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IUPUI - Purdue School of Engineering & Technology

THE BME NETWORK

Newsletter of the **Department of Biomedical Engineering**

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Innovation in hydrogel chemistry and engineering for regenerative biology

L to R: Chien-Chi Lin, John Bragg, Han Shih, Tim Emmel, Tsai-Yu Lin, Tanja Greene

Hydrogels are hydrophilic polymer networks capable of imbibing a large amount of water without dissolving. Hydrogels are increasingly being explored as scaffolds for cell and drug delivery to treat diseases or as platforms to study cell biology in three-dimension (3D). The Lin Research Group at IUPUI is particularly interested in designing polymeric hydrogels with controllable biophysical (e.g., rigidity, stiffness, degradability, permeability, etc.) and biochemical properties (e.g., cell signaling ligands) for a variety of biomedical applications. We are particularly interested in hydrogels that can be prepared via modular approaches (like building a sculpture using individual pieces of mini LEGOs). These hydrogels are ideal for answering important biological questions related to cells and tissues, for releasing therapeutically relevant agents to facilitate disease treatment, and for delivering adult and stem/progenitor cells to accelerate tissue regeneration (Figure 1). Our research is highly interdisciplinary and integrates knowledge from polymer chemistry and engineering, bioconjugate chemistry, biochemistry, cell and molecular biology, and immunology.

In one project, we are developing a multifunctional hydrogel system that initially supports cell proliferation, but the gels can be transformed into a microenvironment to promote cell differentiation towards a specific lineage. The goal of this project is to demonstrate how synthetic gels can be engineered at appropriate space and time to direct cell fate processes in 3D. These well-defined hydrogels are also being used to study pancreatic cancer cell growth, epithelial-mesenchymal transition (EMT), and metastasis (Figure 2A). We are also using a similar gel platform to study liver regeneration (figure 2B). In collaboration with Prof. Guoli Dai in the Department of Biology at IUPUI, we are developing biomimetic hydrogels for restoring polarity and functionality of primary hepatocytes, as well as for re-differentiating hepatocellular carcinoma cells into functional hepatocytes. The successful outcome of this project will not only provide a culture platform for mechanistic understanding of hepatocyte proliferation, but also permit the study of hepatitis viral infection using re-differentiated hepatocytes.

A second focus area of our work is on designing hydrogel coating on pancreatic islets. This thin hydrogel coating provides immuno-isolation against host immune rejection when islets are transplanted in diabetic patients (Figure 2C). The success of this technology is critical because patients receiving islet transplantation are required to take immuno-suppressive drugs to decrease immune rejection, a critical factor limiting the long-term survival of the transplanted islets. With a goal of eliminating immuno-suppressive regimens in islet transplantation, this new technique will improve the design of hydrogel coating while allowing facile conjugation of a myriad of bioactive motifs not only to improve the survival and function of transplanted islets, but also to mitigate host immune rejection.

Finally, we are also working on designing better hydrogel carriers for delivering proteins and small synthetic drugs. Proteins (e.g., growth factors, cytokines, hormones, etc.) play an important role in tissue development and regeneration. The ability of a scaffold to deliver therapeutically relevant proteins with desired dosage and bioactivity holds the key to the success of a tissue engineering strategy. We seek to develop micro-/nano-scale hydrogel particles with tunable properties to sequentially deliver multiple bioactive

See Innovation on p.3

Message from the Chair

Edward J. Berbari
Chancellor's Professor
and Chair of Biomedical
Engineering

Every year as I reflect on the past year in preparation for writing my annual letter for the newsletter, I struggle with topics which would be appropriate and newsworthy for our various constituencies. This year it became obvious that we have a number of alumni pursuing exciting careers and many students moving along new education pathways. I always tell those interested in our programs that I am always amazed at the creativity of our students and where they choose to apply their education. Hence, I only need to introduce you to some of our recent graduates so that you can share in my amazement.

There are three highlighted recent graduates who are sharing their stories: Haili Theriac (BSBME, 2011), Chris Taylor (BSBME, 2012) and David Sempsrott (BSBME, 2009 and MSBME, 2012). They are working in the medical device industry and pharmaceutical industry. Since our first graduates in 2008 we have had 140 students receive their BSBME from our program. Approximately 25% or our graduates pursue further education primarily in MS, PhD, or MD programs. Since 2012, we have had 67 graduates and 6 have gone on to medical school (2 at IU, 1 at Duke, 1 at Texas A&M, and 2 at Johns Hopkins) and 3 have gone into PhD programs (1 at Duke, 1 at Vanderbilt, and 1 at IU). It should be noted that one student is in the prestigious MD/PhD program at Johns Hopkins. The remaining graduates are employed, primarily in the medical device industry. We have lost track of 16 students – please let us know where you are and what path you are on! As a reminder, there is an active group (IUPUI Biomedical Engineering Department Alumni) on LinkedIn-currently with 100 members. Please consider joining and leaving a note from time to time.

Also highlighted in this newsletter is Dr. Chien-Chi Lin and his research lab. He has provided a summary of his research activities, but I would note that he has also received 2 NIH grants since joining us in 2010. This is especially notable in this austere era of sequester at the federal funding agencies. Besides maintaining an active research lab, he also teaches both at the undergraduate and graduate levels. Since coming to our program, he has published over 20 papers in high quality peer-reviewed journals in biomaterials research areas.

The Science and Engineering Laboratory Building opened in January and will provide several resources for Biomedical Engineering. These include a 1400 sq. ft. shared (with Biology) teaching laboratory and 1900 sq. ft. of research laboratory space for cellular biomechanics, tissue culture, and advanced microscopy used by Drs. Julie Ji and Sungsoo Na and their students. In addition, the building will house a state-of-the art vivarium which will support many of our research programs.

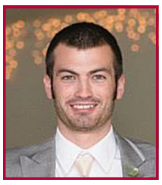
Transitions: Shelly Albertson resigned as our Office Coordinator and has been replaced by Sherry Clemens. Best wishes to Shelly in her new pursuits and welcome to Sherry!

BME Trivia: Identify the undergraduate degrees of our BME faculty. There are 2 electrical engineers, 2 chemical engineers, a bioengineer, a biochemical engineer, an aeronautical engineer, a microbiologist, an aerospace engineer, a mechanical engineer, and 2 biomedical engineers

ALUMNI UPDATE

Haili Theriac, BS BME 2011, Mathematics Minor

I am currently employed at Catalent Pharma Solutions in St. Petersburg, FL as a Softgel Process Engineer. I am responsible for customer-based projects driven by process improvement initiatives. In addition to providing commercial manufacturing support, I also play a role in new product development processes. My BME degree equipped me with problem-solving skills, time/project management skills, software programming, and leadership skills. Learning how to learn is crucial. Always work to learn more and grow professionally and personally.



Chris Taylor, BS BME 2012

I am a Process Development engineer for Cook General Bio-Technology LLC, located in Indianapolis. I developed the manufacturing process of Stemulate, a human platelet lysate stem cell culture media supplement, and control the manufacturing operations of that product for Cook Medical. Currently, I have been spending a lot of my time at a Cook sister company in Denmark to transfer the manufacturing process for European distribution. BME was very valuable to me because it further developed my critical problem solving, time management, and leadership skills.

David Sempsrott, BS BME 2009 & MS BME 2012

I'm currently an R&D Hardware/Software Test Engineer in the Diabetes Care area of Roche Diagnostics. I'm a bit of a jack-of-all-trades in the test engineering world and really enjoy it. My primary responsibility is leading small teams of engineers doing verification testing for our blood glucose meters: we receive documents with specific requirements and specifications for meter behavior, and we write and execute tests to prove that the meter satisfies each requirement, documenting any failures to help the project team troubleshoot and fix them. I also serve an advisory role on review boards for new meter designs to make sure the designs are testable, and I occasionally help develop and maintain hardware/software tools we use in our test efforts. Both of the BME programs taught me important skills that help me do my current job: the undergraduate program helped me develop the analytical mindset of a problem solver, and the graduate program gave me the experience and responsibility of a project I had to own, execute, and communicate to my team.

[Innovation] Continued from page 1

proteins for enhancing the proliferation and differentiation of cells. In collaboration with Prof. Hiroki Yokota, we are also developing strategies to incorporate Salubrinal, a novel synthetic agent that promotes bone fracture healing, into orthopedic implants with a goal of accelerating fracture bone healing.

We are grateful for the following sponsors for their financial support to our work: **National Institutes of Health (NIBIB and NCI), IU Office of the Vice President for Research (OVPR), 100 Voices of Hope, IU School of Medicine Indiana Diabetes Research Center (IDRC), IUPUI Office of the Vice Chancellor for Research (OVCR), Biomechanics and Biomaterials Research Center (BBRC), and the Department of Biomedical Engineering.**

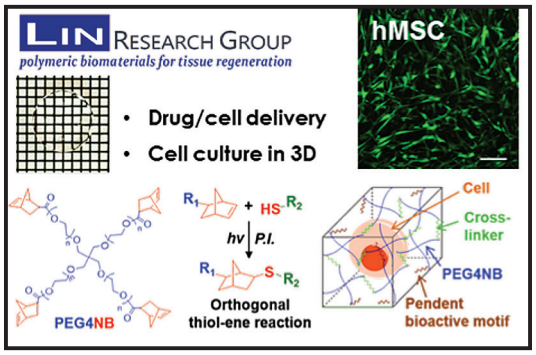


Figure 1. Research focus of Lin Research Group at IUPUI.
The Lin Research Group is interested in designing hydrogels for drug/cell delivery and for cell culture in 3D. These hydrogels are prepared by a mild and rapid light exposure and with properties that can be independently controlled. These hydrogels are cytocompatible (cell-friendly) for a variety of cell types, including pancreatic islets, liver cells, pancreatic ductal adenocarcinoma cells (PDAC), and human mesenchymal stem cells (hMSC, stained green in the upper right image).

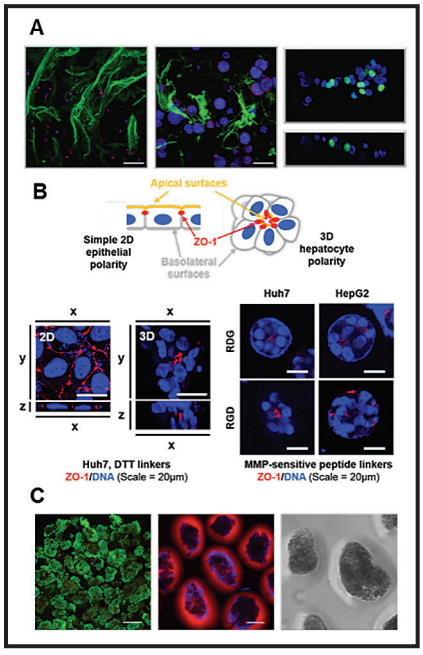


Figure 2. Example projects in the lab.
(A) Modeling pancreatic cancer in 3D hydrogels. Left: pancreatic cancer cells encapsulated in hydrogels dispersed with collagen fibrils right after photo-encapsulation. Middle: After 10-day culture, cells proliferated into spheroids. Right: Irregular cell clusters with random proliferating cells in a hydrogel upon cytokine stimulation. (B) Liver tissue engineering. Hydrogel culture restored 3D liver cell (hepatocyte) polarity. (C) Islet surface hydrogel coating. Left: pancreatic ß-cell aggregates maintained high viability (green staining) after hydrogel coating. Middle: thin layer of hydrogel coating on the surface of the cell aggregates. Right: Hydrogel coating on isolated mouse islets.

The Class of 2014

Congratulations to our undergrad class of 2014!

BME award recipients for 2013-14

Charles H. Turner Award for Outstanding Achievement in the Senior Year:
Daniel French

Bepko Award for Outstanding Achievement in the Junior Year:
Leandro Moretti & Alec Willard

Bepko Award for Outstanding Achievement in the Sophomore Year:
Sultan Almunif

Biomedical Engineering Outstanding Service Award:
Kelsey Lipking

Exemplary Internship or Research Award:
Alycia Berman

Medtronic Outstanding Senior Design Team: *Daniel French, Cho-Hin (Mark) Fung, S. Christopher Hiett, James Holman, and Kyle Kleinline*

Outstanding Engineering Dual Degree BME Student Award:
Heather Keiser

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Sept. 5	Faculty	Dr. Hiroki Yokota, "Mechanical Loading and Bone"
Sept. 19	Adj Faculty	Dr. Randall Roper, IUPUI Biology Dept
Oct. 3	Faculty	Dr. Berbari, "Electrotherapies for Treating Cardiac Arrhythmias"
Oct. 17	Non-BME Faculty	Dr. Steven Lacey, IU Fairbanks School of Public Health
Sept. 19	Adj Faculty	Dr. Randall Roper, IUPUI Biology Dept
Nov. 21	Adj Faculty	Dr. Alexander Robling, IUSM Dept of Anatomy & Cell Biology
Dec. 5	Faculty	Dr. Ji
Dec. 12	Student	BME 696 Presentations

Research Areas of BME Faculty

BIOMATERIALS
Steven Higbee, Ph.D., *Lecturer*
Chien-Chi Lin, Ph.D., *Assistant Professor*
Dong Xie, Ph.D., *Associate Professor*

BIOMEDICAL INSTRUMENTATION
Edward Berbari, Ph.D., *Professor and Chairman*

CARDIOVASCULAR ENGINEERING
Bill Combs, MSEE, *Clinical Assoc. Professor*
Julie Ji, Ph.D., *Associate Professor*

MECHANOBIOLOGY
Sungsoo Na, Ph.D., *Assistant Professor*
Joseph Wallace, Ph.D., *Assistant Professor*
Hiroki Yokota, Ph.D., *Professor*

NEUROENGINEERING
Karen Alfrey, Ph.D., *Senior Lecturer*
John Schild, Ph.D., *Associate Professor*
Ken Yoshida, Ph.D., *Associate Professor*

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