THE FUTURE IS NOW: 3D BIOPRINTING

MEDICAL INNOVATION STARTUP PROGRAM

SFB OFFICER NOMINEES

# BIOMATERIALS FORUM

OFFICIAL NEWSLETTER OF THE SOCIETY FOR BIOMATERIALS

FIRST QUARTER 2021 • VOLUME 43, ISSUE 1

## ALSO INSIDE

OPHTHALMIC AND ORTHOPAEDIC SIG UPDATES

IN MEMORY OF DR. DONALD J. LYMAN (1926-2020)

*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.

It is the policy of the Society For Biomaterials that all articles reflect only the views of the authors. Publication of articles or advertisements within *Biomaterials Forum* does not constitute endorsement by the Society or its agents of products, services or views expressed herein. No representation is made to the accuracy hereof, and the publication is printed subject to errors and omissions. Articles that do not have an author byline may originate from press releases. The Society For Biomaterials retains press releases on file for a period of one year from the date of publication.

Editorial contributions to *Biomaterials Forum* are always welcome. Contributions should be sent to the Executive Editor and are subject to the terms and conditions of the Editorial and Publication Release. Authors should refer to the Author Guidelines, which are available on the Society's website, when writing submissions. The publisher accepts no responsibility for return or safety of artwork, photographs or manuscripts. Submission of editorial content does not guarantee acceptance or publication.

Address corrections should be sent to *Biomaterials Forum*, 1120 Route 73, Suite 200, Mt. Laurel, NJ 08054.

Requests for advertising information should be directed to Lisa Howard-Fusco at lfusco@ahint.com or 856-380-6905. Information is also available on the Society's website, biomaterials.org.



Scientific photos may be submitted for cover consideration in future issues. Submit color photo, no larger than 4" x 6", along with credit information and scientific description, to the Executive Editor.



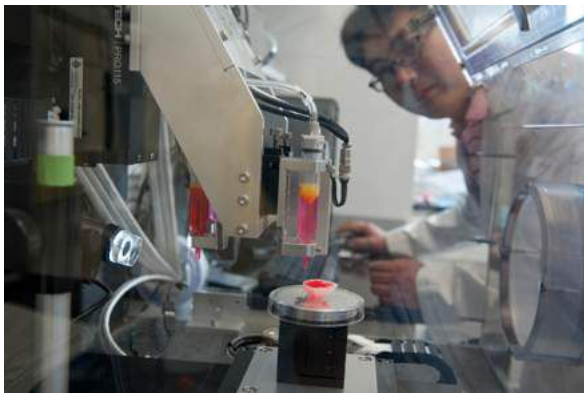
BIOMATERIALS FORUM

The official news magazine of the **SOCIETY FOR BIOMATERIALS** • Volume 42, Issue 4



## SPECIAL INTEREST GROUP REPORTERS

| | |
|---|---|
| **Biomaterials & Medical Products Commercialization** | Puneeth Shridhar • pus8@pitt.edu |
| **Biomaterials Education** | Sarah Rowlinson • sarcorow@gmail.com |
| **Biomaterial-Tissue Interaction** | Antonio Merolli • antonio.merolli@rutgers.edu |
| **Cardiovascular Biomaterials** | Chris Bashur • cbashur@fit.edu |
| **Dental/Craniofacial Biomaterials** | F. Kurtis Kasper • Fred.K.Kasper@uth.tmc.edu<br>Santiago Orrego • sorrego@temple.edu |
| **Drug Delivery** | Eun Ji Chung • eunchung@usc.edu |
| **Engineering Cells & Their Microenvironments** | Scott Wood • scott.t.wood@gmail.com |
| **Immune Engineering** | Yaoying Wu • yw195@duke.edu |
| **Nanomaterials** | Eno Ebong • e.bong@northeastern.edu |
| **Ophthalmic Biomaterials** | Frances Lasowski • lasowsfj@mcmaster.ca |
| **Orthopaedic Biomaterials** | Roche C. de Guzman • roche.c.deguzman@hosftra.edu |
| **Protein & Cells at Interfaces** | Rafael Ramos • ramos.rafael93@gmail.com |
| **Surface Characterization & Modifications** | Shaunak Pandya • pandyasg21@gmail.com |
| **Tissue Engineering** | Abby Whittington • awhit@mse.vt.edu |



# Contents

## THE TORCH



## NEWS & UPDATES



## ON THE COVER

WFIRM's (Wake Forest Institute for Regenerative Medicine) proprietary bioprinter, the Integrated Tissue and Organ Printing System (ITOP), deposits both biodegradable, plastic-like materials to form the tissue "shape." Water-based gels contain the cells to form constructs, like the bladder scaffold shown here.

Photo credit: WFIRM

# From the Editor

*By Roger Narayan, Biomaterials Forum Executive Editor*

I hope that you and your families are having a healthy and productive 2021!

Dan Lemyre, SFB Executive Director, has been hard at work with the production and meetings teams to develop a valuable 2021 Virtual Meeting experience for our community. In the "Staff Update" of this issue, he shares a number of valuable tips related to the platform — including navigation, scheduling, interaction and networking activities — which will help to make your virtual meeting experience as productive and useful as possible.

Although this year's meeting is virtual, the experience will be as if you are walking through a virtual convention center, complete with opportunities for networking. It's really a fun and unique experience, and though it's no substitute for having a few drinks with colleagues in Chicago, I hope that you find it entertaining and valuable!

Lastly, our meeting wouldn't be complete without the support of our sponsors and exhibitors. I encourage you to reach out to them for information about the products and services they offer. It is only with their support that we can make this event successful, and their success relies on you — so please make it a point to visit each of the exhibits. We look forward to "seeing" you at the SFB 2021 Virtual Annual Meeting!

On a sad note, I'd also like to acknowledge the passing of Dr. Jonathan Black, founding member and past President of SFB and author of *the Biomaterials Sciences* textbook, on December 5, 2020. Dr. Jack Lemons has written a brief note about his memories from Dr. Black's era, which I have included below.

Sincerely,

Roger Narayan

# Memories

*By Jack Lemons, PhD*

The early SFB interactions from 1968-1974 were very educational and enjoyable, as they are today. The SFB-USA and international collaborations evolved and expanded since being hosted initially at Clemson University. Meetings and organization transferred to other sponsors, with international locations at about four-year intervals.

At that time, the UAB Executive Secretary was Ms. R. Sellers, and business was conducted through multiple interactions and always guided by the elected officers and committee chairs. The SFB transitioned to establish an independent business office, again selected by the SFB Council. My participation helping with hosting meetings and office activities extended for about a decade, with many fond memories. One participant who enjoyed an active debate was Jonathan Black, and we are very sad about losing him in 2020. Thoughts are extended to his family.

Having participated in more than 50 SFB meetings, I now reflect on the many presentations and posters reviewed and discussed. I also enjoyed the "bash" with extended discussions. All interactions have been fun, especially with students, and I am glad royalties from the *Biomaterials Sciences* book supports students. I look forward to the next meeting.

Sincerely,

Jack Lemons, PhD
University Professor Emeritus
University of Alabama at Birmingham

# From the President

*By Shelly Sakiyama-Elbert, SFB President*

Dear SFB Colleagues,

As spring 2021 begins, we find ourselves reflecting on one year of the pandemic life. I hope despite the many challenges of the past year that you are able to reflect back and find some silver linings. I will definitely appreciate the opportunity to travel and see professional friends in person much more than I have in the past!

We are looking forward to the Society For Biomaterials Annual Meeting coming up April 20-23. The Program Committee and our SFB staff at AH have been working hard to bring you an exciting, high-quality virtual meeting, building on experiences from the last year. We have added Rapid Fire talks for all the "poster" abstracts, so this looks to be a great opportunity to see the latest biomaterials research presented. Registration rates have been reduced to reflect the change in format (and the savings from lack of food/beverage and space charges). Please see the 2021.biomaterials.org website for the latest information.

Also mark your calendars for our Joint Symposium with the Japanese Society for Biomaterials in Hawaii that is *now scheduled for January 8-10, 2022* at the Hilton Waikiki Beach.This is to ensure that all our international colleagues will be able to join us.

This is my last column as President of SFB. I will be turning the reins over to Guigen Zhang for the Second Quarter 2021 issue. I would like to thank all the committed volunteers that allow SFB to operate, especially the Board, Council and Executive Committee, as well as the Committee Members, YSG and SIGs. Thank you for staying engaged, even during the pandemic, and for continuing to bring your great ideas and energy to SFB! I also want to pass on a huge thank you to Dan Lemyre, Shena Seppanen and the whole AH team! Their support has been critical this year as we have had to navigate moving the meeting to a virtual format and partnering with the virtual WBC. It has never been more important to have a knowledgeable and flexible team of staff. Thank you!

I challenge you all to continue your involvement with the Society For Biomaterials (including renewing your membership) and to enhance the impact of our work to improve healthcare through the use of biomaterials while supporting and continuing to build a diverse community. I welcome your suggestions for ways to engage (please email me at sakiyama@utexas.edu).

## CALL FOR COVER ART


### WE WANT TO FEATURE YOUR EXCITING BIOMATERIALS ARTWORK ON THE COVER OF *BIOMATERIALS FORUM!*

**Deadline:** Accepted on a rolling basis.

**Instructions:** Please email artwork (digital images, artistic creations, etc.) to info@biomaterials.org, to the attention of the Executive Editor of the *Biomaterials Forum.* All artwork with biomaterials relevance that have not appeared as a *Forum* cover are welcome. Multiple submissions are permissible.

**Description:** Selected artwork will appear as the cover of a future issue of *Biomaterials Forum* along with a brief "On the Cover" description of the subject and name/affiliation of the creator.

**Format:** High-resolution electronic version in .gif, .tiff or .jpeg file format.

# Officer Nominees

## PRESIDENT-ELECT

*The President-Elect shall become familiar with the duties of the President and shall, at all times, cooperate and assist with the duties of that office. In the absence of the President, the President-Elect shall preside at the meetings of the Society, the Council and the Board of Directors, and perform the duties and exercise the powers of the President. The term of office is for a period of one year without succession. The President-Elect is the Chairperson of the Long-Range Planning Committee.*

**Elizabeth Cosgriff-Hernandez, PhD**
*The University of Texas at Austin*

**Bob Hastings, MS, PE**
*Depuy Synthes, Johnson & Johnson*



## SECRETARY-TREASURER-ELECT

*The Secretary-Treasurer-Elect shall become familiar with the duties of the Secretary-Treasurer, cooperate and assist in carrying out the duties and prepare for eventual succession to that office. In the temporary absence of the Secretary-Treasurer, the Secretary-Treasurer-Elect will perform the duties and exercise the duties of the office. The term of office shall be for a period of two years without succession. The Secretary-Treasurer-Elect shall be the Chairperson of the Finance Committee.*

**Danielle Benoit, PhD**
*University of Rochester*

**Anirban Sen Gupta, PhD**
*Case Western Reserve University*

## MEMBER-AT-LARGE

*The Member-at-Large shall serve as an unencumbered representative of the membership at meetings of both the Board of Directors and the Council. The Member-at-Large shall serve for a period of one year.*

**John P. Fisher, PhD**
*University of Maryland*

**Anita Shukla, PhD**
*Brown University*

For the full Biographical Sketches and Vision Statements of each nominee, see the 2021 SFB Elections: Biographies page on the SFB website. (Only Active and Retired Senior Members have voting privileges. Voting ends Friday, April 2.)

# Member News

*By Joyce Wong, Member-at-Large*

Thank you everyone who submitted their news. Please continue to send me your information – I will still need your help to ensure that we spotlight *all* of our members' news and accomplishments. You can submit your own news or amplify other SFB members' work at any time using this form. If you wish, please include your headshot.

News means not only honors and awards but also publications, books, conferences, grants, outreach, diversity equity and inclusion, promotions, new roles, etc. I am also in the process of collecting **patents** issued within the past five years from our members – please continue to submit your entries. You can also email me at jywong@bu.edu or help us by tagging SFB in your posts on Twitter (@SFBiomaterials), Facebook, and LinkedIn. Please also contact me with suggestions to help me advocate for the broad membership of SFB.

## SFB MEMBER NEWS AND ACCOMPLISHMENTS, PAST QUARTER

**Dr. Christopher M. Jewell,** Minta Martin Professor of Engineering, University of Maryland and Research Biologist, United States Department of Veterans Affairs, has been named an Australian Laureate for 2021. Jewell will be appointed as the Miegunyah Distinguished Visiting Fellow at the University of Melbourne. He will spend the year at the Peter Doherty Institute for Infection and Immunity, collaborating with leading immunologists on new biomaterial-enabled vaccine technologies.

**Dr. Cato T. Laurencin**, Albert and Wilda Van Dusen Distinguished Professor of Orthopaedic Surgery and Chemical, Materials and Biomedical Engineering at the University of Connecticut School of Medicine and CEO, The Connecticut Convergence Institute for Translation in Regenerative Engineering, has received the prestigious 2020 Herbert W. Nickens Award. During his acceptance remarks he announced the release of a landmark publication, *The Impacts of Racism and Bias on Black People Pursuing Careers in Science, Engineering and Medicine*. The publication represents proceedings of a workshop conducted by the National Academies Roundtable on Black Men and Black Women in Science, Engineering and Medicine. Dr. Laurencin serves as Chair of the Roundtable and Editor of the publication.

Dr. Laurencin and his team at the Connecticut Convergence Institute for Translation in Regenerative Engineering have made groundbreaking advancements in unlocking the potential of a molecule called fibroblast growth factor eight (FGF-8), which they discovered controls stem cells in the regeneration of musculoskeletal tissue. This landmark discovery could help curb the progression of osteoarthritis, which is currently projected to remain a major public health issue. According to the CDC, by 2050, the disease will affect more than 130 million people worldwide.

**Colleen Roosa, Jack Whitewolf, Natasha Claxton, Mackenzie Grubb,** PhD Students, University of Virginia, Biomedical Engineering: The University of Virginia (UVA) has been a growing hotspot for interdisciplinary biomaterials research. By definition, "biomaterials scientists and engineers study cells, their components, complex tissues and organs and their interactions with natural and synthetic materials and implanted prosthetic devices, as well as develop and characterize the materials used to measure, restore and improve physiologic function and enhance survival and quality of life." Faculty and graduate students in the School of Engineering at Applied Sciences and the School of Medicine at UVA have spearheaded ground-breaking research that has contributed excellent knowledge to the field of biomaterials. However, four PhD students in the Biomedical Engineering department (**Colleen, Jack, Natasha** and **Mackenzie**) recognized a need for a more structured community for biomaterials researchers at UVA.

In December 2020, these students formed the first nationally recognized chapter of Society for Biomaterials (SFB) at the University of Virginia to encourage the development, dissemination, integration and utilization of knowledge in biomaterials among students, the UVA community, and other members of SFB. This month, the UVA SFB chapter piloted a new Soft Materials Journal Club (SMJC), which aims to create a collaborative space between students and faculty across labs and departments to discuss contemporary literature, pitch grants, give research updates and provide feedback to peers. The first meeting was a successful "grant-brewing" session, where students and faculty brainstormed ideas for a grant proposal focused on the development of biomaterials for cancer screening. Future SMJC meetings will be held bi-weekly, on Mondays from 12-1 pm. The new UVA SFB chapter is excited to foster an inclusive community for biomaterials enthusiasts and expand future programming and events.

**The following SFB Members were elected to the National Academy of Inventors:**

- **Andrés García**, Georgia Institute of Technology
- **Leonard Pinchuk**, University of Miami
- **David Puleo**, University of Mississippi
- **Joyce Wong**, Boston University

**The following SFB Members were elected to the National**

## Member News (continued)

**Academy of Engineering:**

- **Christopher Bowman,** University of Colorado – Boulder
- **Andrés García**, Georgia Institute of Technology
- **David Kaplan,** Tufts University

### DIVERSITY, EQUITY & INCLUSION

**SFB Members Call To End NIH Funding Disparity And #FundBlackScientists**

Recently, a nationwide network of BME women faculty, including several SFB leaders and members, published a commentary in *Cell* describing stark disparities in NIH research funding that have created a barrier to the success of Black scientists. For the past decade, the Black applicant award rates for NIH research funding has been approximately half the rate of similarly trained white investigators. Given that NIH funding is often used in promotion and tenure decisions, this racial disparity in research NIH funding leads to failed tenure cases for Black faculty. Beyond promotion, there is also a high risk of burnout and exit from the academy before reaching the tenure threshold due to the increased burden of twice as much proposal writing to achieve the same funding level as white PIs. This excessive proposal writing burden, on top of substantially more service, leaves Black faculty less time to do research, publish papers, gain exposure and train and inspire diverse students. The loss of Black scientists from the academy and limiting the scientific achievement and career trajectory of those that remain has removed much-needed perspectives, creativity and knowledge of diverse populations from healthcare research. The loss of Black faculty members in the classroom limits our ability to effectively retain and train the next generation of Black scientists. The authors provide a set of NIH policy recommendations in the article to eliminate the funding disparity, as well as action items for fellow scientists, the private sector and academia to overcome the racism that is endemic in the sciences. Lola Eniola-Adefeso and Kelly Stevens are lead authors, and SFB members **Elizabeth Cosgriff-Hernandez, Shelly E. Sakiyama-Elbert, Rebecca K. Willits, Karen L. Christman, Josephine B. Allen, Abigail Koppes** and **Joyce Y. Wong** are among the co-authors.

**Talking points and how you can help:**

- Explicitly state that racism persists in the United States research enterprise and that it must be expelled
- Institute policies to immediately achieve racial funding equity
- Make diversity score-driving criteria, prioritize diverse teams for funding and diversify review panels
- Train and empower NIH leadership, staff and grant reviewers and recipients to recognize and stop racism

# Student Chapter News

## Increasing Engagement with Our Student Members

*By Deanna Bousalis, National Student Chapter President*

Greetings, SFB members!

One of the goals of the National Student Section this year is to engage more SFB student members. I find that many student biomaterials researchers do not even know our organization exists. As a result, at the SFB Annual Meeting, our student chapter meeting often has low attendance, and people that do attend ask, "Why didn't I know about this before?"

One thing that we have done to combat this is to make an official Twitter account for the National Student Section. Our handle is @sfb_students. Please take a look, follow and retweet! On Twitter, we plan to highlight student achievements, local student chapter news and activities and general biomaterials news. We will also occasionally be posting some fun, science-related discussion topics to facilitate discussion amongst the biomaterials community! If you know of any student members or local chapters that are doing something awesome and want to share it, please tweet at us, send us a direct message, or email the information to dbousalis@ufl.edu and we will be sure to post about it!

Other than starting up our Twitter account, we have been planning some exciting programming for the upcoming virtual Annual Meeting. First, we are hosting a panel titled, "Transitioning Technology from Bench to Market," which will feature professionals in the tech transfer and regulatory fields (as well as academics) that have successfully created clinical products from technology developed either in their laboratory or during their time as PhD students. The goal of this event is to provide the audience with advice and insights to keep in mind when working towards developing translatable technologies. Another event we are planning is a collaborative workshop with the Young Scientist Group, which will focus on trainee professional development and success. I am so excited for these informative and inspiring events and encourage you all to attend them in April. We will definitely be advertising these on Twitter as the Annual Meeting draws near!

Finally, we are actively planning a 3-Minute Thesis competition for undergraduate and graduate students. The details are still underway but stay posted for email and Twitter announcements coming soon regarding this event. There will be a high-profile judging panel (a perfect opportunity for those looking to expand their professional network) and prizes for the winners.

# Staff Updates

*By Shena Seppanen, Assistant Executive Director and Dan Lemyre, Executive Director*

Hello from the Society For Biomaterials Headquarters!

The Board, Council, Committees, Special Interest Groups (SIGs) and Student Chapters all continue to remain busy advancing the mission of the Society. In particular, the Program Planning Committee has been diligently organizing and developing the 2021 Annual Meeting, the Finance Committee has been hard at work ensuring that your membership dues continue to provide incredible benefits while sustaining the viability of the Society and the Education & Professional Development and Membership Committees strive to meet your needs and provide you with unparalleled value.

The 2021 Annual Meeting is quickly approaching, and we encourage you to register at the Early Bird rate before April 9! Additionally, those who submitted an abstract have received notification of your acceptance and assigned time slot. Although held virtually this year, the meeting organizers have maintained and deepened the breadth of quality and content. You can see more specific details in the section below.

**"THE 2021 ANNUAL MEETING IS QUICKLY APPROACHING, AND WE ENCOURAGE YOU TO REGISTER AT THE EARLY BIRD RATE BEFORE APRIL 9!"**

Lastly, all Active and Retired Senior Members recently received an online ballot to select their choices for the 2021 Officers Election. Please review all candidate bios, as mentioned within this issue of the *Forum*. The deadline to submit your vote is Friday, April 2, 2021.

Thank you all for your continued dedication to the Society For Biomaterials! If you have any questions, require any additional information or have suggestions for improved services, please contact Society headquarters at info@biomaterials.org.

## WHAT TO EXPECT FROM THE SFB 2021 ANNUAL MEETING & EXPOSITION (NOW VIRTUAL)

### A BRIEF OVERVIEW OF THE PLATFORM, NAVIGATION, SCHEDULING, INTERACTION AND NETWORKING COMPONENTS

**Programming:** A complete agenda for the meeting is available on the "Program" page of the SFB 2021 Website (2021.biomaterials.org). However, when you are logged in to the event website, while sessions are live, you will see a media player, with a "Sli.do" interactive chat and Q&A panel. You'll also have access to each of the abstracts being presented during the session. Questions may be asked of the presenters and on approval of the session moderator, may be "up-voted" by other attendees to help the moderators prioritize their questions. All presentations will be pre-recorded, and all sessions will have a live Q&A portion with each of the presenters in that session. All sessions will be recorded as they occur, and recordings will remain available for 60 days after the event via the event website.

**Rapid Fires:** Our typical poster presentations will be replaced with a three- to five-minute pre-recorded rapid-fire presentation. These rapid-fire presentations will be available through the course of the meeting and for 60 days afterward. There will be a discussion session for rapid fire presentation grouped by theme on Thursday from 3:15pm-5:15 pm CST and on Friday from 3:15-4:15 CST.

**Networking:** Our networking sessions will be held on the Gather.town platform. Here, you'll be able to wander through a virtual convention center (you'll need to login separately, with your name and avatar selection). We'll have focused areas for each of the SIGs, and areas for private discussion. As you wander through this virtual space, you'll note that your microphone and camera are shared (at your control) with those in your immediate proximity.

**Exhibits and Sponsors:** All of our sponsors and exhibitors will be provided with their own landing pages, and we encourage you to visit them for information about the products and services they offer. As an incentive, each time you share your contact information with an exhibitor or sponsor, you'll be entered to win a complimentary registration!

Please note that the SFB Virtual Meeting will function best on the Google Chrome browser. While other browsers may be used, the site, and all of its functionality, is optimized for the Google Chrome browser.

# AIMBE Report

*By Lynne C. Jones, Alan Litsky and Joel Bumgartner*

Never has it been more important to advocate in Washington, D.C. for public policy and funding for medical innovation and science. We have certainly witnessed the importance of research and having an established biomedical science and engineering infrastructure in understanding and combatting COVID-19. COVID-19 also has had a serious effect on our ability to educate future researchers and to be active in our laboratories to make the important discoveries that advance healthcare. We are fortunate to be members of AIMBE; this institution leads our advocacy efforts. How? AIMBE serves as a resource to Congress and other government organizations and teaches our members how to advocate as individuals. AIMBE represents the Society For Biomaterials as well as 14 other scientific organizations (e.g., IEEE Engineering in Medicine & Biology Society, Orthopaedic Research Society, and TERMIS) and 99 universities. AIMBE also forms alliances with other organizations with common advocacy needs such as The Ad Hoc Group for Medical Research and the Coalition for National Science Funding. This collective voice carries much weight with our elected officials and their staff.

The collective advocacy efforts of our professional organizations need strong supplementation by individuals (constituents, voters) who impress upon their legislators the value of our research efforts and the need for continued and expanded support. AIMBE has worked with the Society to make individual involvement in advocacy easy. Simply visit the Society website at biomaterials.org and click on the "Advocacy" tab and you will find many resources, including the AIMBE Advocacy Toolkit, about how to contact and talk to your members of Congress.

AIMBE has partnered with these groups to write letters to key members of our federal government to advocate for specific recommendations regarding public policy, as well as for increased funding for the National Science Foundation and the National Institutes of Health. We would like to take this opportunity to share a recent letter from The Ad Hoc Group for Medical Research addressed to the Honorable Joseph R. Biden, Jr., President of the United States. Please take this opportunity to contact your members of Congress today.

December 4, 2020

The Honorable Joseph R. Biden, Jr.
President-elect
1401 Constitution Ave. NW Washington, DC 20230

Dear President-elect Biden:

The Ad Hoc Group for Medical Research, and the 349 undersigned member organizations representing patients, clinicians, scientists, educators, academic institutions, research organizations and industry, thank you for your steadfast support for science. As the oldest coalition advocating for the federal investment in the National Institutes of Health (NIH) and biomedical, bioengineering, behavioral and social science research, we are grateful that you support increased and sustainable funding growth for the NIH as part of $300 billion in new research and development investments in your Build Back Better plan.

We applaud the steps you and your team have already taken to seek and then follow recommendations from the scientific community during the deadly COVID-19 pandemic, and we appreciate your recognition that investments in scientific discovery are crucial to improving the nation's health and economy in both the near- and long-term. In the months and years ahead, we urge attention to:

- Foundational principles that promote both a thriving scientific enterprise and public trust in science;
- Emergency supplemental funding to allow the NIH to continue to make progress against COVID-19 and to resume pre-pandemic research; and
- Sustained, robust growth for the NIH's base budget across scientific disciplines and disease areas.

**Foundational Principles.** As we turn to a new year, we urge your Administration to keep these foundational principles in mind:

- To improve health for all, supporting medical research must be a top national priority. Beyond robust funding, this includes appointing distinguished scientists to key science advisory and science agency leadership positions as soon as possible, ensuring they have access to the President, as well as the trust of the scientific community.

- Public policies must be evidence-based and guided by sound and transparent scientific discoveries. By ensuring clear communication, we can increase public trust in science.
- Diversity, equity and inclusion are essential to the advancement of the best science and to solving the myriad health and societal challenges we face today, including tackling the health disparities laid bare by the COVID-19 pandemic.
- Support for a strong research workforce pipeline is essential to ensure the U.S. is able to recruit and retain talented scientists into productive careers in medical research.
- Policies should facilitate a societal culture in which science can thrive and global, multi-sector collaboration is possible.

**Emergency Supplemental Funding.** As you know, the NIH plays an instrumental role in funding basic, translational, and clinical research in labs nationwide and facilitating the translation of this knowledge into applications for human health. For example, NIH-funded research has been critical to confronting the COVID-19 pandemic, among the most pressing public health crises of our time. Since the beginning of the pandemic, many NIH-funded researchers have focused on developing diagnostics, treatments and vaccines for COVID-19. The incredible pace of scientific advancements over the past eleven months from the rapid sequencing of the viral genome, to the development of new assays to test for infection, to preclinical and clinical testing of potential vaccine candidates and treatments—has been possible because of decades of NIH-funded basic research. As the world's largest funder of biomedical research, the NIH has invested billions of dollars in developing the technologies, collaborative research networks and a workforce that enabled this accelerated pace of biomedical innovation in the face of the COVID-19 emergency. As the fight against COVID-19 continues apace, we urge continued supplemental investments in the NIH to sustain this work and to ensure that efforts to combat the pandemic do not displace other essential avenues of discovery.

**Strong Commitment Across Disciplines and Disease Areas.** Robust, sustained and predictable funding growth for the NIH base budget is also essential to ensuring that the U.S. is able to meet the scientific challenges beyond the COVID-19 pandemic and that our nation's research institutions are able to rebuild in the face of devastating impacts to the biomedical research workforce. Continued investment in the broad array of biomedical research will be critical to furthering advances against the myriad diseases and conditions facing humankind, ranging from cancer to heart disease to stroke to diabetes to Alzheimer's disease. A robust investment in medical research as a part of support for the broader public health continuum is crucial to improving the health of all.

Historically, and especially over the last five years, Democrats and Republicans have joined forces to prioritize funding the NIH, helping the agency regain some of the ground that it lost after years of effectively flat budgets. This most welcome renewed investment in the NIH has accelerated discovery toward promising therapies and diagnostics, reenergized existing and aspiring scientists nationwide, restored hope for patients and their families, and facilitated critical basic and applied research aimed at ending the COVID-19 pandemic and other threats. Support for the NIH also yields important benefits for local economies. In fiscal year (FY) 2019, NIH-funded research supported more than 476,000 jobs across the U.S. and generated more than $81 billion in new economic activity.

To further realize the potential of medical research, our nation must continue this forward momentum with sustained, robust budget growth. As you consider your administration's budget priorities for FY 2022 and beyond, the Ad Hoc Group recommends an ongoing commitment to meaningful growth above the cost of biomedical research inflation for the NIH. The stability associated with a budget trajectory that not only keeps pace with inflation but also allows investment in new research is essential to ensure we continue to push the boundaries of discovery toward meaningful outcomes for patients.

We are grateful for your outspoken support over many years for biomedical research and your leadership in making these funding and foundational commitments a reality. We offer the Ad Hoc Group and our community as a resource as you determine priorities and formulate budget requests as President. We look forward to working with you and your team toward our mutual goal of improved health.

Sincerely,

**(349 Signatories as of December 3, 2020)**

# Wake Forest Institute for Regenerative Medicine: The Future is Now

*By The WFIRM Communications Office*

The Wake Forest Institute for Regenerative Medicine (WFIRM) was established in January 2004 when Dr. Anthony Atala's research team of 20 individuals moved to Winston-Salem, North Carolina (from his Laboratory for Tissue Engineering and Cell Therapy at Children's Hospital / Harvard Medical School in Boston). That initial team has grown to include over 400 people from all over the world, working together to bring these technologies from the bench to the bedside.

WFIRM is the largest regenerative medicine institute in the world and its researchers hold a record of many "world firsts," including the development and implantation of the first engineered organ inside a patient. WFIRM's mission is to improve patient's lives through regenerative medicine technologies by achieving four key objectives: advancing discovery, training and educating, accelerating clinical translation and serving as a magnet for collaboration in regenerative medicine. All of WFIRM's endeavors are based on three core values: innovation, teamwork and integrity.

Researchers are working to develop cell therapies and replacement tissues and organs for more than 40 different areas of the body. They have now used 15 applications in patients, including regenerative medicine therapies involving skin, muscle, cartilage, bladder and kidney disease. They are working on making these treatments more widely available by scaling up the manufacturing process. To do so, research teams are pursuing multiple strategies, including 3D printing, to meet their ultimate goal — making patients better.

## BROAD CAPABILITIES

With experts in molecular biology, genetics, cell biology, physiology, pharmacology, biomaterials, imaging and nanotechnology, WFIRM has broad research capabilities. This expertise enables the Institute to focus on multiple areas of regenerative medicine.

In addition to engineering tissues and organs, the Institute has teams working to develop cellular and molecular therapies, diagnostic platforms and healing therapies, as well as developing various supporting technologies. For example, to find a solution for the more than 661,000 U.S. patients on dialysis because of kidney failure, the Institute's teams are pursuing various strategies such as a cell therapy using a 3D printer to build replacement organs, and using donor organs as platforms for engineering matching organs for patients.

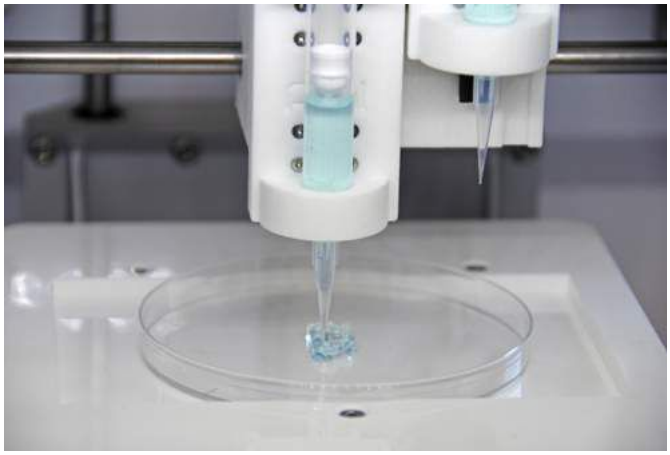
## STRUCTURE AND ORGANIZATION

The Institute is structured and organized for innovation with labs that are designed with an open layout to allow for scientists to collaborate with one another and is set up around core areas of work such as genetics, bioprinting, biomaterials and imaging.

The support infrastructure is designed to accelerate the translation of scientific discoveries to therapies that can benefit patients. WFIRM is unique in that it houses all operations under one roof, including a Manufacturing Development Center (MDC) that is a compliant Good Manufacturing Facility. The MDC is staffed with experts in regulatory pathways and clinical trial design who can work with the FDA to meet its requirements while also saving time and money when a research project is deemed translational.

## SCALING UP

The field of 3D bioprinting has really advanced over the last few years, as the need for these technologies increases. WFIRM scientists have implanted a variety of lab-engineered tissues and organs into patients, but know that to make these treatments more widely available they must scale up the manufacturing process. They turned to 3D bioprinting 20 years ago as one way to accomplish this, resulting in the *in-vivo* implantation of printed tissue in 2007, and the development of the Integrated Tissue and Organ Printing System (ITOP). In early 2016, WFIRM research published in *Nature Biotechnology* showed that they could print tissues, and that when implanted in experimental models, developed a system of nerves and blood vessels. The research showed that these structures had the correct size, strength and function for use in humans, proving the feasibility of printing living tissue structures to replace injured or diseased tissue in patients.



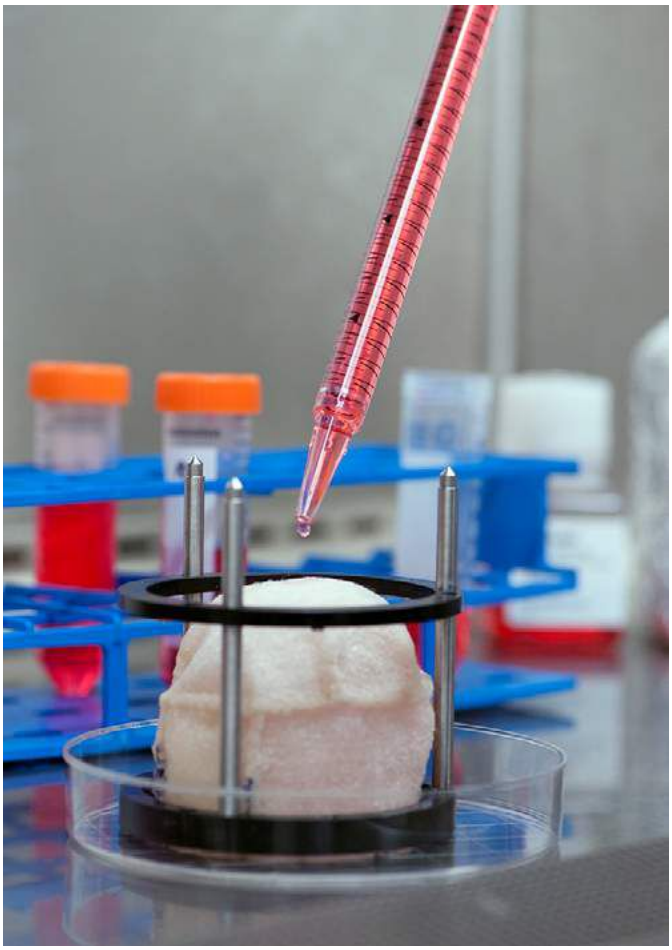
**Bioink for 3D Bioprinting**

## Wake Forest Institute for Regenerative Medicine: The Future is Now (continued)

The WFIRM team is also using the 3D bioprinting process to scale up the production of organoids, or tiny replicas of human organs, to test drugs. Most recently, the Institute's scientists used organoids to test drugs to fight COVID-19 by constructing miniature lungs and gut, two organs particularly affected by the virus. While the science of bioprinting is progressing in the right direction, there is still much work to do in order to be able to bioprint functional solid organs, like the liver for transplant in humans.

### CELL AND GENE THERAPIES

Cell and gene therapies are exciting research areas because of the potential to heal diseased or damaged tissues rather than replace them. For instance, a project at WFIRM focuses on prenatal treatment approaches for genetic disorders, like hemophilia. The idea is to intervene before the baby is born by using stem cell populations and manipulating them through gene therapy or gene editing.



**Integrated Printing Scaffold**

In their experience engineering organs for patients, WFIRM scientists have used "progenitor" cells, a type of cell found in a particular organ that is destined to become that tissue type. The advantage of using a patient's own cells is that there will be no issues with rejecting the engineered organ. In some cases, it may not be possible to use a patient's own cells. In that case, pluripotent or multipotent stem cells may be an option. In 2007, WFIRM scientists published their findings where they identified a source of stem cells in amniotic fluid and placenta that could potentially be banked and used in organ and tissue engineering. These cells, unlike adult stem cells, are highly multipotent and can turn into other tissue types readily, but unlike embryonic and induced pluripotent stem cells, do not form tumors. For example, in work to develop new treatments for burns, as part of the Armed Forces Institute for Regenerative Medicine, scientists are evaluating the stem cells found in amniotic fluid and placenta for enhanced wound healing. Other projects that use stem cells include the development of cell therapies to improve functional recovery after compartment syndrome, a condition associated with blast injuries that can cause tissue death and amputation.

### BIOTECH AND A NATIONAL REGENERATIVE MEDICINE INNOVATION HUB IN NORTH CAROLINA

A number of regenerative medicine companies already operate in the Winston-Salem, North Carolina region at the intersection of bioscience innovation and business, offering expansive resources for entrepreneurs and life science professionals. These companies are dedicated to a broad range of technologies, such as 3D printing, stem cell banking, extracellular matrices and cell and tissue therapies. Additionally, there are also business entities supporting the field in areas such as the production of reagents and diagnostics.

The region has become an epicenter of innovation that has only been possible through the hard work and collaboration of many leaders and visionaries. North Carolina has ranked first nationally in its biotechnology workforce growth for the last decade, and ranks third nationally in the size of its life-science sector. As a result, the Innovation Quarter and the surrounding area in downtown Winston-Salem has been recognized as the fastest growing innovation region in the country, with a focus in areas like biomedical science, information technology, clinical services and advanced materials. Within Innovation Quarter, and with WFIRM as a key anchor, the Winston-Salem Regenerative Medicine Hub has been developed into a dynamic area that houses start-ups and established companies, all of which are supported by local and successful business development programs and the State of North Carolina.

## Wake Forest Institute for Regenerative Medicine: The Future is Now (continued)

The Regenerative Medicine Hub also includes the RegenMed Development Organization (ReMDO), which works to accelerate the discovery and translation of regenerative medicine therapies. ReMDO is a 501(c)3 non-profit organization headquartered in Winston-Salem that manages a clinical translation initiative that includes thought leaders, representatives from leading U.S. research centers, government representatives and companies of all sizes. ReMDO conducts research to de-risk technologies and speed up the translation of regenerative medicine to clinical practice and to the global market.

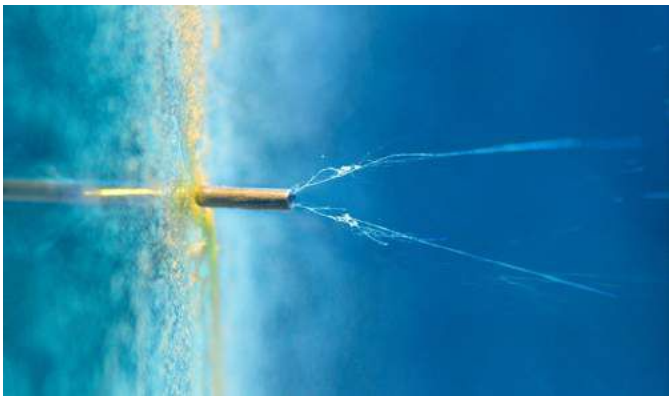
As a means of leveraging the resources developed by ReMDO, a new initiative called ReMDO's RegeneratOR was developed. This initiative consists of three parts:

**1. ReMDO's RegeneratOR Test Bed** – seeks to assist regenerative medicine start-ups and growth companies with new and emerging technologies through access to advanced biomanufacturing equipment, talent and programs to support prototyping and initial product development.

**2. ReMDO's RegeneratOR Business Incubator** – supports innovation from research to commercialization for regenerative medicine start-ups and growth companies by providing space and support, including market potential validation, benefit analysis, financial planning, budgeting and comprehensive business plans.

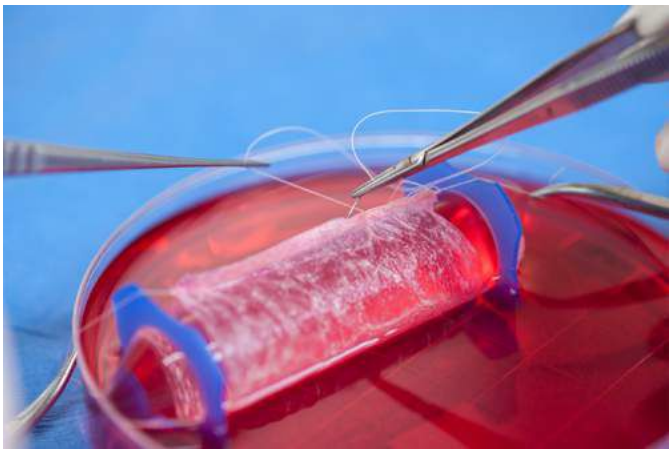
**3. ReMDO's RegeneratOR Workforce Development** – a resource that connects an educational ecosystem of colleges, university programs and technical schools with biomanufacturing staff, engineers and research leaders. With access to training programs across the members of the Regenerative Medicine Manufacturing Society (RMMS) and the Regenerative Medicine Innovation Consortium (RegMIC) (both headquartered in Winston-Salem) and world class talent, regenerative medicine enterprises can rely on a pool of newly-educated individuals, or existing employees who can skill-up with short term courses.

WFIRM, driven by the urgent needs of patients, is a major driver of the Regenerative Medicine Hub, serving the interests of the field internationally. The Institute is making a global difference in regenerative medicine through collaborations with over 400 entities and institutions worldwide, through its government, academic, non-profit and industry partnerships, its start-up entities and through major initiatives in breakthrough technologies such as tissue engineering, cell therapies, diagnostics, drug discovery, biomanufacturing, nanotechnology, gene editing and 3D printing.



**A Close-Up View of Electrospinning, a Technique Used to Make Blood Vessels, As Well As Muscles and Tendons**

**A 3D Printed Bladder Scaffold is "Seeded" with Cells in the WFIRM Lab**



**Engineered Vagina**

# Q&A with Anthony Atala, MD, G. Link Professor and Director of the Wake Forest Institute for Regenerative Medicine

### *BIOMATERIALS FORUM:* WHAT ARE THE BIGGEST CHALLENGES THAT THE FIELD OF TISSUE ENGINEERING FACES TODAY?

**Dr. Atala:** The major challenges in the field of tissue engineering today are associated with the scale-up and adequate manufacturing of products that can be consistent, reliable and at decreased cost. As a result, we are pursuing major biomanufacturing initiatives that will help to standardize the production of these technologies for the field.

### *BIOMATERIALS FORUM:* WHAT CHANGES DO YOU SEE COMING TO CLINICAL OR COMMERCIAL TRANSLATION RELATED TO THE FIELD OF TISSUE ENGINEERING OVER THE NEXT FIVE YEARS?

**Dr. Atala:** In the field, we do see more technologies entering the clinic. We have already seen a small number of technologies that have shown the impact they can have on patients' lives. In the future, we will see more regenerative medicine technologies that will cover even more clinical indications for patients.

### *BIOMATERIALS FORUM:* WHAT DO YOU FORESEE AS THE NEXT TRANSFORMATIONAL STEP FOR THE TISSUE ENGINEERING FIELD?

**Dr. Atala:** 3D printing has already made major transformational changes for the field. However, there is still a lot of room for improvement in terms of speeding up the process for manufacturing. This will involve development of better cell isolation, bioreactors, printers and bioink technologies as well as better methods to deploy these technologies into the clinic.

### *BIOMATERIALS FORUM:* WHAT'S NEXT FOR YOUR RESEARCH TEAM?

**Dr. Atala:** Our research efforts vary as we work to address these challenges and advance more technologies overall to get them through the clinical trial process and to patients as quickly as we can. To date, we have implanted 15 regenerative medicine technologies into patients in small clinical trials. We are working to develop cell therapies and replacement tissues and organs for more than 40 different areas of the body, so there is much work to do. Our research team is excited and encouraged by the ability of regenerative medicine to provide replacement tissue made from a patient's own cells and what it can mean to the patient's recovery and long-term health.

# Q&A with David F. Williams, PhD, Professor, Wake Forest Institute for Regenerative Medicine

### *BIOMATERIALS FORUM:* THE ESSENCE OF BIOMATERIALS RESEARCH HAS ALWAYS BEEN INTERDISCIPLINARY. HOW HAS THE INTERDISCIPLINARY NATURE OF THE FIELD CHANGED OVER TIME?

**Dr. Williams:** Yes, biomaterials science is, by definition, both multi- and inter-disciplinary. However, the major change in the nature of biomaterials research has been associated with the appreciation that there is a difference between these two features. For much of the last 60 to 70 years, the difference between interdisciplinarity and multidisciplinarity has not been understood by many of those working in this area. The subject of biocompatibility, the area I am most familiar with, provides many good examples. Consider a synthetic polymer being evaluated for use as a scaffold, or template, in a tissue engineering process for the generation of soft tissue, say, a ligament. The multidisciplinary nature of the interactions between the polymer and the relevant biological components is seen by the fact that the specifics of polymer structure and chemistry, polymer degradation, surface characteristics, mechanical properties (especially elasticity), extracellular fluid chemistry, ECM protein behavior, inflammation, immunology, cell activation, wound healing and many more features all have some influence over the biocompatibility of the system. Yet, however much and however carefully we study these individual sciences, we do not get to the right answers until we understand the phenomena that link these together. The totality of biocompatibility pathways that control the overall performance represents the different interdisciplinary mechanisms that are involved, including, but certainly not limited to, the internalization of polymer-derived nanoparticles in stem cells, the role of mechanotransduction in tissue regeneration, the mechanisms of both innate and adaptive immune responses to tissue-engineering constructs and the role of microfluidics in organ regeneration within bioreactors.

## Q&A with David F. Williams, PhD, Professor, Wake Forest Institute for Regenerative Medicine (continued)

### *BIOMATERIALS FORUM:* HOW IS THE GROWING INTERNATIONALIZATION OF RESEARCH AFFECTING THE PACE OF BIOMATERIALS INNOVATION?

**Dr. Williams:** Until a few years ago, I would have agreed that internationalization of research, both in our area and many others, was growing. I felt that this was very beneficial to the pace, quality and quantity of biomaterials science and regenerative medicine research. As many readers will be aware, internationalization underpins my whole professional ethos, having worked in the U.K. and Europe for many years and now both in the U.S.A. and South Africa. As Editor-in-Chief of *Biomaterials* and Global President of the Tissue Engineering and Regenerative Medicine International Society (TERMIS), I strongly encouraged and endorsed this international approach. Unfortunately, world-wide political and social instability during the last few years that was centered, but not solely focused, on U.S.-China disagreements and the Brexit/ post-Brexit chaos in Europe is having a profound effect on the ability to perform research internationally. Of course, this has been remarkably influenced by the COVID-19 pandemic and the restrictions of travel and movement of goods. This is going to take quite a few years to resolve.

### *BIOMATERIALS FORUM:* WHAT AREAS OF BIOMATERIALS RESEARCH DO YOU FEEL MAY BE OVERLOOKED BY THE COMMUNITY AND DESERVE ADDITIONAL CONSIDERATION?

**Dr. Williams:** As noted above, fundamental aspects of biocompatibility should receive more attention. It is notable that while medical technologies involving biomaterials provide very effective therapies for millions of people worldwide, there are many situations in which the products fail to achieve satisfactory outcomes, and all too often these happen because of a lack of biocompatibility. Coupled with this, it is very difficult to predict clinical performance from pre-clinical testing. This is not a trivial matter; the host response depends on a multitude of factors, including patient and clinical skill variable. Our understanding of these phenomena must be based on a more personalized approach. This is as much true for tissue engineering processes as for medical device products. A major problem here is that we do not have a thorough list of specifications for scaffold materials; this is exacerbated by a widespread misunderstanding of the necessary biological attributes of a material that is capable of coordinating the molecular and mechanical signaling of the target cells for tissue regeneration — this is the reason why we still largely rely on traditional synthetic biodegradable polymers, with very few new innovative biomaterials for tissue engineering.

### *BIOMATERIALS FORUM:* WHAT ADVICE DO YOU HAVE FOR STUDENTS AND EARLY CAREER SCIENTISTS IN THE FIELD?

**Dr. Williams:** I find it very difficult to give sound advice on these matters to early career scientists who are many decades younger than me. Looking back, I encountered very few of the barriers to career progression that are apparent today. So my advice is more philosophical than practical. Conviction, determination, awareness, honesty and hard work are at the core. I feel strongly about two issues. First, I have had a policy of "never say no." Obviously this has to be qualified, but, based upon a conviction that I know roughly what I want to achieve, if I have been asked to take on a particular action, my response is usually to say yes (sometimes provisionally). I have rarely been let down by this approach to professional matters. Secondly, the caveat at the beginning of the previous sentence (has to be qualified) implies that honesty, both to yourself and to others, is paramount. There are many ways for a professional scientist to deceive the community; sometimes very small infractions, leading up to major scientific fraud. I have seen too many careers destroyed by careless attention to ethical issues.

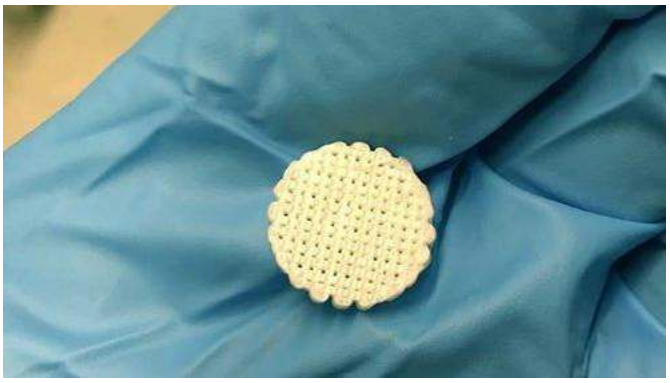
"UNFORTUNATELY, WORLD-WIDE POLITICAL AND SOCIAL INSTABILITY DURING THE LAST FEW YEARS THAT WAS CENTERED, BUT NOT SOLELY FOCUSED, ON U.S.-CHINA DISAGREEMENTS AND THE BREXIT/ POST-BREXIT CHAOS IN EUROPE IS HAVING A PROFOUND EFFECT ON THE ABILITY TO PERFORM RESEARCH INTERNATIONALLY."

# UCSF Rosenman Institute's Innovators Program is a Valuable Resource for Startups

*By Justin Im*

The startup journey in health technology can be long, arduous and lonely. Getting a medical innovation to market remains a daunting challenge and a promising technology can only go as far as the resources and connections of the entrepreneurs behind it.

This was certainly the case for Ben Holmes and Nathan Castro, co-founders of the company Nanochon, a startup working on an orthopedic implant and tissue growth scaffold aimed at helping patients recover from post-cartilage surgery. After receiving a federal Small Business Innovation Research grant in 2017 and obtaining proof of concept in animal models, the company sought to expand its operations. With the goal of obtaining FDA Premarket Approval (PMA), they were looking for opportunities to secure more funding, scale up its manufacturing capabilities and complete a human trial.

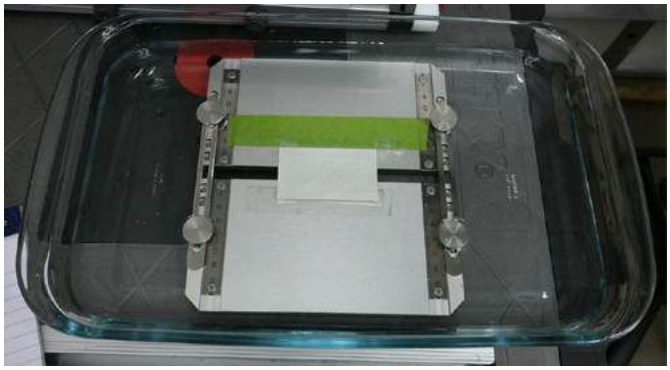


**Nanochon's Novel Orthopedic Implant**

An advisor for the company working in the medical device space had mentioned the University of California, San Francisco (UCSF) Rosenman Institute as a potential resource. Over the phone, Christine Winoto, the Institute's founder and director, informed Ben and Nathan about the Rosenman Innovators program. The apparent benefits, including personalized coaching from industry experts, exposure to potential investors and industry partners and access to in-kind service providers, were more than enough to convince them to apply.

After Ben and Nathan applied online and pitched a panel of 20 judges, Nanochon won one of the 12 coveted spots in the 2020 Rosenman Innovator cohort. From there, they and their company gained a wealth of exposure to the Rosenman ecosystem, working with strategic industry experts in communications, product development, IP, reimbursement, marketing and business strategy. Some of their new connections took on informal advisory roles at Nanochon. Networking with investors at the Rosenman Innovators demo day was also an invaluable resource. Ben and Nathan met some investors interested in joining their first investment round.

The Rosenman Innovator program also introduced them to Bayflex, a company providing endurance testing of various medical devices and components. Nanochon's orthopedic implants were developed with 3D printing technology using synthetic nanomaterials, and while research was able to demonstrate the implant's abilities to induce bone, vascular and cartilage growth in animal models, questions remained about structural integrity and biomechanical strength. From June to October of 2020, Nanochon collaborated with Bayflex to validate their technology, helping the company progress towards commercialization.



**Endurance Testing of Nanochon's Orthopedic Implant in Collaboration with Bayflex**

Currently, Ben and Nathan are working on a go-to-market strategy for Nanochon's orthopedic implant for use in sports medicine. They hope that their new technology offers alternatives to traditional procedures, noting, "Our technology can be an effective alternative to the standard types of cartilage tissue repair and grafting procedures already available." In the future, they hope to develop an orthopedic platform, expanding the material's applications into veterinary work.

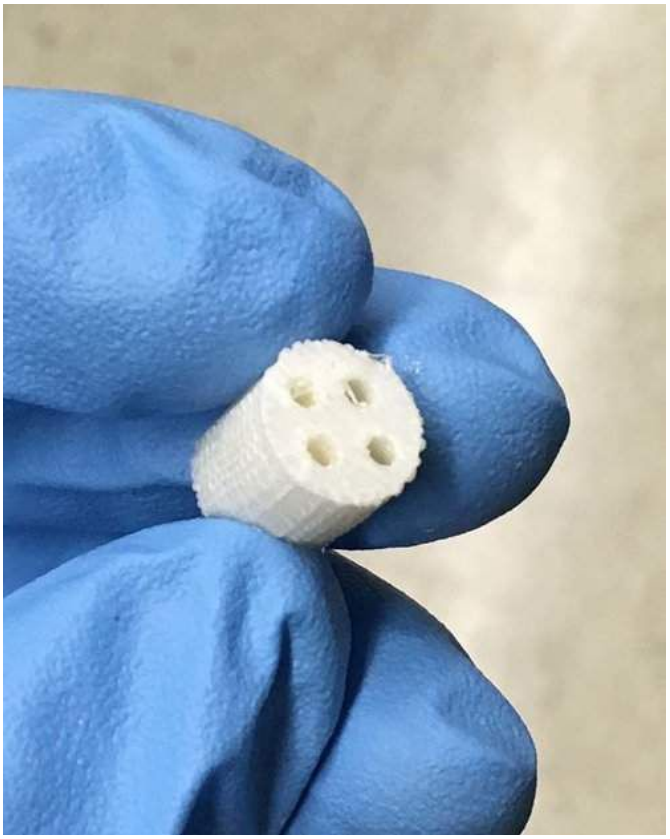
Ben notes that Nanochon was unique in that when it joined the Rosenman Innovator program it already had a robust team of advisors and mentors. But there were still significant benefits.

"What makes the UCSF Rosenman Institute truly unique," he says, "is that it allows you to meet a community of people who want to engage with you and your company. You get to network with people from industry and different stakeholder groups that may not be looking to join a startup but simply want to guide you in your journey as an entrepreneur."

He argues that the Innovators program gave him and Co-Founder Nathan a unique perspective. "It allowed us a long-term view of the future of the company," he says. "Instead of being siloed in short-term strategy, the Rosenman network of coaches, experts and investors gave us exposure to other viewpoints on our technology, as well invaluable advice from individuals with superior knowledge in the orthopedic and 3D printing space."

Nanochon is just one of the many Rosenman stories of growth and success. Founded in 2014, the Institute has blossomed as a catalyst of the healthtech ecosystem in the Bay Area and beyond. It offers financial resources, personalized mentorship and many vital connections for up-and-coming startups. Whether it be organizing a competitive global program for startup companies developing solutions to COVID-19, hosting dinners with thought leaders or offering a fellowship program for rising entrepreneurs, Rosenman fosters a rich, diverse network for the health technology ecosystem. To date, companies supported by the Institute have delivered their product or service to over 1.5 million patients worldwide and raised over $700 million in funding.

The main mission of the UCSF Rosenman Institute is to improve patients' lives by reducing the time to market for innovative solutions, and they do this by supporting hundreds of startups such as Nanochon. Each has their own unique story, challenges and journey to commercialization. That journey may be long and hard, but with support from the UCSF Rosenman Institute, the startup founders are never alone.



**Nanochon's 3-D Printed Joint Replacement for Injured Equine Patients**

**Ben Holmes, Co-Founder of Nanochon**

**UCSF Rosenman Institute Team (left to right):**
**Herminio Neto, Agnes Buenaventura, Regis Kelly, Nora Ke, Christine Winoto, Ioana Aanei, Kaspar Mossman**

# Ophthalmic SIG Update

*By Frances Lasowski, PhD*

Ophthalmology is a branch of medicine dealing with the diagnosis and treatment of eye disorders. Below we highlight two North American research programs that bridge the gap between academic and translational research.

## C20/20 INNOVATION HUB

The C20/20 Innovation Hub is a unique ophthalmic biotechnology hub located at McMaster University in Hamilton, Canada. C20/20 is dedicated to the creation of an advanced portfolio of new ophthalmic products. This includes improved ocular therapeutics and drug delivery systems treating a wide range of diseases and advanced materials to accelerate new contact lenses for the future. These products originate within academia or stem from industrial collaborations.

While eyedrops are a well-accepted method of delivering drugs to the eye, regular instillation of highly concentrated solutions is required to maintain therapeutic concentrations. For chronic diseases, this is onerous, leading, for example, to compliance rates below 30% in the case of glaucoma.[1] Based on the hypothesis that enhancing the efficacy of this well-accepted platform will lead to better therapeutic outcomes, significant effort in the C20/20 Innovation Hub has focused on the development and validation of a mucoadhesive micelle-based eyedrop drug delivery system.[2,3] In addition to using sustained-release formulations, this work enhances the "on eye" drug residence time via the eye's natural components, which is a relatively new discovery.[4-6] Measurement of the increased ocular residence time of the particles, attributable to phenyl boronic acid incorporation, had never been done before and was made possible by adapting the unique chemistry, developed for radiolabelling hyaluronic acid (unpublished data). This work was identified by clinical and industry collaborators as highly impactful, as reducing the dosing regimens for ocular diseases, such as dry eye and glaucoma, would improve patient compliance and increase clinical efficacy. This is key in a field with limited treatment options. Translational concerns have also been addressed, such as adapting the synthetic chemistry to a more scalable free-radical technology. Extensive testing confirmed that micelles prepared using the different chemistries had similar properties, and that the key metrics, including drug loading and drug release, were comparable. This work has been licensed to 20/20 OptimEyes Technologies, a start-up company, for further preclinical development. If successful, this will provide a comfortable treatment option for dry eye suffers that allows them to instill drops less frequently, a key improvement for elderly patients and others who require caregiver assistance. This is being adapted for other diseases currently. Conducting pharmacokinetic studies for the micelles required a significant expansion in the expertise of the team, requiring the development of *in vivo* and analytical methods for evaluating drug concentrations in tissues. By developing these capabilities in-house, the C20/20 Innovation Hub has further enhanced their competencies, both for in-house use and for partnership with collaborators and industry.

**Dr. Heather Sheardown, Scientific Director of the C20/20 Innovation Hub at McMaster University, Hamilton. Photo Credit: JD Howell**

**"IN ADDITION TO USING SUSTAINED-RELEASE FORMULATIONS, THIS WORK ENHANCES THE 'ON EYE' DRUG RESIDENCE TIME VIA THE EYE'S NATURAL COMPONENTS, WHICH IS A RELATIVELY NEW DISCOVERY."**

## SWINDLE-REILLY LAB

When Katelyn Swindle-Reilly, PhD, left a career in industry to join Ohio State University, she knew she wanted to return to research on ophthalmic biomaterials, which she had been introduced to and thoroughly enjoyed as a graduate student. Ohio State is unique in that it has several faculty members dedicated to ophthalmic research in Biomedical Engineering, and has a College of Optometry, Department of Ophthalmology at the College of Medicine that conducts clinical trials, and has a College of Veterinary Medicine with veterinary ophthalmologists that foster collaboration and innovation. Since 2016, her research group has been expanding upon their expertise on the vitreous humor, the gel inside the eye, in order to make better vitreous substitutes and intravitreal drug delivery systems. The materials used for implants and drug delivery systems in the lab are composed of polymers, which have a rich history of use in ophthalmology.

## Ophthalmic SIG Update (continued)

**Ohio State Assistant Professor Katelyn Swindle-Reilly with recent PhD graduates Nguyen "Archie" Tram (left) and Pengfei Jiang (right). Photo credit: Ohio State University Wexner Medical Center**

Clinical collaborator Matthew Ohr, MD, head of the Retina Division and a vitreoretinal surgeon at Ohio State, brought up challenges associated with treating wet age-related macular degeneration (AMD). In order to prevent blindness, patients must receive frequent (often monthly) and costly intravitreal injections, which is a burden to the healthcare system. While intravitreal injections have become the clinical standard for delivering drugs to the back of the eye, as with eye drops high concentrations of solutions and frequent administration are required to maintain therapeutic concentrations due to short half-life in the vitreous.[7] Recent work at Ohio State has focused on development of ocular drug delivery systems to treat AMD by sustaining release for several months.[8-10] The team initially developed bilayered polymeric microparticles with an inner cationic chitosan layer to electrostatically bind the negatively charged therapeutic and coated it with slowly biodegradable poly(caprolactone) (PCL).[8] However, with traditional particle preparation techniques, therapeutic encapsulation efficiency is often low. Therefore, the team applied a combination of materials processing techniques including electrospinning, salt leaching and sintering, to develop hollow injectable capsules out of the same polymers. The hollow design allows for drug loading after preparation of the device, minimizing therapeutic loss. *In vitro* testing demonstrated therapeutic release for 6 to12 months with maintained bioactivity.[9] This demonstrates one application where polymeric biomaterials can be modulated to control release and biodegrade over longer periods of time. This patent pending work is being licensed out of the university to start-up company Vitranu, LLC for full preclinical development. If successful, this will reduce injection frequency for patients with AMD, which will be a key improvement for these elderly patients and their caregivers who often drive them monthly to see the ophthalmologist for injections.

### REFERENCES


1. Tatham AJ, Sarodia U, Gatrad F, Awan A. Eye drop instillation technique in patients with glaucoma. *Eye (Lond).* 2013 Nov;27(11):1293-8.
2. Mangiacotte N, Prosperi-Porta G, Liu L, et al. Mucoadhesive nanoparticles for drug delivery to the anterior eye. *Nanomaterials (Basel).* 2020;10(7):1400.
3. Prosperi-Porta G, Kedzior S, Muirhead B, Sheardown H. Phenylboronic-acid-based polymeric micelles for mucoadhesive anterior segment ocular drug delivery. *Biomacromolecules.* 2016;17(4):1449-57.
4. Liu S, Jones L, Gu FX. Nanomaterials for ocular drug delivery. *Macromol Biosci.* 2012;12(5):608-20.
5. Maisel K, Ensign L, Reddy M, et al. Effect of surface chemistry on nanoparticle interaction with gastrointestinal mucus and distribution in the gastrointestinal tract following oral and rectal administration in the mouse. *J Control Release.* 2015;197:48-57.
6. Xu Q, Ensign LM, Boylan NJ, et al. Impact of surface polyethylene glycol (PEG) density on biodegradable nanoparticle transport in mucus ex vivo and distribution in vivo. *ACS Nano.* 2015;9(9):9217-27.
7. Seah I, Zhao X, Lin Q, et al. Use of biomaterials for sustained delivery of anti-VEGF to treat retinal diseases. *Eye.* 2020;34:1341-1356.
8. Jiang P, Jacobs KM, Ohr MP, Swindle-Reilly KE. Chitosan-polycaprolactone core-shell microparticles for sustained delivery of bevacizumab. *Mol Pharm.* 2020;17(7):2570-2584.
9. Jiang P, Chaparro FJ, Cuddington CT, et al. Injectable biodegradable bi-layered capsule for sustained delivery of bevacizumab in wet age-related macular degeneration. *J Control Release.* 2020;320:442-456.
10. Jiang P, Choi A, Swindle-Reilly KE. Controlled release of anti-VEGF by redox-responsive polydopamine nanoparticles. *Nanoscale.* 2020;12:17298-17311.

# Orthopaedic SIG Update

## MATLAB FOR ANALYSIS OF ORTHOPAEDIC STRUCTURES IN DICOM, PART 1: 2D REGION

*By Roche C. de Guzman, PhD*

Orthopaedic structures, including bones and radiodense biomaterial implants, are imaged using a variety of noninvasive modalities (x-ray, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, etc.) and are then data stored as Digital Imaging and Communications in Medicine (DICOM®) standard files containing metadata and digital image information.[1] Default photo viewers in Windows and Macintosh operating systems do not have the capability to open and view these DICOM files. Academic institutions, particularly the engineering, health and science departments, often have subscriptions to the MATLAB® programming language (mathworks.com). For students, the MATLAB suite that comes with commonly-used science and engineering toolboxes is also inexpensive.[2] The text in this article describes some strategies using MATLAB to evaluate DICOM CT files, which can be helpful in the orthopaedic biomaterials discipline.

Analysis of DICOM in MATLAB rely on the image processing toolbox containing an app (called a DICOM Browser) and several built-in functions (fx).[3] The **dicomBrowser** fx is entered in the Command Window to open the app, which is a user interactive figure (uifigure) for viewing DICOM images. However, this app is still poorly developed; thus, users can get more functionality by writing custom scripts (or collection of ordinal line-by-line commands packaged as files).

After opening MATLAB, three essential windows are recommended to be displayed: The Command Window (for entering commands including variable creation and using fxs), the Workspace (to view stored variables and their properties such as size and class) and the Current Folder (scripts and other files present here are included in the path for MATLAB access). The Current Folder directory is changed by browsing to the folder containing the DICOM series of interest. To verify that a file is indeed DICOM formatted, **isdicom** fx with a character (char class) filename input is used and the output is a logical 1 (true) variable (Figure 1). Batch processing employs a script (.m) file (Figure 2) containing the following sections to ultimately show the images with guides corresponding to their actual dimensions. The file can be downloaded in MATLAB Central File Exchange using the address provided.[4]

DICOM check uses **cellfun** with @isdicom (@ converts the fx to function_handle class) to all filenames in the folder, generating a vector (1D array) output without a for loop (Line 6). Metadata including private information (patient name, age, sex, etc.) are stored in files and must be removed or anonymized with the **dicomanon** fx with inputs: original and anonymized filenames (which also removes the confidentiality warning message) (Line 9).

A struct (structure) class variable is created using **dicominfo** with fields corresponding to DICOM tags[5,6] or attributes such as Modality (e.g., CT) and image properties: Width and Height (in pixel (px)), and SliceThickness and PixelSpacing (in mm) (Line 13). Scaled sizes (e.g., in cm) are obtained by the corresponding products of pixel spacing or resolution with dimensions in px and conversion factor from the mm unit (Line 17). Integer image data are acquired with **dicomread** (Line 19) as a cell class variable and converted to the default numeric class in MATLAB, the **double** (for double-precision floating-point number = 64 bits). For CT data, it is useful to calculate the image intensity values in the Hounsfield scale (in Hounsfield unit (HU)) for proper tissue identification (such as to locate bones).[7] Rescale slope (m) and intercept (b) values are obtained and the linear formula (mx+b) implemented with cellfun for HU image change (Line 21), then saved as a MATLAB data file (.mat) for later retrieval. A preliminary display of image and colorbar is initiated to determine the axes position (Line 27). Additionally, the script creates a video of the image slices (Line 30). A **for loop** (with required **pause** and **drawnow** fxs) is implemented to visualize the images (Figure 3) as an animation using **imshow** with indexed cell image

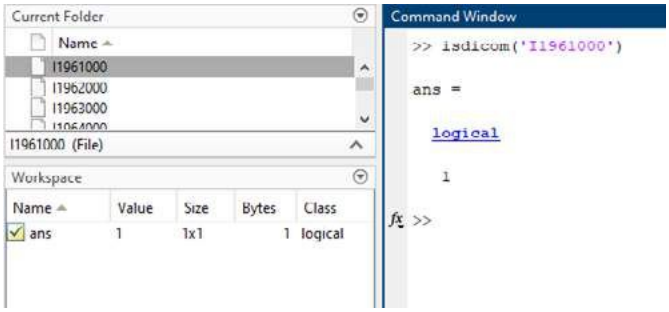



**Figure 1. MATLAB Windows Showing the File, Entered Command, and the Produced Variable**

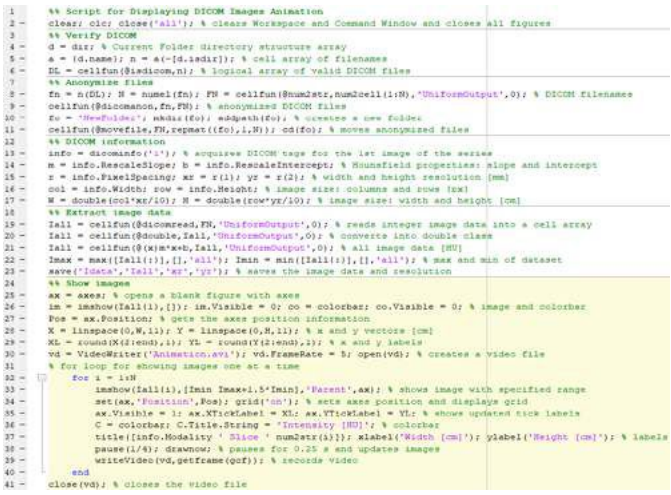



**Figure 2. Script Commands in the Editor Window to Visualize DICOM Files**

## Orthopaedic SIG Update (continued)

array (curly braces indexing), fixed vector range (to normalize all intensities) and property name-value pair for axes handle as inputs (Line 33), then image position **set** afterwards.

Tick labels (from the struct field) are updated based on the actual scale (e.g., cm). The grayscale **colorbar** (Line 36) acts as an

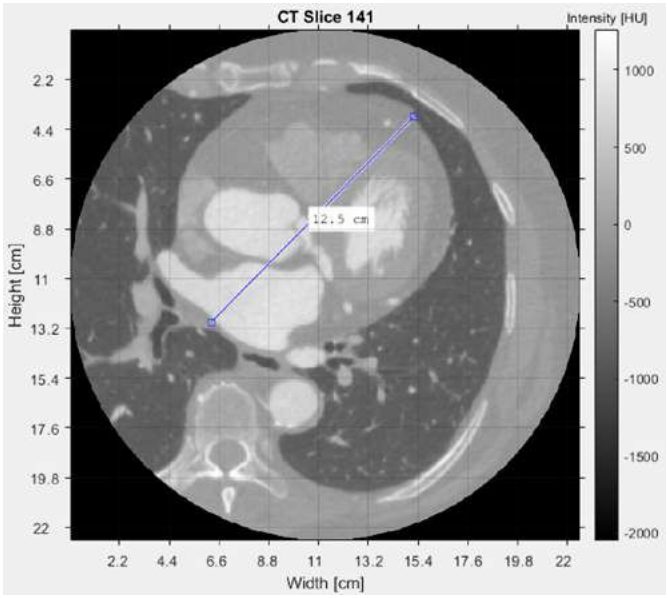



**Figure 3. Processed DICOM CT Image Example**

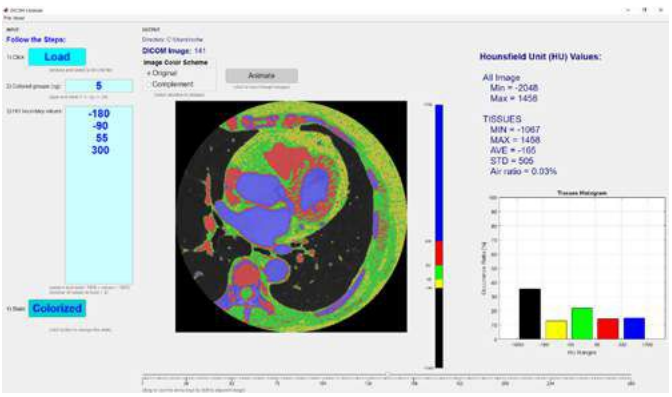



**Figure 4. Custom MATLAB App for Colorizing DICOM CT Based on HU**

HU intensity colormap guide. The DICOM CT image example in Figure 3 shows an axial plane section of a human heart according to its actual size (of about 12.5 cm or 5 inches long). A thoracic vertebra (T7) can also be seen at the bottom left with intensities within the expected bone HU range of 300 to 400 for trabecular and 500 to 1000+ for cortical regions.[8] A DICOM Colorizer uifigure app (still currently in development) (Figure 4) can be implemented to colorize specific ranges of HU values for contrasted (using iodinated agents) CT scans (e.g., minimum to -180 for background (black), -180 to -90 for fat (yellow), -90 to 55 for parenchyma (green) including muscle, 55 to 300 for blood (red), and 300 to maximum for bone (blue)).

The fx, **imdistline** is employed to make an interactive line segment distance measurement (Figure 5). A custom fx is added within the script[4] to obtain the endpoints position, then converted to the scaled unit (e.g., cm), distance calculated using **norm** with position vector difference as input, and calibrated distance displayed via **setLabelTextFormatter** formatted[9] to display 1 decimal and the cm unit. This custom fx is activated with a callback when the endpoints are moved to new positions by the user.

To obtain a rectangular region of interest (ROI) and subsequently crop the image, **imcrop** is employed (Figure 6) in a script.[4] The output image data can be further evaluated using **drawassisted**, an ROI-creation convenience fx to create freehand ROI with assistance from image edges.[10] This tool is helpful in tracing a chosen structure within the image, e.g., the biomaterial implant or the T7 vertebra (Figure 6). All events related to the ROI handle class is obtained via **class** within the **events** fx. A custom fx is written (Action) containing the default 2 inputs: event source (which is the same as the ROI handle) and event data and an added third input: cell array of variables required within the fx (image data and conversion factors for image scaling). The actual size-scaled ROI area (e.g., in $cm^2$) is measured by utilizing the **createMask** fx with event source input, obtaining the **sum** of the mask logical array, and multiplying by the conversion factors. Image intensity (in HU) statistics such as minimum, maximum, average and standard deviation are calculated using

```
%% Draw and measure line
h = imdistline; % activates the fx for drawing and measuring line
setLabelTextFormatter(h,'measure'); % start message
addNewPositionCallback(h,@(pos)ShowDistance(pos,h,xr,yr)); % new position callback
%% Custom fx
function ShowDistance(pos,h,xr,yr)
    X = pos(:,1)*xr/10; Y = pos(:,2)*yr/10; % converts x and y positions [cm]
    d = norm(diff([X Y])); % distance [cm]
    setLabelTextFormatter(h,[num2str(d,'%.1f') ' cm']); % updates measurement
end
```

**Figure 5. Distance Measurement Commands**

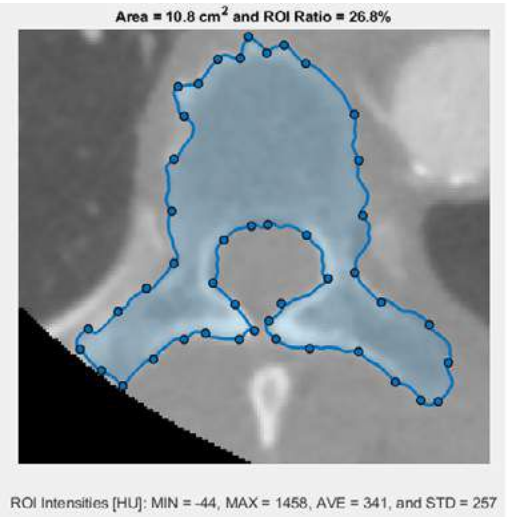
## Orthopaedic SIG Update (continued)

the respective fxs: **min**, **max**, **mean**, and **std**, from the masked imaged data. These results can be conveyed into the **title** and x-axis label (**xlabel**) (Figure 6), triggered and updated when the ROI is clicked or moved, using the **listener** fx.

In summary, MATLAB scripts using built-in and custom fx commands can read, anonymize, process, store and visualize DICOM image data with a variety of display options and configurations. Moreover, 1D and 2D measurements, including those in actual units can be implemented. The follow-up article (part 2: 3D region) will discuss 3D reconstruction and analysis of DICOM CT series, further expanding our analytical capabilities using MATLAB.


**REFERENCES:**

1. About DICOM: overview. Dicom. https://www.dicomstandard.org/about. Accessed January 23, 2021.
2. New license for MATLAB student R2020b. MathWorks. https://www.mathworks.com/store/link/products/student/SV?s_tid=ac_buy_sv_but1. Accessed January 26, 2021.
3. Read and write image data from files. MathWorks. https://www.mathworks.com/help/images/basic-import-and-export.html?s_tid=CRUX_lftnav. Accessed January 26, 2021.
4. de Guzman RC. ShowDICOM script for animation of CT series and movie output. MathWorks. https://www.mathworks.com/matlabcentral/fileexchange/86528-showdicom-script. Accessed January 28, 2021.
5. DICOM standard browser. Innolitics. https://dicom.innolitics.com/ciods. Accessed January 27, 2021.
6. DICOM Tags. Dicom Library. https://dicomlibrary.com/dicom/dicom-tags/. Accessed January 27, 2021.
7. DenOtter TD, Schubert J. Hounsfield Unit. 2020 May 11. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. PMID: 31613501.8.
8. Formatting text. MathWorks. https://www.mathworks.com/help/matlab/matlab_prog/formatting-strings.html. Accessed January 29, 2021.
9. ROI-based processing. MathWorks. https://www.mathworks.com/help/images/roi-based-processing.html. Accessed February 3, 2021.


```
%% Crop a rectangular ROI
Is = imcrop; % after ROI selection, right click and select: Crop Image
figure; mag = 300; % new figure and magnification set to mag [%]
imshow(Is,[],'InitialMagnification',mag); % shows cropped region
%% Assisted draw ROI and analyze
roi = drawassisted; evs = events(class(roi)); n = numel(evs); % event source and all class events
props = {Is xr yr}; % input properties for the custom fx grouped as a cell
cellfun(@listener,repmat({roi},n,1),evs,repmat({@(x,y)Action(x,y,props)},n,1)); % all events listener
%% Custom fx
function Action(source,data,props)
    ev = data.EventName; % event detected
    switch ev
        case {'ROIClicked' 'ROIMoved'} % events of interest and actions
            Is = props{1}; xr = props{2}; yr = props{3}; % image data and resolutions
            mask = createMask(source); % mask logical array for the ROI
            As = sum(mask,'all'); A = numel(Is); RAs = (As/A)*100; % ROI area [px^2] and ratio [%]
            Ascm = As*(xr/10)*(yr/10); % ROI area [cm^2]
            Im = Is(mask); minI = min(Im); maxI = max(Im); aveI = mean(Im); stdI = std(Im); % intensities
            % displays results to title and xlabel
            title({['Area = ' num2str(round(Ascm,1)) ' cm^2 and ROI Ratio = ' num2str(round(RAs,1)) '%']};
            xlabel({['ROI Intensities [HU]: MIN = ' num2str(minI) ', MAX = ' num2str(maxI)...
                ', AVE = ' num2str(round(aveI)) ', and STD = ' num2str(round(stdI))]});
    end
end
```

**Figure 6. Assisted ROI Selection and 2D Properties Commands Including Scaled Area**

# Industry News

*By Gopinath Mani, Industry News Editor*

**ReGelTec, Inc.**, a medical device company developing a percutaneous treatment for chronic low back pain, announced today that it has received Breakthrough Device designation from the Center for Devices and Radiological Health (CDRH) of the U.S. Food and Drug Administration (FDA).[1] The company's leading product is HYDRAFIL™, a patented hydrogel that is heated prior to injection into the nucleus of a degenerated disc via a 17-gauge needle.[1] When HYDRAFIL cools to body temperature, it forms a contiguous implant within the nucleus to augment the disc, restore the biomechanical properties of that spinal segment, and alleviate pain.[1] The Breakthrough Device program is intended to help patients receive faster access to technologies that can provide more effective treatment or diagnosis for life-threatening or irreversibly debilitating conditions. Under the program, the FDA will provide ReGelTec with priority review and interactive communication regarding device development and clinical trial protocols continuing through the premarket review process. Once approved, the HYDRAFIL™ System will offer a non-surgical treatment option to patients suffering from chronic back pain due to degenerative disc disease.[1]

**Avenda Health**, a software and medical device company developed out of UCLA, focuses on improving patient outcomes through artificial intelligence (AI).[2] They have developed a focal laser ablation system and continue to develop investigational AI cancer margin prediction software.[2] Recently, the company has announced that the FDA has cleared their image-guided focal laser ablation system, which is designed to ablate soft tissue in a physician's office and requires no general anesthesia.[2] It uses a proprietary laser needle and thermal optical sensor to precisely target and treat soft tissue while minimizing the impact on healthy tissues.[2] The company will focus its commercialization efforts to urology applications.[2]

**SafKan Health**, a medical device company that has developed the first automated ear cleaning device, announced that the FDA has granted the company 510(k) Clearance to market its product, the OtoSet, an ear cleaning system.[3] OtoSet was inspired by primary care physicians' need for a quick, safe, effective and mess-free device to remove impacted earwax, which affects about 35 million Americans and is a leading cause of conductive hearing loss.[3] Currently, the standard of care for the earwax removal procedure is the ear & bladder syringe. OtoSet combines irrigation and microsuction technologies into an automated and wearable device that offers clinicians unprecedented ease for a quick earwax removal procedure and also offers patients a safe, effective and mess-free procedure.[3] According to the American Academy of Otolaryngology, excessive or impacted earwax is present in 1 in 10 children, 1 in 20 adults and more than one-third of the geriatric population.[3]

The new, FDA-cleared **XO Score® System** was successfully used to dilate multiple challenging fibrotic and calcific lesions in hemodialysis patients with stenotic and occluded fistulas.[4] Percutaneous transluminal angioplasty balloons are used millions of times per year to dilate narrowed, or stenosed, arteries and veins. Hospitals typically stock hundreds of angioplasty balloons of different diameters and lengths to cover diverse patient needs.[4] However, calcified and/or fibrous vessels are difficult to dilate and often require high-pressure and/or scoring & cutting systems.[4] The XO Score technology allows users to convert basic angioplasty balloons in the hospital's existing inventory into sophisticated scoring, cutting and infusion/delivery devices.[4] During an XO Score procedure, clinicians insert a basic angioplasty balloon into the ultra-thin XO Score sheath and advance the combined balloon and XO Sheath to the stenosis.[4] When the balloon is inflated, up to 22 evenly spaced XO Score struts expand with the balloon and rotate 90 degrees to score & cut the narrowed vessel.[4] When the balloon is deflated, the struts rotate 90 degrees back to an atraumatic position to assist balloon rewrap and removal.[4] The XO Score system is FDA-cleared to dilate stenotic material in iliac, femoral, ilio-femoral, popliteal, infra-popliteal and renal arteries and for the treatment of obstructive lesions of native or synthetic arteriovenous dialysis fistula.[4] **Transit Scientific** designs, develops and commercializes medical devices, including the FDA-cleared XO Score scoring sheath and XO Cross® microcatheters.[4]

**TheraLight, LLC**, an international photomedicine company and a leader in light therapy and photobiomodulation, announced that Health Canada has approved the TheraLight 360 full body photobiomodulation system for use in Canada.[5] Photobiomodulation is a non-invasive and painless light-based treatment used for pain management and inflammation reduction from conditions such as arthritis, tendonitis and acute joint or muscle injuries.[5] This innovative system offers a drug-free and surgery-free option for pain relief and recovery. Instead of just treating symptoms that may provide temporary benefits, photobiomodulation is a superior treatment option because it provides energy to cells in the body that trigger a chemical response, resulting in the body to heal itself.[5] Each TheraLight system utilizes red and near-infrared light in four wavelengths that deliver maximized treatment coverages so patients can receive the best results.[5] Because of the unattended feature of the TheraLight system, these are simple to operate and do not require manual operation like many other pain management devices.[5]

## Industry News (continued)

The FDA approved **Myovant Sciences**' Orgovyx (relugolix) for treatment of adults with advanced prostate cancer.[6] The drug was granted Priority Review and is the first and only oral gonadotropin-releasing hormone (GnRH) receptor antagonist for men with advanced prostate cancer.[6] The approval was based on data from the Phase III HERO trial.[6] Also, the FDA approved **AstraZeneca's** Tagrisso (Osimertinib) for adjuvant treatment of adults with early-stage epidermal growth factor receptor-mutated (EGFRm) non-small cell lung cancer (NSCLC) after tumor resection with curative intent.[6,7] The drug is indicated for EGFRm patients whose tumors have exon 19 deletion or exon 21 L858R mutations.[6,7] The approval was made under the agency's Real-Time Oncology Review (RTOR) pilot program.[6,7] Five other countries participated in a concurrent submission and review process via the FDA's Project Orbis.[6,7]

The FDA approved **Ridgeback Therapeutics' Ebanga (ansuvimab-zykl)** for treatment of *Zaire ebolavirus* infection in adults and children.[8] Ebanga is a human monoclonal antibody that blocks binding of the ebolavirus to the cell receptor, preventing its entry into the cell.[8] Zaire ebolavirus is one of four ebolavirus species that can cause the potentially fatal disease.[8] The therapy was evaluated in the PALM trial during the ebola outbreak in the Democratic Republic of the Congo (DRC) in 2018-2019.[8] The trial was led by the U.S. National Institutes of Health and the DRC's Institut National de Recherche Biomedicale.[8] Ebanga was granted an Orphan Drug designation, which provides incentives to assist and encourage drug development for rare diseases.[8] Additionally, the agency granted Ebanga a Breakthrough Therapy designation.[8]

The FDA approved the **Osseoanchored Prostheses for the Rehabilitation of Amputees (OPRA) Implant System**, the first implant system marketed in the U.S. for adults who have transfemoral (above-the-knee) amputations and who have or are anticipated to have rehabilitation problems with, or cannot use, a conventional socket prosthesis.[9] A conventional leg prosthesis uses a specially-fitted, cup-like shell called a socket that fits over the remaining portion of the patient's leg (the residual limb remaining after amputation) to secure the device to the leg.[9] Some patients may not have a long enough residual limb to properly fit a socket prosthesis or may have other conditions, such as scarring, pain, recurrent skin infections or fluctuations in the shape of the residual limb that prevent them from being able to use a prosthesis with a socket.[9] The OPRA Implant System is surgically anchored and integrated into the patient's remaining thigh bone to allow connection to an external prosthetic limb.[9] The OPRA Implant System has been on the market under a humanitarian device exemption since 2015.[9] Humanitarian use devices are intended to benefit patients in the treatment or diagnosis of a disease or condition that affects or is manifested in not more than 8,000 individuals in the U.S. per year.[9] Today's approval expands the patient population eligible for this device. The OPRA Implant System is manufactured by **Integrum AB** in Mölndal, Sweden.[9]

### REFERENCES


1. ReGelTec receives FDA breakthrough designation for its HYDRAFIL™ System. Businesswire. https://www.businesswire.com/news/home/20201209005150/en/. Accessed Jan 26, 2021.
2. Avenda Health receives FDA clearance for their Focal Laser Ablation System. PRNewswire. https://www.prnewswire.com/news-releases/avenda-health-receives-fda-clearance-for-their-focal-laser-ablation-system-301193694.html. Accessed Jan 26, 2021.
3. New FDA cleared automated ear cleaning device brings ear care into the 21st century. Biospace. https://www.biospace.com/article/releases/new-fda-cleared-automated-ear-cleaning-device-brings-ear-care-into-the-21st-century/?s=93. Accessed Jan 26, 2021.
4. New angioplasty system dilates calcified & fibrotic vessels.PRNewswire. https://www.prnewswire.com/news-releases/new-angioplasty-system-dilates-calcified--fibrotic-vessels-301171696.html. Accessed Jan 26, 2021.
5. Health Canada approves TheraLight Photobiomodulation Systems. PRNewswire. https://www.prnewswire.com/news-releases/health-canada-approves-theralight-photobiomodulation-systems-301210395.html. Accessed Jan 26, 2021.
6. Four recent FDA drug approvals: Myovant, Integrum, AstraZeneca and Ridgeback. Biospace. https://www.biospace.com/article/4-recent-fda-drug-approvals-myovant-integrum-astrazeneca-ridgeback/?keywords=four+recent+fda+drug+approvals+myovant. Accessed Jan 26, 2021.
7. Tagrisso approved in the US for the adjuvant treatment of patients with early-stage EGFR-mutated lung cancer. https://www.astrazeneca.com/content/astraz/media-centre/press-releases/2020/tagrisso-approved-in-the-us-for-early-lung-cancer.html. Accessed Jan 26, 2021.
8. FDA approves treatment for ebola virus. https://www.fda.gov/drugs/drug-safety-and-availability/fda-approves-treatment-ebola-virus. Accessed Jan 26, 2021.
9. FDA approves prosthetic implant for above-the-knee amputations. https://www.fda.gov/news-events/press-announcements/fda-approves-prosthetic-implant-above-knee-amputations. Accessed Jan 26, 2021.


IF YOU HAVE INDUSTRY NEWS TO SHARE WITH *BIOMATERIALS FORUM* READERS, SEND IT TO GOPINATHMANI.BME@GMAIL.COM.

# Government News

*By Carl Simon, Government News Editor*

## TRANSLATIONAL SCIENCE INTERAGENCY FELLOWSHIP (TSIF)

The TSIF program provides training in both translational science and regulatory science to new MDs and PhDs.[1] The program is jointly sponsored by the National Center for Advancing Translational Sciences (NCATS) of the National Institutes of Health (NIH) and the U.S. Food and Drug Administration (FDA). The TSIF provides three years of support and the candidate splits time at FDA and NCATS. "Fellows will be trained in preclinical translational science, technology development and regulatory research and review. By combining training in translational science and research-related regulatory review, this program will enable fellows to build awareness of regulatory requirements into the early stages of medical product development, improving efficiencies in both the development and review processes. Fellows in this program will develop skills of value to future careers in academia, the pharmaceutical industry and government."

## NASEM WORKSHOP: APPLYING SYSTEMS THINKING TO REGENERATIVE MEDICINE

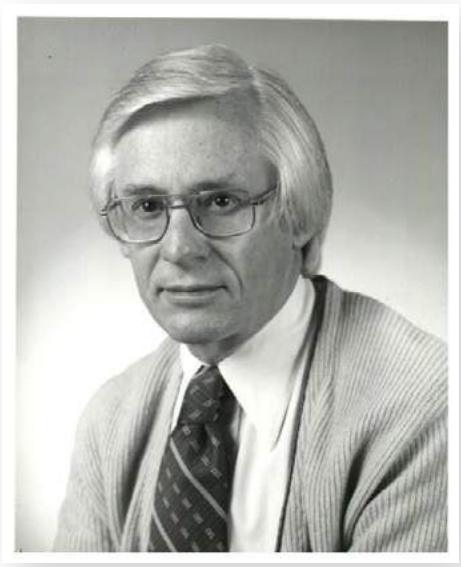
The National Academies of Sciences, Engineering and Medicine (NASEM) held a workshop entitled, "Applying Systems Thinking to Regenerative Medicine" on October 23-24, 2020.[2] The workshop was organized by representatives from NIH, FDA, NIST, academics, patient advocacy and industry. "The current approach to characterizing the quality of a regenerative medicine product and the manufacturing process often involves measuring as many endpoints as possible, but this approach has proved to be inadequate and unsustainable." The workshop explored "how cross-disciplinary systems thinking approaches can support the identification of relevant quality attributes and streamline manufacturing and regulatory processes of regenerative medicine products." Participants discussed "new advances in data acquisition, data analysis and theoretical frameworks and how systems approaches can be applied to the development of regenerative medicine products." The meeting materials are posted on the website, including slides from talks and videos of talks.

## NIST FLOW CYTOMETRY STANDARDS CONSORTIUM

The National Institute of Standards & Technology is starting a new consortium on flow cytometry.[3] Although flow cytometry is one of the most common methods for characterization of therapeutic cell preparations, results are challenging to compare over time and space. Different operators, instruments, laboratories and data analytics lead to variability in results, making it difficult to assess manufactured cell quality in a comparable, consistent manner. "The Consortium will develop standards for flow cytometry applications and reference materials for instrument calibrations" in order to improve the consistency and reliability of flow cytometry measurement capabilities.

### REFERENCES


1. Translational science interagency fellowship. National Center for Advancing Translational Sciences. https://ncats.nih.gov/training-education/training/TSIF. Accessed February 24, 2021.
2. Applying systems thinking to regenerative medicine: a workshop. The National Academies of Sciences Engineering Medicine. https://www.nationalacademies.org/event/10-22-2020/applying-systems-thinking-to-regenerative-medicine-a-workshop. Accessed February 24, 2021.
3. NIST Flow Cytometry Standards Consortium. The National Institute of Standards & Technology. https://www.nist.gov/programs-projects/nist-flow-cytometry-standards-consortium. Accessed February 24, 2021.



# *In Memoriam*
# DONALD J. LYMAN
## (1926-2020)

*By Elizabeth Lyman*

Dr. Donald J. Lyman — scientist, researcher, educator, mentor and visionary — passed away at home on November 8, 2020, a few days after his 94th birthday. Throughout his long and distinguished career in industry, research institutes and academia, his love of science was palpable and infectious, a love that was first sparked by the book he read as an adolescent, *The Microbe Hunters* by Paul De Kruif. It introduced him to a world of inexhaustible discoveries, one that he would explore through chemistry. Equipped with the Gilbert chemistry set his parents bought him as a boy, he built his first chemistry lab in the basement of his parents' home. The beauty of the natural world awed him and never ceased to inspire his curiosity and passion for learning.

Gifted with imagination, a nimble mind open to new ideas and the ability to reduce complex ideas to understandable nuggets, Dr. Lyman had a knack for reaching people of all ages and backgrounds, drawing them into his world of science. An international leader in the field of biomedical polymers, he advocated for an interdisciplinary and cooperative approach among researchers to successfully tackle the challenges posed by the complexities of repairing the human body. He cautioned that the sharp distinctions drawn between various specialties, while being useful human contraptions for organizing the world around them, disappeared in nature and carried the danger of contributing to a myopia that could hinder cooperation and innovation.

Dr. Lyman began his research career at the Pioneering Research Laboratory of E.I. DuPont de Nemours after receiving his PhD in organic chemistry from the University of Delaware in 1952. At DuPont, he focused on polymer synthesis and structure/property relationships under the direction of Dr. William Hale Charch. With the premature death of Dr. Charch in 1958, Dr. Lyman began looking beyond DuPont to expand into other areas of polymer research. Professor Herman Mark at the Polytechnic Institute of Brooklyn suggested that he contact Dr. Maurice Huggins who was looking for a synthetic polymer chemist. Dr. Huggins invited Dr. Lyman to join his team at the Stanford Research Institute. The move to SRI in 1961 was a pivotal turning point for Dr. Lyman.

Soon after arriving at SRI, Dr. Lyman attended a lecture at Stanford's medical school by Dr. Belding Scribner describing the first 15 patients kept alive on chronic dialysis using an arteriovenous shunt he developed at the University of Washington. Until then, fresh cuts in a patient's arm were made to access the artery and vein each time the patient was dialyzed, which severely limited the number of procedures since the same access sites could not be reused in most cases. After the talk, Dr. Lyman approached Dr. Scribner with some ideas on developing membranes to remove toxins during dialysis. This led to Dr. Scribner funding Dr. Lyman's first year of membrane research. Funding from the John Hartford Foundation and the National Institute of Arthritis and Metabolic Diseases soon followed.

Dr. Lyman also began working on the effects of polymer structure and surface properties on the coagulation of blood. This research to synthesize thromboresistent polymers was supported by the National Heart Institute. One of the polymers developed, a new copolyether urethane urea, was later used in fabricating the first generation of the Utah artificial heart designed by Dr. Clifford Kwan-Gett.

Because of his work at SRI, Dr. Lyman was elected in 1964 as a member of the American Society for Artificial Internal Organs. At the time, Dr. Lyman was among only a half dozen or so PhDs among a sea of MDs. There he crossed paths with Dr. Willem Kolff, who at the time was the Scientific Director of Artificial Organs at the Cleveland Clinic. In 1967, Dr. Kolff left for the University of Utah to

## In Memoriam: Donald Lyman (continued)

direct the Division of Artificial Organs that was started by Dr. Keith Reemstma, Head of University of Utah's Department of Surgery and Acting Dean of the College of Medicine.

On the recommendation of Dr. Kolff, Dr. Reemstma invited Dr. Lyman in early 1969 to join the University of Utah, offering him research and teaching appointments in both the College of Medicine and the College of Engineering. Attracted not only by the opportunity to work with Dr. Kolff but equally by the atmosphere of excellence and cutting edge research that permeated the University under the leadership of President James Fletcher (who later headed NASA) and others such as Dr. Reemtsma and the renowned hematologist Dr. Maxwell Wintrobe, Dr. Lyman embarked on a 20-year stint at the University of Utah.

Dr. Lyman's continued interest in the synthesis and characterization of polymers and the broader applications of polymers as implants led him to pursue his own research programs. From early in his research on biomaterials, one of Dr. Lyman's long-range goals was to develop polymer implants that would repair the injury in the acute phase but then function as scaffolding to promote healing to ultimately reduce or replace the body's reliance on the implants. He obtained numerous grants from several agencies including the National Science Foundation, the National Heart Institute and the National Institute of General Medical Science. The largest of these programs was the Biomedical Engineering Center for Polymer Implants funded by NIGMS in 1978 and directed by Dr. Lyman. An interdisciplinary team of leading researchers in different specialties was brought together to work on a variety of implant areas, including vascular graft, ureter, esophageal and nerve repair. The Center was the first of its kind in the United States.

In addition to his research, Dr. Lyman taught both undergraduate and graduate courses in biomaterials and chemistry throughout his tenure. His courses were popular among students but none more so than his polymer synthesis class, a hands-on graduate level lab course taught every summer quarter through the Chemistry Department. Space was limited and there was always a waiting list of students wanting to enroll.

Dr. Lyman's research attracted graduate students, post docs, fellows and visiting professors both domestically and internationally. As faculty advisor to over two dozen masters and doctoral students, Dr. Lyman was both demanding and approachable. He also trained surgical residents on research methods through the Surgery Department. He enjoyed teaching, hoping to challenge students to think independently and question conventional wisdom. Generous with his time and sparing no effort to help his students achieve their goals, his students will remember getting back numerous red-lined drafts of their thesis and dissertation and the countless hours spent rehearsing their oral presentation in front of Dr. Lyman and their colleagues, to prepare for the main event. It was particularly helpful to those for whom English was not their first language.

Dr. Lyman retired from the University of Utah in 1989. During his tenure, he held appointments in four academic departments — Materials Science and Engineering, Surgery, Bioengineering and Chemistry. The Department of Bioengineering was created in no small measure from the vision and efforts by him and Dr. Joseph Andrade to fill the need for an academic department focused on biomaterials. He was appointed as emeritus professor of both Materials Science and Engineering and Bioengineering in 1989.

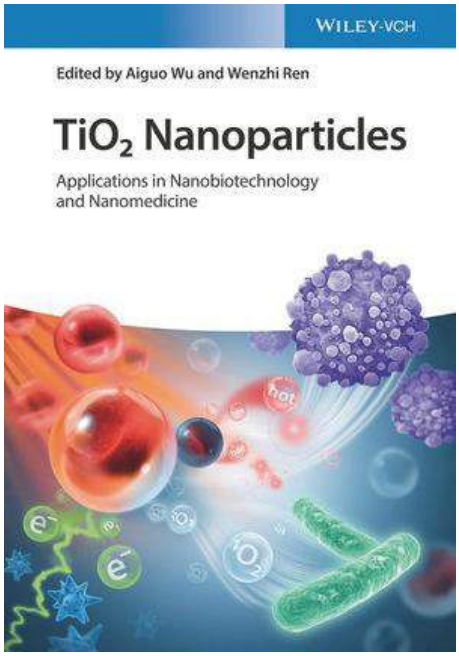
Dr. Lyman's research continued after leaving the University and moving to Washington State. From 1994 to 2003, he was the Director of Polymer Chemistry at the Hope Heart Institute, a research institute in Seattle, Washington founded by the late Dr. Lester Sauvage, a world-renowned heart surgeon. Dr. Lyman's last research took him into an entirely new area of study — that of using Fourier transform infrared spectroscopy to study the molecular changes that breast cancer appeared to initiate in the morphology of hair. His foray into this research was accidental. He learned from his longtime friend, the late Dr. Maxwell Feughelman (University of New South Wales, Australia), that a former graduate student of his (Dr. Veronica James) detected shifts in the pattern of hair structure in the presence of breast cancer using Synchrotron x-ray diffraction. Though these pattern shifts were observable, x-ray diffraction could not explain the molecular changes causing the shifts. Having used Fourier transform infrared spectroscopy extensively in his polymer research to study molecular structures, Dr. Lyman thought it might be able to shed light on what was happening at the molecular level to cause these pattern shifts. His last two papers reported his findings.

Dr. Lyman's achievements are many. He authored and co-authored nearly 170 scientific papers and book chapters. He is the holder of several patents and the recipient of many awards and honors, including University of Utah's Distinguished Research Award for 1982-1983, the Clemson Award for Basic Research (Society For Biomaterials) for 1982, visiting professorships and invited lectureships. He served on editorial boards, think tanks and steering committees. He was also a founding member of the Society For Biomaterials.

These achievements would not have been possible were it not for his many colleagues, students, staff and friends (too many to name), but the list would not be complete without mentioning Dr. Dominic Albo, a professor of surgery whom Dr. Lyman began working immediately with upon arriving in Utah and whose friendship helped sustain Dr. Lyman during trying times.

# TiO2 Nanoparticles: Applications in Nanobiotechnology and Nanomedicine

BY LYNNE C. JONES, PHD AND SACHIN MAMIDWAR, MBBS, MS




Editors: Aiguo Wu, Wenzhi Ren
Publisher: Wiley – VCH
ISBN: Print: 978-3-527-34724-7 June 2020
E book: 978-3-527-82544-8 February 2020

I [Lynne Jones] was introduced to nanoparticles by *Prey*, a science fiction novel written by Michael Crichton in 2002. A few years later, I learned how the technology of nanoparticles and nanotubes could be applied to cancer diagnosis and therapy during a presentation at an Annual Meeting of the Society For Biomaterials. The potential uses of nanoparticles fascinated me, especially as applied to cancer. When selecting a book for review, I found this textbook that provides an overview of the use of $TiO_2$ nanotechnology as applied to medicine. I thank my co-author, Sachin Mandimar, for agreeing to review this book with me.

The field of biomaterials is rapidly evolving towards the use of nanomaterials for various biomaterial-related applications. Ceramic, polymeric and metallic nanomaterials and sometimes their nanocomposites are being studied for various clinical indications. This particular book, titled, *$TiO_2$ Nanoparticles: Applications in Nanobiotechnology and Nanomedicine,* provides a fairly basic overview of the properties of $TiO_2$ nanoparticles and its various crystalline types, ways of synthesizing them, their properties and applications of those properties for various clinical indications.

"Chapter 1: $TiO_2$ Nanoparticles: Properties and Applications" begins with a detailed introduction to various crystalline types (anatase, rutile, brookite) of $TiO_2$ nanoparticles. There is considerable interest in TiO2 nanoparticles because of their low production costs, mechanical and chemical stabilities, thin film transparency, bio- and chemical inertness, hydrophilicity, high light conversion efficiency and corrosion resistance. This chapter discusses various properties of $TiO_2$ nanoparticles including crystalline, optical and electromechanical properties. It gives brief information about how electromechanical properties are helpful for dental implants. Various methods to synthesize $TiO_2$ have also been discussed. Other properties like optical property, use in drug delivery, use in phototherapy, sonodynamic therapy, chemotherapy, role in water purification and air cleaning is briefly discussed.

"Chapter 2: Toxicity of $TiO_2$ Nanoparticles," states that while $TiO_2$ nanoparticles can be effective for a variety of applications, they are able to participate in cellular and molecular interactions and, therefore, can have toxic side effects. The authors provide a thorough description of the potential side effects and their mechanisms. They do note that there are recent reports of negligible toxicity of black TiO2 (b-TiO2) nanoparticles, which indicates their potential for biomedical application.

In "Chapter 3: Antibacterial Applications of $TiO_2$ Nanoparticles," the antibacterial effects of $TiO_2$ nanoparticles are reviewed in great detail. Mechanisms of antibacterial effects include photocatalytic mechanism under UV and visible light, and cell membrane disruption because of the opposite charges of $TiO_2$ nanoparticles and cells. This chapter explores the research that has been conducted regarding anion doping, as well as doping with transition metal ions. Doping using nitrogen, nitinol or carbon can improve the biocompatibility and the antibacterial properties of the nanoparticles. Doping with Ag, Zn and Cu is also discussed. For example, Ag doping has been shown to improve the crystallization, increase the surface area, increase volume of pores and improve the absorption of visible light. However, almost all of the studies that were referred in this chapter for the antibacterial properties were *in vitro* studies. The chapter ends with a discussion on antibacterial applications of doped $TiO_2$ nanoparticles, briefly noting applications for wound and implant infections, as well as dental applications.

"Chapter 4: Surface-Enhanced Raman Spectrum of $TiO_2$ Nanoparticles," discusses the role of surface-enhanced raman spectrum (SERS) for the manufacture of various nanoparticles. It

## Book Review (continued)

describes how semiconductor SERS substrates with super strong enhancement factors (EFs), like defective $TiO_2$ nanoparticles and $TiO_2$ arrays, have been developed. SERS substrate composed of Ag, Au or Cu can reach ultrahigh detection sensitivity even to single molecule level, making SERS an excellent trace analysis tool for biomedical applications. Studies of non-metal platforms (such as the graphene, carbon nanotubes) are also discussed. SERS $TiO_2$ nanoparticles has many advantages due to its relatively high stability, enhanced light scattering, versatile interface functionalization, self-cleaning performance and spectrum recyclability. Based on the studies reviewed, it is expected that SERS TiO2 nanoparticles will have useful applications in biosensors.

"THE LITERATURE REVIEWED IN THIS CHAPTER SUPPORTS THAT W-TIO2 NANOPARTICLES HAVE MANY ADVANTAGES LIKE BIOCOMPATIBILITY, PHOTOSTABILITY AND LONG CIRCULATION BECAUSE OF ITS ROLE AS INORGANIC PHOTOSENSITIZERS."

"Chapter 5: Cancer Theranostics of White $TiO_2$ Nanomaterials," discusses theranostics, as applied to cancer, and as it relates to the integration of simultaneous cancer imaging and therapy. This chapter describes the basic concepts of photodynamic therapy and sonodynamic therapy. White $TiO_2$ (W-$TiO_2$) has excellent biocompatibility, high stability and excellent light/ultrasound responsive properties. The literature reviewed in this chapter supports that W-$TiO_2$ nanoparticles have many advantages like biocompatibility, photostability and long circulation because of its role as inorganic photosensitizers. W-$TiO_2$-based sonodynamic therapy has excellent advantages of non-photo damage and non-radiation damage. Additionally, easy functionalization helps W- $TiO_2$ nanoparticles bind to drugs enabling them to be used as drug delivery vehicles. However, as the authors indicate, various additional studies are needed before clinical application of W-$TiO_2$.

"Chapter 6: Cancer Theranostics of Black $TiO_2$ Nanoparticles," discusses various methods of manufacturing and properties of black TiO2. Although W-$TiO_2$ has amazing properties, it needs UV light for it to be functioning well or to generate reactive oxygen species (ROS) for cancer photodynamic therapy (PDT). However,UV light often harms normal cells as well. In contradistinction, black $TiO_2$ can function well in the presence of near infrared (NIR) light. This chapter further describes how black $TiO_2$ can be used for phototherapy (including photothermal and photodynamic therapy), image-guided phototherapy, synergistic chemo-photo therapy and synergistic sonodynamic-photothermal therapy. The authors conclude with an outstanding discussion of the current limitations in our understanding of the application of black $TiO_2$ nanoparticles for photodynamic and photothermal imaging. They note that further research is needed regarding the stability of black $TiO_2$, the mechanism of optical performance, the use of hydrophilic polymer to modify black $TiO_2$ and the *in vivo* behavior that is needed before black $TiO_2$ can be used for clinical application.

In "Chapter 7. Neurodegenerative Disease Diagnostics and Therapy of $TiO_2$ Nanoparticle Therapy of $TiO_2$-Based Nanoparticles," the authors lay the foundation for the application of TiO2 nanoparticles to the diagnosis and treatment of neurodegenerative diseases (NDs) by describing the types of NDs, potential causes and the current status of detection and treatment of these diseases. NDs affect several million people all over the world and are seriously debilitating for the affected individual. There is enthusiasm in the medical community regarding the potential of $TiO_2$ for the diagnosis and treatment of NDs, but this is tempered by concerns regarding the agglutination of proteins associated with their use and the potential to aggravate NDs such as Alzheimer 's disease. This chapter is a good stand-alone chapter that can be used to provide students an overview of $TiO_2$ nanoparticles for a specific medical application.

This book could be useful for students, faculty and researchers working in the specific field of $TiO_2$ nanomaterials. References given at the end of every chapter are fairly detailed and would be useful to them. However, there is some redundancy in a few of the chapters that could have been avoided. The brief conclusion at the end of every chapter is useful; several of the chapters also provide their perspective on future directions that remain to be explored.


Society For
Biomaterials
2021
ANNUAL
MEETING &
EXPOSITION
BIOMATERIALS RESEARCH:
Hitting all the right notes, and
avoiding the translational blues
NOW VIRTUAL
APRIL 20–23, 2021
www.biomaterials.org