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IUPUI - Purdue School of Engineering & Technology

THE BME NETWORK

Newsletter of the Department of Biomedical Engineering

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Visualizing Mechanotransduction: Seeing is Believing

The Na Lab (L to R – Sungsoo Na, Qiaoqiao Wan, Yu-Hui Lai)

Mechanotransduction is the process by which cells sense and respond to their physical microenvironments and convert them into biochemical signaling that affects their various functions including growth, survival, differentiation, and migration. Changes in physical microenvironments, such as magnitude and frequency of mechanical forces or stiffness and geometry of extracellular matrices, result in altered mechanotransduction signaling, and consequently lead to, or at least contribute to, physiological or pathophysiological outcomes of tissue and organ development and functions. Moderate, physiological mechanical stress, for example, decreases proteolytic activity of chondrocytes in the articular cartilage, whereas excessive mechanical stress increases the activity. In bone, application of mechanical loading accelerates bone formation and fracture healing, whereas removal of loading due to microgravity or bed rest leads to bone loss. In the cardiovascular system, laminar flow has an atheroprotective effect, while disturbed flow can develop atherosclerotic regions. In addition, stiffness of the extracellular matrix is shown to control the differentiation of mesenchymal stem cells towards the neuronal cell lineage on soft matrix and the osteogenic cell lineage on rigid matrix. Thus, understanding the molecular mechanism of mechanotransduction has important implications in human health and disease. On the molecular level, however, the mechanism by which how cells sense and transduce mechanical signals has been largely elusive. The measurement and visualization of such activities at the sub-cellular or molecular level require tools of high spatial and temporal resolution and sensitivity.

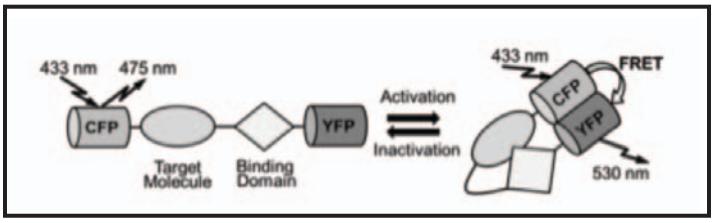

Figure 1. Structure of a FRET-based biosensor. The biosensor changes its conformation upon activation of the molecule, resulting in the changes in FRET between CFP and YFP.

Our laboratory employs fluorescence resonance energy transfer (FRET) technique together with various mechanical loading tools to monitor and manipulate target proteins in living cells. FRET is a phenomenon that occurs when two fluorescent proteins, namely donor and acceptor,

See Visualizing Mechanotransduction on p.3

Message from the Chair

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

I just had a visit from one of our 2011 graduates who was visiting the campus and representing her company for recruitment purposes. She was able to bring me up to date on several students from her class and mentioned her connections with many of our alumni. The relationships we make throughout our life can be longer lasting than ever with the addition of social networking resources. So I recently joined LinkedIn and indeed found many of our alumni inhabiting this space. I am always interested in finding out what our graduates are doing so an email or invite is quite welcome! We ask all of you to keep us informed as your career progresses. The faculty and staff are always pleased to hear from you.

This year's newsletter will highlight Dr. Sungsoo Na's research lab, a few of our alumni, and the most recent campus awards for several of our undergraduates. We recently hired a new staff member, Zachary Bart, and a new faculty member, Steven Higbee. Zach is our Academic Laboratory Supervisor. He received his BSBME from Purdue and an MSBME from our program. He will have primary responsibility for our laboratory resources used in the undergraduate curriculum. In addition, he will serve as the laboratory assistant our two sophomore courses, BME 222 and BME 241. Steve Higbee just completed his Ph.D. in BME at Rice University and is joining us a Lecturer. Along with his teaching duties he will be the Coordinator of Undergraduate Research. We plan to highlight him and this new job responsibility in our next newsletter.

The campus will open a new building which will serve as the Science and Engineering Laboratory Building (SELB) in November. Besides providing new research resources to the department we will share a new instructional wet lab with the Biology department. With this new resource our faculty members have undertaken a curriculum revision effort of a few junior level courses to take advantage of a dedicated teaching lab. Towards this end the department has purchased over $200,000 in new equipment in the past 18 months to support the undergraduate laboratories. The combination of new faculty and staff, teaching labs, and equipment demonstrates our continued dedication to the undergraduate program and will keep our graduates at the forefront of our field.

In recent years the BME department had research expenditures which averaged over $3.5 million per year. However, the government sequester had a strong impact on research efforts across the country and while our expenditures were significantly reduced this past year our publication productivity has remained high with our faculty publishing over 40 peer reviewed journal publications, most with student co-authors. In the past year we saw the promotion and tenure process succeed with Dr. Julie Ji becoming a tenured Associate Professor; Dr. Ken Yoshida becoming tenured at his current rank of Associate Professor; and Dr. Karen Alfrey being promoted to Senior Lecturer. Three of the research faculty were also promoted in rank: Jenny Susana Choy, M.D. to Associate Research Professor; Xiaomei Guo, M.D. to Associate Research Professor; and Xiao Lu, Ph.D. to Research Professor. My personal congratulations go to these faculty members for reaching new levels of academic recognition.

ALUMNI UPDATE

Muller Soliman,
M.S. BME 2012, B.S. BME 2010

I am currently in the 2-year Naval Acquisition Development Program of the Department of The Navy (DON) which supports the mission of the DON. We design, develop, and sustain the US Maritime Electronic Warfare systems. I'm a lead engineer working on maximizing the reliability of a system in the design process by creating a failure mode, effects, and criticality analysis and diagnostics design. My BME education helped me with research, software programming and data statistical analysis.

Nathan & Nichole (Leahy) Glass,
B.S. BME 2009 & B.S. BME 2010

Nathan is the Senior Product Development Engineer at InHealth Technologies located in Indianapolis, IN. The most critical tools Nathan uses from the BME Program are how to identify accurate scientific references, the importance of the balance between collaboration and individual efforts, and the value of clearly communicating ideas. They married in 2012 and Nichole is currently focusing on raising their two children: Evelyn, 18 months and William, 3 months.

[Visualizing Mechanotransduction] Continued from page 1

are in proximity (~10 nm) and the emission spectrum of the donor overlaps the excitation spectrum of the acceptor. FRET-based biosensors consist of a pair of fluorescent proteins fused together with a target molecule and a specific binding domain (Fig. 1). When the molecule of interest is at its rest (inactive) state, donor and acceptor fluorescent proteins (CFP and YFP, respectively, in the example in Fig. 1) are far apart and excitation of CFP only results in the emission of CFP. When the molecule is activated, the high affinity and interaction between the molecule and the binding domain causes conformational change of the biosensor, resulting in FRET from CFP to YFP and increase in YFP emission. Therefore, the molecular activity can be represented by the FRET changes (e.g., the emission ratio of CFP to YFP or YFP to CFP) of the FRET-based biosensor.

We are interested in signaling proteins that play an important role in cartilage development and degradation, particularly Rho family GTPases, such as RhoA, Rac1, and Cdc42. Using a FRET based RhoA biosensor together with a fluid flow system that applies shear stress to the cells, we have shown that chondrocytes exhibit shear stress magnitude-dependent RhoA activity (Fig. 2A). High shear stress (20 dyn/cm2) increases RhoA activity, whereas intermediate shear stress (5 dyn/cm2) decreases the activity. Furthermore, these two-level activities of RhoA by shear stress are closely linked to the shear stress-induced alterations in actin cytoskeleton and intracellular tension, which are essential in maintaining chondrocyte phenotype (Fig. 2B and 2C). It is expected that current developments in molecular biology and tissue engineering as well as integration of FRET imaging and mechanical loading will accelerate our understanding of cellular mechanotransduction and its linkage to physiological and pathological outcomes.

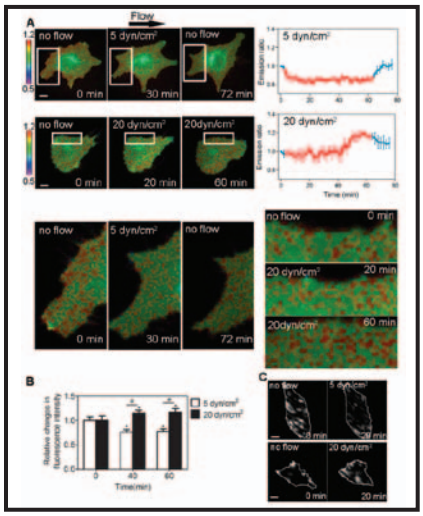

Figure 2. Shear stress-induced dynamics of RhoA activity is linked to actin cytoskeleton remodeling and intracellular tension. (A) Chondrocytes exhibit shear stress magnitude-dependent RhoA activity. (B) Relative changes in fluorescent intensity of actin cytoskeleton under 5 and 20 dy/cm2 of shear stress. (C) Changes in intracellular tension revealed by dynamic traction map in response to 5 and 20 dy/cm2 of shear stress. Scale bars, 10μm.

The Class of 2013

Congratulations to our undergrad class of 2013!

BME award recipients for 2012-13

Charles H. Turner Award for Outstanding Achievement in the Senior Year:
Andrew Fraser

Bepko Award for Outstanding Achievement in the Junior Year:
Kelsey Lipking

Bepko Award for Outstanding Achievement in the Sophomore Year:
Alycia Berman

BME Exemplary Internship Award:
Chad Harding

BME Outstanding Service Award:
Katie Wight

Medtronic Outstanding Senior Design Team: *Jimmy Corcoran, Andrew Fraser, Rachel Hale, Andrew Laird (Project: Pessary for Uterine Prolapse)*

Outstanding EDDP Student:
Daniel French

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BME Seminar Schedule 2013-14

Location: SL056

Sept. 6	Dr. Joey Wallace	IUPUI BME Department
Sept. 20		Practice presentation for students presenting at BMES
Oct. 4	Dr. Xie	IUPUI BME Department
Oct. 18		Practice presentation for students presenting at NER and Neuroscience
Nov. 1	Dr. Lin	IUPUI BME Department
Nov. 22		Practice presentation for graduating MS students
Dec. 6	BME696	Directed Project research 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*
Ghassan Kassab, Ph.D., *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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