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IUPUI
Indiana University–Purdue University Indianapolis
Purdue School of Engineering and Technology
723 W. Michigan St., SL 220
Indianapolis, IN 46202
www.engr.iupui.edu/bme

IUPUI - Purdue School of Engineering & Technology

THE BME NETWORK

Newsletter of the Department of Biomedical Engineering

Mechanobiology: How Cells Respond to Their Physical Environment

The endothelial lining of the blood vessel wall plays a critical role in the initiation and progression of cardiovascular diseases such as atherosclerosis which remains the leading cause of death in developed countries. Besides biochemical and molecular signals, the continual hemodynamic forces of blood flow are also important regulators of endothelial functions in pathological processes such as inflammation and wound healing. Understanding fully how cells respond to not only their biochemical but also mechanical microenvironments will allow us to better manipulate and mimic the desired cellular responses for therapeutic purposes. Our lab is dedicated to understanding mechanotransduction pathways that collectively bring about changes in endothelial functions such as apoptosis and migration.

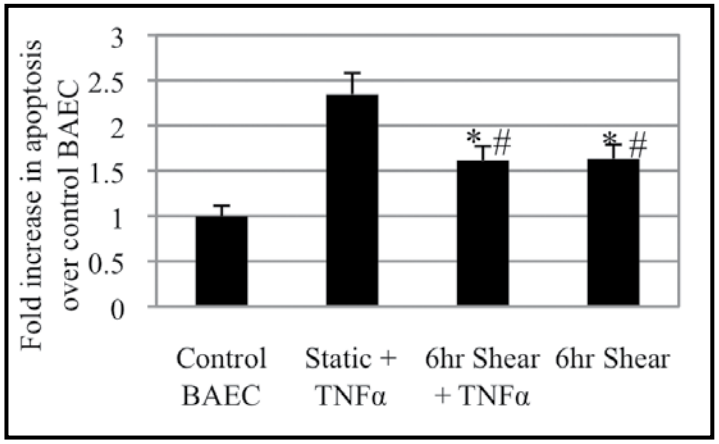

Figure 1. TUNEL apoptosis results based on flow cytometry († $P < 0.01$ vs. control, * $P < 0.05$ vs. TNFα, and # $P < 0.05$ vs. control cells).

ABOVE – The Vascular Mechanobiology Lab is led by Julie Ji, Ph.D., who has been an Assistant Professor at IUPUI since 2007. (L to R – Heather Teach, Julie Ji, Mustafa Mavi, Keith Rennier, Arman Nayebosadri.)

In endothelial cells, misdirected programmed cell death, apoptosis, can leads to pathological conditions such as inflammation, while physiological shear stress is protective against apoptosis. We found that while cytokines such as tumor necrosis factor (TNF) induces cell death, adding shear stress significantly suppressed apoptosis. Death-associated protein kinase (DAPK) is a promoter of apoptosis. Due to its location on the cytoskeleton, DAPK is potentially susceptible to mechanical stresses. We found that shear stress modulates DAPK activity in suppressing apoptosis (Figures 1), suggesting the potential crosstalk of mechanotransduction and

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Message from the Chair

Edward J. Berbari

Chancellor's Professor and Chair of Biomedical Engineering

We continue to see successes for our Biomedical Engineering Department in the form of student awards, alumni achievements, and research accomplishments of our students and faculty. Some of these accomplishments are highlighted in the newsletter as we review Dr. Julie Ji's research and some of the most recent campus awards for several of our undergraduates.

One of our major campus honors is the annual selection of the Top 100 students. Since our first graduating class in 2008 numerous students have obtained this prestigious classification. It is further narrowed to the top 10 male/female students and the top male and female student. In 2008 we had the top female student (Rachel Meyer); in 2011 the top male student (Asad Raza) and again this past year the top male student (Andrew Fraser). Additionally, a BME student was elected the president of the campus student government in 2010 and again in 2011. Currently, Andrew Fraser is the president of the Student Council for the Purdue School of Engineering and Technology. Hence our students are being recognized for their strong academic achievements and their leadership skills. These are outstanding forms of recognition for our students; we have almost begun to expect such high levels of achievement!

Despite the slow growing economy we are finding that our graduates are landing great career opportunities both within Indiana as well as across the country. Regional firms such as Cook and CRI as well as large multinational companies such GE Healthcare, Roche Diagnostics, Covance, and Boston Scientific are now the workplace home for many of our recent graduates. In addition we see a high percentage of our graduates going forward with advanced education. We ask all of you to keep us informed as your career progresses. The faculty and staff are always pleased to hear from you.

The new Science and Engineering Laboratory Building (SELB) is now under construction with completion scheduled in about 12 months. This building will provide the department with much needed wet lab instructional space as well as an expansion of our research space. This building will also house a state of the art vivarium.

The BME department had another very productive year in research with annualized funding over $2.5 million and over 50 peer reviewed journal publications, many with student co-authors. Of some note in achieving our research success is the fact that we have over 12 post-doctoral fellows and research faculty in our department. These individuals bring a wide range of expertise and accomplishment. For example, there are currently four foreign trained physicians in these roles. They not only participate in the research with their faculty mentors, but engage our students in their many research projects. All of this teamwork advances both our educational and research missions and I am very proud of their achievements.

The Class of 2012

Congratulations to our undergrad class of 2012!

BME Award Recipients for 2011-12

- *Charles H. Turner Award for Oustanding Achievement in the Senior Year:* Perez Agaba
- *Bepko Award for Outstanding Achievement in the Junior Year:* Andrew Fraser
- *Bepko Award for Outstanding Achievement in the Sophomore Year:* Christopher Hiett *and* Kelsey Lipking
- *BME Exemplary Internship Award:* Perez Agaba
- *BME Outstanding Service Award:* Andrew Fraser
- *Medtronic Outstanding Senior Design Team:* Joyce Jiang, Kelly McKenna, Amanda Meyer, *and* Sarah Phelps
- *Outstanding EDDP Student:* Kelly McKenna

STELLAR STUDENTS

ANDREW FRASER is a senior BME student and a researcher in Dr. Lin's lab where he helps create and design biomaterials that can be used as delivery devices for drugs to cells. Andrew's main research focus is to engineer tissues that can be transplanted to replace failed and diseased organs. The long term goal is for his findings to be transferred into useful technologies for the treatment of disease such as Type I Diabetes. In addition to his undergraduate study, Andrew is involved with the Engineering Student Council through Purdue University. Andrew has great interest in student leadership and helps in Introduction to Engineering courses as a teaching assistant. Among many other awards received, he was named the Top Male Student at IUPUI in April 2012. Post -graduation Andrew would like to attend an international graduate program. Outside of school, Andrew attends a local book club, enjoys spending time with his younger siblings, and plays basketball.

PEREZ AGABA, originally from Uganda, graduated with his B.S. in BME in 2012. He is currently working in Dr. Christie Orschell's lab at Indiana University Medical School where he does Oncology research as well as at the VA Hospital in Indianapolis where he analyzes dialysis data from patients. As a student athlete with the IUPUI Men's soccer team, he was voted the Summit League Scholar Athlete of the Year (2011, 2012), an ESPN 1st Team Academic All American (2010) and was named one of IUPUI's Top 10 Male Students in 2012. He has received many other awards and scholarships on top of those. Perez spent the past two summers at Yale University working on a tissue engineering based study focused on the Vinculin Association in Neutrophil Focal Adhesions. During his undergraduate program, he helped peers as a math tutor and mentor for the freshman engineering students. In the future, he hopes to attend medical school and work as a medical doctor.

Physical Environment Continued from p.1

DAPK-apoptosis pathways. We are currently further exploring the role of DAPK in endothelial apoptosis under shear, which may lead to new approaches to treatment of vascular diseases.

We are also looking at the effects of shear stress on the nucleus level, by studying the anti-inflammatory nuclear glucocorticoid receptor (GR). Normally localized primarily in the cytoplasm, GR translocates to the nucleus upon binding to an agonist (dexamethasone). We have shown that shear stress alone also activates the receptor, and we have developed a novel image analysis method based on Bayesian statistics to quantify its intracellular movement of fluorescently-tagged GR (Figures 2). Furthermore, we have observed that the nuclear lamina is not required for GR nuclear translocation, but does effect transcription regulation. We are continuing to look at the effects of shear on GR and its potential role in suppressing vascular inflammatory responses in cardiovascular diseases.

Proper endothelial wound healing is vital for maintaining vascular homeostasis and preventing pathological conditions. Our group is also looking at wound closure of endothelial cells while under shear stress since wound recovery in the endothelium must occur under in vivo hemodynamic forces of the vasculature. We are evaluating the effect of treatment with shear stress and substrate and direction-dependent differences in wound recovery. Through these projects, we continue to investigate the effect of shear stress and other mechanical stimuli on endothelial mechanotransduction.

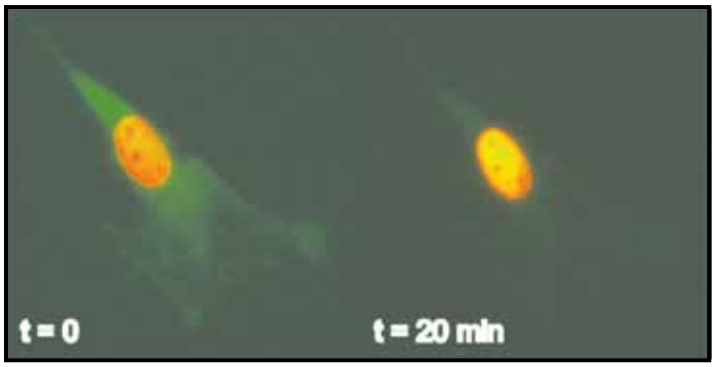

Figure 2. A cells expression RFP tagged lamin A/C and GFP-GR. Dexamethasone induction induced complete nuclear localization of GFP-GR in 20 minutes.

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723 W. Michigan St., SL 220
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Phone: 317.278.2416
Fax: 317.278.2455
E-mail: eberbari@iupui.edu

www.engr.iupui.edu/bme

BME Seminar Schedule 2012-13

9/28/2012	David Umulis Ph.D., Purdue University	Utilization of Biological Image Data to Develop, Optimize, and Test Models of Bone Morphogenetic Protein Regulation
10/19/2012	BME Students, IUPUI	Presentations of Research Work
11/30/2012	Andy Hudmon, Ph.D., IU School of Medicine	Novel Mechanisms Underlying CaMKII Substrate Selection
1/25/2013	Lilian Plotkin, Ph.D., IU School of Medicine	Connexins, Osteocyte Survival and Regulation of Osteoclastogenesis: Novel pathways with Therapeutic Potential
2/22/2013	Paul Territo, Ph.D., IU School of Medicine	Dynamic Bioluminescence Imaging: Development of a Physiological Pharmacokinetic Model of Tumor Metabolism
3/22/2013	Edward Bartlett, Ph.D., Purdue University	Measurement and Modeling of The Central Auditory Pathway in Young and Aged Rats
4/26/2013	Gudrun Schmidt, Ph.D., Purdue University	Design of Elastomeric and Adhesive Hydrogels for Tissue Engineering

Research Areas of BME Faculty

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

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

CARDIOVASCULAR ENGINEERING
Ghassan Kassab, Ph.D., *Professor*
Julie Ji, Ph.D., *Assistant Professor*
Bill Combs, MSEE, *Clinical Assoc. Professor*

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

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

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