MUSCULOSKELETAL RESEARCH CENTER

MUSCULOSKELETAL RESEARCH CENTER at Washington University

http://muscoloskeletalcore.wustl.edu

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Avioli Musculoskeletal Seminar Series

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

11/9	**Charles Farber, PhD** Univ. of Virginia
11/16	**Amel Didakovic, PhD** Mayo Clinic
11/23	**No Seminar** Holiday
11/30	**Steve Mumm, PhD** Bone & Mineral Diseases
12/7	**Alexander Robling, PhD** Indiana Univ. School of Med.
12/14	**James Iatridis, PhD** Icahn School of Medicine
12/21	**TBA** TBA
12/28	**No Seminar** Holiday
1/4	**Jie Shen, PhD** Orthopaedic Surgery

MRC Annual Symposium

February 20, 2019
Eric P. Newman Educational Center

Core B Advisory Committee

We would like to hear the ideas and opinions of our Core B users. In an effort to facilitate this, we would like to form a Core B Advisory Committee. If you would be interested in having your voice heard, please self-nominate yourself for the committee!

For nominations, please contact Dr. Matthew Silva (silvam@wustl.edu).

Call for Proposals: Pilot & Feasibility Studies

Proposals Due: November 12, 2018

Project Start Date: April 1, 2019

The Washington University Musculoskeletal Research Center requests proposals for Pilot & Feasibility studies in the broad area of musculoskeletal research and arthritis (basic science, translational and preclinical). The goal of the P&F program is to foster projects that will generate preliminary data to support future applications for independent research support through conventional NIH granting mechanisms. For more information regarding eligibility, application guidelines and application review, please visit the following website:

http://www.musculoskeletalcore.wustl.edu/content/Pilot-amp-Feasibility-Grants/2990/Call-for-Proposals.aspx

Support for the P&F program is provided by the Musculoskeletal Research Center.

Inquiries

Informal inquires can be directed to Dr. Roberta Faccio (faccior@wustl.edu or 314-747-4602).

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

Christine Pham, MD |

Director - Division of Rheumatology
Professor of Medicine and Pathology and Immunology

One of the focuses in the Pham lab is to develop novel approaches to deliver therapeutics that will halt or reverse joint inflammation and degeneration in preclinical models of rheumatoid arthritis and osteoarthritis, with the ultimate goal of translating these findings to the clinic. These projects represent a team-science, interdisciplinary approach to arthritis research, combining the Pham lab expertise in basic mechanisms underpinning these rheumatic conditions with innovative bioengineering advances in nanomedicine and regenerative medicine pioneered by outstanding collaborators in the Departments of Orthopaedics and Bioengineering.

We collaborated with Drs. Linda Sandell, Farooq Rai, Farshid Guilak, and Sam Wickline (currently at University of South Florida) to deliver a peptide-siRNA nanocomplex targeting the NF-kB pathway to mitigate inflammation in murine models of rheumatoid arthritis and post-traumatic osteoarthritis. We have shown that peptide- NF-kB p65 siRNA nanocomplex suppresses experimental rheumatoid arthritis. We also leveraged the expertise and support of the Musculoskeletal Research Center, specifically the Structure and Strength Core and the Musculoskeletal Histology and Morphometry Core to conduct a murine model of controlled knee joint impact injury to test the hypothesis that delivery of peptide- NF-kB p65 siRNA nanocomplex in the immediate aftermath of joint injury will prevent cartilage degeneration and the eventual development of post-traumatic osteoarthritis. We showed that peptide-siRNA nanocomplex suppresses NF-kB activation (Figure 1) and mitigates several important early events post injury, including chondrocyte apoptosis, thus reducing the extent of cartilage injury and reactive synovitis. In addition to structural changes, we have now shown that treatment with peptide-siRNA nanocomplex is associated with improvement in pain sensitivity post injury. These findings may lead to the development of a first-in-class disease-modifying nanotherapeutic approach to prevent post-traumatic osteoarthritis.

More recently we have also collaborated with Dr. Guilak and

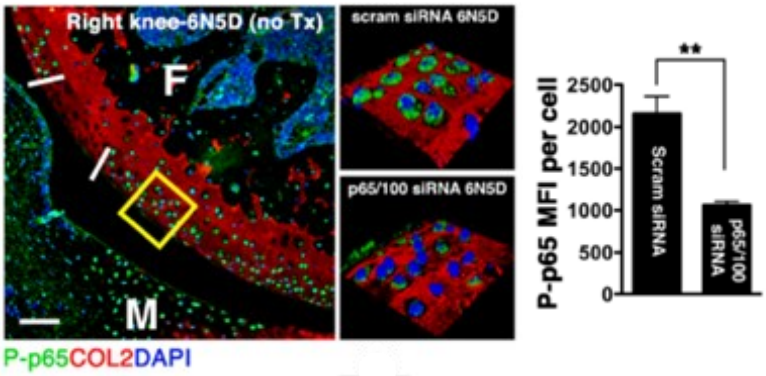

*Figure 1. Mouse knees were loaded with 6 Newtons on day 0 and and left untreated or injected IA with 0.1 mg of peptide-p65 siRNA nanocompex immediately and at 48 h after impact injury; knees were harvested on day 5 for analysis. Mean fluorescent intensity (MFI) of phospho (P)-p65 per chondrocyte in p65 siRNA or scrambled (scram) siRNA nanocomplex-treated knees was measured in the boxed area just outside of the impact zone (demarcated by white lines) from z-stack confocal images. Values represent mean ± SEM. N = 4 mice per treatment group. Scale bars = 100 mm. COL2 (red), type II collagen; F, femur; M, meniscus. DAPI (blue) stains nuclei. **P < 0.01 (Yan et al, PNAS 2016; 113:E6199-E6208.).*

stem cell-based system with autoregulated cytokine antagonist delivery to mitigate inflammation in a robust murine model of rheumatoid arthritis. The system employs genome-engineered pre-differentiated iPSCs to deliver anti-cytokine therapeutics, the production of which is driven by endogenous levels of inflammatory cytokines. Our data suggest that this "SMART" cell-based delivery of IL-1 receptor antagonist suppresses inflammation, prevents bone erosions and mitigates pain induced by inflammatory arthritis.

In addition to work in pre-clinical models of diseases, our lab is also actively involved in several translational projects. Our translational work is partially supported by the Washington University Rheumatic Diseases Research Resource-based Center (WU-RDRRC), a NIAMS-funded mechanism. WU-RDRRC's mission is to promote cross-disciplinary collaborations and to stimulate the development of new initiatives that will advance the pace of discovery, with the goal of disseminating and implementing research findings into the practice of personalized medicine.

Core A - Administration

Director
Matthew Silva, PhD
silvam@wustl.edu

Associate Director
Roberto Civitelli, MD
rcivitel@wustl.edu

Associate Director
Deborah Veis, MD, PhD

Associate Director
Linda Sandell, PhD

Core B - Structure & Strength

Director
Matthew Silva, PhD
silvam@wustl.edu

Associate Director
Simon Tang, PhD
tangs@wustl.edu

Associate Director
Gretchen Meyer, PhD
meyerg@wustl.edu

Core C - Histology

Director
Deborah Veis, MD, PhD
dveis@wustl.edu

Core D- Animal Models

Director
David Ornitz, PhD
dornitz@wustl.edu

If you have any questions regarding the MRC, contact:

Kamilla McGhee | *Core Coordinator*
314.747.5993 | kjm@wustl.edu