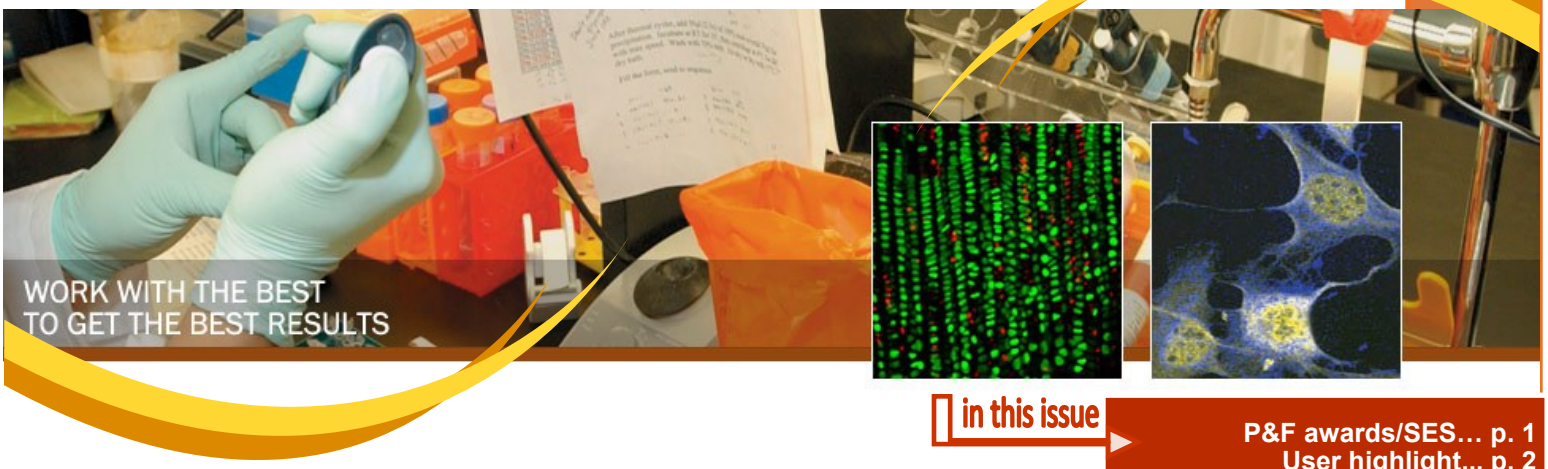
Musculoskeletal Research Center

Vol 6|Issue 3|May 2014

MUSCULOSKELETAL RESEARCH CENTER at Washington University



in this issue

2014 P&F Awards

Congratulations! The 2014 Musculoskeletal Pilot & Feasibility awards went to the following investigators:

Michael Gardner, MD
The Effects of Systemic Hedgehog Pathway Modulation on Fracture Healing

Simon Tang, PhD
In Vivo Contrast-enhanced MicroCT Imaging of the Murine Intervertebral Disc

Conrad Weihl, PhD, MD—Translation from Bench to Bedside
Preclinical Studies to Assess Autophagic Flux in Human Skeletal Muscle

Avioli Musculoskeletal Seminar Series

BJCIH Bldg. | 11th floor
A/B Conference Room
Fridays @ 9am

5/2 Ernesto Canalis, MD
Univ. of Connecticut

5/9 Richard Loeser, MD
Wake Forest School of Medicine

5/16 Alix Black, PhD
Thomopoulos Lab

5/23 Emel Esen
Long Lab

2014 Summer Educational Series

Fridays @ 9am
BJCIH Bldg. | 11th floor
A/B Conf. Rm.

6/20 **Dr. Matthew Silva** (Orthopaedic Surgery)
"Bone Imaging & Mechanical Testing"

6/27 **Rebecca Riley Vargas & Nichole Mercier** (WU)
"Evaluating Academic Inventions" & "How to Patent Your Inventions"

7/11 **Dr. Deborah Novack** (Bone & Mineral Diseases)
"What's New in Histomorphometry"

For more information about the MRC and the Cores, please click here:
http://muscoloskeletalcore.wustl.edu

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

Core D News

David Ornitz, PhD & Fanxin Long, PhD

New mouse allele now available for conditional targeting of the periosteum, endosteum, and articular surface.

Mouse line: Fgf18-CreER knockin mouse

FGF18 is a growth factor that is essential for skeletal development. Existing information suggests that *Fgf18* is expressed in the perichondrium and periosteum during embryonic development and during postnatal bone growth. *Fgf18* expression is also induced during skeletal fracture healing. Additional information suggests that *Fgf18* is expressed in postnatal articular chondrocytes.

Tools to conditionally target the endosteum, periosteum, and articular surface in postnatal mice would be useful to understand the function of many genes that are thought to function in these tissues. To establish new and potentially better tools for musculoskeletal research, we have designed a mouse line in which we have inserted a splice acceptor (SA), driving a GFP:CreERT2 fusion gene into an intron in the *Fgf18* gene (Figure 1). This vector was designed to allow GFP:CreERT2 expression in endogenous *Fgf18* expression domains in the perichondrium, periosteum, endosteum, and articular surface.

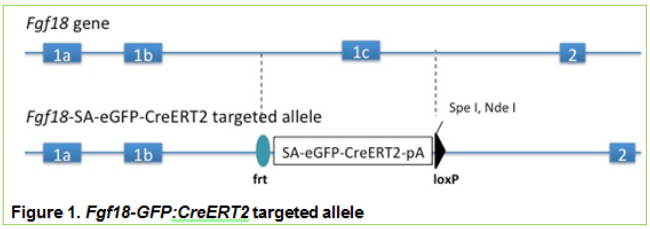


Figure 1. *Fgf18-GFP:CreERT2* targeted allele

Core D has successfully generated a knockin mouse line with the SA-GFP:CreERT2 insertion (*Fgf18-CreER*). Initial functional testing involved mating the *Fgf18-CreER* allele to a Cre-dependent reporter, such as *ROSA26-Lox-Stop-Lox (LSL)-tdTomato* allele. In the presence of tamoxifen, which activates the CreER fusion protein, the LSL cassette is deleted, allowing tdTomato expression driven by the ubiquitous ROSA26 promoter and inserted chicken beta-actin enhancer. Cre activation in this context can thus be used to trace the lineage of cells that express the *Fgf18-CreER* gene at the time of tamoxifen administration. The images in Figure 2 demonstrate that tamoxifen administration to postnatal day 3-7 mice efficiently marks the lineage of endosteal, periosteal, and articular surface cells. The GFP part of the GFP:CreER fusion protein is not expressed at high enough levels to visualize in these sections at this time point. Further experiments are underway to examine expression and function of the *Fgf18-CreER* gene at other developmental and postnatal time points.

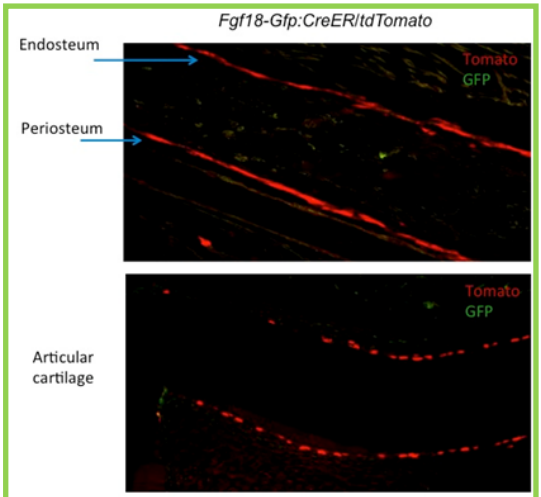


Figure 2. Expression patterns of *Fgf18-CreER*, *ROSA26-tdTomato*, injected with tamoxifen at postnatal day 3,5,7, analysis at P11. *Note that the GFP part of the GFP:CreER fusion protein is not visible.*

Through core D, we are now making this allele available to the Washington University musculoskeletal research community. If you are interested in using this mouse please contact David Ornitz.

Images provided by Kannan Karuppaiah

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