Penn Center for Musculoskeletal Disorders awarded $4 million to continue research

Congratulations the Penn Center for Musculoskeletal Disorders in the Perelman School of Medicine at the University of Pennsylvania was awarded a five-year, $4 million grant from the National Institutes of Health to continue its research on musculoskeletal injury and repair.

The Center conducts investigations in many areas of musculoskeletal biology and medicine: bones, muscles, tendons, ligaments, cartilage and discs. The funding will support research aimed at improving the prevention, diagnosis and treatment of conditions such as osteoporosis, osteoarthritis, low back pain and rotator cuff tears.

Penn is one of only five institutions nationally to receive funding for a Musculoskeletal Center and is already the longest running of these Centers nationally. The Penn Center began its NIH funding in 2006.

According to the NIH review panel, the Center features “a strong leadership team and well-organized administrative structure; state-of-the-art technologies and an exceptional education and enrichment program. Furthermore, the reviewers consider the overall environment and the institutional commitment to be outstanding.” Additionally, they cite the “high level of success in operation and productivity of the existing center over the past ten years.” They concluded that “this is an exceptional application with high impact to the field of musculoskeletal research.”

Looking Forward to the 2016 PCMD Annual Scientific Symposium — November 9, 2016

Preparations are underway for the 13th Annual Penn Center for Musculoskeletal Disorders Scientific Symposium in the BRB Auditorium/Lobby to be held on November 9, 2016.

This year’s keynote speaker will be Matthew Warman, M.D. from Harvard Medical School, Harriet M. Peabody Professor of Orthopaedic Surgery, Director, Orthopaedic Research Laboratories at Boston Children’s Hospital. His lecture is titled “Strategies for improving bone properties in patients with Osteogenesis Imperfecta.”

The day will begin at 9am with registration and poster set-up followed by scientific presentations from new Center Full and Affiliate members and PCMD Pilot Grant recipients.

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 4:00-5:30pm in the BRB lobby. Registration is free but required.

To register please visit the PCMD website at https://www.med.upenn.edu/pcmd/2016-annual-symposium.html

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

Cite Grant NIH/NIAMS P30AR050950 from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases of the NIH.
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We are grateful to the NIH and the National Institute of Arthritis and Musculoskeletal and Skin Diseases Special Emphasis Panel for this important funding,” said Louis J. Soslowsky, the Fairhill Professor in the department of orthopaedic surgery and founding director of Penn’s Center. “Whether through injury, work, sports or intrinsic bodily features, millions of Americans are affected by musculoskeletal disorders. The resulting pain and reduction in quality of life affect families, friends and co-workers, as well as the sufferers themselves. These trends will grow as the baby-boom generation ages and people live longer with chronic conditions. The Center brings together Penn’s globally recognized experts to expand our research and understanding of these debilitating afflictions.”

Penn’s Musculoskeletal Center will provide funds for three cores of musculoskeletal research:

- Micro-computed Tomography Imaging Core, which offers a wide range of imaging approaches to evaluate musculoskeletal tissue injury and repair. (Micro-CT is akin to 3-D x-ray imaging on a small scale with extremely increased resolution.)
- Biomechanics Core, which develops and provides a large array of biomechanical approaches to evaluate musculoskeletal tissue injury and repair.
- Histology Core, which uses and develops a wide range of approaches for the microscopic study of the structure, composition and function of tissues and bones.

In addition to Dr. Soslowsky, other investigators participating in the grant include Maurizio Pacifici, Felix Wehrli, X. Sherry Liu, Robert L Mauck and Robert Pignolo. The Center has 128 faculty members, 112 from five Penn schools and 16 from local institutions.

“This new funding will allow the rich collaborations that have been occurring at the Center over its ten-year history to expand and flourish,” Dr. Soslowsky said. “We will continue to work diligently on behalf of the many millions of people worldwide with musculoskeletal disorders.”

2016 PCMD Pilot and Feasibility Grant Recipients Announced

The Penn Center for Musculoskeletal Disorders Pilot and Feasibility Grant Program has awarded four investigators with one year of funding for their pilot grant projects with a start date of July 1, 2016.

Joseph Baur, Ph.D., Assistant Professor of Physiology Institute for Diabetes, Obesity and Metabolism, “Targeting NAD metabolism in muscular dystrophy”

Yongwon Choi, Ph.D., Leonard Jarett Professor of Pathology and Lab Medicine, “Cell adhesion regulation of multiple-myeloma induced bone destruction”

X. Sherry Liu, Ph.D., Assistant Professor of Orthopaedic Surgery and Bioengineering, “Mechanical Consequences of Modeling- vs. Remodeling-Based Bone Formation”

Hongtao Zhang, Ph.D., Research Assistant Professor, Department of Pathology and Lab Medicine, “Novel cartilage-targeting Fc fusion proteins as novel and effective treatments for osteoarthritis”

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@mail.med.upenn.edu
A Novel Molecular Mechanism in Dystrophic Muscle Stem Cells

Duchenne Muscular Dystrophy (DMD) is the most common recessive chronic skeletal muscle disorder. It affects ~1/3500 males and exhibits a particularly severe phenotype, which includes progressive muscle weakness and ultimately death during adolescence. The inability of mice carrying the same mutations as humans (called mdx) to manifest the severity of DMD phenotype was a limiting factor in understanding the basic molecular events leading to exhaustion of muscle regeneration in patients. We recently developed a new mouse model (dystrophic mice with shortened telomeres, mdx/mTR) (Sacco, Mourkioti, *Cell*, 2010 and Mourkioti, *Nat Cell Biol*, 2013), which i) replicates the DMD phenotype seen in patients and ii) uncovered a new role of diseased muscle stem cells (MuSCs) in reducing damage-repair cycle due to their telomere defects. Analyzing the regeneration abilities of the mdx/mTR mouse, we recently identified that NF-κB activation is a potential molecular pathway affected by uncapped telomeres during the advancement of DMD. In corroboration, MuSCs isolated from DMD patients had increased NF-κB levels and shorter telomeres compared to aged matched controls (Fig. 1), providing further evidence of the biological significance of our mouse findings. We are currently performing experiments to determine the involvement of the NF-κB axis in directing cellular telomere defects. These experiments will provide insights into genome wide molecular changes that can be targeted in the future to sustain telomere length and increase the functionality of MuSCs for both DMD and potentially other skeletal muscle diseases with muscle stem cell defects.

Figure 1. Signaling dynamic and telomere shortening leading to muscle stem cell exhaustion in diseased muscle stem cells (MuSCs) (a) Representative image showing telomere assay in isolated MuSCs from healthy and DMD patients, (b) MuSCs from DMD patients exhibit reduction in their telomere length compared to age matched controls. N>45 cells per condition, (c) Elevated levels of NF-κB in MuSCs from patients, *** p<0.001.

Acknowledgement:
Upcoming Events

PCMD Visiting Professorship Series

Tuesday, September 20, 2016, 1:30-2:30pm/JMB Class of ’62 Auditorium
Mechanisms of Chondroprotection by TGF-β.
Rosa A. Serra, PhD
Professor, Department of Cell, Developmental and Integrative Biology
University of Alabama at Birmingham

Tuesday, October 25, 2016, 1:30-2:30pm/JMB Class of ’62 Auditorium
Musculoskeletal Adaptation to Space Flight.
Henry J. Donahue PhD
Professor and Chair, Department of Biomedical Engineering
Virginia Commonwealth University, Richmond

ANNUAL SCIENTIFIC SYMPOSIUM
Wednesday, November 9, 2016, 9:00-5:30pm/BRB Auditorium
Strategies for Improving Bone Properties in Patients with Osteogenesis Imperfecta.
Matthew Warman, MD
Professor, Department of Genetics, Harvard Medical School

Tuesday, December 13, 2016, 1:30-2:30pm/JMB Class of ’62 Auditorium
Osteocytes and Bone Remodeling: They’re Just Dying to do the Job.
Mitchell B. Schaffler, PhD
CUNY and Wallace Coulter Distinguished Professor of Biomedical Engineering
Chairman, Department of Biomedical Engineering
The City College of New York, City University of New York

Tuesday, January 10, 2017, 1:30-2:30pm/CRB Austrian Auditorium
Studying Bone as a Complex Adaptive System Reveals Inter-Individual Differences in Skeletal Growth and Aging.
Karl Jepsen, PhD
Professor, Associate Chair of Research, Department of Orthopaedic Surgery
University of Michigan

Tuesday, February 7, 2017, 1:30-2:30pm/CRB Austrian Auditorium
Cell-independent Manipulation of Bone Matrix Properties: A Novel Treatment Strategy for Osteoporosis and Type 2 Diabetes.
David Burr, PhD
Professor of Anatomy & Cell Biology Profess, Department of Biomedical Engineering
Indiana University