Spring 2017



Musculoskeletal Messenger



Inside this issue:

| Research Updates—PCMD Members | 2 |
|----------------------------------|---|
| In the News | 3 |
| Upcoming events | 4 |
| New Members | 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 P30AR06919 from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases of the NIH.

University of Pennsylvania Penn Center for Musculoskeletal Disorders

Looking Forward to 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. Atha-



nasiou. Ph.D. Distinguished Professor, Department of Biomedical Engineering, University of

California. His lecture is titled "Articular Cartilage Bioengineering".

The day will begin with registration and poster set up at 7:30am followed by scientific presentations from new Center Full and 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-annualsymposium.html

2017 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, 2017.

Susan Volk, VMD, PhD, DACVS will receive funding for her grant titled "The Regulatory Roles of Type III Collagen in the Cartilage Collagen Network: Implications for Osteoarthritis Prevention and Treatment".

Yanging Gong, PhD will receive funding for her grant titled "Role of Plasminogen in Mesenchymal Stem Cell Function and Post-injury Bone Regeneration".

Nathaniel Dyment, PhD will receive funding for his an expected submission grant titled "Murine Anterior Cruciate Ligament Reconstruction Model to Understand the Cellular **Origins and Mechanisms**

of Repair".

Carla Scanzello, MD, PhD will received funding for her grant titled "Importance of Macrophage Responses in Osteoarthritis".

New applications will be accepted starting January 2. 2018 for the next round with deadline of February 22nd. Official announcement to follow.

Research Updates from PCMD Members

Sunday O. Akintoye, BDS, DDS, MS

Depletion of Jaw Osteoprogenitors by Radiation-associated Hypoxia Promotes Onset of Jaw Osteoradionecrosis

A major orofacial complication of head and neck cancer radiotherapy is jaw osteoradionecrosis (ORN). Although ORN is attributed to development of radiation-induced hypoxic-hypocellular-hypovascular tissues, the modulatory roles of hypoxia in the pathogenesis of ORN is still evolving. To further define the contribution of radiation-induced tissue hypoxia, we tested whether disproportionate jaw bone cell susceptibility to hypoxia heightens the incidence of jaw ORN. We have found that human jaw trabecular bone (HTB, osteoblast-like) cells readily succumb to radiation effects compared to Iliac crest (hip) bone (Figure 1A). We also found that mesenchymal stem cells (MSCs) from the jaw (OFMSCs) and iliac crest (ICMSCs) were unaffected by moderate hypoxia (2% O_2), but severe hypoxic stress (0.1% O_2) caused a disparate decrease in survival (Figure 1B) and decrease in the number of αSMA^+ and CD146⁺ OF-MSCs (Figure 2A-D). Since α SMA, CD146 as well as STR01 are markers of undifferentiated early MSC osteoprogenitors, our group is currently pursuing the hypothesis that radiation-induced osteoblast loss and hypoxic depletion of osteoprogenitors apparently dysregulate post-irradiation jaw bone healing to initiate osteoradionecrosis.

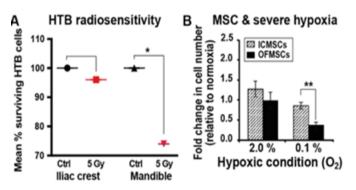


Figure 1. Site-disparity in human trabecular bone (HOB) cells radiosensitivity and human MSC responsiveness to hypoxia. Mandible HTB cells displayed consistent lower survival within 48 hours exposure to 5 Gy radiation (A, red color). Although both OFMSCs and ICMSCs survived moderate hypoxia ($2\% O_2$) OFMSCs more readily succumbed to severe hypoxia at 0.1% O_2 (B). This site-dependent responsiveness of jaw bone cells to irradiation and radiation-associated hypoxic stress supports jaw susceptibility to ORN [*= p<0.05; **=p <0.01; Ctrl=control].

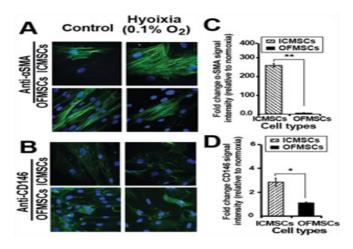


Figure 2. Hypoxia suppressed undifferentiated OF-MSCs. Under hypoxia at (0.1% 0₂), immunofluorescent staining with two common stem cell markers, α SMA (A, C) and CD146 (B, D) indicated severe suppression of undifferentiated OFMSCs relative to IC-MSCs. This suggests hypoxia apparently depletes jaw osteoprogenitors vital for bone healing [* = p < 0.05; ** = p<0.01].

Penn Center for Musculoskeletal Disorders is moving!

We are excited to announce that the PCMD is moving! This July we are relocating to the newly renovated space of Stemmler Hall. The center will be temporarily housed on the ground and first floor while construction is being done on the permanent space. The anticipated completion of the permanent space to be spring/summer 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.

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

In the News!

Felix Wehrli, PhD awarded the 12th Annual Lodwick Award

The Lodwick Award: presented to Felix W. Wehrli, PhD on October 4th, 2016: 12th Annual Lodwick Award for "A Surrogate Measure of Cortical Bone Matrix Density by Long T2-Suppressed MRI" in J Bone Miner Res. Founded in 2004, the Lodwick Award recognizes excellence in academic literature in the fields of musculoskeletal radiology, medicine or physiology. It is presented annually by the Division of Musculoskeletal Imaging & Intervention in the Department of Radiology at Massachusetts General Hospital to the author of the paper with the largest impact in the field of musculoskeletal radiology, medicine or physiology. It is named after Gwilym Lodwick, MD, a renowned musculoskeletal radiologist and former member of the Department of Radiology at Mass General. Each year, members of the Division of Musculoskeletal Imaging & Intervention review thousands of papers published in more than 20 general and subspecialty journals. The winner is selected by the Division's staff radiologists, fellows and radiology residents.



Congratulations to Dr. Wehrli!

2017 Orthopaedic Surgery New PhD Faculty Recruited



Please welcome Nathaniel (Nat) Dyment, PhD who has joined Penn as Assistant Professor of Orthopaedic Surgery in January 2017. Dr. Dyment obtained his PhD from the University of Cincinnati in Tendon Tissue Engineering. His research interests are tendon and ligament injury, repair and regeneration stem/progenitor cell lineage.

If you would like to contact Dr. Dyment, please do so at Dyment@mail.med.upenn.edu.

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

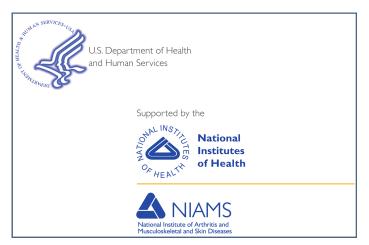
Funding through this mechanism is available by submitting the one page proposal along with the summary statement to pcmd@mail.med.upenn.edu



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Remember to include reference to support from the Center in your abstracts and publications. Cite Grant NIH/NIAMS P30AR06919 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.

Upcoming Events

PCMD Visiting Professorship Series Winter 2017/Spring 2018

| Tuesday, September 12, 2017 1:30-2:30pm/Location TBD | Joint Research Laboratories Kolling Institute of Bone and Joint | Tuesday, January 2018/TBD |
|--|--|----------------------------|
| "Cartilage Repair and Osteoarthri- tis in Genetic Mouse Models" | Research University of Sydney | Tuesday, February 2018/TBD |
| Linda Sandell, PhD | | Tuesday, March 2018/ TBD |
| Mildred B. Simon Research Profes- | ••• | |
| sor, Director of Research | Wednesday, November 15, 2017 | Tuesday, April 2018/ TDB |
| Director, Center of Musculoskele- | 7:30am-6pm/BRB Auditorium | |
| tal Research, | "Articular Cartilage Bioengineer- | Tuesday, May 2018/TDB |
| Washington University | ing" | |
| | Kyriacos A. Athanasiou, Ph.D., Dis- | Tuesday, June 2018/TBD |
| Tuesday, October 2017 1:30- | tinguished Professor of Biomedical | |
| 2:30pm/Location TBD | Engineering, University of Califor- | |
| "How can we improve translation | nia | |
| of pre-clinical osteoarthritis re- | | |
| search to patients?" | Tuesday, December 2017/ TBD | |
| Christopher Little, BVMS, PhD | | |
| Director, Raymond Purves Bone & | | |



Welcome to the New Members of Penn Center for Musculoskeletal Disorders January 2015-June 2017

Full Members

Manju Benakanakere, Ph.D., Research Assistant Professor of Periodontics Shelley L. Berger, Ph.D., Daniel S. Och University Professor, Cell and Developmental Biology Ellen Casey, M.D., Assistant Professor, Physical Medicine and Rehabilitation Anil Chauhan, M.D., Assistant Professor, Radiology Nat Dyment, Ph.D., Assistant Professor, Orthopaedic Surgery John Fischer, M.D., M.P.H., Assistant Professor, Plastic Surgery Yanging Anna Gong, Ph.D., Research Assistant Professor, Medicine Atul Kamath, M.D., Assistant Professor, Orthopaedic Surgery Bekir Karabucak, D.M.D., M.S., Interim Chair & Associate Professor of Endodontics & Director, Postdoctoral Endodontics Program Robert Levy, M.D., Professor, Pediatrics & Pharmacology, CHOP Diane C. Lim, M.D., M.T.R., Assistant Professor, Medicine, Division of Sleep Medicine Matthew Maltese, Ph.D., Research Assistant Professor, Anesthesiology and Critical Care Medicine, CHOP Paris Margaritis, DPhil, Research Assistant Professor, Pediatrics, CHOP Kyla Ortved, D.V.M., Ph.D., Assistant Professor, Large Animal Surgery, New Bolton Dipti Pitta, Ph.D., Assistant Professor, Ruminant Nutrition, New Bolton Center Alexander M.Reiter, Dipl. Tzt., Associate Professor, Dentistry & Oral Surgery, Veterinary Medicine Ronnie A. Sebro, M.D., Assistant Professor of Radiology

Associate Members

Pedro P Alvarez-Urena, Ph.D., Postdoctoral Researcher in the Department of Bioengineering
Josh Baxter, Ph.D., Director, Human Motion Lab
Peeyush Goel, Ph.D., Postdoctoral Fellow/TMRC
Joanne Haughan, D.V.M., Research Associate, Clinical Studies New Bolton
Mazen Mohamed Ibrahim, M.D., Ph.D., Postdoctoral Research Fellow / Pediatric Orthopaedics
Hyeran Helen Jeon, D.D.S., M.SD.,. DSc.D., Instructor, Department of Orthodontics
M. Noelle Knight, VMD/PhD Student
Fouad M. Moussa, Ph.D., Postdoctoral Researcher, Translational Research Program in Pediatric Orthopaedics, CHOP
Danielle R. Rux, Ph.D., Postdoctoral Researcher, Translational Research Program in Pediatric Orthopaedics, CHOP
Thomas P. Schaer, B.S., V.M.D., Director, Translational Orthopaedic Research & Preclinical Studies
Feikun Yang, Ph.D., Postdoctoral Fellow, Department of Hematology, CHOP

Affiliate Members

Jonathan Akins, Ph.D., Assistant Professor, Biomedical Engineering, Widener University Xu Cao, Ph.D., Lee Riley Professor, Orthopedic Surgery, Johns Hopkins University Antonia Chen, M.D.. M.B.A., Assistant Professor, Orthopaedics, Rothman Institute, Thomas Jefferson University Yury Gogotsi, D.Sc., Distinguished University Professor & Trustee Chair of Materials Science & Engineering, Drexel University Li-Hsin Han, Ph.D., Assistant Professor, Mechanical Engineering & Mechanics, Drexel University Noreen J. Hickok, Ph.D., Associate Professor, Orthopaedic Surgery, Thomas Jefferson University Yibin Kang, Ph.D., Warner-Lambert/Parke-Davis Professor, Molecular Biology Princeton University Megan Leigh Killian, Ph.D., Assistant Professor, Biomedical Engineering, University of Delaware Christopher Li, Ph.D., Professor, Materials Science, Drexel University David Logerstedt, PT, PhD, MPT,SCS, Assistant Professor, Physical Therapy, University of the Sciences Karin Grävare Silbernagel, PT, Ph.D., A.T.C., Assistant Professor, Department of Physical Therapy University of Delaware Michele Staud Marcolongo, Ph.D., Department Head and Professor, MSE, Drexel University Surena Namdari, MD, MSC, Assistant Professor, Shoulder & Elbow Surgery, Rothman Institute, Thomas Jefferson University Joel Rosenbloom, M.D., Ph.D., Department of Dermatology & Cutaneous Biology, Thomas Jefferson University Ryan E. Tomlinson, Ph.D., Assistant Professor, Department of Orthopaedic Surgery, Thomas Jefferson University Ani Ural, PhD, Associate Professor, Mechanical Engineering, Villanova University