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).
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-κB pathway to mitigate inflammation in murine models of rheumatoid arthritis and post-traumatic osteoarthritis. We have shown that peptide-NF-κB 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-κB 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-κB 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 Drs. Linda Sandell, Farooq Rai, Farshid Guilak, and Sam Wickline to conduct a murine model of controlled knee joint impact injury to test the hypothesis that delivery of peptide-NF-κB p65 siRNA nanocomplex 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).