Winter 2010

Musculoskeletal Messenger

University of Pennsylvania Penn Center for Musculoskeletal Disorders

Inside this issue:

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A Look Back at the PCMD Annual Scientific Symposium — November 17, 2010

We are thrilled to announce that 223 registrants participated in the 7th Annual Penn Center for Musculoskeletal Disorders Scientific Symposium in the BRB Auditorium/Lobby making this year's event the largest ever!

The keynote speaker, Michael J. Yaszemski, M.D., Ph.D., Professor of Orthopaedics and Bioengineering at the Mayo Clinic, and the Director of the Tissue Engineering and Biomaterials Laboratory, gave an outstanding lecture titled "Musculoskeletal Regenerative Medicine."

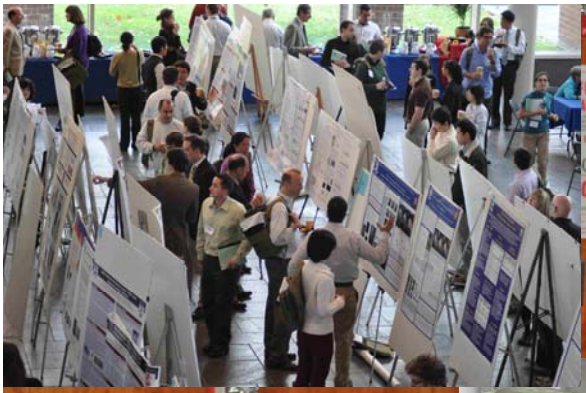
Symposium attendees enjoyed eight scientific presentations from new Center members Drs. Neil Malhotra, Arjun Raj, Yair Argon, Michael Pack and PCMD Pilot Grant recipients Drs. Ling Qin, Toby Ferguson, Sherrill Adams and Robert Mauck.

The day also included a poster session in which 48 posters were judged in four categories. Poster awards were awarded to Alock Malik, Motomi Enomoto-Iwamoto and Meiqi Xu for their 1st, 2nd and 3rd place winning posters in the Proteomics and Genomics category; Kris Miller, Megan Farrell and Lachlan Smith for their 1st, 2nd and 3rd place winning posters in the Structure-Function category; Matthew Fenty, Rachel Berger and Henry Ong/Yusuf Bhagat for their 1st, 2nd and 3rd place winning posters in the Imaging category, and Elizabeth Sweeney's lab, Wei en Tung and Andria Culbert for their 1st, 2nd and 3rd place winning posters in the Miscellaneous category.

We are looking forward to next year's symposium to take place late October/early November. Stay tuned for more details!

Thanks to all of our Center members for making this year's symposium a great success.

Photos from the event are available on our web site and a few are shown below clockwise from top left:: poster session, Dr. Neil Malhotra, Dr. Arjun Raj, and lunch break.



Did you know that funds are available to support projects within each Research Core (in addition to the Pilot Grant Program)? For more information, please contact the Core Directors-

Donald Baldwin, Ph.D.- dbaldwin@mail.med.upenn.edu (microarray)

Dawn Elliott, Ph.D.- delliott@mail.med.upenn.edu (structure-function biomechanics)

Felix Wehrli, Ph.D.- wehrli@mail.med.upenn.edu (imaging)

7T MRI Scanner Available to PCMD Members

The 7T Siemens Whole Body MRI Scanner was dedicated on November 11th, 2008 in a ceremony hosted by the Center for Magnetic Resonance and Optical Imaging (CMROI) formerly the Metabolic Magnetic Resonance Research and Computing Center http:www.mmrrcc.upenn.edu).

The magnet is housed in B1 Stellar Chance Laboratory building located at UPenn. Acquisiton of the ultra high field magnet was made possible through a two million dollar grant awarded to the University by the National Center for Research Resources.

This 7T Whole Body Magnet has a 90 cm diameter bore prior to Gradient coil insertion. The length of the bore is 3.4m which is longer than the current clinical service scanners. The finished diameter after shim and gradient insertion is 60cm. This is the same as other standard Siemens systems. The system has multinuclear imaging, simultaneous RF excitation (8 channels) and, 32 channels receive capability.

Currently, the system has two operational head imaging coils, one extremity coil, and a small contingent of multinuclear coils for imaging or spectroscopy. For additional information, please-contact: Mark Elliott, Ph.D. Technical Director of CMROI at

mark@mail.mmrrcc.upenn.edu or visit the website:
www.mmrrcc.upenn.edu

Figure: Dr. Ravinder Reddy at the 7T Siemens Whole Body MRI Scanner

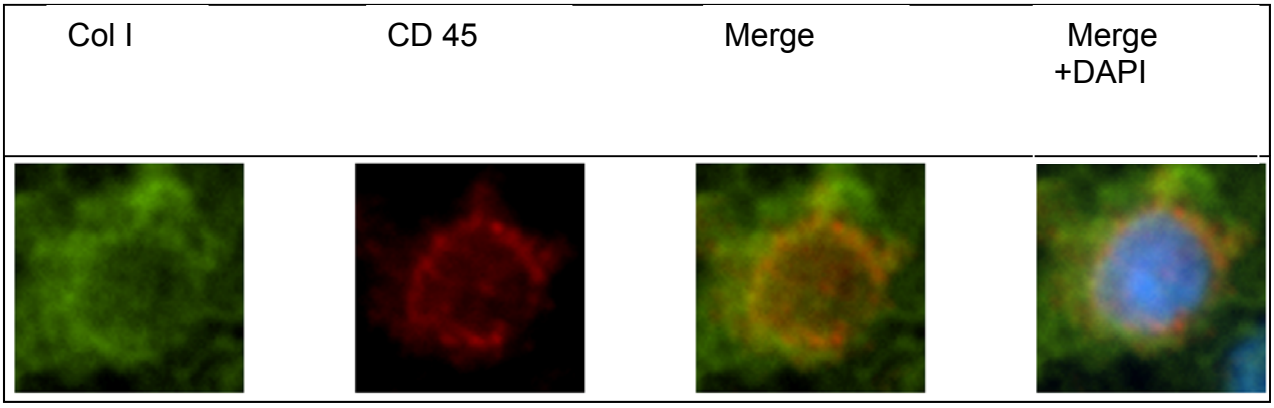


Figure (article to right): Identification of COP cells in an early fibroproliferative region of HO by a combination of markers.

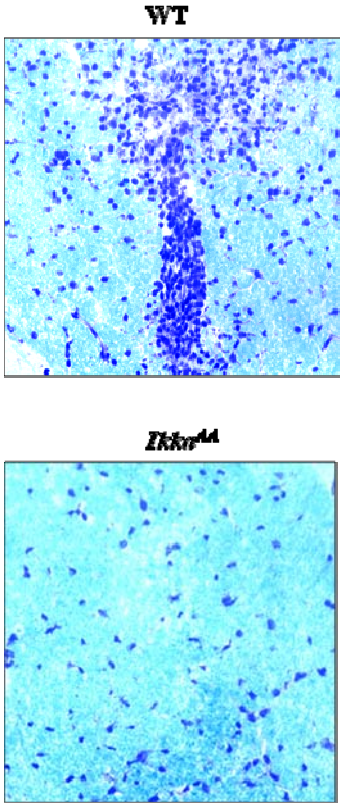
Research Updates from PCMD Members

Transcriptional Regulation of the Th17 Immune Response by IKKα – Youhai H. Chen, M.D., Ph.D.

Li Li*, Qingguo Ruan*, Brendan Hilliard*, Jennifer DeVirgiliis*, Michael Karin#, and Youhai H. Chen*.

*Department of Pathology and Laboratory of Medicine, University of Pennsylvania School of Medicine, Philadelphia, PA 19104. #Department of Pharmacology, University of California, San Diego, CA 92093.

Th17 cells are a new subset of T cells that play crucial roles in the pathogenesis of inflammatory diseases. We report here the identification of IKKα (inhibitor of NF-κ B kinase-α as a key transcriptional regulator of the Th17 lineage. *Ikkα*^{AA} knock-in T cells, which express an inactivatable form of IKKα, were significantly compromised in their ability to produce IL-17A and to initiate neural inflammation. IKKα is present in the nuclei of resting CD4^{+} T cells; and upon Th17 differentiation, it selectively associated with the *Il17a* locus, and promoted its histone H3 phosphorylation and transcriptional activation in a manner independent from NF-κB. These findings indicate that nuclear IKKα maintains the Th17 phenotype by activating the *Il17a* gene.



Figures: WT (n=9) and IkkαAA (n=6) C57BL/6 mice were immunized with MOG to induce EAE. Mice were sacrificed at the end of the experiment, and their spinal cords and brains sectioned and stained with luxol fast blue and cresylviolet. The upper panel shows the spinal cord of a WT mouse with a clinical score of 4; the lower panel is of the spinal cord of an IkkαAA mouse with no signs of EAE. Original magnifications, x200.

Circulating Osteogenic Cells: Implications for Injury, Repair, and Regeneration – Robert J. Pignolo, M.D., Ph.D.

Circulating osteogenic precursor (COP) cells are blood-borne cells that express a variety of osteoblastic markers and are able to form bone in vivo. Experimental evidence supports that COP cells seed sites of injury and inflammation in response to homing signals and are involved in processes of pubertal growth, fracture, and diverse conditions of heterotopic bone formation (HO). In the mature adult skeleton, new bone formation is normally restricted to regeneration of osseous tissue at sites of fracture. However, HO or the formation of bone outside the normal skeleton, can occur within muscular, adipose, or non-muscle fibrous connective tissue.

We have identified COP cells which are derived from bone marrow, have the capability to form bone, and are identified by the co-expression of the osteogenic marker type 1 collagen and the hematopoietic marker CD45 (Figure). There is a strong association between the presence of COP cells and early fibroproliferative lesions of genetic and non-hereditary forms of HO, including periarticular HO that may occur after musculoskeletal trauma, following CNS injury, with certain arthropathies, or following injury or surgery that is often sustained in the context of age-related pathology.

Our studies indicate that osteogenic cells in the blood home to distant sites where they are associated with formation of HO caused by diverse traumatic conditions. The role of COP cells in physiologic and pathophysiologic conditions of de novo bone formation suggests that they may serve as future targets for diagnostic measurements and therapeutic interventions.

(See opposite page for Figure)

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Upcoming Events

PCMD Visiting Professorship Series 2010-2011

Tuesday, December 14, 2010, 1:00-2:00pm/ BRB 251
Oxygen Sensing in Cartilage and Bone Development
Ernestina Schipani, M.D., Ph.D.
Associate Professor of Medicine, Division of Endocrinology
Massachusetts General Hospital-Harvard Medical School

Tuesday, January 18, 2011, 1:00-2:00pm/ BRB 253
Between a Muscle and a Hard Bone: The Regulation of Tendon Induction and Differentiation
Ronen Schweitzer, Ph.D.
Associate Professor, Shriners Hospital-Research
Dept. of Cell and Developmental Biology, Oregon Health and Science University

Tuesday, February 1, 2011, 1:00-2:00pm/ BRB 253
Adult Stem Cells in Joint Aging and Osteoarthritis
Martin Lotz, M.D.
Professor and Head, Division of Arthritis Research
The Scripps Research Institute, La Jolla, California

Tuesday, March 1, 2011, 1:00-2:00 pm/ BRB 252
The Effects of Mechanical Stability on Fracture Repair
Theodore Miclau, III, M.D.
Professor and Vice Chair, Trauma/ Problem Fracture, Dept of Orthopaedic Surgery
University of California, San Francisco

Tuesday, April 5, 2011, 1:00-2:00pm/ BRB 252
Acoustoelasticity Analysis of Ultrasound Signals for Biomechanical Behavior
Ray Vanderby, Jr., Ph.D.
Professor of Orthopaedic Surgery and Biomedical Engineering
University of Wisconsin, Madison

Tuesday, May 3, 2011, 1:00-2:00pm/ location tba
tba
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