Center for Musculoskeletal Research

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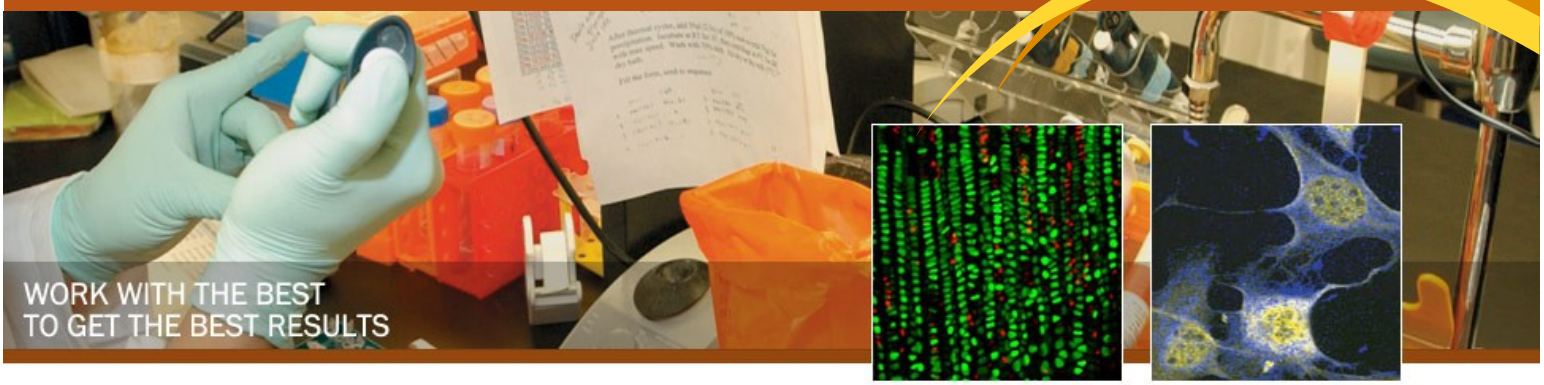
http://musculoskeletalcore.wustl.edu/home.aspx



1st Annual Winter Symposium

January 27, 2011
1-5pm

Call or email Kami McGhee
to reserve your seat.
mcgheek@wudosis.wustl.edu
314-747-5993

Core Highlight

Core C - In Situ Molecular Analysis

The **In situ Molecular Analysis Core** provides histological services for the identification and analysis of molecular phenotypes of our target tissues, bone, cartilage, muscle, tendon and ligament, in developing and adult mice. Our services include preparation of tissues and tissue sections; a reagent/protocol bank for immunohistochemistry and in situ hybridization; and facilities and training in deconvolution microscopy and histomorphometry. Our overall goal is to provide support for all facets of histological analysis of mouse musculoskeletal phenotypes.

Our main histology core facility can process decalcified bone for paraffin embedding and undecalcified bone for MMA (plastic) embedding. Sectioning for these as well as frozen sections is also available, including specific orientations of tissue. A variety of histochemical stains can also be ordered. The **advantage** of using the core is the level of experience and expertise with bone and cartilage, including special tricks for dealing with suboptimally decalcified specimens and special stains. In the coming months, we will get the CryoJane system up and running, to allow preparation of frozen sections from nondecalcified specimens. The core is open to **everyone** within the P30 grant's research base, and new groups with interest in musculoskeletal tissues can join. We aim for a 2-week turnaround time for paraffin-embedded tissue, and a 4-week turnaround time for plastics. Specimen submission forms and price lists are available on 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

1/7	**Cecelia Lo** **"Genetic analysis suggests a central role for the cilium in the pathogenesis of congenital heart disease"** *University of Pittsburg*
1/14	***Colonna Lab:* Alex Barrow** *Washington University*
1/18	**Chris Little** **Special Tuesday Seminar** **"Osteoarthritis in mice – modeling whole joint pathology and cartilage repair"** *12pm Brown Room*
1/21	**Steve Thomopoulos** *Washington University*
1/27	**Hank Kronenberg** **Thursday Symposium** *EPNEC @ 4pm* ***Harvard University***
2/4	**Weilbaecher Lab**
2/11	**Phil Osdoby**
2/18	**Linda Sandell** **"Genetic Mouse Models of Cartilage Regeneration and Osteoarthritis"** *Washington University*
2/25	**Keith Hruska**

Who's using our Cores?

Muhammad Farooq Rai, Ph.D *(Department of Orthopaedic Surgery)*

We are currently employing the services of Core C for our large-scale mouse project which creates a unique resource for the study of the mechanism(s) of how a gene or a group of genes contribute to cartilage regeneration and osteoarthritis (OA) development. In this project, we aim at establishing a genetically defined mouse model for articular cartilage regeneration in recombinant inbred (RI) lines generated from the intercrosses between the LG/J (large, healer) and SM/J (small, non-healer) strains. RI lines have been used to map complex genetic traits and each recombinant genome is replicated in the form of an entire isogenic line with genotypic variance concentrated among lines and eliminated between lines. Nine strains from RI lines (4, 5, 6, 18, 19, 33, 35, 46 and N48) selected for the present project enjoy a unique genetic composition and carry a defined genetic makeup derived from the healer LG/J strain. Our approach involved the introduction of full-thickness articular cartilage lesions on the trochlear groove of 8-weeks old mice through microsurgery. At 12 or 16 weeks post-surgery knee joints were harvested, decalcified and commissioned to Core C for histology processing. Serial sagittal sections stained with toluidine blue from each knee were analyzed by microscopy and graded for cartilage repair through a well-established scoring system.

We have identified that only one strain from RI line namely strain 6 is capable of cartilage regeneration at 16 weeks post-surgery while others strains showed no or poor healing. LG/J and another healer MRL/MpJ strains also showed a complete healing of cartilage lesions as compared to SM/J strain. As the cartilage regeneration and development of OA are interlinked and because the genetic composition of these mice is known, our findings will enable us to identify specifically those (10–20) genes that contribute to articular cartilage regeneration and thus to OA. Our current findings are both significant and novel and have been accepted as NIRA poster at the forthcoming Orthopaedic Research Society meeting in Long Beach, CA. From these data a manuscript is emerging soon which is currently in preparation for submission to PNAS. Next step is to analyze over 600 more mice from Advanced Intercross (AI) line which have already been operated for cartilage lesions. The AI line will further narrow our quest to identify the genes to 5–10 genes that are responsible for cartilage regeneration (and development of OA).

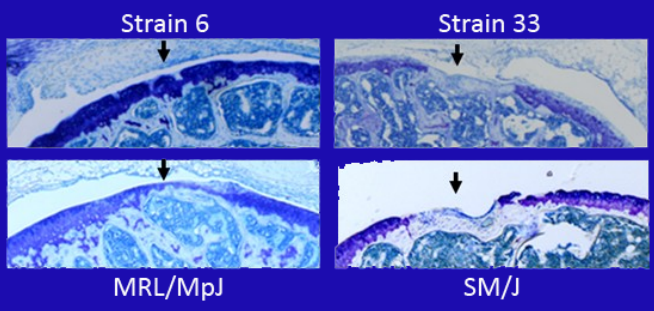
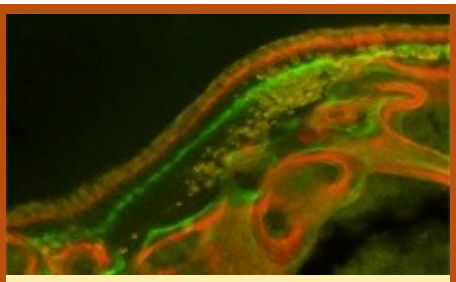


Figure 1: Analysis of articular cartilage lesions in selected strains of mice. Representative sagittal sections of full-thickness cartilage defects from strains 6, 33, MRL/MpJ and SM/J stained with toluidine blue for proteoglycan are shown. Strain 6 and MRL/MpJ mice regenerated their cartilage and showed significant proteoglycan deposition compared to the strains 33 and SM/J which remained unable to repair their cartilage and their defect site (arrow) showed no proteoglycan deposition.

Over 7500 slides have been stained with toluidine blue from 600 knees harvested from 300 mice. It would have not been possible to complete this project in a timely-fashion without the congenial help from Core C staff especially from Crystal Idleburg who took our work as precedence and accepted our speedy decalcification protocol.

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

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



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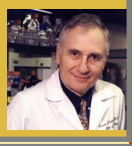

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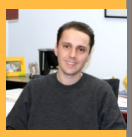

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