Spring 2017

Musculoskeletal Messenger

University of Pennsylvania Penn Center for Musculoskeletal Disorders

Inside this issue:

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for
Musculoskeletal Disorders
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If you have any news or information that you would like included in the next issue of this newsletter, please email us at:

pcmd@pennmedicine.upenn.edu

Remember to include reference to support from the Center in your abstracts and publications.

Cite Grant NIH/NIAMS P30AR069619 from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases of the NIH.

Registration is now open for the 14th Annual PCMD Scientific Symposium —November 15, 2017

Preparations are underway for the 14th Annual Penn Center for Musculoskeletal Disorders Scientific Symposium in the BRB Auditorium/Lobby to be held on November 15, 2017.

This year's keynote speaker will be Kyriacos A. Athanasiou, Ph.D. Distinguished Professor, Department of Biomedical Engineering, University of California, Irvine. His lecture is titled "Toward Bioengineering Translation".

The day will begin with registration and poster set up starting at 8:00am followed by scientific presentations from new Center members, Affiliate members, and PCMD Pilot Grant recipients. We will also have a session on basic research translation to the clinic and market.

The symposium will also include lunch and a judged poster session with prizes awarded in four categories.

The day will conclude with a reception from 4:45-6pm in the BRB lobby.

Please register (no charge, but registration is required) by going to: https://www.med.upenn.edu/pcmd/2017-annual-symposium.html

PCMD Pilot and Feasibility Grant Program Opportunity

The Penn Center for Musculoskeletal Disorders (PCMD) will continue to enhance the research productivity of, and provide critical resources and programs to, investigators to address multidisciplinary research strategies for musculoskeletal problems. The PCMD is once again accepting applications for its Pilot and Feasibility Grant Program. Submissions should be related to musculoskeletal tissue injury and repair which is the broad focus of the Center and Grants are only eligible for Full Members (if you are not a full member but would like to become one, please visit the "Become a Member" page of the PCMD website click the link below. https://www.med.upenn.edu/pcmd/become-a-member.html

Pilot grants will be due on February 22, 2018 with a planned start date of July 1, 2018 and we are expecting to award 3 grants in this round. *It is expected that one of these awards will go to a CHOP-based faculty member.*

For more information on our Cores and Center in general, please see our website at http://www.med.upenn.edu/pcmd

Pilot Grant Deadline

02/22/2018

Research Updates from PCMD Members

Mary Mullins, PhD

Pathogenic signaling mechanism of the Fibrodysplasia Ossificans Progressiva (FOP) altered receptor using a zebrafish model

FOP is a rare genetic disorder characterized by extra-skeletal ossification. FOP is caused by gain-of-function mutations in the Type I BMP receptor gene, ACVR1, which result in over-activation of Bone Morphogenetic Protein (BMP) signaling. However the mechanism by which the FOP mutation causes disease is still unknown. Zebrafish have been used extensively in the study of BMP signaling and more recently have been recognized as a model of human disease. In collaboration with Drs. Eileen Shore and Fred Kaplan of the Department of Orthopaedic Surgery, we use zebrafish development as a method to determine the aberrant FOP signaling mechanism and develop potential therapeutics. We tested the activity of the human FOP-causing ACVR1 R206H, G328R, G328E, and G328W mutations in our zebrafish assays. We found that all FOP mutant receptors cause BMP signaling overactivity in wild-type embryos, embryos defective for endogenous Acvr1 function, as well as embryos lacking BMP ligand. Results show that the human FOP receptors signal independently of BMP ligand and the endogenous Acvr1 receptor. We are now testing if BMP and other TGFb ligands enhance activity of these mutant receptors, as well as examining the roles of the Type II and other Type I BMP receptors in this aberrant signaling mechanism.

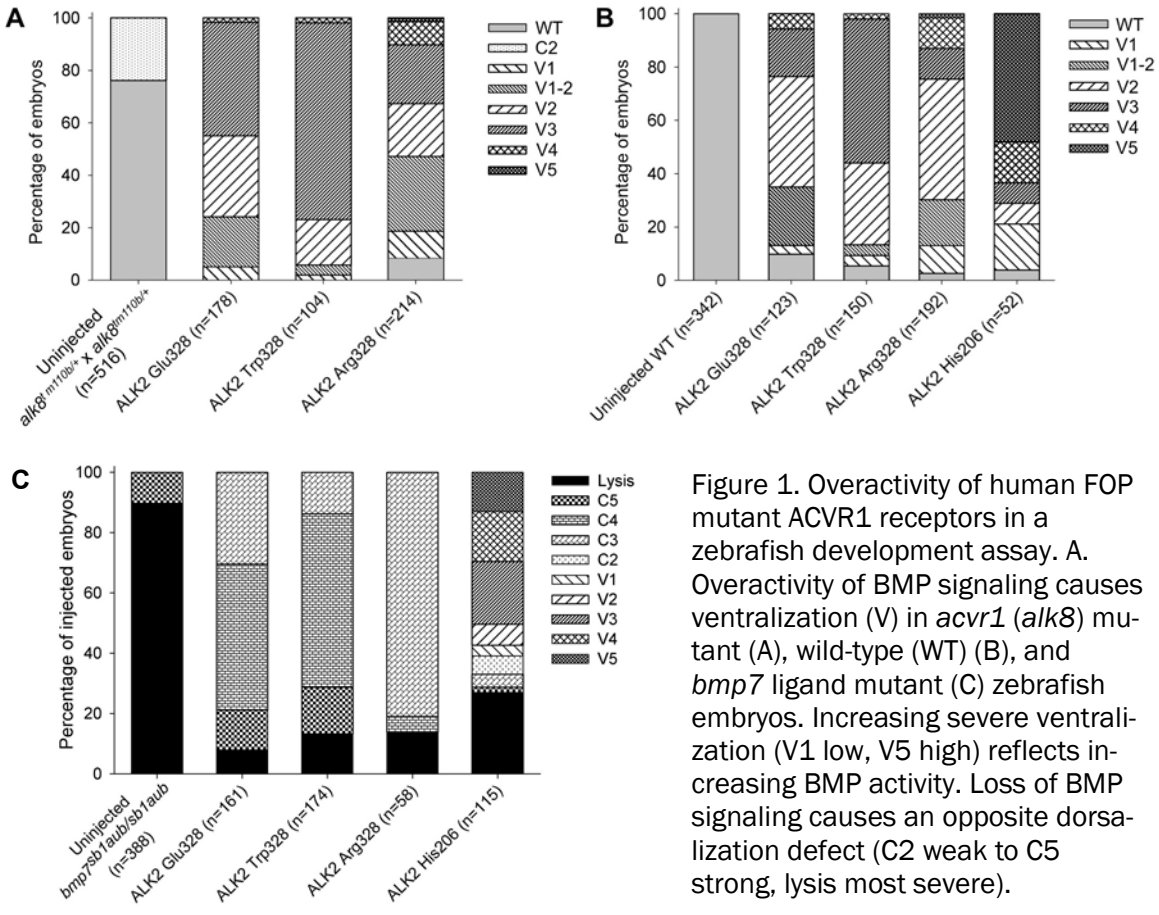
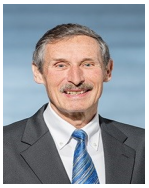


Figure 1. Overactivity of human FOP mutant ACVR1 receptors in a zebrafish development assay. A. Overactivity of BMP signaling causes ventralization (V) in *acvr1* (*alk8*) mutant (A), wild-type (WT) (B), and *bmp7* ligand mutant (C) zebrafish embryos. Increasing severe ventralization (V1 low, V5 high) reflects increasing BMP activity. Loss of BMP signaling causes an opposite dorsalization defect (C2 weak to C5 strong, lysis most severe).

Acknowledgement: Studies performed by Dr. Bettina Mucha-LeNy and supported by a T32 Postdoctoral Research Training Grant (NIH/NIGMS "Medical Genetics Research Training") to BML and a Cali Developmental Grant to MM.

In the News!



Thank you to Felix Wehrli, Ph.D.

The Penn Center for Musculoskeletal Disorders (PCMD) and its members would like to express our thanks and our sincere appreciation to Dr. Felix Wehrli for his many years of service and dedication as director of the MicroCT Imaging Core and previous Imaging Core. Thank you Felix for all your efforts on our behalf!!

Orthopaedic Surgery New Ph.D. Faculty Recruited

Please welcome Joel Boerckel, PhD who joined Penn as Assistant Professor of Orthopaedic Surgery and Bioengineering in August 2017. Dr. Boerckel obtained his PhD from the Georgia Institute of Technology in mechanical engineering, followed by a Ruth L. Kirchstein postdoctoral fellowship in cell and developmental biology at the Cleveland Clinic. Dr. Boerckel's laboratory studies mechanobiology in the contexts of development and tissue regeneration. He applies reverse engineering approaches to understand how mechanical forces influence morphogenesis and designs approaches to recapitulate these processes for tissue engineering.

If you would like to contact Dr. Boerckel, please email him at boerckel@pennmedicine.upenn.edu

New MicroCT Core Director—Sherry Liu, Ph.D.

X. Sherry Liu, Ph.D received her PhD in Biomedical Engineering from Columbia University in 2007 and completed her postdoc training in the Endocrinology Division at Columbia University Medical Center. In 2012, Dr. Liu joined the department of Orthopaedic Surgery and Bioengineering at the University of Pennsylvania as an assistant professor. She has been the associate director of the PCMD Imaging core since 2013. Dr. Liu's current research focuses on in vivo imaging of bone remodeling, mechanisms of and anabolic effect of parathyroid hormone, and influence of female reproduction on bone quality. Dr. Liu has published more than 70 peer-reviewed journal articles. She is a recipient of a new investigator recognition award from the Orthopaedic Research Society (2009), Harold Frost Young Investigator Award (2009) and John Haddad Young Investigator Award (2012) from the American Society of Bone and Mineral Research, and Nan SF CAREER award (2017).

Rob Mauck, Ph.D. awarded the Berton Rahn Research Award

The Berton Rahn Research Award was presented to Rob Mauck, PhD on June 30th, 2017 at the TERMINS European Chapter Meeting. The Berton Rahn Research Award was established in recognition of Berton Rahn's immense contribution to the AO Foundation. The award is chosen from submissions from AO Foundation's start up grants (including consortia and clinical division mini grants and regional grants) from the AO Foundation's Clinical Divisions and Institutes and is decided within the AO Research Institute Davos' Advisory Committee (ARI AC) and approved at the AO Foundation's R&D platform.

Congratulations to Rob!

McKay Orthopaedic Research Laboratory Seeking Endowed Chair in Musculoskeletal Research

The Department of Orthopaedic Surgery at the Perelman School of Medicine, University of Pennsylvania seeks candidates for a newly established Endowed Professorship in Orthopedic Surgery, with appointment at the Full Professor level. Responsibilities will include maintaining and expanding an independent, extramurally-funded research program in the McKay Laboratory for Orthopaedic Surgery Research, as well as collaborating with other research and clinical faculty in Orthopaedic Surgery, across the Penn Center for Musculoskeletal Disorders, and elsewhere in the Penn community. The successful applicant will have an international reputation in musculoskeletal education and research in areas such as: orthopedic biomechanics at the organismal and/or tissue level, soft tissue bioengineering, developmental biology, musculoskeletal molecular and/or stem cell biology, wound repair and inflammation, or drug discovery and molecular biophysics as it applies to the musculo-

PCMD FUNDS AVAILABLE: Summary Statement Driven Funding Request

If you have a recent summary statement from an NIH grant (eligible NIH mechanisms include all "R" grants such as R03, R21 and R01 and "K" grants such as K01, K08 on their first submission—please inquire regarding eligibility of other proposal mechanisms) which requires you to run additional experiments, gather additional data, provide feasibility for an approach, or similar, we can provide small funds ($1,000-$15,000) with a very short turn-around time in order to allow you to complete these experiments and resubmit your proposal with the best chance of success. Requests for funding will be evaluated on a rolling basis and priority will be given to Assistant Professors with encouraging initial review priority scores better than ~30-35%. The format of the "Summary Statement Driven Funding Request", which is limited to **one page**, is as follows:

- Name of PI (must be a PCMD full member)
- Title of Project Request
- Specific Purpose of Request with Stated Outcome/Goal Referring Explicitly to the Summary Statement for Justification
- Research Design and Methods
- Budget with Brief Justification

Funding through this mechanism is available by submitting the one page proposal along with the summary statement to pcmd@pennmedicine.upenn.edu

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U.S. Department of Health and Human Services

Supported by the National Institutes of Health

NIAMS National Institute of Arthritis and Musculoskeletal and Skin Diseases

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Penn Center for Musculoskeletal Disorders Temporary Move Is Complete!

We are excited to announce that the move of the PCMD and the McKay Research Laboratory is complete! The center is temporarily housed on the ground and first floor of Stemmler Hall while construction is being done on the permanent space. The anticipated completion of the permanent space to be summer/fall of 2018 at that time we will move the third floor and occupy more than 18,000 square feet. Note that email and website information will remain the same. The Biomechanics, Histology and MicroCT Cores are fully functional.

Please direct any questions or concerns about the Cores during the move to the Core Directors.

Upcoming Events

PCMD Visiting Professorship Series Winter 2017/Spring 2018

Tuesday, September 12, 2017 1:30-2:30pm, CRB Austrian Auditorium
"Cartilage Repair and Osteoarthritis in Genetic Mouse Models"
Linda Sandell, PhD
Mildred B. Simon Research Professor, Director of Research
Co-Director, Center of Musculoskeletal Research,
Washington University

Tuesday, October 24, 2017 1:30-2:30pm, CRB Austrian Auditorium
"How can we improve translation of pre-clinical osteoarthritis research to patients?"
Christopher Little, BVMS, PhD
Director, Raymond Purves Bone & Joint Research Laboratories
Kolling Institute of Bone and Joint Research
University of Sydney

Annual Scientific Symposium
Wednesday, November 15, 2017 8am-6:30pm/BRB Auditorium
"Toward Bioengineering Translation"
Kyriacos A. Athanasiou, Ph.D., Distinguished Professor of Biomedical Engineering
University of California, Irvine

Tuesday, December 5, 2017, 1:30pm – 2:30pm, CRB Austrian Auditorium
"Osteocytes and bone remodeling: They're just dying to do the job"
Mitchell B. Schaffler, Ph.D.
Wallace Coulter Distinguished Professor and Chairman of Biomedical Engineering
The City College of New York

Tuesday, January 16, 2018, 1:30pm – 2:30pm, CRB Austrian Auditorium
"Parathyroid hormone and related peptides signaling to the nucleus of osteoblasts"
Nicola C. Partridge, Ph.D.
Professor and Chair
Departments of Medicine, Biochemistry & Molecular Pharmacology, & Basic Science & Craniofacial Biology, College of Dentistry
New York University School of Medicine

Tuesday, February 13, 2018, 1:30pm – 2:30pm, CRB Austrian Auditorium
"Notch Signaling and the Skeleton"
Ernesto Canalis, M.D.
Professor of Orthopaedic Surgery and Medicine, Director of Center for Skeletal Research
University of Connecticut

Tuesday, March 27, 2018, 1:30pm – 2:30pm, CRB Austrian Auditorium
"Modular inductive high-density cell culture systems for engineering complex tissues."
Eben Alsberg, Ph.D.
Professor of Biomedical Engineering and Orthopaedic Surgery
Director of ASCENT Lab
Case Western Reserve University

Tuesday, April 2018—TBD

Tuesday, May 2018—TBD