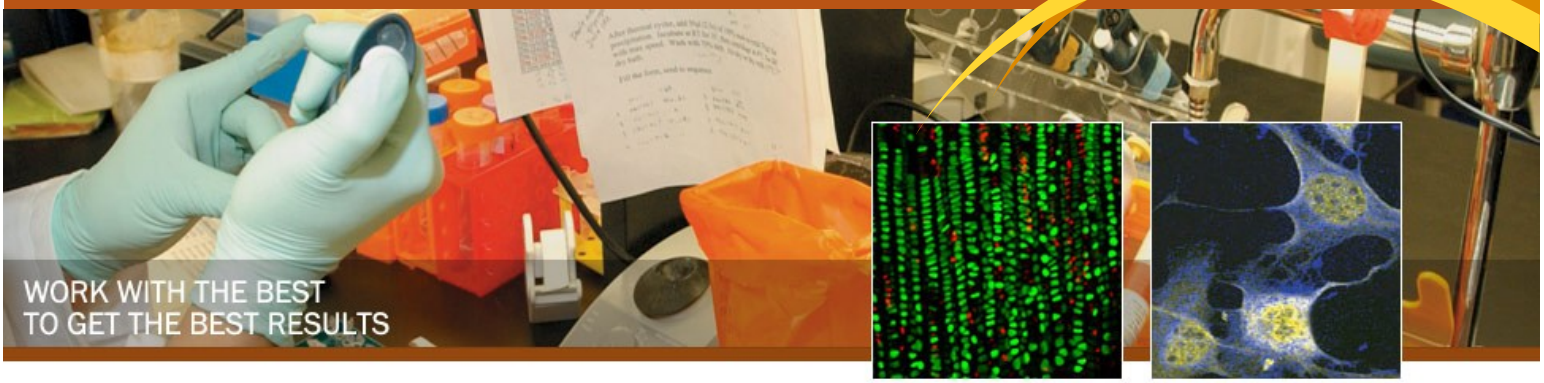
Center for Musculoskeletal Research

Vol 2|Issue 2|Nov 2010

http://musculoskeletalcore.wustl.edu/home.aspx



In the November issue of our newsletter, we would like to highlight one of our Cores, and one of our Core users. We have also included the November/December schedule for the Musculoskeletal Seminar Series. As always, we welcome your comments, please feel free to call or send an email.

Core Highlight

Core B - Musculoskeletal Structure and Strength

The goal of Core B is to facilitate assessment of musculoskeletal structure and/or strength in animal models. Our main focus is bone imaging and mechanical testing, although we have worked with tendon, ligament and cartilage. To assess structure, we have several x-ray imaging options ideally suited for bone imaging and density measurement. Most of these can be used for either post-mortem specimens or live animal imaging. Investigators can use these systems themselves or you can hire us to do the work. Instruments we have include: Faxitron plane radiography (MX20); GE/Norland Piximus Dual-Energy X-Ray Absorptiometry (DXA, for bone density scanning); Norland/Stratec pQCT scanner; Scanco uCT40 microCT scanner specimen; Scanco VivaCT40 microCT scanner. To assess strength, we can test your bone or other tissue samples using one of three Instron mechanical testing systems. These are used to provide quantitative measures of stiffness, strength and other mechanical properties.

Examples of work done in Core B recently include: in vivo microCT scanning of mouse bones to measure changes in bone volume in response to temporary paralysis, in vivo DXA and microCT scanning of mutant mice to assess skeletal phenotype (increased or decreased bone mass), in vivo microCT scanning to assess club foot deformity in mice, post mortem microCT to assess bone changes after knee injury in mice, bending tests to assess mechanical properties of femurs from ~1000 mice to identify genes related to bone strength.

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

this issue

Washington University
Department of Orthopaedic Surgery
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St. Louis | MO | 63110

Avioli Musculoskeletal Seminar Series

Fridays @ 9am | Brown Room Steinberg Building

11/5	**Faccio Lab: *Viviana Cremasco*** "Regulatory Mechanisms of Osteo-immune Activation Dur ing Inflammatory Bone Loss"
11/12	**Georg Schett** "Osteoclasts in Inflammatory Disease" *University of Erlangen-Nürnberg*
11/19	**Farshin Guilak** "Osteoarthritis and Fat: The Good, the Bad, and the Ugly" *Duke University*
11/26	**No Seminar**
12/3	**Teitelbaum Lab: *Wei Zou***
12/10	**Long Lab**
12/17	**Towler Lab**
12/24	**No Seminar**

Save the Date
1st Annual
Winter Symposium
January 27, 2011
(abstracts due 12/29/10)

Who's using our Cores?

Scott Saunders, MD, Ph.D. (*Pediatrics, Developmental Biology*)

We are making use of Core D for the purpose of generating *Gpc6*-deficient mice to allow us to directly test the hypothesis that *GPC3* and *GPC6* are functionally non-redundant and have opposing loss of function phenotypes in bone. *GPC3* and *GPC6* play an essential and complex role in the continuous balance of antagonistic and synergistic signaling events during development that serve to control the precise balance of skeletal growth. The epiphyseal growth plate in developing bone is regulated by a feedback signaling loop initiated and terminated within its specialized cartilaginous cells, and involves the FGF, BMP, and IHH signaling pathways. Despite involving entirely unrelated ligands and receptors, each of these signaling pathways shares in common their functional modulation by a class of glycoproteins known as heparan sulfate proteoglycans (HSPGs). Because of the potential for HSPGs to modulate multiple signaling pathways, we have hypothesized that HSPGs have evolved to simultaneously balance these interacting signaling pathways, and that structurally defined subfamilies of HSPGs may well have evolved with distinct activities to further fine tune the balance of these functions. We have focused on understanding the functions of the glypican gene family and specifically *Gpc3* and another glypican discovered by our laboratory, *Gpc6*, which are the only glypican family members expressed by growth plate chondrocytes during development.

Loss-of-function mutation in *GPC3* causes an X-linked disorder in humans known as Simpson Golabi Behmel syndrome (SGBS). This human disorder is associated with several abnormalities including defects in skeletal patterning, overgrowth of bone and tall stature. Mice created by our laboratory bearing mutations in *Gpc3* model this disease. Recently, loss-of-function mutations in *GPC6* in humans have been shown to cause autosomal recessive Omodysplasia, a disease associated with restricted growth of bone and short stature. In addition to supporting our more general hypothesis that these two genes were critical to the control of skeletal growth, these opposing effects on human skeletal growth directly supports our long-standing hypothesis that *Gpc3* and *Gpc6* have evolved to balance opposing signals and would therefore have fundamentally opposite phenotypes.

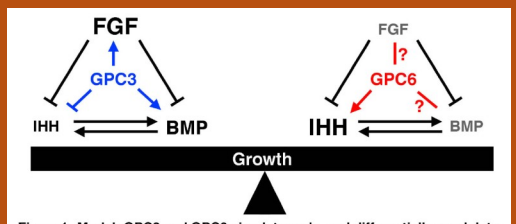


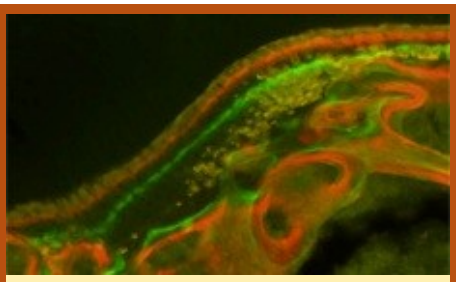
Figure 1. Model: GPC3 and GPC6 simulateously, and differentially, modulate multiple growth factor signals to coordinate and balance skeletal growth.

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

Each publication, press release or other document that cites results from NIH grant-supported research must include an acknowledgment of NIH grant support and disclaimer such as:

"The project described was supported by Award Number P30AR057235 from the National Institute Of Arthritis And Musculoskeletal And Skin Diseases. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institute Of Arthritis And Musculoskeletal And Skin Diseases or the National Institutes of Health."

If you have any questions regarding the Core, please contact:
Kamilla McGhee | *Core Coordinator* | 314.747.5993 | mcgheek@wustl.edu



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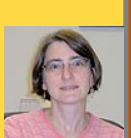

Core C

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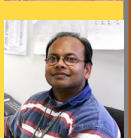

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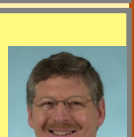

Core D

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