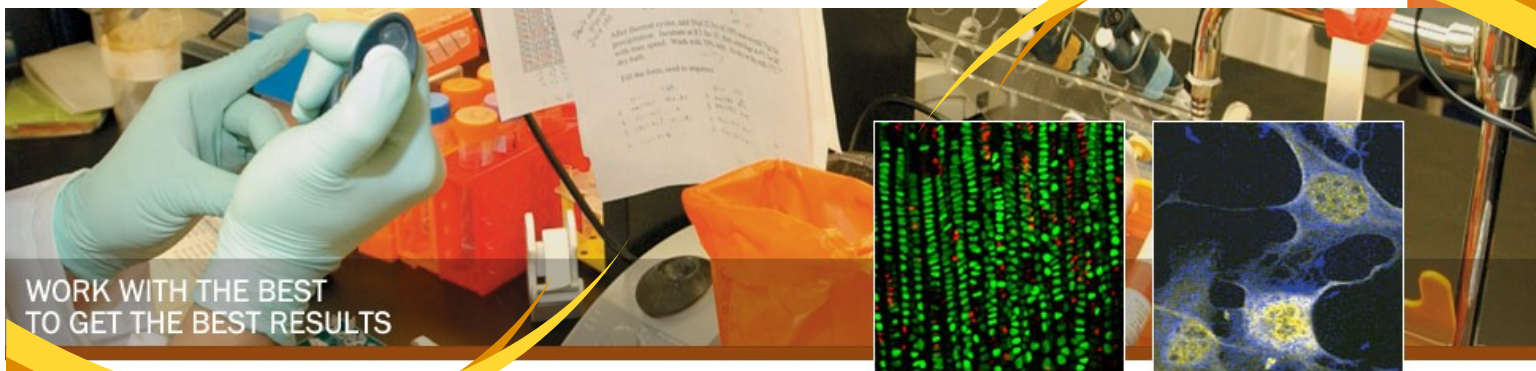


<http://musculoskeletalcore.wustl.edu/>



WORK WITH THE BEST  
TO GET THE BEST RESULTS

## Pilot & Feasibility Awards—Year 3

In this issue we would like to highlight the work of one of our two Pilot & Feasibility awardees for Year 3 of the P30 grant.



**Dr. Gabriel Mbalaviele, PhD**, is a Research Associate Professor of Medicine in the Division of Bone and Mineral Diseases at Washington University Medical School.

NLRP3 is one of the most studied members of the family of intracellular NOD-like receptors (NLRs), and one of the few NLRs shown to form inflammasome. Dr. Mbalaviele's research is focused on the role of the Leucine rich Repeat with a Pyrin domain 3 (NLRP3) inflammasome in bone. They are investigating whether and to what extent NLRP3 inflammasome mediates low grade aseptic inflammation as a component of the so-called "non-targeted bone remodeling" i.e. basal remodeling not induced by specific stimulators or damage. As unresolved inflammation can exacerbate tissue damage or disorders caused by other etiologies, they are also investigating how NLRP3 inflammasome contributes to some forms of pathological bone remodeling.

### P&F funding from the Center for Musculoskeletal Research:

Since systemic inflammation occurs in NOMID mice due to the broad expression of mutant NLRP3, the bone phenotype observed in these mice might be secondary to a direct super-activation of osteoclasts or to an indirect effect via cytokine production by non-hematopoietic cells. In the latter case, cells of the osteogenic lineage represent the most likely candidate since they express NLRP3 and pro-

this issue

P & F: Mbalaviele... p.1  
Symposium, publications... p.2

## Avioli Musculoskeletal Seminar Series

Fridays @ 9am  
Cam Bldg. | Conf. Rm. #2

- 9/30 Haibo Zhao  
*University of Arkansas*
- 10/7 Laurie McCauley  
*University of Michigan*
- 10/14 Jean B. Regard  
*National Institute of Health*
- 10/21 Solnica-Krenzle Lab:  
Ryan Gray  
*Washington University*
- 10/28 NO SEMINAR

**WASHINGTON UNIVERSITY**  
Department of Orthopaedic Surgery  
660 S. Euclid  
Yalem Research Bldg.  
Campus Box 8233  
St. Louis | MO | 63110

*For more information on the Cores, please click on the links below:*

- [Core A—Administrative Core](#)
- [Core B—Structure and Strength Core](#)
- [Core C—In Situ Molecular Analysis Core](#)
- [Core D—Mouse Genetics Models Core](#)

Remember to include reference to support from the Core Center for Musculoskeletal Biology and Medicine in your abstracts and publications. **Cite Grant # P30AR057235** from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases.

## Mbalaviele, cont.

The huge impact of the P&F funding has been the in-depth characterization of the phenotype of NOMID mice, the execution of in vitro mechanistic studies and the ongoing acquisition of floxed mice in which NLRP3 activation is restricted to the myeloid lineage (lysozyme M driven Cre expression). This funding was instrumental in generating data which were used for an RO1 application in June 05, 2011, an abstract selected for oral presentation at the ASBMR 2011 Annual Meeting, September 16-20, 2011 at San Diego, and a manuscript in preparation.

Dr. Mbalaviele anticipates that these studies will not only unravel an important role of NLRP3 inflammasome in physiological or pathological bone development and remodeling, but also position this inflammasome as a potential new target for therapeutic intervention in bone diseases.

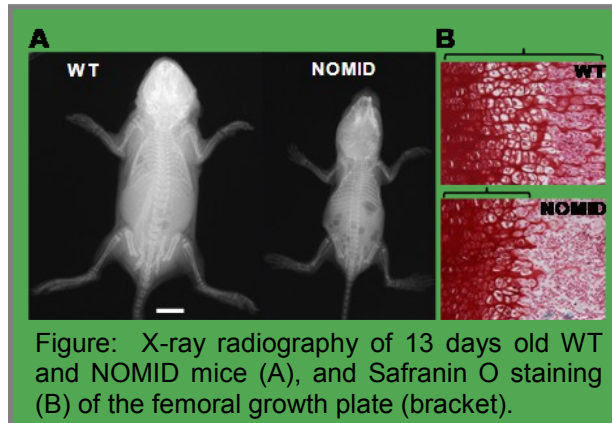


Figure: X-ray radiography of 13 days old WT and NOMID mice (A), and Safranin O staining (B) of the femoral growth plate (bracket).

## Recent Publications

[Healing of non-displaced fractures produced by fatigue loading of the mouse ulna.](#) Martinez MD, Schmid GJ, McKenzie JA, Ornitz DM, Silva MJ (2010) Bone 46: 1604-1612.

[Pitx1 haploinsufficiency causes clubfoot in humans and a clubfoot-like phenotype in mice.](#) Alvarado DM, McCall K, Aferol H, Silva MJ, Garbow JR, Spees WM, Patel T, Siegel M, Dobbs MB, Gurnett CA. Hum Mol Genet. 2011 Aug 2. [Epub ahead of print]

[Site-1 Protease Is Essential to Growth Plate Maintenance and Is a Critical Regulator of Chondrocyte Hypertrophic Differentiation in Postnatal Mice](#) Debabrata Patra, Elizabeth DeLassus, Shinya Hayashi, and Linda J. Sandell J. Biol. Chem., Aug 2011; 286: 29227 - 29240.

[CD8+ T Cells Regulate Bone Tumor Burden Independent of Osteoclast Resorption.](#) Zhang K, Kim S, Cremasco V, Hirbe AC, Novack DV, Weilbaecher K, Faccio R. Cancer Res. 2011 Jul 15;71(14):4799-808. Epub 2011 May 20.

Save the Date

## Center for Musculoskeletal Research 2nd Annual Winter Symposium

February 2, 2012 | 1-6pm

Keynote Speaker: Dr. Gerard Karsenty, MD, PhD

(abstracts will be due December 30, 2011)

If you have any questions regarding the Core, please contact:

Kamilla McGhee | Core Coordinator | 314.747.5993 | [mcgheek@wustl.edu](mailto:mcgheek@wustl.edu)

## Core Directors

### Director

Linda J. Sandell  
314-454-7800  
[sandelll@wustl.edu](mailto:sandelll@wustl.edu)



### Associate Director

Matthew Silva  
314-362-8585  
[silvam@wustl.edu](mailto:silvam@wustl.edu)



### Associate Director

Steven Teitelbaum  
314-454-8463  
[teitelbs@wustl.edu](mailto:teitelbs@wustl.edu)



### Director

Matthew Silva  
314-362-8585  
[silvam@wustl.edu](mailto:silvam@wustl.edu)



### Associate Director

Steve Thomopoulos  
314-362-8605  
[thomopouloss@wustl.edu](mailto:thomopouloss@wustl.edu)



### Associate Director

Roberto Civitelli  
314-454-8408  
[rcivitel@dom.wustl.edu](mailto:rcivitel@dom.wustl.edu)



### Director

Deborah Novack  
314-454-8472  
[novack@wustl.edu](mailto:novack@wustl.edu)



### Associate Director

Debabrata Patra  
314-454-8853  
[patrad@wustl.edu](mailto:patrad@wustl.edu)



### Associate Director

Conrad Weihl  
314-747-6394  
[weihlc@neuro.wustl.edu](mailto:weihlc@neuro.wustl.edu)



### Director

David Ornitz  
314-362-3908  
[dornitz@wustl.edu](mailto:dornitz@wustl.edu)



### Associate Director

Fanxin Long  
314-454-8795  
[flong@wustl.edu](mailto:flong@wustl.edu)

