MUSCULOSKELETAL RESEARCH CENTER

http://muscoloskeletalcore.wustl.edu

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MUSCULOSKELETAL RESEARCH CENTER at Washington University

contents

Avioli Musculoskeletal Seminar Series

Fridays @ 9am
BJCIH Bldg. | 5th flr
Allison Conf. Rm.

5/4	**Elizabeth Mellins, MD** *Stanford Univ.*
5/11	**Carol Wise, PhD** *Univ. of Texas SW Med. Center*
5/18	**Wei Zou, MD, PhD** *Pathology & Immunology*
5/25	**Deneen Wellik, PhD** *Univ. of Michigan Med. Sch.*
6/1	**Tim Peterson, PhD** *Bone & Mineral Diseases*
6/8	**Clarissa Craft, PhD** *Bone & Mineral Diseases*

Summer Educational Series 2018

Fridays @ 9am
BJCIH Bldg. | 5th flr
Allison Conf. Rm.

6/15	**Gretchen Meyer, PhD** *Muscle Analysis*
6/22	**Kathyrn Trinkaus, PhD** *Power Analysis for Pre-Clinical Studies*
7/13	**Matthew Silva, PhD** *microCT*
7/27	**Deborah Veis, MD, PhD** *Histomorphometry*

Histology Core Update

The BioQuant software was recently updated to the 2018 version and the computer has been replaced.

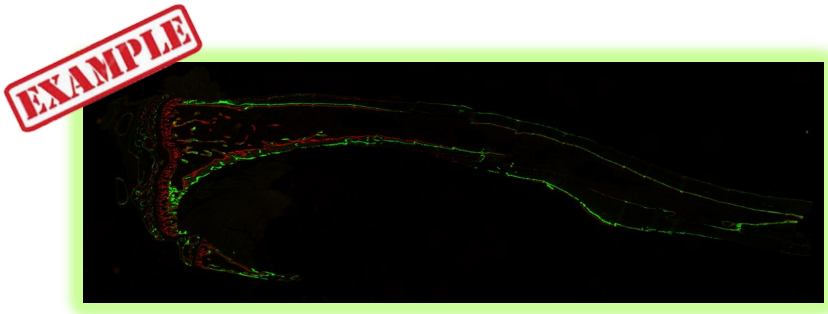
- The 2017 version will be active until July 31, so please finish any open project before then and begin new ones in the 2018 version.
- When starting a new project, export data after you analyze the first image to verify everything is working. With a new computer, there are some permissions changes that could affect your data output (i.e. you get NO data).
- You will need to make a new calibration file for your files (the only one currently loaded is Nanozoomer 20x image exported at 100%)
- There is now an option available to convert your images to .bif files. This encodes calibration into the image so you don't accidentally change calibration array for some of your analysis variables. See 2018 release notes page 10.

As always, feel free to contact BioQuant technical support by phone or email if you have specific questions.

Histology Core (Core C)—Call for Images

The MRC would like to start highlighting images derived from the histology core (Core C) resources!

If you have a great image that you have gotten from a resource provided by Core C, please send it to us with a short caption. We'd like to highlight the techniques that are available through Core C. These images will then be highlighted in our MRC newsletter.



Tile scan of unstained plastic section of mouse tibia, labeled in vivo with calcein and alizarin red, captured on new Leica confocal system in histology core (Core C).

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.

Research Highlight

Aaron N. Johnson, PhD

Assistant Professor, Department of Developmental Biology

Our skeletal muscle is an amazing organ that not only produces voluntary movements, but also regulates our breathing and maintains our core body temperature. To complete these essential functions, individual skeletal muscle cells make functional connections to tendons during development. Compared to our understanding of muscle cell fate specification and early muscle morphogenesis, relatively little is known about the mechanisms that guide muscle cells to tendon attachment sites. The Johnson lab is focused on understanding how skeletal muscles make functional connections during development, and how defects in this process contribute to muscle disease.

As a platform for gene discovery, we performed large-scale genetic screens in *Drosophila* and identified a myriad of factors that direct muscle cell growth and navigation. This genetic analysis has uncovered essential components of the muscle 'connectome' including highly conserved signal transduction pathways, RNA binding proteins, previously uncharacterized kinases, and intracellular regulators of the cytoskeleton. A major advantage for using *Drosophila* as model is that we can watch muscle development proceed *in vivo* and accurately assess how specific molecules guide muscle cells to the correct connection point. These studies have provided some of the first inroads into the mechanisms that ensure muscle cells make the correct functional connections.

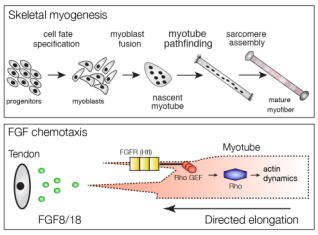


*Figure #1:**Mechanisms of muscle morphogenesis.** Skeletal myogenesis is a multistep process. We have identified FGF8/18 orthologues and the FGFR Heartless (Htl) as conserved regulators of muscle morphogenesis.*

We are currently pursuing multiple projects to understand how the muscle connectome contributes to mammalian muscle development and disease. With support from an MRC pilot and feasibility award, we are asking if Fibroblast Growth Factor (FGF) signaling, which regulates muscle cell navigation in our insect model, also directs muscle morphogenesis in mice. The mechanisms by which individual mammalian muscles acquire unique shapes and sizes are largely unknown, and we predict that FGF guided muscle-tendon connections underlie overall muscle morphology.

We have also expressed a number of congenital myopathy disease variants in insect muscles and found that these variants disrupt functional muscle connections and muscle morphology. Congenital myopathies are often diagnosed at birth due to extreme muscle weakness, and many myopathy patients will require lifelong mechanical assistance to maintain mobility and sufficient respiratory function. In collaboration with the GEiC and the hESC core, we are characterizing the impact of myopathy disease variants on human muscle fiber differentiation. Our prediction is that these disease variants will drastically alter myofiber morphology and size, and may even disrupt sarcomere assembly.

Our lab is actively recruiting at all levels. Email us at anjohnson@wustl.edu to learn more about these and other exciting myo-projects!

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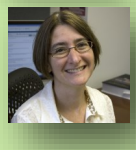

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