MUSCULOSKELETAL RESEARCH CENTER

http://muscoloskeletalcore.wustl.edu

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MUSCULOSKELETAL RESEARCH CENTER at Washington University

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Skeletal Biology Mini-Course

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

9/7	**M. Farooq Rai, PhD** Orthopaedic Surgery
9/14	**Marian Young, PhD** NIH, Bethesda, MD
9/21	**Mary Beth Humphrey, MD, PhD** Univ. of Oklahoma, Oklahoma City, OK

Save the DATE

February 20

MRC Annual Symposium

February 20, 2019
Eric P. Newman Educational Center
1:00-5:30pm

Featured Speaker:
Dr. Jennifer Elisseeff
Johns Hopkins

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. Eligible applicants include: 1. Early Stage Investigators without current or past NIH support (e.g. R01 or P01) as a Principal Investigator; 2. Postdoctoral fellows within their last 1-2 years of training who are moving toward independence. 3. Established investigators who are entering into new studies related to musculoskeletal research. 4. Investigators who have a current P&F MRC award are eligible to submit a renewal proposal for a 2nd year.

For more information regarding eligibility, application guidelines and application review, please visit the following website:

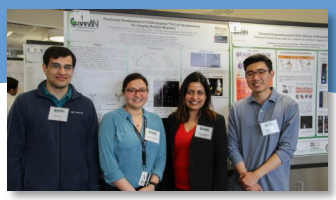
http://www.musculoskeletalcore.wustl.edu/content/Pilot-amp-Feasibility-Grants/2990/Call-for-Proposals.aspx

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).

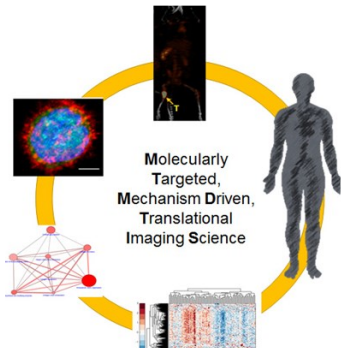
Research Highlight



The Shokeen Group is part of the ORL at the Mallinckrodt Institute of Radiology (MIR)

Monica Shokeen, PhD | *Assistant Professor, Radiology*

Shokeen Lab Research Philosophy. The Shokeen Lab is focused on developing novel approaches for imaging cancer and cardiovascular disease. Our research environment is interdisciplinary, comprising the disciplines of cancer biology, chemistry and imaging sciences. We are a part of the Optical Radiology Lab (ORL), whose overarching theme includes research, education and translation. We are also investigators in the National Cancer Institute funded Center for Multiple Myeloma Nanotherapy (CMMN). CMMN is a center of cancer nanotechnology excellence dedicated towards improving the treatment outcomes of those afflicted with multiple myeloma.



As imaging scientists driven by patient needs, we are involved in all aspects of bench to bedside translation. Our research program is dedicated towards developing and evaluating different molecular constructs, such as small molecules, peptides, multi-functional nanoparticles, and antibodies for imaging myeloma with high sensitivity and specificity. The engineers in our group are also designing efficient and accurate image analysis techniques by developing high-throughput methods for extracting molecular features from structural and functional imaging data. One of the unique aspects of the lab is that we use multi-modal nuclear, optical, and magnetic resonance imaging platforms for mechanistic evaluations. We believe that imaging sciences will continue to unravel the unknown, and we are dedicated to playing our part in this endeavor.

Selected Research Projects.

MOLECULAR IMAGING OF TUMORS AND TUMOR MICROENVIRONMENT FOR DETECTION, STAGING AND STRATIFICATION

1. Correlating changes in receptor expression (functional readout of tumor-stroma interactions) with the changes in tumor metabolism pre and post-therapy.

RECEPTOR TARGETED NUCLEAR IMAGING. Our oncologic imaging efforts are focused on multiple myeloma. Multiple myeloma is the second most commonly diagnosed hematologic cancer and is characterized by immunoglobulin secreting plasma B-cells. The interactions of myeloma cell surface integrins with the stromal environment play a defining role in the pathogenesis of multiple myeloma. Activated forms of the receptor very late antigen-4 (VLA-4; also known as integrin α4β1) are strongly expressed on the surface of multiple myeloma cells. With NIH support, we have pioneered the VLA-4 targeted molecular imaging of multiple myeloma in different *in vitro* and *in vivo* models. After completing successful pre-clinical evaluation, we are currently leading the first in-human translation of a VLA-4 targeted imaging agent, ^{64}Cu-LLP2A, for multiple myeloma diagnosis. This work will fulfill a significant unmet need in myeloma patient care by evaluating a specific imaging agent for multiple myeloma that will complement current imaging techniques for multiple myeloma.

2. Molecular imaging of multiple myeloma with [^{18}F]-FDOPA and [^{11}C]-ACETATE PET/CT. Metabolic imaging is helpful in the diagnosis, management, and evaluation of treatment response in a variety of cancer types. The current clinical metabolic imaging modality for multiple myeloma is [^{18}F]-fluorodeoxyglucose (FDG) PET/CT; however the sensitivity of FDG can be reduced in hypoproliferative multiple myeloma lesions. [^{18}F]-DOPA has shown promise preclinically and clinically in various cancers expressing the L-type amino acid transporter (LAT1). We are evaluating the application of [^{18}F]-DOPA for transporter-based imaging in myeloma mouse models. The long term goal is to stratify patients for tailored therapies. In collaboration with the Weilbaecher group, we have found that myeloma cells are dependent on acetate and monocarboxylic acid anabolic metabolism. These underlying mechanisms can be utilized for optimizing treatment regimens for myeloma patients.

3. Imaging of bone marrow with MRI. The overarching goal of this project is to demonstrate that small-animal magnetic resonance imaging (MRI) can provide quantitative and functional information in disseminated syngeneic multiple myeloma mouse models. Working with Prof. Veis and the MRC, we have validated our imaging results using bone histology (**Figure 1**). These results are broadly applicable to bone metastasis resulting from different cancers.

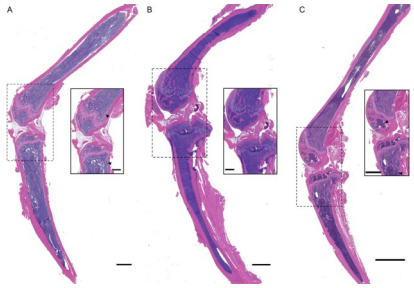


Figure 1. Collaborative work with MRC. Representative H&E sections. (A) Non-tumor bearing, (B) Untreated tumor-bearing week 4, and (C) Bortezomib treated tumor-bearing week 6. Black arrowhead represents non-tumor; gray arrowhead represents tumor. Scale bar, 1mm; Inset scale bar, 500μm.

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