AIMM/ASBMR JOHN HADDAD
YOUNG INVESTIGATORS MEETING
April 3, 4 pm version of program

April 3 – 7, 2023

SNOWMASS, COLORADO

The purpose of this conference is to bring scientists and clinicians together in a format of open verbal communication that permits the translation of basic science advances into clinical concepts. Physicians and scientists working in the field of bone and mineral metabolism are encouraged to participate.

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of the Minnesota Medical Association and AIMM. The Minnesota Medical Association (MMA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The Minnesota Medical Association designates this live activity for *AMA PRA Category 1 Credit(s)*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

2023 AIMM/ASBMR John Haddad Young Investigator Awardees

Above, from left to right:
Diana Athonvarangkul, MD, PhD, Yale School of Medicine
Stacyann Bailey, PhD - University of Massachusetts Amherst
Po-Jung Chen, DDS - University of Nebraska Medical Center
Madison Doolittle, PhD - Mayo Clinic College of Medicine and Science
Elise Jeffery, PhD - UT Southwestern Medical Center

Above, from left to right:
Ben Kirk, PhD - University of Melbourne's Medical School
Jessica Hathaway-Schrader, PhD - Medical University of South Carolina
David Maridas, PhD - Harvard School of Dental Medicine
Jun Sun, PhD - Weill Cornell Medicine
Samantha Weaver, PhD - Mayo Clinic

2023 AIMM Young Investigator Awardee

Francisca Maria Acosta, PhD
UT Health San Antonio

2023 Charles Turner Young Investigator Awardee

Roy Byung-Jun Choi, MSc
Indiana University

SUPPORTED IN PART BY EDUCATIONAL GRANTS FROM:

NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASE

NATIONAL INSTITUTE OF AGING

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AIMM/ASBMR JOHN HADDAD YOUNG INVESTIGATOR MEETING

PROGRAM

April 3 – 7, 2023, Monday – Friday
The Stonebridge Inn, Snowmass, Colorado
https://aimmmeeting.org/
All events at the Stonebridge first floor conference room/dining areas
Breakfast begins at 6:15am each day

Times provided are in Mountain Time (MT)

SUNDAY, APRIL 2
2:30 - 6:00 pm Registration

MONDAY, APRIL 3
Registration continues
Breakfast begins at 6:15am

Morning 7:00 - 9:30 am
7:00-7:15 am Mary Barbe, PhD, Temple University, *AIMM President*: Introduction and Welcome

Session 1: Updates on bone mechanoresponsiveness (basic/translational)
Chair: Alexander G Robling, PhD, IUPUI (2004 Young Investigator (YI))
Co-Chair: Perla Reyes Fernandez, PhD, IUPUI (2022 YI)

Speakers
7:15-8:00 am: Virginia Ferguson, PhD, University of Colorado at Boulder - "Bone and osteocyte responses to disuse in spaceflight"
8:00-8:45 am: Joe P Stains, PhD, University of Maryland – "Microtubules, Osteocyte Mechanotransduction, and the Surprising Regulation of Sclerostin"
8:30-8:45 am: Break
8:45-9:15 am: Roy Byung-Jun Choi, MSc, Indiana University (Charles Turner Young Investigator 2023) – "Development of inhibitors to accessory Wnt antagonists for synergistic osteoanabolic action"
9:15-9:30 am: Discussion and Overview

Learning Objectives:
Ferguson's:
Describe mechanisms by which osteocytes detect and respond to changes in mechanical stimuli.
Describe how osteocyte function and bone tissue properties are altered by disuse.
Describe how impaired osteocyte function with reduced mechanical stimuli in disuse leads to elevated fracture risk.
Stain's:
Describe how microtubules may serve as a strain sensor tuning osteocyte mechano-responsiveness.
Describe a new model for the post-translational regulation of an important bone regulating protein, sclerostin.
Assess new data suggesting an important role for Calcium/calmodulin-dependent protein kinase type II (CaMKII) in the acquisition of bone mass.
Choi's:
Understand new approaches to improving bone properties by co-inhibition of Sost and other Wnt antagonists.
Learn about strategies for addressing off target effects of pharmaceutical agents.

12:00-1:30pm: Mid-day consultations between Young and Established Investigators, including Mentoring Sessions

Afternoon 3:00 - 4:00 pm
Meet the Professor #1
Session Chair: Shirley Wang, PhD, Massachusetts General Hospital (2022 YI)

Meet the Professor speaker John Williams, PhD, Health Scientist Administrator**,** NIH/NIA **-** National Institute on Aging's Division of Aging Biology in the Aging Physiology Branch.

4:00-4:30 pm break

Afternoon to Evening Session 4:30 -7:00 pm

Session 2: Kidney and bone interactions (Translational – phosphate sensing)
Session Chair: John Wysolmerski, MD, Yale University (2000 YI)
Co-Chair: Perla Reyes Fernandez, PhD, IUPUI (2022 YI)

Speakers
4:30-5:15 pm: Eugene Rhee, MD, Massachusetts General Hospital – "Kidney glycolysis as a mammalian phosphate sensor"
5:15-6:00 pm: Petra Simic, MD, Massachusetts General Hospital – "Phosphate and FGF23 regulation in kidney injury"
6:00-6:15 pm: Break
6:15-6:45 pm: Samantha Weaver, PhD, Mayo Clinic (John Haddad Young Investigator, 2023) – "GIRK3 deletion increases bone mass, alters circulating cytokines, and perturbs hematopoiesis in adult mice"
6:45-7:15 pm: Diana Athonvarangkul, MD, PhD, Yale School of Medicine (John Haddad Young Investigator, 2023) – "Osteocytic osteolysis in lactation requires functional osteoclasts"

Learning Objectives:
Rhee's:
Understand how phosphate stimulates kidney glycolysis and G-3-P production.
Understand the key roles for Npt2a, Gpd1, and NAD+ recycling in kidney phosphate sensing.
Simic's:
Learn about mineral bone disorder in kidney disease.
Understand interaction between kidney injury and bone.
Dissect the mechanism of FGF23 regulation in acute kidney injury.
Weaver's:
Define Girk3 as a negative regulator of bone mass.
Discuss mechanisms for how Girk3 deletion regulates osteoblast and osteoclast differentiation and activity.
Determine how Girk3 regulates the immune / hematopoietic axis.
Athonvarangkul's:
Identify factors that coordinate and regulate osteocytic osteolysis in lactation.
Identify technical challenges to working with osteocytes and to troubleshoot solutions to these issues.

8 pm: Welcome Reception for registrants (no guests)

TUESDAY, APRIL 4
Breakfast begins at 6:15am

Morning 7:00 - 9:30 am
Session 3: Tumor biology (Clinical & Basic Science)

Session Chair: Gabriel Pagnotti, PhD, MD Anderson (2019 YI)
Co-Chair: Diego Grinman, PhD, Yale University (2022 YI)

Speakers
7:00-7:45 am: Yangjin Bae, PhD, Baylor College of Medicine (2014 YI) – "Dysregulation of Notch signaling in osteosarcoma"
7:45-8:35 am: Chris Collier, MD, Indiana University – "Cancer and bone from bedside to bench, with a Case"
8:35-8:50 am: Break
8:50-9:20 am: Stacyann Bailey, PhD - University of Massachusetts Amherst (John Haddad Young Investigator 2023) **-** Extracellular matrix quality and clinicopathologic factors associated with tumor-induced bone fragility
9:20-9:30 am: Discussion and Overview

Learning Objectives:
Bae's:
Understand how dysregulation of Notch signaling in the bone leads to disruption of bone homeostasis and bone malignancy.
Collier's:
Review the unmet clinical needs for patients with primary bone sarcomas.
Review the unmet clinical needs for patients with metastatic bone disease.
Explore the systemic effects of cancer and cancer treatment on bone.
Bailey's
Determine the influence of metastatic lesion types on vertebral bone architecture, composition, and mechanical properties.
Identify targetable patient factors to mitigate tumor-induced bone fragility.
Quantify the expression of osteoimmunological markers that mediate remodeling in bone metastasis.

9:30 am GROUP PHOTO

12:00-1:30pm: Mid-day consultations between Young and Established Investigators, including Mentoring Sessions

3:30-4:15 PM

A. SPECIAL SESSION - Promoting Diversity in Science
Speaker: Kristy Nicks, PhD, NIH/NIAMS - "NIH initiatives to promote diversity in science"

B. Meet the Professors Session #2– *locations to be announced with the Stonebridge common areas anticipated for these informal events*
Erica L. Scheller, D.D.S., Ph.D.

4:15-4:30 Break

Afternoon to Evening 4:30 pm -7:00 pm

SPECIAL SESSION – TECHNIQUES
4:30-5:15 pm: Speaker: Jeff Moffitt, PhD, Harvard – "Imaging the transcriptome: Using spatial transcriptomics methods to create cellular atlases"

Learning Objectives:
1. The landscape of spatial transcriptomic methods and their performance
2. Multiplexed-error robust fluorescence in situ hybridization (MERFISH)
3. The use of MERFISH to discovery, define, and map cell types in a range of tissues

5:15-5:30 pm: Break

Session 4: Young Investigator Sessions
Chair: Courtney Karner, PhD, UTSouthwestern (2017 YI)
Co-Chair: Shirley Wang, PhD, Massachusetts General Hospital (2022 YI)

5:30-6:00 pm: Jessica Hathaway-Schrader, PhD, Medical University of South Carolina (John Haddad Young Investigator 2023) – "C3a/C3aR Signaling Axis: A Dynamic Regulator of Commensal Microbiota Actions in Skeletal Health"
6:00-6:30 pm: Francisca Maria Acosta, PhD - UT Health San Antonio (AIMM Young Investigator 2023) – "Osteocytic Connexin Hemichannel Regulation of Adiposity"
6:30-7:00 pm: David Maridas, PhD, Harvard School of Dental Medicine (John Haddad Young Investigator 2023) – "Smad1/5/8 and Smad2/3 signaling compete to regulate trabecular bone mass"

Learning Objectives:
Hathaway-Schrader's:
Appreciate the role of the Gut-Bone Axis in health and disease.
Describe the complement signaling cascade and its effects on the skeleton.
Elucidate C3a/C3aR signaling in connection to the commensal microbiota and bone.
Acosta's:
Osteocytic connexin 43 (Ocy Cx43) is a transmembrane protein expressed in bone that forms hemichannels (HCs) that facilitate the communication of cells among themselves and with their environment; we aimed to identify the role that Ocy Cx43 may play in the modulation of adipose tissue, and consequently metabolism and disease progression.
Using a combined approach of transgenic mice models, a monoclonal Cx43 HC targeting antibody, and *in vitro* cell studies, we highlight how signaling molecules, originating from Ocy Cx43 HCs, can contribute to adipose tissue formation.
Maridas's:
Discuss the role of Smad1/5/8 and Smad2/3 signaling in trabecular bone acquisition and age-related bone loss.
Discuss the competition between Smad1/5/8 and Smad2/3 signaling for the regulation of osteoblastic genes.

8-10:00 pm: Welcome Dinner for registrants and guests

WEDNESDAY, APRIL 5
Breakfast begins at 6:15am

Morning 7:00 - 9:30 am
Session 5: Neural innervation of bone (basic/translational)
Session Chair: Mary Barbe, PhD, Temple University
Co-Chair: Seoyeon Bok, PhD, Weill Cornell Medicine (2022 YI)

Speakers
7:00-7:45 am: Erica Scheller, DDS, PhD, Washington University (2014 YI) – "New lessons in skeletal innervation"
7:45-8:30 am: Ryan Tomlinson, PhD, Thomas Jefferson University (2018 YI) – "NGF-TrkA Signaling in Bone"
8:30-8:45 am: Break
8:45-9:15 am: Jun Sun, PhD, Weill Cornell Medicine (John Haddad Young Investigator 2023) – "Discovery of a vertebral stem cell lineage driving spine metastasis"
9:15-9:30 am: Discussion and Overview

Learning objectives:

Scheller's:
Understand the basic features of peripheral nerve distribution and function as it relates to the skeletal system.
Discuss key mechanisms underlying the bidirectional communication between nerve and bone and the role of these signals in bone homeostasis.
Tomlinson's:
Understand nerve growth factor (NGF) expression and function in the skeleton.
Assess efforts to utilize NGF-TrkA signaling for therapeutic applications.
Sun's:
Identify stem cells for vertebral bone which display a unique biology from other skeletal sites.
Provide a stem cell basis for the long-standing clinic observation that vertebral bone attracts metastases from a wide range of solid tumors at a much higher rate than other skeletal sites.

Meet the Professors Session 2: 9:45-10:30 am - *locations to be announced with bar, lobby, meeting room anticipated for these informal events*

A. Jeff Moffitt, PhD, Harvard
B. Joe P Stains, PhD, University of Maryland

1-2:30: NASTAR SKI RACE [Please note that the time has changed]

Cheerleaders are encouraged; warm cider and cookies are served at the ski race base for all!

Afternoon to Evening Session 4:00 -7:00 pm

4:00-5:00 pm Business Meeting – election of new Board Members, discussion of future sessions

Session 6: Clinical sessions (Young Investigator + Late Breaking Clinical/Transl Abstracts and Cases)
Session Chair: Michael Mannstadt, MD, Massachusetts General Hospital
Co-Chair: Xiangli Elefteriou, PhD, Baylor College of Medicine (2004 YI)

5:15-5:45 pm: Ben Kirk, PhD, University of Melbourne's Medical School (John Haddad Young Investigator 2023) - "Bone and muscle interactions in older adults: clinical insights"
Learning Objectives:
Understand the relationship between bone fragility (osteopenia/osteoporosis) and muscle weakness (sarcopenia) with aging, and their shared risk factors and health outcomes.
Understand current recommendations for diagnosis and treatment.
Identify knowledge gaps for future research.

5:45-7:15 pm **LATE BREAKING CLINICAL/TRANSLATIONAL ABSTRACTS AND CASES**
Robert Wermers/Yves Sabbagh: INZ-701 in Adults with ENPP1 Deficiency
Joshua Sakon: Deliver of FGF for fracture healing (PoC)
Tyler Vesey/Tamara King: Sex differences in knee joint pain
Stephen Harris: Organoid system to study amelogenesis
Dana Gaddy: Respiratory distress in sheep with hypophosphatasia
Robert Tower et al: Itaconate-producing neutrophils regulate local and systemic inflammation following trauma.

8-10:00 pm: Past-Presidents Dinner for Young Investigators and Invited Speakers

THURSDAY, APRIL 6
Breakfast begins at 6:15am

Morning 7:00 - 9:30 am

Session 7 Formation and Degeneration of the Spine (Basic/Translational)

Session Chair: Florent Elefteriou, PhD, Baylor College of Medicine (2004 YI)
Co-Chair: Thomas Ambrosi, PhD, UC Davis (2022 YI)

Speakers

7:00-7:45 am: Chitra Lekha Dahia, PhD, Hospital of Special Surgery, NY – "Role of Sonic Hedgehog Signaling in the Intervertebral Disc"

7:45-8:30 am: Nilsson Holguin, PhD, Icahn School of Medicine at Mount Sinai, NY – "Bone therapeutics for disc degeneration"

8:30-8:45 am: Break

8:45-9:15 am: Po-Jung Chen, DDS, University of Nebraska Medical Center (John Haddad Young Investigator 2023) – "Senolytics alleviate the degenerative disorders of temporomandibular joint in old age"

9:15-9:30 am: Discussion and Overview

Learning objectives:

Dahia's:

Understand the development and anatomy of the intervertebral disc.
Learn about the signaling crosstalk that maintains intervertebral disc growth and health.
Learn how disc pathologies lead to its innervation and pain.
Assess how treatment of disc pathologies can reduce pain.

Holguin's:

Anti-sclerostin antibody and raloxifene injections for osteoporosis augment intervertebral disc structure.
The beneficial adaptation of the disc to injections may not require the stimulation of bone cells.

Chen's:

Evaluate the effect of senolytics on the TMJ dysfunction with aging.
Discuss the long-term effect of the elimination of senescent cells using senolytics on OA of the TMJ.

12:00-1:30pm: Mid-day consultations between Young and Established Investigators

SPECIAL SESSION – TECHNIQUES

3:15-4:15 pm: Speaker: Steve Harris, PhD, UT Health San Antonio – "Integration of genetic and genomic data to support human disease research"

Learning Objectives:

1. Introduce the use of the musculoskeletal knowledge port (mskp) to find human genetic variants associate with musculoskeletal disease. The focus on this talk will be to explore genetic variants associated with Bone Mineral density, BoneFracture Risk, and/or Osteoporosis(BMD-BFR-Osteop) and integration of this data into known genomic regions associated with gene function.
2. Introduce the UCSC Genome Browser and use in exploring genetic, epigenetic, and gene regulation data that is primarily derived from ENCODE, and integrating this type of data with the BMD-BFR-Osteop human genetic variants.
3. We will then integrate the chromatin regulatory regions (scATAC) with the human genetic variants in our BDM-BFR-Osteop data base we derived from the mskp, allowing us to prioritize further studies of human genetic variants associated with bone health.

Afternoon to Evening 4:30pm - 7:00 or 7:15 (no later) pm

Session 8 Young Investigators and Late Breaking Basic Science/Translational Abstracts

Session Chair: Daniel Perrien, PhD, Emory University School of Medicine
Co-Chair: Tamara King, PhD, University of New England

Speakers:

4:30 - 5:00 pm: Madison Doolittle, PhD, Mayo Clinic College of Medicine and Science

(John Haddad Young Investigator 2023) – "Unraveling the heterogeneity of senescent cells in the aged skeleton"
5:00-5:30 pm: Elise Jeffery, PhD, UT Southwestern Medical Center (John Haddad Young Investigator 2023) –"The unexpected fate of periosteal skeletal stem and progenitor cells in bicortical fracture healing"

Learning Objectives:
Doolittle's:
Present technique for single-cell analysis of senescent cells.
Establish defining factors for senescence in skeletal cells.
Demonstrate aged cell types targeted by senolytic approaches.
Jeffery's:
Understand the roles of bone marrow and periosteal skeletal stem/progenitor cells in bicortical fracture healing.
Understand the alterations that occur in the bone marrow microenvironment after fracture healing.

5:30-5:40 break

5:40 – 7:15 pm **LATE BREAKING BASIC SCIENCE ABSTRACTS**
Birol Ay/Murat Bastepe: Hypercalcemia caused by $G\alpha_{11}$ deficiency is associated with extra-skeletal production and increased levels of fibroblast growth factor-23 (FGF23).
Jingwen Yang, Yuji Mishina: Augmentation of BMP signaling causes midfacial defects in mice via a metabolites-epigenomic signaling.
Eri Takematsu/Charles Chat: Molecular engineering a synthetic BMP2 analog for specific targeting of the skeletal stem cell niche.
van Wijnen: Mechanism-Based Epigenetic Drugs with Bone Anabolic Properties ('Epibolics')
Hui Zhe/Joy Wu: Role of vesicle trafficking genes in osteoblast differentiation and function.
Sierra Root and Kalajzic: Hematopoietic and stromal DMP1-Cre positive cells form a unique niche in the bone marrow
Sanja Novak and Kalajzic: Transcriptional changes in periosteum of NICD1 overexpressing osteoprogenitors in fracture healing

8:00 –10 pm Awards Ceremony (dinner included)

April 7, Friday
Breakfast begins at 6:15am

Morning 7:00 - 9:30 am
Session 9 Age-associated fracture treatment and outcomes (Clinical)
Session Chair: Kurt Hankenson, DVM, PhD, University of Michigan (2003 YI)
Co-Chair: Claire Acevedo, PhD, University of Utah (2018 YI)

Speakers
7:00-7:45 am: Alex Lambi, MD, PhD, University of New Mexico - "Upper Extremity Fragility Fractures are Underappreciated Sentinel Events in Osteoporosis Management"
7:45-8:30 am: Prism Schneider, MD, PhD, University of Calgary – "Balancing Fragility Fracture Management With Patient Fears and Expectations"
8:30-9:15 pm: Kurt Hankenson, DVM, PhD, University of Michigan (2003 YI) – "The biology of impaired fracture healing"

Learning Objectives:
Lambi's
Discuss the prevalence of upper extremity fragility fractures and resulting increased risk in future osteoporotic fractures.

Discuss the role of fracture liaison services in osteoporosis screening and treatment in fragility fracture patients.
Discuss screening options, other than DXA, that can be used by surgeons to identify patients at risk for osteoporosis.

Schneider ‘s

Discuss the balance between pharmacotherapy for osteoporosis management and potential complications.
Review current concepts in atypical femur fracture etiology and management.
Understand the value of early patient engagement in lifelong bone health care.

Hankenson’s:

Challenges and opportunities in real-world implementation of evidenced-based management of medical frailty and osteoporosis in orthopaedic trauma patients.
Translational gaps in knowledge: how can we better leverage our clinical experiences and patient data to improve real-life applications of laboratory and 'basic science' knowledge.
Understanding cellular and molecular mechanisms underpinning altered fracture healing.

Thank you for your attendance!

See you next year - April 8-12, 2024