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BioMET Now

Center for Biomedical Engineering and Technology - University of Maryland School of Medicine
in conjunction with the Fischell Department of Bioengineering, School of Engineering, University of Maryland, College Park

New Guy on the Block

With the retirement of Tim Hughes effective December 31, 2010 (see *BioMET Now*, Vol. 13, No. 6), BioMET found itself without an assistant director. The position took some time to set up with Human Resources and applications had only begun to arrive the beginning of January. The committee assigned to review applications consisted of Drs. Mervyn Monteiro and Joseph Kao, and Tim Hughes himself, as a volunteer. The committee quickly sent a short list to Dr. Lederer and he interviewed two of the final three candidates. After some quick negotiations and timely paperwork, BioMET's new Assistant Director was named. He is Brian Hockenberry, formerly Research Administrator in UMB's School of Nursing. Brian began his tenure at BioMET on February 21.

Brian received a Bachelor of Science degree in Health Policy and Administration from Pennsylvania State University and a Masters in Health Services Administration from Central Michigan University through a program located in Washington D.C. He also served in the US Army and Pennsylvania National Guard. He has a strong background in grants and contracts, and also served as the Administrative Officer for the Children's Oncology Group, a large cooperative agreement effort with the National Cancer Institute. He came to the University of Maryland School of Nursing in 2002. Brian is the proud parent of five children ranging from college age to infancy, and his wife is an emergency room Physician's Assistant in a hospital near their home in Bowie. In his spare time Brian enjoys coaching his son's lacrosse team and watching his daughter compete at various dance competitions.

Brian is thrilled to be at BioMET. "This is really a growth opportunity for me," said Brian. "I am looking forward to developing new skills and using them to help contribute to the mission of BioMET." He has also been impressed with the staff and faculty at BioMET. "I love the collaborative atmosphere. There is a real sense of camaraderie and working together." When asked how the transition was going, he was very enthusiastic. "Everyone has made coming in easier than expected.

Jami [Kasco, Business Manager], Olivia [Sterrett, HR], Pamela [Wright, Assistant to the Director], and both Mike's [McCrea, Facilities Manager, and Kelly, IT] have been here a long time and really know their jobs. Their combined knowledge and skill sets are phenomenal. Hopefully my existing skills and knowledge of the campus will compliment what is already established and help the Center grow in this new era." Brian mentioned that

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UMB



UMCP

The new UMB Strategic Plan initiative, entitled “Redefining Collaboration” has begun. BioMET Director W. Jonathan Lederer is on one of the many committees looking at various aspects of UMB’s future. BioMET faculty and staff are encouraged to participate in the town meetings and surveys that are ongoing. As a relatively new group to UMB, our perspective can be of great value in planning changes for the future.

Congratulations to Dr. Patrick Kanold of the Department of Biology and Affiliate Faculty of the Institute of Systems Research, A. James Clark School of Engineering at UMCP. The Alfred P. Sloan Foundation has named him a 2010-2011 Sloan Research Fellow. He is the only person in the state of Maryland to be so honored this year. Dr. Kanold is an active collaborator of BioMET faculty member, Dr. Joseph Kao (see below). They both work in the neurosciences.

College Park Ties

Collaboration has been and continues to be the legacy of the University of Maryland Biotechnology Institute (UMBI). BioMET faculty have always actively embraced collaboration, as much for its stimulating effect on their science as for the leverage it gives to a small group to successfully compete with larger entities. This legacy coincides nicely with the mandate given to BioMET to be a bridge between UMB and UMCP in biomedical engineering.

BioMET faculty have a long history of collaboration with UMCP, both with the UMBI faculty whose laboratories were there and are now UMCP faculty members, and with other faculty members in various scientific departments. While many of these collaborations are informal, some have resulted in some interesting research.

One ongoing collaboration is between BioMET’s Acting Associate Director, Dr. Joseph Kao, and Dr. Patrick Kanold, Department of Biology, investigating neonatal microcircuits.¹ The research was funded by a joint Seed Grant entitled “Study the brain circuitry of live animals using an inert molecule coupled with new imaging technology.” Dr. Kao also has ongoing projects with Drs. Silvia Muro and Ian White of the Fischell Department of Bioengineering. Dr. Shengyun Fang is currently collaborating with Dr. Shuwei Li, Department of Chemistry and Biochemistry and the Institute of Bioscience and Biotechnology Research, a spin-off of UMBI’s Center for Advanced Research in Biotechnology now part of the Fischell Department of Bioengineering. Dr. W. Jonathan Lederer is pursuing possible stem cell projects with Dr. John Fisher, also at Bioengineering. Drs. Muro and Fisher are past speakers at BioMET’s annual retreat.

Indeed, seminars are often the start of many collaborations. Drs. Kao, Baskakov, Fang and Lederer have all given seminars at College Park. Dr. Lederer was the Keynote speaker at last year’s Annual Fischell Festival held in honor of the department’s namesake.

Dr. Lederer is also on the Science Advisory/Formation Board for the Robert E. Fischell Institute of Biomedical Devices at College Park.

As UMCP is a teaching institution, BioMET faculty have volunteered to be involved with that aspect as well. Dr. Baskakov hosted Blake Billmyre, a student in GEM program, as a summer intern in 2008, as well as being on Blake’s advisory committee along with Dr. Kao. The internship resulted in a publication.² Dr. Kao

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Research Proposal Review Meeting

Within the last year or two, NIH has radically changed the reviewing process for research proposals, as well as the structure of the proposal itself. Not only has the number of pages been reduced from 25 to 12, but the traditional sections (Background and Significance, Preliminary Results, Experimental Design) have been either eliminated or condensed. The new NIH proposal structure consists of three sections (Significance, Innovation, Experimental Design). Preliminary Results are expected to be included in the relevant Experimental Design rationales, and Background information is to be included only for clarity. The new sections Significance and Innovation are supposed to emphasize justification for the funding and its future potential. In addition, progress reports for competitive renewals have to be within the new page limits.

In conjunction with the new structure, the reviewing process itself has been streamlined. More proposals are to be triaged and not reviewed; reviews are bulleted lists and not full critiques; and the numerical scoring system has been revamped. Reviewers and submitters are still not clear on the new process, according to BioMET faculty who act in both capacities. With the uncertain funding climate, proposal writing has taken on new significance and new strategies to increase the quality of submissions are needed.

With this in mind, BioMET Director W. Jonathan Lederer proposed that the faculty begin doing mock reviews for proposals before submitting them. This suggestion was enthusiastically supported by the faculty and the first meeting was set for February 21 to review two pending NIH R01 submissions—a competitive renewal by Dr. Mervyn Monteiro and a resubmission by Dr. Mariusz Karbowski. Draft versions of the proposals were sent around three days earlier and reviewing faculty were to use the new NIH reviewer guidelines, but add more detailed criticisms to help in rewriting the proposals before submission.

While the results of the meeting will have to wait for the actual NIH reviews to be received, Dr. Karbowski called the meeting “very helpful.”



Grants.gov is the online submission site for most government granting agencies. OER refers to NIH's Office of Extramural Research, which organizes and administers the proposal process.

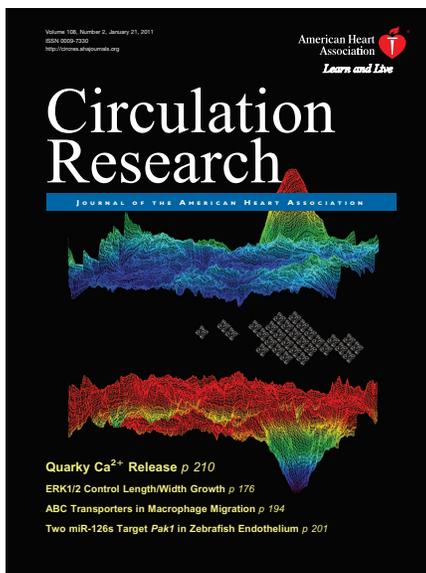
Lederer Lab Goes Viral (Sort of) Again

In the last issue, we reported that the published version of an article from the Lederer laboratory was one of the top accessed articles for the month of December. The full version came out in January, and it too went “viral” with over fourteen hundred downloads! In addition, it became the cover for the January Issue of *Circulation Research*.

Besides the honor of the cover, the article also elicited an editorial and a highlight in the same journal.

The Lederer lab is internationally known for its work on calcium signaling in heart. The article documents the reality of a previously hypothesized signaling phenomenon called a calcium quark. This signal is the smallest intracellular calcium signal, representing the opening of just one or a small group of 2-3 calcium channels. Conclusive data as to their existence had remained elusive. Since calcium signaling underlies heart rhythm, understanding calcium signaling mechanisms that control that rhythm have a significant impact on heart health, as arrhythmias of many types (abnormal heart rhythms) are a common cause of heart failure.

Brochet, Didier. X.P., Xie, Wenjun., Yang, Dongmei., Cheng, Heping., Lederer, W. Jonathan. (2011) Quarky Calcium Release in the Heart. *Circulation Research*, 108:210-218.



BioMET Happenings

Publications

Gonzalez-Montalban N, Makarava N, Ostapchenko VG, Savtchenk R, Alexeeva I, Rohwer RG, **Baskakov IV**. Highly efficient protein misfolding cyclic amplification. *PLoS Pathog*. 2011 Feb 10;7(2):e1001277.

Xu S, Peng G, Wang Y, Fang S, **Karbowksi M**. The AAA-ATPase p97 is essential for outer mitochondrial membrane protein turnover. *Mol Biol Cell*. 2011 Feb;22(3):291-300.

Xu X, Vogel BE. A secreted protein promotes cleavage furrow maturation during cytokinesis. *Curr Biol*. 2011 Jan 25;21(2):114-119.

Brochet DX, Xie W, Yang D, Cheng H, **Lederer WJ**. Quarky calcium release in the heart. *Circ Res*. 2011 Jan 21;108(2):210-218.

Mears JA, Lackner LL, **Fang S**, Ingerman E, Nunnari J, Hinshaw JE. Conformational changes in Dnm1 support a contractile mechanism for mitochondrial fission. *Nat Struct Mol Biol*. 2011 Jan;18(1):20-26.

Neutzner A, Neutzner M, Benischke AS, Ryu SW, Frank S, Youle RJ, **Karbowksi M**. A Systematic Search for Endoplasmic Reticulum (ER) Membrane-associated RING Finger Proteins Identifies Nixin/ZNRF4 as a Regulator of Calnexin Stability and ER Homeostasis. *J Biol Chem*. Epub 2011 Jan 4.

Grants and Contracts

Dr. W. Jonathan Lederer, 1/1/2011, NIH, NHLBI, "Stretch-Dependent Calcium Signaling in Heart," \$325,000, yr 1 of 4.

Talks and Travels

Dr. W. Jonathan Lederer, Annual Meeting, Outside Advisory Committee, Virtual Cell Research Resource, University of Connecticut Medical Center, 1/5/2011

Dr. Ilia Baskakov, invited talk "Mammalian prions: from protein to disease", Program in the Biology of Model Systems, University of Maryland School of Medicine, Columbus Center, 1/26/2011.

Dr. Shengyun Fang, invited talk, "Protein quality control in the endoplasmic reticulum". Department of Chemistry and Biochemistry, University of Maryland College Park, 2/15/2011.

Dr. W. Jonathan Lederer, Session Speaker, "Stretch-dependent Ca²⁺ signaling in rat and mouse cardiac ventricular myocytes," *Molecular Cardiology: Disease Mechanisms and Experimental Therapeutics*, Keystone Meeting, Keystone, CO, 2/22/2011-2/27/2011.

College Park, continued

has been on a number of College Park thesis advisory committees, in part because of his regular collaborations there. Dr. Shengyun Fang is a member of the MEES (Marine Estuarine Environmental Sciences) Graduate program.

BioMET faculty are expected to continue to collaborate with their counterparts at College Park, and to expand those collaborations as much as possible.

¹Zhao C, Kao JP, Kanold PO. Functional excitatory microcircuits in neonatal cortex connect thalamus and layer 4. *J Neurosci*. 2009 Dec 9;29(49):15479-88.

²Yongjin Zou, John Pisciotta, R Blake Billmyre and Ilia V Baskakov. Photosynthetic microbial fuel cells with positive light response. *Biotechnol Bioeng* 2009 104(5):939-46.

Xu and Vogel Research Highlighted

In the February 8, 2011 issue of *Current Biology*, a report entitled "Cytokinesis: Thinking Outside the Cell," highlighted an article in the same issue by BioMET faculty member, Dr. Xuehong Xu and Bruce Vogel on an unexpected role for an old protein. The protein is hemicentin, an extracellular matrix protein that has been the focus of Dr. Vogel's research for over a decade. Extracellular matrix proteins are generally found outside the cell and are what keep cells stuck together to form tissues, with some other functions in cell migration and signal transduction. Drs. Xu and Vogel found that it also plays a role in cytokinesis, that is cell division. The work began with studies in the model organism, *C. elegans*. This humble round worm has been extremely useful in teasing out components of basic biological processes. In this case, hemicentin has mammalian counterparts, several of which have been implicated in diseases such as macular degeneration.

In this study, hemicentin was found to have a role in maintaining the cell membrane furrow that develops after the nucleus has divided. The furrow will eventually deepen and fuse, pinching the cytoplasm into halves that eventually yield two daughter cells. When a defect in the mammalian version of hemicentin was introduced into transgenic mice, embryogenesis was halted by the 4-cell stage. Instead of complete daughter cells being formed, the nucleus divided correctly, but incomplete or abnormal cytoplasmic division produced multinucleated cells. Given the fundamental and critical nature of cell division, this study opens up a new area of study for extracellular matrix proteins, one that may yield new insight into diseases defects in cell division and infertility.

The paper has been given an "exceptional" rating (FFa12) on the Faculty of 1000 web site.

X. Xu and B.E. Vogel, A secreted protein promotes cleavage furrow maturation during cytokinesis. *Current Biology* 21 (2011), pp. 114-119.

New Guy, continued

his transition would not have been as successful if it wasn't for the generous amount of time spent with Tim Hughes in the weeks leading up to his start date. "I owe Tim a world of thanks. The investment of time and insight from Tim and the others have made the transition easier and much more manageable; more than I ever thought possible."

Besides meeting his new colleagues and staff, Brian also got a tour of the building and a treasure trove of stories from long-time Facilities Manger, Mike McCrea,

BioMET Director, Dr. W. Jonathan Lederer, is just as enthusiastic about Brian. "We have been very fortunate in finding Brian. Tim's shoes were going to be hard to fill, but Brian is doing an outstanding job in doing just that."

Welcome, Brian.