Center for Musculoskeletal Research

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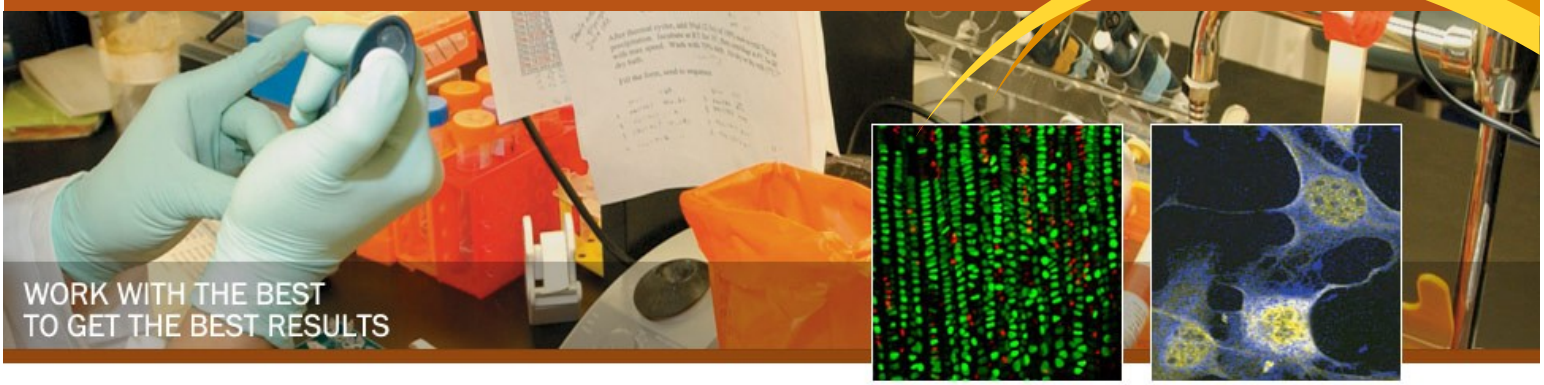
http://musculoskeletalcore.wustl.edu/home.aspx



In the September issue of our newsletter, we would like to highlight one of our Cores (ph. 1), and one of our Core users (pg.2). We have also included the schedule for the first few weeks of the Musculoskletal Seminar Series. As always, we welcome your comments, please feel free to call or send an email.

Core Highlight

More services! Less cost!

Core D—Mouse Genetics Models Core

Core D is designed to enhance the usage of mouse genetic models in musculoskeletal research. Although it has become common for investigators to use exisiting mouse models, creation of new strains uniquely useful for musculoskeletal research remains a bottleneck and has hindered progress in the field. To help alleviate this problem, Core D aims to encourage investigators to develop novel mouse strains to best address their questions in vivo. To this end, Core D funnels the core users through the existing and proven core facilities at Washington University, and provides substantial subsidies (up to 80%) to the cost associated with these services. For further information on the fee schedule and application for the usage of the Core, please visit the Core website.

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

660 S. Euclid

Yalem Research Bldg.

Campus Box 8233

St. Louis | MO | 63110

Avioli Musculoskeletal Seminar Series

Fridays @ 9am | Brown Room
Steinberg Building

9/10	Cell Bio Noon Seminar
9/17	David Linehan
9/22(Wed)	Ian Reed
(CAM Bldg	*3rd Floor Conf Rm #1)*
10/1	Civitelli Lab
10/8	Deb Patra
10/15	ASBMR
10/22	Silva Lab, Akhilesh Kotiya
10/29	Rajeev Aurora

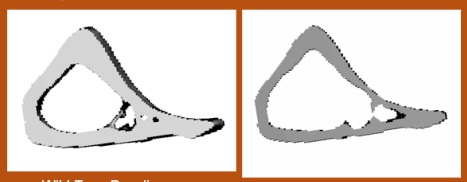
Save the Date
1st Annual
Winter Symposium
January 27, 2011

Who's using our Cores?

Susan K. Grimston, Ph.D. (Civitelli Laboratory)

One of the research focuses of the Civitelli Laboratory is to investigate the role of the gap junction protein Connexin43 (Cx43) in bone health. One of the factors important to bone health is mechanical loading. In an attempt to elucidate the role of Cx43 in mechanical loading we have induced an unloading situation in bone with the use of Botulinum toxin type A (Botox). A single injection of Botox in the musculature of the lower limb will temporarily paralyze the muscles and result in a disuse scenario in bone. Over time the muscle regenerates and reloading of the bone gradually occurs. In order to study the role of Cx43 in this scenario, we have bred mice lacking the Cx43 gene in osteoblasts and osteocytes (cKO) and subjected them to a Botox injection in the right hind limb, comparing these mice to their wild type littermates. To monitor the bone changes in each genotype due to Botox injection we have used the in vivo microct machine of the Musculoskeletal Core Facility. Repeated monthly in vivo microct scans were taken of the mice over a 20 week period, allowing for the longitudinal analyses of bone changes in both the wild type and cKO mice. We have found that the loss of Cx43 in osteoblasts and osteocytes leads to a cortical bone shape characteristic of bone in disuse, with an enlarged marrow cavity and thin cortices. These changes were observed in the wild type mice as a result of muscle paralysis due to Botox injection and were primarily due to a significant increase in endocortical osteoclasts. We also found that the absence of Cx43 results in a delayed recovery of trabecular bone mass. Furthermore, mechanical testing to failure in 3 point bending revealed a reduction in overall bone strength in the cKO mice and in the wild type mice injected with Botox. The availability of the in vivo microct machine minimized the number of mice required for the study, and provided detailed 3 dimensional analyses of the bone changes due to Botox. The mechanical testing to failure provided a biologically relevant endpoint for the study. These data were presented as an oral presentation at the 2010 Orthopedic Research Society meeting. A manuscript detailing the results from this study is currently in preparation and is targeted for the Journal of Bone and Mineral Research.

Figure demonstrating the changes in cortical morphology for the Wild Type mice following Botox. The cKO mice at baseline have a morphology similar to the Wild Type Botox, and show minimal changes due to Botox.



Wild Type Baseline | Wild Type 3 weeks post Botox

cKO Baseline | cKO 3 weeks post Botox

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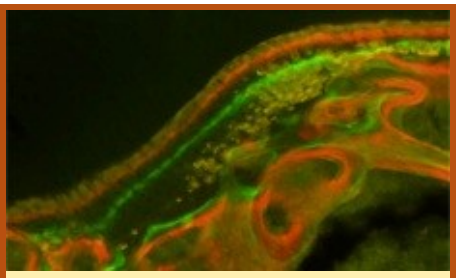

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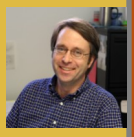

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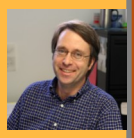

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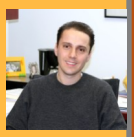

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