Winter 2016

Musculoskeletal Messenger

University of Pennsylvania Penn Center for Musculoskeletal Disorders

Inside this issue:

Pilot Grant Opportunity PMCD Funds Available	2
Research Updates	3
In the News	4
Upcoming events	5

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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@mail.med.upenn.edu

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.

A Look Back at the PCMD Annual Scientific Symposium — November 19, 2015

We are pleased that the 12th Annual Penn Center for Musculoskeletal Disorders Scientific Symposium was a great success. The symposium was held in the BRB Auditorium/Lobby on November 19, 2015.

The keynote speaker, Nancy Lane, MD, from the University of California at Davis, Director for the Center for Musculoskeletal Health gave a well received lecture titled *"Treatment of Musculoskeletal Diseases with a little help from your own Stem Cells".* Symposium attendees enjoyed scientific presentations from new Center members Drs. Songtao Shi, Eric Granquist, and George Hajishengallis While at the symposium, attendees had the opportunity to view more than 50 posters which were judged in five categories.

The following poster presenters received prizes:

Brian Cosgrove (1st place), Ben Freedman (2nd place), Qing Li (3rd place) for their winning posters in the Biomechanics Category; Abhishek Chandra (1st place), Rebekah Decker (2nd place), Yu Usami (3rd place) for their winning posters in the Histology Category; Sarah Gullbrand (1st place), Ravi Nanga (2nd place), Elizabeth Kobe (3rd place) for their winning posters in the Imaging Category. Michael Conventi (1st place), Claire McLeod (2nd place), Girish Ramaswa,y (3rd place) for their winning posters in the Miscellaneous Category.

Pictures from the Symposium are available at: http://www.med.upenn.edu/pcmd/2015SymposiumPictures.shtml

PCMD Pilot and Feasibility Grant Program Opportunity

The Penn Center for Musculoskeletal Disorders 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 contact us at (pcmd@mail.med.upenn.edu). Pilot grants are due on February 29, 2016 with a planned start date of July 1, 2016 and we expect to award 3 grants in this round.

Submissions should be related to musculoskeletal tissue injury and repair which is the broad focus of the Center. For more information on our Cores and Center in general please see our website at http://www.med.upenn.edu/pcmd

Categories of applicants are:

1. Established investigators with a proposal to test the feasibility of a new or innovative idea in musculoskeletal tissue injury and repair representing a clear and distinct departure from their ongoing research

(continued on page 2)

PCMD Pilot and Feasibility Grant Program Opportunity (cont'd)

2. New investigators without significant extramural grant support as a Principal Investigator to develop a new project.

- Pilot and Feasibility Grants must use at least one of the Center's Research Cores.
- Pilot project awardees are eligible for one year, with a second year to be considered (budgets will be for $25-50,000 per year and timelines should be for one or two years).
- The second year of funding, the dollar amount of which would only be for up to half the year one budget, will be considered based on the progress report submitted after the first year of funding and funding availability in the Center. Please note that second year funding will most often not be awarded, and when awarded, will be done so primarily to new investigators; second year funding to senior investigators will be quite rare.
- It is expected that these Pilot grants will lead to funding through other independent, extramural mechanisms. Therefore, the likelihood of future extramural funding will enter into the evaluation of these proposals. For format guidelines, please visit our website at: http://www.med.upenn.edu/pcmd/pilotgrants.shtml

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

COMING SOON!

NEW AND EXCITING UPDATED WEBSITE FOR THE PENN CENTER FOR MUSCULOSKELETAL DISORDERS

Research Updates from PCMD Members

Motomi Enomoto-Iwamoto, D.D.S. , Ph.D.

Pharmacological inhibition of lactate synthesis improves tendon repair in the mouse

Incomplete tendon healing leads to significant mobility restriction, pain and health care cost. To develop novel targeted therapies for tendon injury, it is necessary to define the molecular changes and mechanisms governing the tendon healing process. Up-regulation of glycolysis and lactate synthesis occurs in wound, inflammation, immune response and cancer, and is critical for growth/survival of cancerous tumors and polarizing of macrophages. We hypothesize that modifying metabolic changes would be an effective therapeutic approach for tendon repair and regeneration. We analyzed activities of glycolysis and lactate synthesis in injured tendons and examined the effects of dichloroacetate (DCA), an inhibitor of lactate synthesis, on recovery of biomechanical properties in the mouse Achilles tendon injury model. A complete transverse incision was made at the midpoint of the right Achilles tendon in C57/BL6 mice. 13C-glucose (400mg/kg) was peritoneally injected 1 h prior to euthanization. The uninjured or injured tendons were subjected to analysis of 13C-metabolites and intermediates by combination of LC-MS and MC-MS. The molar percent enrichment of 13C-latate and 13C-glyceraldehyde, a metabolite in glycolysis pathway was strongly increased at 1 week post-injury and remained high after 4 weeks (Fig. 1). DCA-treated samples had smaller cross sectional areas (Fig. 2A). Biomechanical assessments demonstrated that modulus and maximum strength were significantly higher in the DCA-treated tendons than the vehicle-treated tendons (Fig. 2B and C). The findings indicate that injured tendons reprogram glucose metabolism and that metabolic drugs can modify this alteration and improve tendon healing

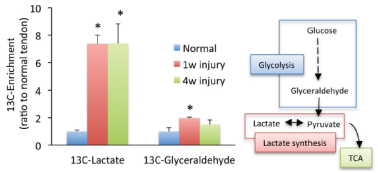


Figure 1. Injured tendons increased an influx of glucose to glycolysis and lactate synthesis pathway. ^{13}C-glucose was injected 1 h in prior to euthanization. The uninjured or injured tendons (1 or 4 weeks postinjury) were harvested and subjected to metaboromics analysis to measure the molar percent enrichment of ^{13}C-metabolites. *, p<0.05

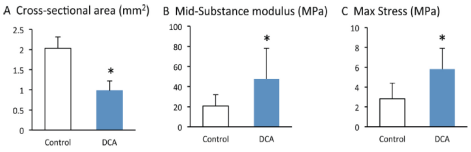


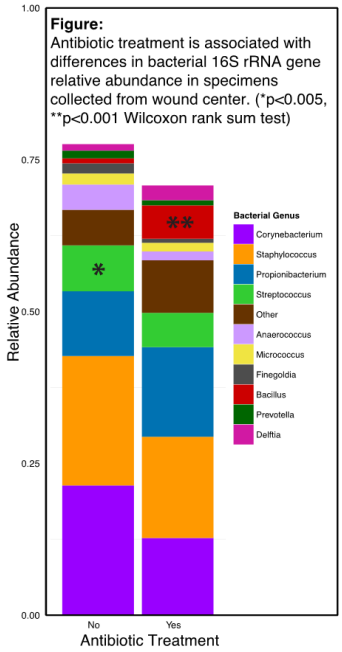
Figure 2. DCA treatment stimulated tendon repair. DCA (100 mg/kg) or PBS vehicle was given to the mice for 4 weeks after tendon injury surgery. The DCA-treated tendon had smaller cross-sectional area and showed better fiber alignment and higher values of mid-substance modulus and max stress compared to the control injured tendons. *, p<0.05

Acknowledgement: The study is performed in collaboration with Drs. K. Zhang, L.J. Soslowsky, M. W. Hast and M. Iwamoto. The study was supported in part through a pilot grant for the Penn Center for Musculoskeletal Disorders (PCMD). We also thank Dr. I. Nissim, Co-Director of Metabolomics Core at CHOP.

Elizabeth Grice, Ph.D.

Temporal dynamics of microbiota colonizing open fractures and association with complication

Microbial communities, in the context of the skin and wound healing, are the major focus of research in the Grice laboratory. In collaboration with Samir Mehta, MD from the Department of Orthopaedic Surgery, their work is exploring a type of wound healing beyond the skin—traumatic open fractures. Some patients with open fractures will develop infection-related complications, and the colonizing microbiota may, in part, modulate healing and complication. The objective of their current work is to systematically evaluate whether the traumatic open fracture microbiome is a source of clinically relevant markers that are predictive of outcomes. Microbiota collected from open fracture specimens are characterized using culture-independent, DNA sequence-based methods (i.e., 16S rRNA gene sequencing). Their findings, thus far, show a much greater diversity of microbes colonizing open fractures than previously appreciated using traditional lab based culture techniques, including Staphylococcus, Propionibacterium, Corynebacterium, and Acinetobacter. Clinical features of the injury (i.e., mechanism, severity, and location) and patient-level factors (i.e., antibiotic treatment, as illustrated in the Figure, BMI) were associated with aspects of the colonizing microbiota. Currently, analyses are focusing on the predictive nature of the microbiome. The long term objective of this work is to better understand the role of the colonizing microbiota in modulating healing and complication in traumatic wound healing and to improve early identification of patients at elevated risk for complication.



Acknowledgement: This project was funded by the Orthopedic Trauma Association, Grant No. 29, to Samir Mehta.

In the News!

Louis J. Soslowsky, PhD to be Honored as ORS 2016 Distinguished Mentoring Award Recipient

The award notice states "Lou has been an exemplary mentor to PhD's and MD's alike. He has mentored trainees in basic and clinical research, advocated for trainees far beyond his research program, developed educational programs to support trainee development, and developed the careers of graduate students, residents, fellows, and junior faculty. As a testament to his abilities, his trainees have achieved great success in orthopaedic research and clinical practice."

Congratulations to Dr. Soslowsky!

Penn Cartilage Center
Penn Medicine

Penn Center for Advanced Cartilage Repair and Osteochondritis Dissecans Treatment has been recognized as a Teaching Centre by the International Cartilage Repair Society

CONGRATULATIONS!

http://cartilage.org/society/teaching-centres-overview/

PENN
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DISORDERS

Our NIH sponsored Penn Center for Musculoskeletal Disorders is already the longest running research center of its kind in the country. At the review meeting this past fall – to continue five more years of support – we were awarded a truly outstanding score and are optimistic we will be able to serve the musculoskeletal research community for many years to come.

SAVE THE DATE

Penn Center for Musculoskeletal Disorders Annual Scientific Symposium

Thursday, November 9, 2016
BRB II/III Auditorium/Lobby

Keynote Speaker:
Matthew Warman, M.D.
Harriet M. Peabody Professor of Orthopedic Surgery and Professor,
Department of Genetics, Harvard Medical School
Director, Orthopaedic Research Laboratories at Boston Children's Hospital

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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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Upcoming Events

PCMD Visiting Professorship Series Winter/Spring 2016

Tuesday, January 19, 2016, 1:30-2:30pm/CRB Austrian Auditorium
Role of Connexin43 in Cortical Bone Adaptation to Mechanical Load
Roberto Civitelli, MD, PhD
Professor of Orthopaedic Surgery and of Cell Biology and Physiology
Washington University, St. Louis

Tuesday, February 16, 2016, 1:30-2:30pm/CRB Austrian Auditorium
Unravelling the neurobiology of osteoarthritis pain
Anna-Marie Malfait, MD, PhD
Associate Professor of Medicine and Biochemistry
Rush University Medical Center

Tuesday, March 22, 2016, 1:30-2:30pm/JMB Class of 62 Auditorium
Scar Wars: New Frontiers in Flexor Tendon Repair
Hani Awad, PhD
Professor of Biomedical Engineering and Orthopaedics
University of Rochester Medical Center

Tuesday, April 19, 2016, 1:30-2:30pm/CRB Austrian Auditorium
Genome and Epigenome editing for Gene Therapy and Programming Cell Fate
Charles Gersbach, Ph.D.
Associate Professor of Biomedical Engineering
Associate Professor of Orthopaedic Surgery
Duke University

Tuesday, May 17, 2016, 1:30-2:30/ TBD
TENTATIVE
David J. Glass, MD
Novartis Institutes for Biomedical Research