, b) tissue macrophages migration and activation, and c) attraction and induction of fibroblasts to secrete collagen fibers. Accordingly, the extracellular material of this walling-off network is mostly collagen while the majority of the cellular components are macrophages and fibroblasts localized at the inner and outer sublayers, respectively (Figure 1). Collagen is the ubiquitous structural protein in our body produced by fibroblasts. Hence, fibroblasts signaled to deposit collagen through activated macrophages can occur mostly throughout, as foreign-body fibrous capsule (FBC) formation has been observed in the subcutaneous, intraperitoneal, subglandular, submuscular, intramuscular and other regions of the body where the implant was placed. The FBC can grow to have a thickness of about a millimeter and may remain at that condition for a few years.

Figure 1.



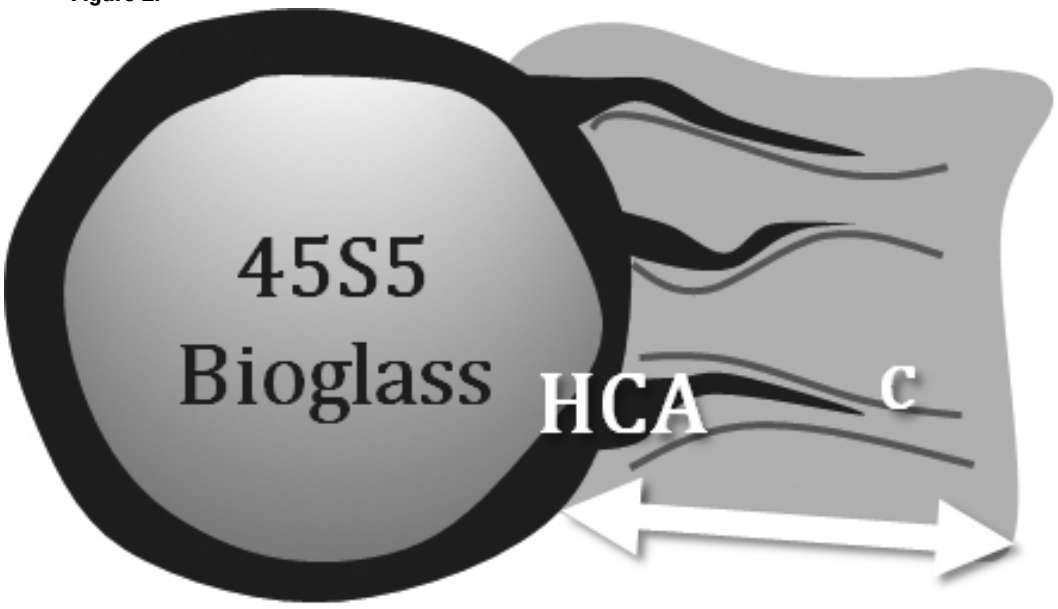
Fibrous capsule (double arrow) composed of collagen fibers (c) secreted by fibroblasts (f) with macrophages (m) and foreign-body giant cells (g) surrounding the implant.

At certain situations however, like when implantable materials and their degradation products are incompatible or when the body's physiological balance is altered, macrophages fuse and form the multi-nucleated foreign-body giant cells in the attempt to phagocytose the relatively large object. These giant cells, as well as the mono-nucleated macrophages, may induce the T-cell mediated immunity[4] causing a granuloma chronic inflammatory response and fibrosis in which fibroblasts are continuously activated to secrete collagen fibers, thereby constantly increasing the thickness of the FBC layer. In this diseased state, fibroblasts may also be signaled to differentiate into myofibroblasts (cells with smooth muscle cells and fibroblasts phenotype) that enable contraction of the capsule.[5,6] Orthopaedic implants that require stability and host-tissue integration, therefore, do not benefit from this fibrous membrane isolation and the FBC structure can even lead to more incidence of device failure.[7]

45S5 Bioglass monoliths (mm-spatial dimensions) and microparticles avoid the formation of FBC and allow for direct bone tissue binding.[8] Dissolution and release of charged calcium and phosphate species from Bioglass assemble and thermodynamically organize into hydroxyapatite crystals on its surface. Carbonates normally present in extracellular fluids[9] react to form hydroxycarbonate apatite (HCA), which is also the natural bone mineral. Collagen fibers within bone tissues, particularly their positively-charged amino acids enable the precipitation and assembly of hydroxyapatite and HCA.[10] Consequently, adjacent Bioglass, acting as depot of calcium and phosphate ions and HCA crystals, will further promote these nucleation and growth processes of bone minerals (Figure 2); thus a mechanism of Bioglass integration to bone and collagen fiber-containing tissues.

Additionally, the thin HCA layer deposited on the Bioglass surface promotes native protein adsorption and ultimately leading to mesenchymal stem cell attraction, attachment, differentiation into osteoblasts, and deposition of bone matrix.[8] Interestingly, other exogenous and synthetic biomaterials such as silicone and polyethylene glycol polymers also promote surface adsorption of host proteins but resulting in FBC formation[11] instead of bone tissue

Figure 2.



Bone tissue (double arrow) binds to Bioglass through direct attachment of hydroxycarbonate apatite (HCA) layer to collagen fibers (c).

integration. The type, conformation, composition and properties of adsorbed proteins on Bioglass versus those on other FBC-inducing biomaterials may be different and subject for further investigation.

Bioglasses (45S5 and other bioactive glasses) have been employed for integration with soft and non-bony tissues for a variety of tissue engineering applications: vascularization, wound healing and repair of laryngeal, lung, heart, nerve, gastrointestinal and urinary tract tissues.[12] It was hypothesized that the HCA layer on the Bioglass surface binds to the soft tissues' extracellular matrices and stabilized by infiltrating tissue-specific cells; very similar to the mechanism of Bioglass-bone interaction. If fully understood, then Bioglass can be utilized to universally connect the biomaterial non-living world to the biological system towards further improvement of functionalities of medical devices including orthopaedic implants and enhancement of strategies for complete tissue repair and regeneration.

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AN EXAMPLE OF PEER MENTORSHIP IN STEM EDUCATION

BY YUSUF KHAN, EDUCATION NEWS CONTRIBUTING EDITOR

In the past, this column has described programs around the country that are designed to encourage and support the participation of underrepresented minorities in the science, technology, engineering and math (STEM) fields. Today I present a newly funded initiative at UCONN Health in Farmington, Connecticut: the Biomedical Science and Engineering (BSE) Summer School. This National Science Foundation-funded initiative was developed by its Principal Investigator, Syam Nukavarapu, Assistant Professor of Orthopaedic Surgery and Biomedical Engineering at the University of Connecticut. Professor Nukavarapu currently conducts research in the field of orthopaedic biomaterials and musculoskeletal tissue engineering. He has previously worked with colleagues in funded research and mentorship programs, such as Research Experience and Mentoring (funded by NSF), and Building Infrastructure Leading to Diversity (funded by NIH).

Education Quote of the Quarter:

Mentoring is a brain to pick, an ear to listen, and a push in the right direction.

–JOHN C. CROSBY

The goal of the BSE Summer School program is to train and mentor underrepresented minority students in biomedical sciences and engineering related fields. This Summer School at UCONN Health is particularly focused on biomaterials, stem cells and engineered grafts for bone and bone-cartilage interfacial tissue engineering. The BSE Summer School will provide research and mentorship experience to prepare them for careers in STEM areas, but what makes this program unique is its intention to allow undergraduate mentees to learn about medical/dental school while simultaneously obtaining research training under the guidance of a mentor.

During the six- or eight-week program, participants will be assembled into groups consisting of both undergrads and medical/dental students. These groups will receive hands-on research experience in biomaterials processing, three-dimensional porous matrix development, cell culture techniques and biomaterial/matrix culture with cells for biocompatibility evaluation. Using these topic areas they will learn the basic experimental techniques required to perform biomaterials science and engineering-related research with a focus on bone and bone-cartilage defect repair. Additionally, the participants will receive training in scientific writing, professional development and general communication skills, all areas critical to student development in the STEM fields. The twist, however, is the composition of the assembled groups. By combining undergraduate students with currently enrolled medical and dental students, the undergrads will have immediate and lasting access to students currently under medical and dental training, giving them a birds-eye view of what life is like in those graduate programs. The belief is that pairing undergraduate students with medical and dental students will allow undergrads to ask questions, allay fears, learn strategies and gain valuable insight into the application process, lifestyle and demands of a medical or dental education. Knowing these elements going into the application process may give them a leg up on the competition and better prepare them for their future endeavors; all this while simultaneously pursuing their STEM interests. At the end of the program, the participants will have earned a mentor for life for whenever they may be at a cross-roads and need career guidance in choosing the best path forward. Conversely, medical/dental students will have opportunity to perform biomedical research so that they can pursue the dream of becoming a clinician scientist one day. While doing so, they will also have opportunity to mentor undergraduate students on their way to becoming the next generation of mentors. Facilitating this mentor-mentee relationship in a way that initially places the counterparts as equals or peers is an interesting approach to mentorship and one that has found favor in other programs nationally.

The program will recruit four undergraduate and two medical/dental students from the underrepresented minority groups (as defined by NSF) in the state of Connecticut, but based on its initial success future plans are to expand it to a national-level program. If you are interested please contact Dr. Syam Nukavarapu **(syam@uchc.edu)** for additional information regarding BSE Summer School.

Do you have a similar program at your institution? Contact me and we can highlight it here in future issues.

INTRODUCTION TO ASTM BIOMATERIALS MEDICAL PRODUCT STANDARDS

BY KATE CHALFIN, F04 COMMITTEE STAFF MANAGER

Biomaterials have become an important part of the medical world, and in response the ASTM International Committee F04 on Medical and Surgical Materials and Devices has taken on the task of developing technical standards in this important area. Formed in 1962, ASTM Committee F04 develops standards and guidance for medical and surgical materials and devices. There are a number of subcommittees throughout Committee F04 related to biomaterials; such as the P04.13 ceramics subcommittee, the P04.12 metals subcommittee and the P04.11 polymers subcommittee. However, most of the focus on biomaterials can be found within two of its subcommittees. Subcommittee F04.42 on biomaterials and biomolecules for tissue engineered medical products (TEMPs) develops standards that "identify the normal biological functional characteristics that would be required of a tissue-engineered medical product." Key standards include ASTM F2150 *Standard Guide for Characterization and Testing of Biomaterial Scaffolds Used in Tissue-Engineered Medical Products;* ASTM F2900 *Standard Guide for Characterization of Hydrogels used in Regenerative Medicine;* and ASTM F2027 *Standard Guide for Characterization and Testing of Raw or Starting Biomaterials for Tissue-Engineered Medical Products.*

Another subcommittee within F04 that addresses biomaterials is subcommittee F04.43 on cells and tissue engineered constructs for TEMPs. Subcommittee F04.43 develops standards for the structural and mechanical characterization of a TEMP. Key standards related to biomaterials include ASTM F2664 *Standard Guide for Assessing the Attachment of Cells to Biomaterial Surfaces by Physical Methods* and ASTM F2739 *Standard Guide for Quantitating Cell Viability Within Biomaterial Scaffolds.*

In addition to these two subcommittees' efforts, several other F04 subcommittees maintain standards dealing with biomaterials. One such subcommittee, subcommittee F04.16 on biocompatibility, has addressed tissue response to biomaterials in ASTM F981 *Standard Practice for Assessment of Compatibility of Biomaterials for Surgical Implants with Respect to Effect of Materials on Muscle and Insertion into Bone.* To view the complete list of subcommittees within Committee F04, and the approved standards and proposed new standards in each subcommittee, visit **www.astm.org/COMMIT/SUBCOMMIT/F04.htm.**

Committee F04's membership of over 900 members from around the world maintains approximately 300 standards across 23 technical subcommittees. Biomaterials scientists and engineers are welcome to participate in the ASTM standards development process by joining Committee F04 in the important work of the development of new standards and revision of existing standards. In-person working meetings are held twice a year, in May and November, although standards development activity continues all year long through the use of electronic tools and virtual meetings. Some of the benefits of membership include the ability to network with professionals worldwide, direct input into the development of new and revised standards, and a free volume of the *Annual Book of ASTM Standards.* Find more information about ASTM membership at **www.astm.org/MEMBERSHIP/index.html** or by contacting Kate Chalfin at **kchalfin@astm.org.**

Staff Update (continued from page 7)

opportunities for our students. The officers this year are excited to utilize all of the resources our organization provides such as the Special Interest Groups (SIGs) and Biomaterials Day events to use current member benefits in more proactive ways.

SPECIAL INTEREST GROUPS

REPRESENTATIVE BRENDON HARLEY, PhD

Proposed SIG budgets have been submitted and were reviewed by the board in November. In an effort to help ensure that SFB continues to offer and outstanding scientific program that includes ground-breaking research, members of each SIG were encouraged to submit abstracts to 2017 sessions being sponsored or co-sponsored by their respective SIGs.

NEW! YOUNG SCIENTIST COMMITTEE

CHAIR COLE DEFOREST

This new sub-committee will fall under the purview of the Education & Professional Development Committee and will provide a melting pot for career development ideas, where senior members guide grads, postdocs and junior faculty on the path toward impactful research and outreach, fulfilling an unmet need within the biomaterials community. If you are just starting out in your career and want to be part of this exciting new group, pcontact SFB headquarters at **info@biomaterials.org.**

Industry News

BY STEVE LIN, EXACTECH

FDA has approved **Abbott Laboratories'** fully resorbable cardiac stent, less than a year after Boston Scientific won the agency's approval for a similar device. Abbott's Absorb GT1 Bioresorbable Vascular Scaffold System releases the drug everolimus to limit the growth of scar tissue, and is gradually absorbed by the body in approximately three years, according to an FDA statement. Abbott is claiming that the Absorb is the first fully resorbable cardiac stent, although Boston Scientific says its Synergy stent dissolves even faster, in about three months. Abbott has spent some 15 years developing Absorb, and physicians had been anxiously following clinical trials related to the device, which promised to address some of the complications of heart patients treated with stents, including thrombosis and restenosis. Absorb was studied in a large randomized clinical trial in the United States (ABSORB III) that compared Absorb with the XIENCE metallic stent. The trial enrolled 1,322 patients treated with Absorb and 686 patients treated with XIENCE. All patients will be followed for five years.

Zimmer Biomet Holdings, Inc., the Warsaw, Indiana, company, just announced that it will acquire French surgical robotics maker **Medtech S.A.** for more than $133 million. It's the second acquisition for Zimmer Biomet in just a few months. In June, the company announced it would acquire spinal device company LDR Holding Corp. (Austin, Texas) for $1 billion. One year earlier, Zimmer and Biomet joined together in their own $14 billion mega-merger. Medtech was founded in 2002 by Bertin Nahum. Its products include the Rosa Spine, a spinal surgical robot that won a PMA from FDA in January 2016. In December 2015, the agency approved the Rosa Brain robot, which the company likened to "a GPS for the brain" and dubbed "the only robotic assistant approved for neurosurgical procedures in clinical use in Europe, the United States and Canada." FDA approved the first version of the Rosa robotic arm in 2009. The Medtech acquisition will give Zimmer Biomet entry into the surgical robotics market, following competitor **Smith & Nephew's** January 2016 purchase of **Blue Belt** (Plymouth, Minnesota) for $275 million. Blue Belt's Navio handheld, robotic-assisted technology guides the surgeon in creating a virtual surgical plan that removes the need for standard mechanical cutting guides and jigs.

FDA recently approved an intraocular lens to help cataract sufferers improve the sharpness of their vision at near, intermediate and far distances—providing a level of eyesight improvement not seen in other IOL lenses. The approval of Abbott's Tecnis Symfony IOL could be good news for the one-fifth of Americans expected to develop cataracts by age 65, potentially requiring cataract surgery to replace the clouded natural lens with an IOL. The lens includes a proprietary diffractive echelette design feature. The design feature's light diffraction pattern elongates the focus of the eye, extending vision range. FDA approval came after the agency reviewed results of a randomized clinical trial that compared 148 cataract patients implanted with the Tecnis Symfony IOL with151 cataract patients with a monofocal IOL. More than 75 percent of the patients with the Tecnis Symfony IOL had good vision without glasses at intermediate distances, versus 34 percent for the monofocal IOL group. When it came to near distances, the patients implanted with the Tecnis Symfony IOL saw two additional, progressively smaller lines on a standard eye chart. Distance vision was comparable for both groups.

Nestlé Health Science (NHSc) and **Phagenesis** announced that NHSc is entering into a staged, milestone-based acquisition of Phagenesis, a medical device company that has developed a new treatment for dysphagia. Under the terms of the agreement, NHSc will make an upfront payment, followed by milestone-based funding, while Phagenesis completes the clinical evaluation of Phagenyx®*. The staged acquisition will be based upon successful completion of European and US development programs anticipated by 2019. Financial terms have not been disclosed. Phagenyx® is based on groundbreaking research that establishes a mechanism of action of delivering Pharyngeal Electrical Stimulation (PES) to treat the neurological cause of dysphagia. Dysphagia, the inability to swallow safely, is a condition with high prevalence as well as high clinical and health economic burden. Dysphagia occurs in around 29 percent to 55 percent of stroke patients, with 15 million people worldwide suffering a stroke every year. It is also a common consequence of numerous other diseases, and is often under-diagnosed in various patient populations (e.g., in the ICU). Dysphagia is a debilitating condition that frequently leads to life-threatening complications, including aspiration pneumonia, malnutrition and dehydration. Furthermore, patients with dysphagia experience a dramatic reduction in quality-of-life.

Stryker's endoscopy division has purchased New Jersey-based **Ivy Sports Medicine**, developer of the only FDA-approved collagen meniscus implant (CMI) on the market, for an undisclosed amount. CMI is a biological and completely absorbable implant made from highly purified collagen type 1 with a porous structure. The implant is arthroscopically attached to fill the void resulting from damaged and lost meniscal tissue in acute and chronic meniscus injuries, and makes use of the body's own ability to regenerate tissue. CMI, previously called Menaflex, was initially developed by ReGen Biologics and received FDA approval in 2008, according to Healthpoint Capital. FDA rescinded its clearance in 2010, a decision that was challenged by ReGen in court. ReGen was acquired by Ivy Sports in 2011, and in 2014 won the suit filed by ReGen, paving the way for the implant to again be cleared for the U.S. market.

In line with its strategy to grow through inorganic means, **Zimmer Biomet Holdings, Inc.,** has completed yet another mega acquisition. This musculoskeletal major has now announced the buyout of **Clinical Graphics, B.V.,** an imaging company that works on 3D range-of-motion simulation technology needed for common hip conditions. According to the company, this acquisition is a strategic fit as post integration, the 3D imaging platform of Clinical Graphics should expand the company's hip preservation portfolio. However, the company did not disclose the financial terms of the agreement. Zimmer Biomet is highly optimistic about this inclusion. According to the company, as the next generation of treating joint pain, 3D imaging has become an extremely important treatment option in the musculoskeletal market. Clinical Graphics' 3D interactive range-of-motion simulation particularly addresses common hip conditions like femoroacetabular impingement and dysplasia.

Abbott Laboratories will sell its vision care business, Abbott Medical Optics, to **Johnson & Johnson** for $4.325 billion. The deal is expected to close in early 2017 pending customary closing conditions, including regulatory approvals. Abbott's vision care business has products for cataract surgery, laser vision correction (LASIK) and corneal care. It boasts world-class intraocular lenses used in cataract surgery. However, Abbott has been strategically focused on developing leadership positions in cardiovascular devices and expanding diagnostics, CEO Miles White said in a news release.

Abbott is in the process of acquiring **St. Jude Medical** and its extensive cardiovascular device portfolio for $25 billion. It also previously planned to acquire diagnostics company **Alere** for about $6 billion, but has apparently gotten cold feet after Alere disclosed a federal grand jury subpoena related to a U.S. Foreign Corrupt Practices Act investigation. The Abbott-Alere deal is now heading into legal mediation.

GE, which has a medical device operation among the world's largest, is spending $1.4 billion to acquire 3D printing equipment makers **Arcam AB** (Mölndal, Sweden) and **SLM Solutions Group** (Lübeck, Germany). Both companies will report to GE Aviation CEO David Joyce, who will lead 3D printing initiatives across the entire company. The acquisition comes on top of the $1.5 billion GE has already invested in manufacturing and additive technologies since 2010. GE officials think they can grow their new 3D printing business to $1 billion by 2020. A $68-million-a-year business with roughly 285 employees, Arcam is a metal-based additive manufacturing pioneer, credited with inventing the electron beam melting machine. It also produces advanced metal powders. SLM meanwhile has a $74-million-a-year, 260-employee business producing laser machines for metal-based additive manufacturing. SLM boasts that its systems simplify the manufacturing process for dental components including tooth caps and crowns. The company also supplies the dental sector with CoCr nickel-free metal powder.

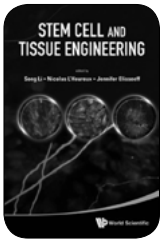
Government News

STANDARDS COORDINATING BODY FOR REGENERATIVE MEDICINE IS ESTABLISHED

BY CARL G. SIMON JR.

A "Standards Coordinating Body (SCB) for Gene, Cell and Regenerative Medicines and Cell-Based Drug Discovery" has been established (www.regenmedscb.org). The SCB is a non-profit organization that will advance the development of industry-wide standards for cell therapy, gene therapy, regenerative medicine and cell-based drug discovery. Morrie Ruffin, managing director for the Alliance for Regenerative Medicine (**alliancerm.org/),** is the founding director of the SCB. "The SCB brings together product developers, tools and service providers, professional societies, government entities and academic centers with the intent to support standards development via coordination, prioritization, resource compilation, inter-laboratory data generation, participation in consensus Standards Development Organization (SDO) activities, education and implementation for standards." The SCB is a multi-stakeholder consortium that comprises members from industry, academia and government. "The SCB will serve as a source of information, knowledge, experience and data collection related to process, material and reference standards to enable more efficient and successful development, manufacture and testing of advanced therapies and cell-based drug discovery." Stay tuned as plans for the SCB are refined.

BY LYNNE JONES, BOOK REVIEW EDITOR



Stem Cell and Tissue Engineering,
Eds. Li, Nicolas L'Heureux, and Jennifer Elisseeff
World Scientific Publishing Co., Pte Ltd., Hackensack, New Jersey and London, England, 2011; 448 pp.
ISBN-13 978-981-4317-05-4; ISBM-10 981-4317-05-5

With our knowledge of stem cells growing at an exponential rate, it is important to appreciate both the historical context of the field, as well as the potential of stem cells to transform the treatment of disease and trauma in the future.

Incremental discoveries about multipotent calls over the last several decades have created momentum in this area of study. Much of the early research focused on the role of these cells in embryogenesis. As our knowledge grew, we became interested in cell-based therapies for the treatment of disease. The next stage was understanding the potential of stem cells for tissue engineering and regeneration.

To explore the application of stem cells to tissue engineering, we must first understand how stem cells are characterized and how they behave. One can review the medical and scientific literature to gain a full appreciation. Recently, I was searching the stem cell literature to find a single resource that would synthesize current research on the topic. I came across the book, *Stem Cells and Tissue Engineering*. This book, edited by Song Li, Nicholas L'Heureux and Jennifer Elisseeff, consists of 20 chapters written by leaders in the field.

As Robert Nerem says in chapter 1 (p. 8), "Only with the combination of research on basic stem cell biology and research on stem cell processing will it be possible to translate the basic benchtop science into future applications and patient therapies."

This book provides students and researchers with a foundation in the current concepts regarding the use of stem cells in tissue engineering. The chapters cover the basics, medical applications, state-of-the art technologies, and quality control and regulatory issues. I found the chapter regarding somatic cell reprogramming (chapter 2; Kim and Park) to be an effective introduction to a topic that can be quite complex; I would recommend it to students just beginning to learn about induced pluripotent stem (iPS) cells. Chapter 3: Hematopoietic Stem Cells (Trowbridge) and Chapter 4: Mesenchymal Stem Cells for Tissue Regeneration (Huang and Li) discuss the basics, including characterization of stem cells, cell sources, applications and challenges/future directions for tissue engineering. These are presented at a level that is easily accessible to undergraduates. Chapter 5 (Friedman and Leach) introduces the concept of mesenchymal stem cell (MSC) delivery in tissue repair. The authors begin by stating that delivery of MSCs can be hindered by a failure to understand "the appropriate physiologic context with the relevant microenvironmental and mechanical tools." This is a key concept often underappreciated by novices in the field. This chapter includes examples of applications to cardiovascular, skin, osteochondral, and bone regeneration. The next 11 chapters describe specific medical applications: Cardiac Tissue Engineering (Young, Christman, Engler); Tissue-Engineered Blood Vessels (Sawh-Martinez, McGillicuddy, Villalona, Shin'oka, Breuer); Vascular Regeneration (Dickinson, Gerecht); Wound Repair (Ko, Nauta, Gurtner, Longaker); Cartilage: Basics, Scaffolds, and Biomaterials (Coburn, Elisseeff); Cartilage: Adult Stem Cells (Saha, Kirkham, Wood, Curran, Yang); Disc Repair (Allon, Buser, Berven, Lotz); Skeletal Tissue (Paneltta, Gupta, Longaker); Oral Bone Reconstruction (McAllister, Haghighat); Spinal Cord (Beattie, Bresnahan); and Neurodegenerative Disease (Auclair-Daigle, Berthod). Chapter 17: High Throughput Systems (Brafman, Willert, Chien) introduces us to high-throughput systems for stem cell engineering. The authors discuss platform fabrication, data acquisition and data analysis and mining. They also discuss extrinsic (altering the extracellular environment) and intrinsic (altering the intracellular signaling pathways and transcriptional networks) manipulation. They describe basic techniques used in the study of stem cells. Chapter 18: Microscale Technologies (Nichol, Bae, Kachouie, Zamanian, Masaeli, Khademhosseini) discusses both top-down (cell-seeded scaffolds for replacement) and bottom-up (assembling building blocks with specific microstructural features into larger engineered tissues) approaches. They stress the relevance of the bottom-up approach to both the creation of engineered tissues, as well as to the study of cell behavior within specific microenvironments. Chapter 19: Quality Control (Dussere, McAllister, L'Heureux) and Chapter 20: Regulatory Challenges (McAllister, Iyican, Dusserre, L'Heureux) are essential reading for anyone engaged in the clinical translation of cell-based tissue engineering. These chapters offer pragmatic discussions of many of the obstacles to bringing tissue engineering constructs to market.'

As a biologist and educator, I strongly recommend that students and researchers in this field first study the basic concepts of cell biology. One textbook that provides an introduction to the necessary concepts is *Essential Cell Biology, 4th ed.,* by Alberts et al. (New York; Garland Science, 2013). I highly recommend *Stem Cells and Tissue Engineering* as an outstanding textbook for both undergraduate and graduate courses and as a valuable resource for one's personal library.

FY: Interestingly, being a good parent or a faculty member require many similar qualities: hard work, the ability to multi-task, patience, resilience and willingness to adapt and grow with the ongoing changes. I had my son before I became a faculty member, and my role as a mom prepared me (unintentionally) for the challenges that I would face later when I started my independent group. I was also wondering if there is a secret to strike a balance for work and life. Fortunately, I have seen role models of women faculty, including my own PhD advisor, who have done both well, so while I realize it takes lots of hard work, it is "mission possible." From observing other women faculty and from my own experience, I have come to the conclusion that there is no perfect balance, and there is never enough time for everything. As such, it is important to prioritize and choose what NOT to do, so we can save time for people and tasks that are most critical. I block time out for my son and family life (Fig. 2), and stay flexible and adjust my schedule as needed. Besides work, I enjoy reading or hiking with my son, taking him to soccer games and cooking for my family. As a mother of a young son, I have also had the unique advantage of understanding his interests, which enables me to develop outreach activities for young kids in an age-appropriate manner. For example, one educational component of my NSF CAREER grant is developing an outreach program called "The Magic of Repairing Human Body" for young children in local elementary schools. The idea was inspired initially by a discussion I had with my son, after he shared with me a book he borrowed from his school library on the topic of the human body. Using story-telling, animations and interactive games, we teach children how different cell types in our body work together to help healing when we get sick. This program is very successful in stimulating passion in science in young children, and we all have so much fun together!

GZ: Looking ahead, what challenges do you see in realizing the impact you would like to make through your innovative research work?

FY: Most projects in our lab start with materials synthesis, characterizing cell-materials interactions in vitro, and then validating them in vivo using small animal models. To realize the impact in translating these therapies from bench to bedside, it would be critical to further validate them in large animal models and move into clinical trials. Looking forward, our next step is to secure right partners, resources, and funding support to help move these exciting new technologies forward to help patients in the near future.

GZ: You mentioned several times about the needs to collaborate and work with the right partners and clinician scientists, how do you identify the right ones?

FY: When I started out as a new faculty member, I initially focused on establishing my group and developing my lab's core platforms and strengths, and then sought collaborations as opportunities arise naturally over time. This helps foster more productive collaborations over long periods of time without losing focus. For junior faculty at a new school, you will run in to many new researchers and get to know their research, and the vice versa. This "freshness" offers lots of opportunities for new collaborations. In my experience, the most rewarding collaboration comes in when all parties are genuinely passionate about solving a research problem of common interest while bringing in complimentary expertise and perspectives.

Highlights of the Latest Biomaterials Research from Nature Medicine (continued from page 13)

larger versus the IMN group (Figure 2a,b). Micro-CT results also showed Mg-IMN facilitates the fracture healing (Figure 2c). Importantly, four-point bending biomechanical test at week 12 showed a significantly greater maximum compressive load of the femoral shafts in Mg-IMN group, as compared to IMN group (Figure 2d). More periosteal woven bone accompanied with elevated CGRP expression within the callus at week two was seen in the Mg-IMN group compared to the IMN group (Figure 2e). Finally, they also confirmed the indispensable role of CGRP receptor in Mg-IMN-facilitated bone fracture healing (Figure 2f,g).

In conclusion, a previously unrecognized CGRP-mediated crosstalk between peripheral nerves and PDSCs has been identified as a major mechanism underlying magnesium-induced bone formation (Figure 2h). The released Mg^{2+} enters DRG neurons via Mg^{2+} transporters or channels (i.e., MagT1 and TRPM7), and promotes CGRP-vesicles accumulation. The DRG-released CGRP, in turn, activates the CGRP receptor (consisting of Calcrl and Ramp1) in PDSCs, which triggers phosphorylation of CREB and expression of genes contributing to osteogenic differentiation. An innovative Mg-IMN system has been developed and shown therapeutic potential for low-energy osteoporotic fracture. It may be also possible to deliver Mg^{2+} or recombinant CGRP to specific healing sites in the bone. Therefore, the present findings may have boarder implications in the treatment or prevention of other bone diseases or injuries, such as high-energy fractures resulting from sports injuries and other traumas.

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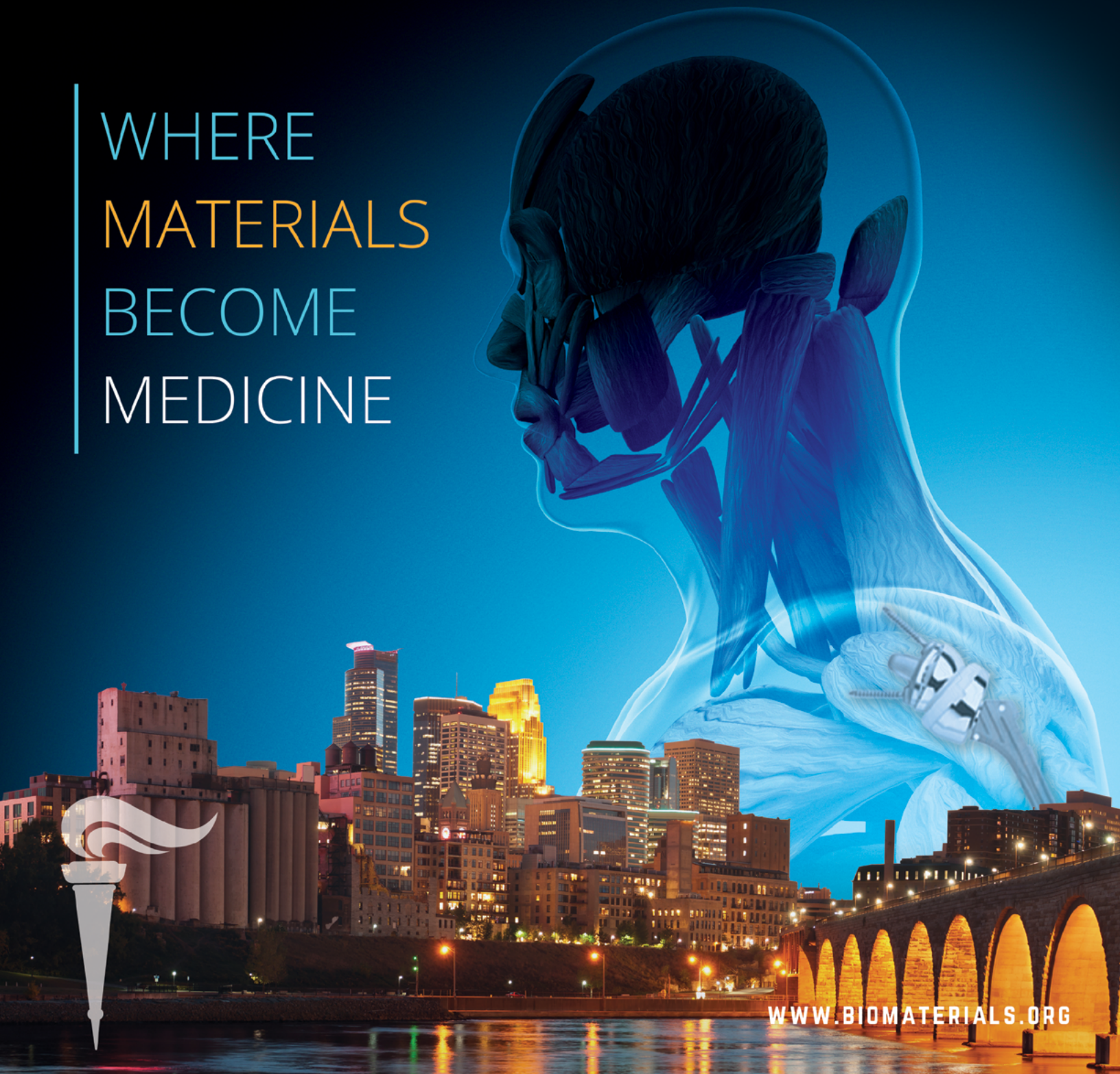

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