



Musculoskeletal Messenger



Inside this issue:

Research Updates PMCD Members	2
In the News Histology Core Update Look back symposium PCMD Funds Available	3
Upcoming events	4

Penn Center for Musculoskeletal Disorders

Congratulations to the PCMD on 5 more years!

We are proud to announce that the Penn Center for Musculoskeletal Disorders was renewed for another five years by the National Institute of Arthritis, Musculoskeletal, and Skin Diseases (NIAMS) of the National Institutes of Health (NIH). The additional \$4 million in funding will continue the center's investigations into all types of musculoskeletal tissue injury and repair. Operating since 2006, it is the longest-running NIH-sponsored musculoskeletal research center in the United States. Since its start, the Penn Center for Musculoskeletal Disorders' research has delved into the fundamental understandings of the cause, development, diagnosis, treatment, and prevention of a spectrum of conditions, ranging from osteoporosis to rotator cuff tears. Today, the Penn Center for Musculoskeletal Disorders has 204 faculty members, 76 more than it had the last time the grant was renewed, five years ago. Five different schools at Penn participate, including the Perelman School of Medicine, the School of Engineering and Applied Sciences, the School of Den-

tal Medicine, the School of Veterinary Medicine, and the School of Arts and Sciences. And members of the center have \$169 million in annual extramural funding, an increase from \$105 million just five years ago.

Much of the focus in this round of funding will address developing a deep bank of researchers and infrastructure for continued high-level research. The center has three specific aims in its mission made possible by the new grant:

- To provide innovation within key areas that cross disciplines, such as microCT imaging, Biomechanics, and Histology
- To provide a grant program for pilot of new ideas and collaborations before seeking outside funding
- Development of educational programs spanning tissue types and research approaches so that investigators can learn from leaders in the field and each other

Penn Center
for
Musculoskeletal Disorders
University of Pennsylvania
Stemmler Hall, 3rd floor
3450 Hamilton Walk
Philadelphia, PA 19104-6081

Phone: 215-898-8653
Fax: 215-573-2133
www.med.upenn.edu/pcmd

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.

2020 PCMD Pilot and Feasibility Grant Recipients Announced

The Penn Center for Musculoskeletal Disorders Pilot and Feasibility Grant Program has awarded three investigators with one year of funding for their pilot grant projects with a start date of September 1, 2021.

Christop Thaiss, Ph.D. will receive funding for his grant titled "Microbiome Control of Musculoskeletal Physiology"

Melike Lakadamyaki, Ph.D. will receive funding for her grant titled "Chromatin Structural Regulation of Chondrocyte Fate in Cell Therapy"

One more award to be announced (awaiting NIH approvals).

Research Update from PCMD Members

Ernestina Schipani, M.D., Ph.D.

Hypoxia and Mitochondria in Skeletal Development, Disease and Regeneration

Dr. Schipani laboratory studies the role of hypoxia-driven pathways and mitochondria metabolism in skeletal development with the overall goal of unveiling both novel aspects of the cellular adaptation to hypoxia and new avenues for treating cartilage and bone diseases.

In particular, the team has established that the transcription factor HIF1 is a survival and differentiation factor for growth plate chondrocytes during fetal development, and suppression of mitochondrial respiration mediates those functions. They are now further investigating the cross-talks between hypoxia-driven pathways and mitochondrial respiration during skeletal development. Along those lines, the team has recently shown that loss of HIF1 in the presomitic mesoderm impairs somitogenesis and causes spine and rib malformations that closely mimic those observed in patients with Jarcho-Levin Syndrome, a rare form of spondylothoracic dysplasia. They are now studying whether the impairment of somitogenesis secondary to loss of HIF1 is due to dysregulation of mitochondrial respiration in the presomitic mesoderm.

The Schipani laboratory has also demonstrated that loss of the transcription factor HIF2 in osteoblastic cells increases bone mass by augmenting bone formation. The

laboratory is now investigating whether pharmacological inhibition of HIF2 phenocopies the genetic experiment. Inhibiting HIF2 could represent a therapeutic approach for treating low bone mass observed in chronic diseases, osteoporosis, or aging. Additionally, they are using unbiased approaches to establish how the loss of osteoblastic HIF2 promotes bone formation.

Lastly, the laboratory is studying the role of the hypoxia-driven pathways in cartilage regeneration and in the development of fibroproliferative lesions of the soft tissue.



Figure legend: Staining of a fetal growth plate with the marker of hypoxia EF5 (Genes Dev. 2001 Nov 1;15 (21):2865-76)

Josh R. Baxter, Ph.D.

Leveraging Mechanical Loads to Improve Muscle-Tendon Healing After Achilles Tendon Injuries

Effective physical rehabilitation is critical for alleviating symptoms and restoring patient mobility after Achilles tendon injuries. Our group uses preclinical models, musculoskeletal simulations, and observational clinical studies to identify how mechanical loading can be personalized to promote healing and accelerate return to activity. To maximize our impact on clinical care, we are studying two different Achilles tendon injuries: ruptures and tendinopathy. We recently found that Achilles tendon ruptures stimulate rapid - and sometimes permanent - structural changes in the calf muscles that explain functional deficits in both patients and small animals. We are now experimentally determining the loading profiles that promote tendon healing while preserving muscle quality. Unlike tendon ruptures that are typically acute injuries, Achilles tendinopathy is a chronic and painful tendon pathology that limits function. We are monitoring Achilles tendon loading in a large cohort of patients with tendinopathy to identify different tendon loading profiles that explain improvements in tendon structure, pain, and patient outcomes using advanced statistical modeling. Once we determine what loading profile has the greatest potential for clinical

care, we will test the clinical effectiveness of personalized rehabilitation to treat Achilles tendon injuries (Figure), which we believe will vertically advance clinical care by equitably and effectively delivering rehabilitative care to Penn Medicine patients.



Figure Caption: Personalized rehabilitation will leverage tendon status and patient factors to guide care. Our group's advances in leveraging wearable sensors to monitor Achilles tendon loading are now being used to monitor how patients load their tendons throughout rehabilitation. In addition to determining the tendon loading profiles that promote healing, we are also determining ultrasound imaging biomarkers that quantify tendon damage and exploring the impacts of sex hormones on tendon healing. By integrating these important tools and patient factors, we are exploring techniques to deliver equitable and effective rehabilitative care to Penn Medicine patients.

Acknowledgments: Our work is supported by the PCMD pilot award program (P30AR069619), NIH/NIAMS (K01AR075877 & R01AR078898), and the American Orthopaedic Foot & Ankle Society.

In the News!

CORES UPDATES

Histology Core Updates

The Histology Core continues to provide an expansive range of musculoskeletal histology services to members of the Penn community and those from nearby institutions. We are pleased to report that all core services have returned to their pre-pandemic levels, with capacity restrictions on self-service users lifted. Visitors to the core must continue to follow University guidelines for covid-safe work practices, as outlined on the core website. We would like to remind current and prospective users to take advantage of our popular protocol development service, where we will work with you at no charge to optimize techniques for new tissue types and applications.

We are pleased to announce that our fall learning lunch entitled “Tips and Tricks for Top Quality Musculoskeletal Histology” will be held virtually on Thursday October 28th at 12pm. Content will include expert tips for every step of the MSK histology process, from fixation, to processing, sectioning and staining, with ample time for questions and discussion. <https://bluejeans.com/4876705489>

Looking Back on the Virtual 2020 PCMD Annual Scientific Symposium

We are pleased that the 17th Annual Penn Center for Musculoskeletal Disorders Scientific Symposium was a great success despite being held virtually due to COVID restrictions. The symposium was held on Wednesday, November 18, 2020.



The keynote speaker, Richard L. Lieber, PhD from Northwestern University gave a well received lecture titled “*Intraoperative And Laboratory Studies Of Human Muscle Contractures*”. Symposium attendees enjoyed scientific presentations from new Center members Drs. Jenny Bencardino and Anna Massie; Affiliate members Drs.

Ben Binder-Markey from Drexel University and Liyun Wang from the University of Delaware. In addition to the above, Dr. Joel Boerckel gave a presentation on his Pilot Grant

titled “Mechanobiology Of Bone Development And Repair”. While the symposium was virtual, attendees had the opportunity to view more than 30 posters and to discuss in breakout sessions. Though we did not have poster prizes, all submissions were winners. Please browse the Symposium [booklet](#) and [posters](#) that were submitted.

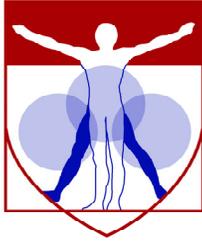
With the announcement of 5 more years for the Penn Center for Musculoskeletal Disorders Center, we are writing to let you know that we are planning to hold the next Symposium in late May or early June of 2022 with hopes that we can have an in person symposium (no symposium this fall). Stay tuned for more information on the Spring symposium.

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 to pcmd@penncardiology.upenn.edu



PENN
CENTER for
MUSCULOSKELETAL
DISORDERS

Penn Center for Musculoskeletal Disorders
University of Pennsylvania
3rd Fl Stemmler Hall, 3450 Hamilton Walk
Philadelphia, PA 19104-6081

Phone: 215-898-8653
Fax: 215-573-2133
www.med.upenn.edu/pcmd

If you have any news or information that you would like included in the next issue of the Musculoskeletal Messenger newsletter, please email the information to:

pcmd@pennteam.upenn.edu

Supported by the

**National
Institutes
of Health**



U.S. Department of Health
and Human Services



NIAMS
National Institute of Arthritis and
Musculoskeletal and Skin Diseases

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. Support has also been provided by the Perelman School of Medicine at the University of Pennsylvania.

PCMD Visiting Professorship Series

**Tuesday, September 14, 2021,
1:30pm-2:30pm Virtual
(Co-Sponsored by IRM)**

"Biomanufacturing, Biomaterials and Biomechanics for Improved Treatment of Volumetric Muscle Loss Injuries"

George Christ, Ph.D., Professor of Biomedical Engineering and Orthopaedic Surgery

Mary Muilenburg Stamp Professor of Orthopaedic Research
Director of Basic and Translational Research in Orthopaedic Surgery
University of Virginia

**Tuesday, October 12, 2021, 1:30pm-
2:30pm Virtual
(Co-Sponsored by IRM)**

"Skeletal muscle postnatal growth and regenerative decline with age"

Joe V. Chakkalakal, Ph.D., Dean's Associate Professor of Pharmacology and Physiology, University Rochester Medical Center

**Tuesday, November 9, 2021, 1:30pm
– 2:30pm Virtual**

"Pharmacological approaches for manipulating bone quality and mechanics"

Matthew R. Allen, Ph.D., Assistant Dean for Faculty Affairs and Professional Development; Associate Professor of Anatomy & Cell Biology
Indiana University School of Medicine

**Tuesday, December 7, 2021, 1:30pm-
2:30pm Virtual
(Co-Sponsored by IRM)**

"Combining heat, light, and sound based biofabrications to address musculoskeletal tissue engineering challenges"

Yunzhi Peter Yang, Ph.D., Professor of Orthopaedic Surgery, Stanford University

Looking forward to in person seminars beginning in 2022!

**Tuesday, January 25, 2022, 1:30pm
– 2:30pm, CRB Austrian Auditorium**

"Advances in Regenerating Musculoskeletal Tissues"

Warren Grayson, Ph.D., Professor of Biomedical Engineering and Director, Laboratory for Craniofacial and Orthopaedic Tissue Engineering, Johns Hopkins

Tuesday, February 2022 Stay tuned

**Tuesday, March 22, 2022, 1:30pm –
2:30pm, CRB Austrian Auditorium**

"Hypoxia and the Skeleton"

Clare Yellowley, Ph.D., Professor of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine
University of California, Davis

Tuesday, April 2022 Stay tuned

Tuesday, May 2022 Stay tuned

Tuesday, June 2022 Stay tuned