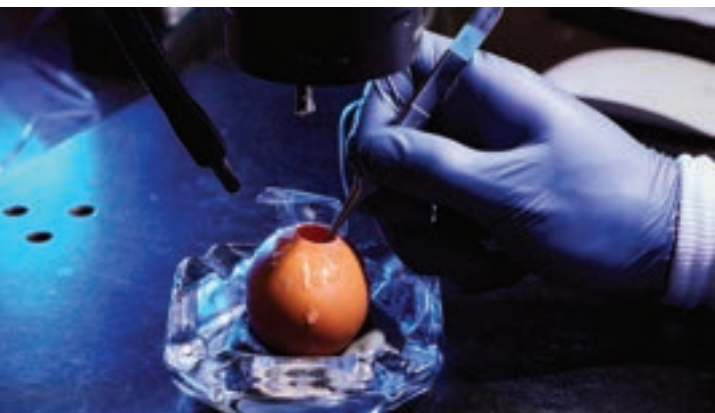


Research Report

Highlights in Musculoskeletal Research 2024



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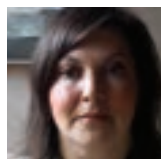
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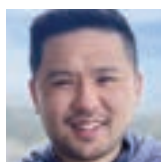
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UCSF Department of
Orthopaedic Surgery

Cover Photos

Main Photo: Kristen Chan, MS, a junior specialist in the Laboratory of Musculoskeletal Crosstalk led by Kelsey Collins, PhD, investigates mechanisms between adipose and musculoskeletal tissues and cells, pioneering new approaches to revolutionize osteoarthritis therapies

Bottom Left: Researchers in the Laboratory for Development and Evolutionary Skeletal Biology prepare a chick embryo to detect the presence of cartilage and bone formation

Bottom Right: Dr. Peter I-Kung Wu discusses a diagnosis with a patient at the UCSF Orthopedic Institute in San Francisco. UCSF Department of Orthopaedic Surgery's Spine Division leads patient-centered clinical research and care, striving to enhance outcomes and quality of life



Message from the Chair of the UCSF Department of Orthopaedic Surgery and Vice Chair of Research

Dear colleagues and friends,

As you will appreciate when reviewing this annual Research Report, our programs are both broad in scope and rich in detail. Research is woven into the fabric of the UCSF Department of Orthopaedic Surgery as is our commitment to improving musculoskeletal health and health equity worldwide.

Collectively, we strive to advance science through basic discovery research and translating promising findings into improved patient care.

The quality of our science is evidenced by our consistent ranking at, or near, the top in peer-reviewed NIH funding relative to other Orthopaedic programs in the nation. This past year, we received over \$8 million dollars in extramural funding.

The themes of our basic science programs span many musculoskeletal tissues, including bone, cartilage, spinal discs, muscle, and ligaments and tendons.

Success in these areas is supported by leveraging diverse collaborations and advanced methodologies from across all of UCSF's research ecosystem – facilitated by the Musculoskeletal Center and the long-running Core Center for Musculoskeletal Biology and Medicine (CCMBM).

We are also fortunate to be the home of several multi-disciplinary research centers supporting translation research. These include the NIH funded Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (UCSF REACH), the NSF-funded Center for Disruptive Musculoskeletal Innovations (CDMI), and the Center for Dental, Oral, and Craniofacial Tissue and Organ Regeneration (C-DOCTOR).

As detailed in this report, these translational centers bring together clinical experts, basic researchers, data scientists, and industry partners from across the U.S. to nurture promising diagnostics and therapeutics into FDA-regulated human clinical trials.

Our culture of excellence provides a solid foundation for training scientists and clinicians. Fueled by a newly funded NIH Training Grant, the Department is well positioned to leverage our research and clinical strengths to inspire and inform the next generation of scientific and clinical leaders.

We are very proud of our research team for this remarkable year and their contribution to musculoskeletal science. With a changing landscape of federal funding looming for us and all our colleagues across the U.S., we are reminded that our success has been derived from our unwavering spirit to innovate, discover and transform human health. These guiding principles will help assure our continued success well into the future as we explore new ways to diversify support for our mission.

We look forward to sharing our successes in 2025 and beyond!

Warm Regards,



C. Benjamin Ma, MD

Chair, Department of Orthopaedic Surgery
Dr. Peter and Sophie Pappas Endowed Chair
V-nee Yeh Endowed Professor
of Orthopaedic Surgery
University of California, San Francisco



Jeffrey C Lotz, PhD

Professor and Vice Chair of Research
David S. Bradford, MD, Endowed Chair
of Orthopaedic Surgery
University of California at San Francisco

Our Vision

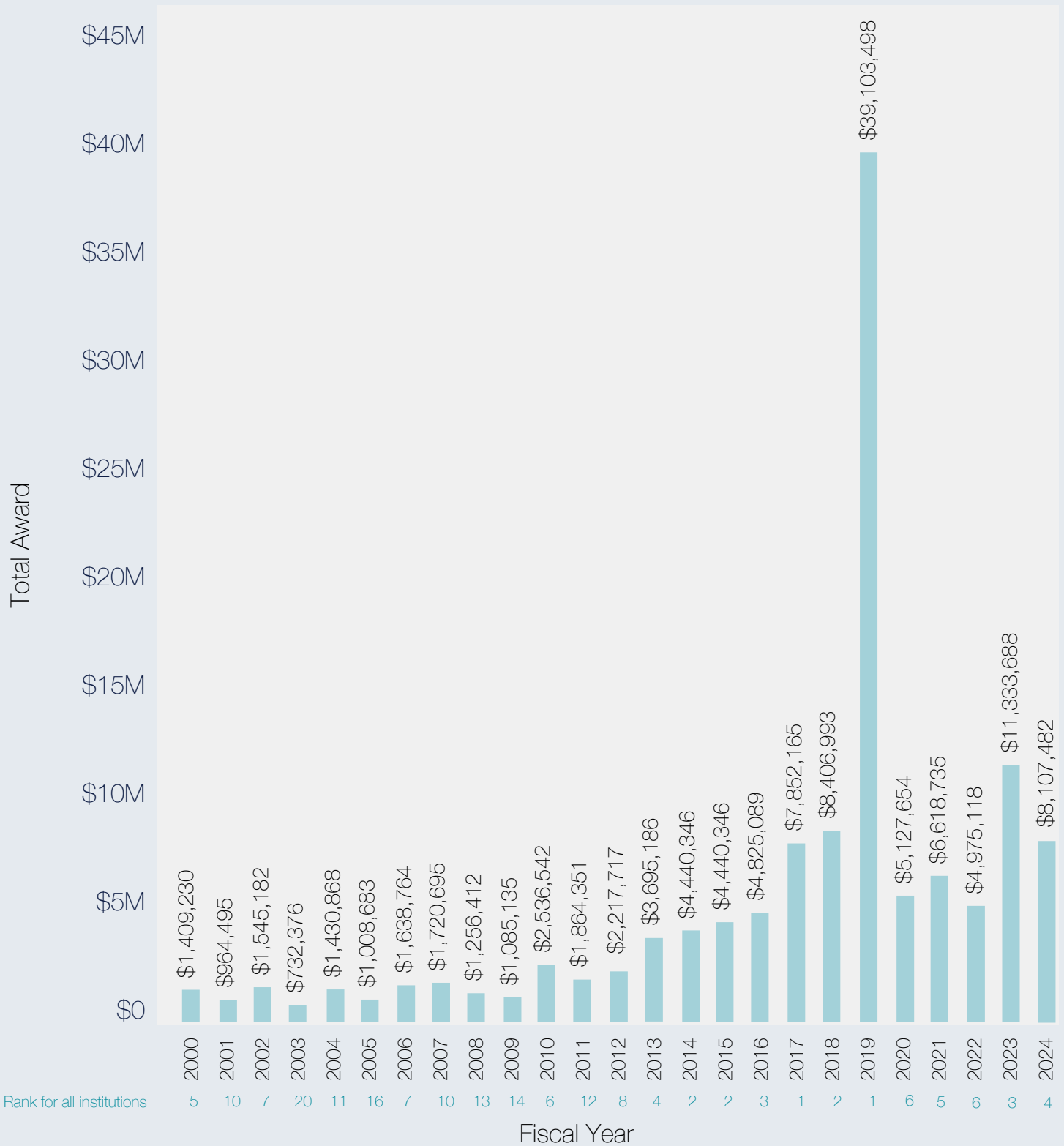
Pioneering musculoskeletal discovery and innovative care to transform lives.

Researchers from the Department participate in more than fifty scientific meetings and conferences throughout the year. Pictured here are, from left to right, Cleo Liu, BS, Hannah Herzog, BS, and Aditi Dubey, MS from Hernandez Research Group presenting a poster on orthopaedic research at the annual UCSF Orthopaedic Surgery Research Retreat.

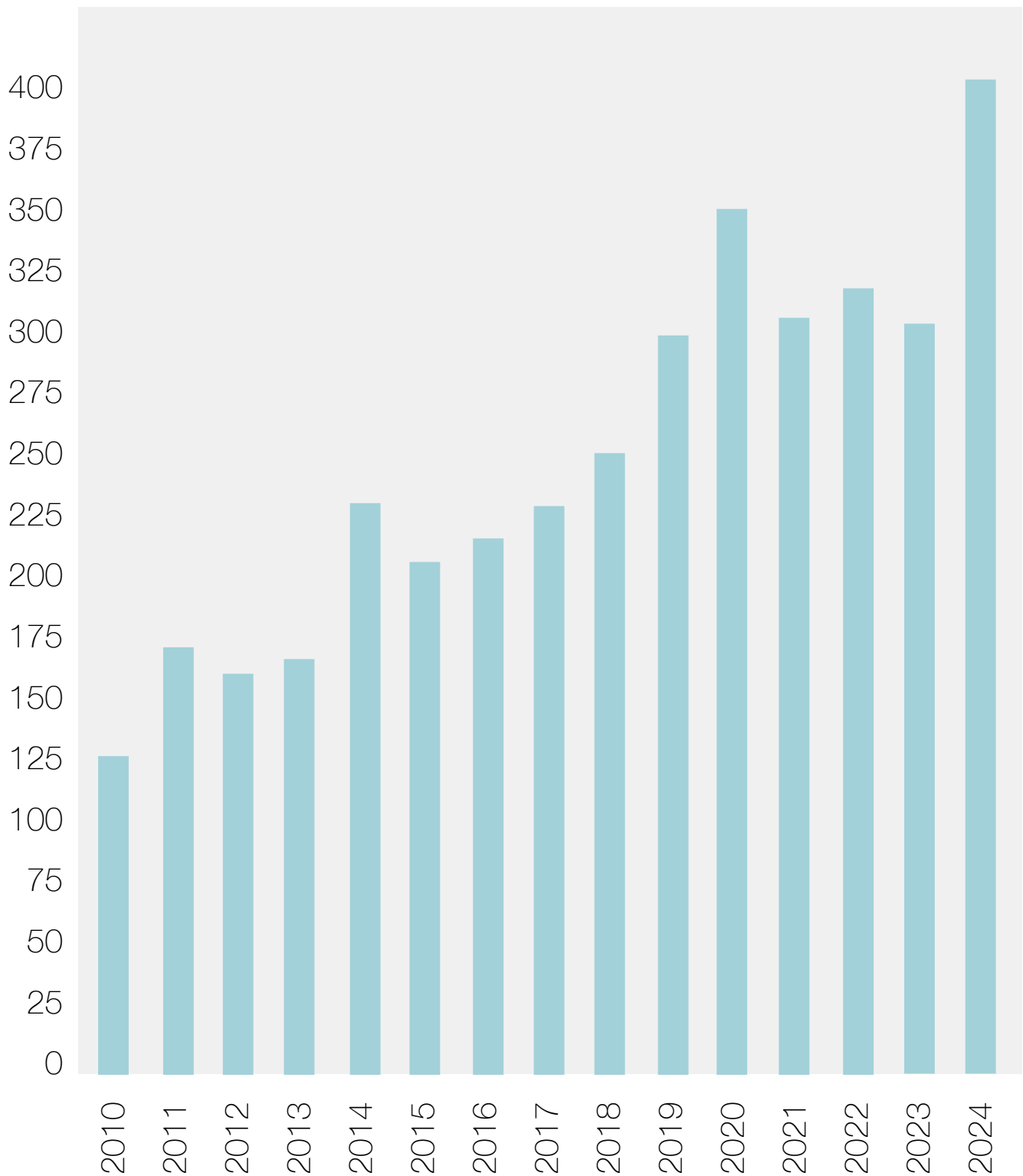


NIH Ranking

NIH Research Grants for UCSF Department of Orthopaedic Surgery



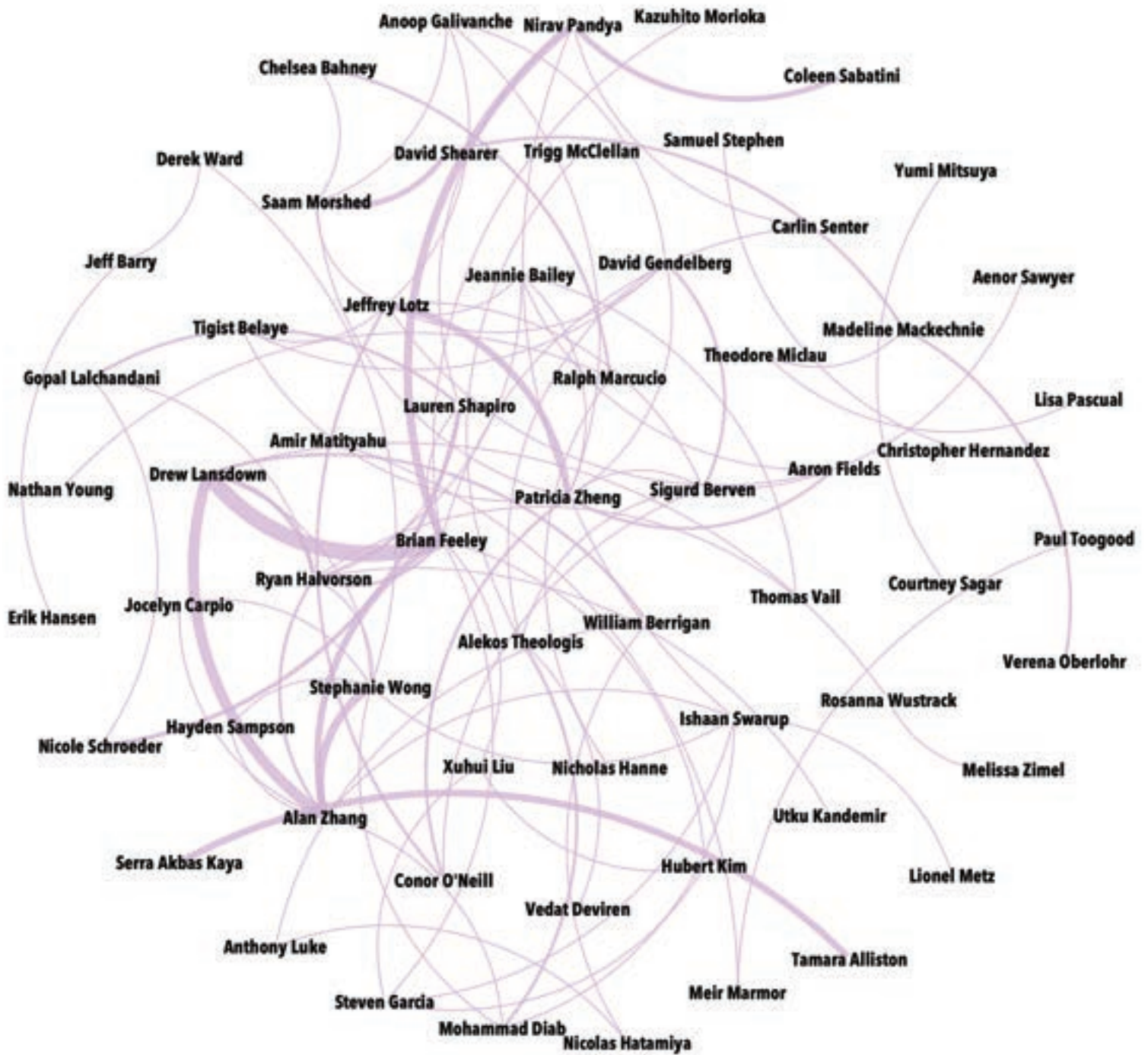
Research: UCSF Publications



Journals of our Published Research

Computer Methods in Biomechanics and Biomedical Engineering Journal of Rehabilitation and Assistive Technologies Engineering Clinical Spine Surgery Journal of Shoulder and Elbow Surgery Journal of Consulting and Clinical Psychology Arthroscopy Techniques Strategies in Trauma and Limb Reconstruction International Journal of Spine Surgery Frontiers in Bioengineering and Biotechnology JSES Reviews Reports and Techniques Spine Deformity Eur Spine J J Am Acad Orthop Surg Glob Res Rev Journal of Pediatric Orthopedics JSES International JOR Spine Journal of the American Academy of Orthopaedic Surgeons Journal of Orthopaedic Trauma Journal of the Pediatric Orthopaedic Society of North America Arthroscopy Current Reviews in Musculoskeletal Medicine J Bone Joint Surg Am Instructional Course Lectures OTA Int Journal of Hand Surgery Arthroscopy Sports Medicine and Rehabilitation OTA International The Open Access Journal of Orthopaedic Trauma Clinical Orthopaedics and Related Research J Neurosurg Spine Orthopaedic Journal of Sports Medicine Journal of Arthroplasty American Journal of Sports Medicine

Co-authorships within Department



2024 Grants and Fellowships



Tamara Alliston, PhD

NIH Natl Inst Arthr,
Musculoskel & Skin R01
Osteocytic mechanisms
required for spatiotemporal
control of bone quality
9/5/2024-8/31/2029
\$3,500,586

NIH Natl Inst Arthr,
Musculoskel & Skin P30
Core Center for
Musculoskeletal Biology and
Medicine
7/17/2024-4/30/2029
\$4,048,440

NIH Center for Scientific
Review - UC Los Angeles R34
Interdisciplinary Clinical
Advances and Research
Excellence in TMDs (ICARE 4
TMDs) Collaborative
1/1/2024-9/18/2024
\$10,830



Chelsea Bahney, PhD

NIH Natl Inst Arthr,
Musculoskel & Skin R01
Therapeutic Application of
Painless Nerve Growth Factor
to Accelerate Endochondral
Fracture Repair
8/1/2024-7/31/2026
\$1,272,144



Jeffrey Barry, MD

Smith & Nephew, Inc.
A Multi-Centre Study in
Patients Undergoing Total
Hip Arthroplasty with the
Smith+Nephew CATALYST™
Primary Hip System
9/17/2024-9/16/2029
\$387,853

American Assoc of Hip and
Knee Surgeons
AAHKS Fellowship
7/1/2024-6/30/2025
\$13,800



Shane Burch, MD

AO North America, Inc.
AO SNA Fellowship Program
2024
8/1/2024-7/31/2025
\$15,000
Medtronic, Inc. - Fellowship
Complex Spine, Data/AI
Therapies Fellowship Award -
Application MDT230036353
8/1/2024-6/30/2025
\$50,000



Michael Chau, MD

2024 ISHA Hip Preservation
Traveling Fellowship
\$12,500



Kelsey Collins, PhD

NIH Natl Institute on Aging
Unraveling Fundamental
Mechanisms of Interorgan
Crosstalk in Osteoarthritis
9/15/2024-8/31/2027
\$1,476,001



Wyatt David, MD

Orthopaedic Research and
Education Fdn. (OREF)
Establishing Crosswalks
Between Common Hip-
Specific Patient Reported
Outcomes Measurements
Utilized for Assessment of
Symptoms and Treatment
in Femoroacetabular
Impingement Syndrome
10/1/2024-09/30/2025
\$5,000



Sara Kiani, MD, MPH

Orthopaedic Research and
Education Fdn. (OREF)
Erector Spinae Plane Blocks
for Pediatric Scoliosis Posterior
Spinal Fusion
10/1/2024-9/30/2025
\$5,000



Drew Lansdown, MD

Howmedica Osteonics
Corporation
Patient Matched Reversed
Glenoid Outcomes
1/11/2024-1/10/2029
\$250,621



Xuhui Liu, MD

US Dept of Veterans Affairs
IPA-Xuhui Liu, M.D.
3/1/2024-2/28/2026
\$108,155

2024 Grants and Fellowships



Jeffrey Lotz, PhD

CALIF Inst for Regenerative
Medicine

2024 Center for Dental, Oral,
& Craniofacial Tissue & Organ
Regeneration (C-DOCTOR)
Annual Spring Conference

6/1/2024-7/31/2024

\$37,500



Kazuhito Morioka, MD, PhD

US Dept of Veterans Affairs
IPA for Kazuhito Morioka

6/1/2024-5/31/2026

\$59,635



**Sanjeev Sabharwal, MD,
MPH**

OrthoPediatrics Corp
Fellowship

8/1/2024-7/31/2025

\$127,833



Lauren Shapiro, MD, MS

NIH Natl Inst Arthr,
Musculoskel & Skin K23

Addressing Cross-Cultural
Adaptation of Patient Reported
Outcome Measures for Distal
Radius Fractures

4/1/2024-3/31/2029

\$840,926

Orthopaedic Research and
Education Fdn. (OREF)

Addressing Cross-Cultural
Adaptation of PROMs for Distal
Radius Fractures

10/1/2024-9/30/2025

\$20,000



Lacey Smith, MD

Orthopaedic Research and
Education Fdn. (OREF)

Quantifying the Burden of
Musculoskeletal Disease in
Tanzania

10/1/2024-9/30/2025

\$5,000



Ishaan Swarup, MD

Scoliosis Research Society
Preoperative Patient
Expectations in Patients
Undergoing Spinal Deformity
Surgery for Adolescent
Idiopathic Scoliosis (AIS)

9/1/2021-8/31/2025

\$30,000



Stephanie Wong, MD

American Orthopaedic Soc for
Sports Med

Sex differences in FAIS hip
synovium leading to differences
in outcomes

1/1/2024-1/1/2026

\$40,000



Alan Zhang, MD

Arthroscopy Association of
North America – Fellowship

AANA 2024 Fellowship

8/1/2024-7/31/2025

\$5,924

2024 Center-Related Grants

CCMBM



Kelly Wentworth, MD

Identifying Therapies for Fibrous Dysplasia of the Bone Using a Drug Repositioning Strategy

NIH NIAMS P30AR075055 (CCMBM Pilot Feasibility Grant)

11/14/2024-11/30/2025

\$40,000



Daehyun Yoon, PhD

Ultra-short Echo Time MRI for Aiding in the Detection of Vessels in Cortical Bone Pore Space

NIH NIAMS P30AR075055 (CCMBM Tools & Technology Grant)

01/11/2024-12/31/2024

\$7,440



Bethany Andoko, BA

NIH NIAMS P30AR075055

February 2024 – Junior Investigator Grant Development Award

\$330



Joe Baal, MD

NIH NIAMS P30AR075055 (Junior Investigator Travel Award)

April 2024 – OARSI 2024 World Congress on Osteoarthritis

\$200



Laura Chen, MS1

NIH NIAMS P30AR075055 (Junior Investigator Travel Award)

April 2024 – European Congress of Radiology 2024

\$200



Hannah Greenfeld, PhD

NIH NIAMS P30AR075055 (Junior Investigator Travel Award)

April 2024 – 12th European Zebrafish Meeting 2024

\$200



Chiho Kadota-Watanabe, PhD

NIH NIAMS P30AR075055

October 2024 - Junior Investigator Grant Development Award

\$162



Verima Pereira, PhD

NIH NIAMS P30AR075055 (Junior Investigator Travel Award)

February 2024 – ORS 2024

\$200

August 2024 - Junior Investigator Grant Development Award

\$80.63



Priscilla Tjandra, PhD

NIH NIAMS P30AR075055 (Junior Investigator Travel Award)

May 2024 – PURPOSE Annual Meeting

\$200



Betsy Young, PhD

NIH NIAMS P30AR075055

June 2024 – Junior Investigator Grant Development Award

\$250

CCMBM STRETCH Scholars



Phiphi Dinh

Department of Bioengineering,
UC Riverside

Project: Noninvasive
Assessment of Tendon
Mechanics for Grip
Rehabilitation

Mentors: Chung-Hao Lee,
PhD (UC Riverside) and Grace
O'Connell, PhD (UC Berkeley)



Kaajal Sharma

Department of Cell Biology and
Neuroscience, UC Riverside
Project: Structural and
Functional Integration of the
Neuromusculoskeletal System

Mentors: Natalie Holt, PhD (UC
Riverside), Richard Schneider,
PhD (UCSF) and Ralph
Marcucio, PhD (UCSF)

C-DOCTOR



Sarah Knox, PhD
Chelsea Bahney, PhD

Hydronovo: Salivary Gland
Regeneration

NIH NIDCR A135216

05/01/24-04/30/25

\$300,000



MSK Center T32



Eva González Díaz, PhD

Postdoctoral Scholar,
Orthopaedic Surgery

Project: Investigating the Role
of the Gut Microbiome in
Musculoskeletal Tissue Aging

Mentor: Christopher
Hernandez, PhD



Ryan Halvorson, MD

Resident, Orthopaedic Surgery

Project: Markerless Motion
Capture and Movement Quality
Algorithms to Predict Injury
Risk in High School Sports

Mentors: Jeannie Bailey,
PhD and Brian Feeley, MD



Zsafia Torok, PhD

Postdoctoral Scholar, Cellular
and Molecular Pharmacology

Project: Identifying Sex-Specific
Pathways of Hypothalamic-
Ventricular Crosstalk in Bone
Homeostasis

Mentor: Holly A. Ingraham,
PhD

Research Programs and Activities



Diane Hu, basic science researcher, works in The Molecular and Cellular Biology Laboratory to examine the process that occurs during bone regeneration after traumatic injury.

Basic, Translational, and Clinical Research

The UCSF Department of Orthopaedic Surgery has a diverse and broad basic science and translational research program in musculoskeletal biology. Areas of focus include molecular and cell biology, developmental and stem cell biology, tissue regeneration, biomechanics, imaging, and biomaterials. These research areas complement our clinical research program, which spans all orthopaedic subspecialties.

The major goal of our research is to bring new insights to the understanding of the musculoskeletal system in order to develop novel treatments for defects, diseases, conditions, and injuries that affect musculoskeletal function. We are driven by the desire to improve the delivery and outcomes of orthopaedic care.

Over the past decade, we have established large collaborative networks both within UCSF as well as with national and international researchers. This has enhanced the impact and depth of our research.

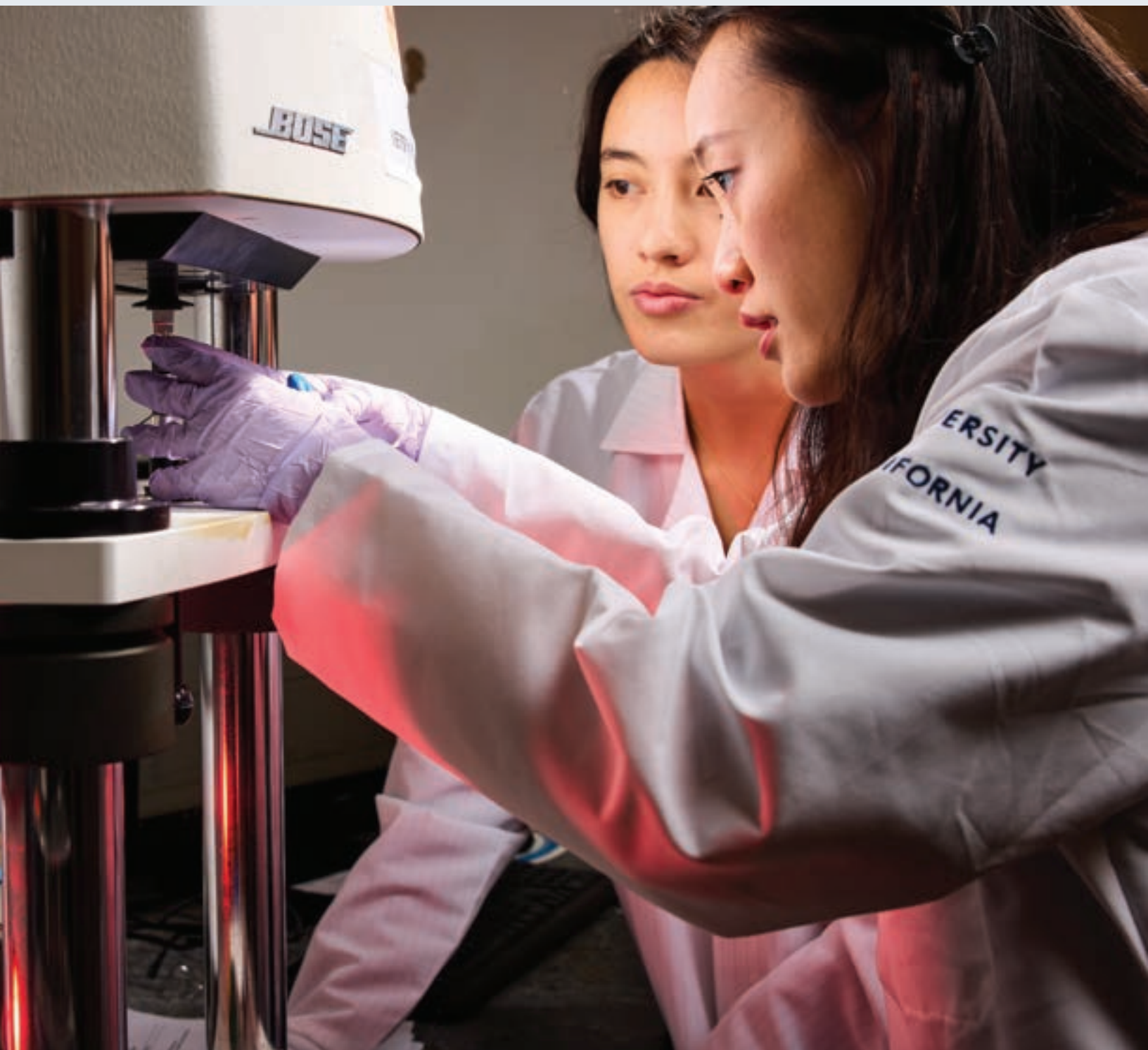
Last year, our basic, translational, and clinical research was published in high impact journals including *Bone*, *eLife*, *FASEB Journal*, *The Journal of Bone and Mineral Research (JBMR)*, *Proceedings of the National Academy of Sciences (PNAS)*, as well as major orthopaedic journals including the *Journal of Bone & Joint Surgery (JBJS)*, *Journal of Orthopaedic Trauma (JOT)*, *The*

Spine Journal, *JOR Spine*, *European Spine Journal*, *Journal of Pediatric Orthopaedics (JPO)*, *Clinical Orthopaedics and Related Research (CORR)*, and the *American Journal of Sports Medicine (AJSM)*, among others.

Our faculty, fellows, and residents have presented at numerous national and international conferences such as those held by the American Academy of Orthopaedic Surgeons (AAOS); American Association for Anatomy (AAA), Orthopaedic Research Society (ORS); the American Orthopaedic Society in Sports Medicine (AOSSM); the International Society of the Study of the Lumbar Spine (ISSLS); the American Society for Bone and Mineral Research (ASBMR); the Gordon Research Conferences (GRC), International Society of Arthroscopy, Knee Surgery and Orthopaedic Sports Medicine (ISAKOS); the Hip and Knee Society; and the Orthopaedic Trauma Association (OTA).

While the individual projects are too numerous to list in detail, we highlight here several collaborative research projects related to spine surgery, chronic low back pain, osseointegration, 3D printing, shoulder arthroplasty and instability, imaging, global health through UCSF's Institute for Global Orthopaedics and Traumatology (IGOT), sports medicine, and pediatrics.

UCSF Orthopaedic Research Laboratory at Parnassus Heights



At Parnassus Heights, our basic science laboratories collaborate to investigate mechanisms underlying different orthopaedic conditions ranging between skeletal deformity, osteoporosis, and joint degeneration. PhD students Natasha Hunt, at left, and Cleo Liu, investigates bone tissue using a state-of-the-art BOSE machine at the biomechanics lab on the Parnassus campus. Dr. Hernandez and his team are dedicated to exploring the impact of the gut microbiome on musculoskeletal tissues and orthopaedic surgery.



Laboratory for Skeletal Mechanobiology

UCSF Parnassus Heights

The Laboratory for Skeletal Mechanobiology is directed by **Tamara Alliston, PhD.**

Tamara Alliston, PhD, directs the Laboratory for Skeletal Mechanobiology. Dr. Alliston and her lab investigate the molecular pathways controlling skeletal cell behavior, how these pathways coordinate with physical cues to influence mechanical integrity of healthy bone and cartilage, and how they can be harnessed to repair tissue damaged in degenerative skeletal diseases like osteoporosis and osteoarthritis. To answer these questions they combine molecular, cellular, physiologic, and materials science approaches. In particular, they seek to define the function of TGF β in synergistically coordinating physical and biochemical cues in bone and cartilage cells. Since TGF β is a powerful regulator of homeostasis throughout the skeleton, understanding this signaling pathway has helped their team uncover fundamental new cellular mechanisms that participate in skeletal health and disease.

The lab's ongoing research focuses on the systemic and skeletal roles of osteocytes, a head-to-toe network of mechanosensory cells embedded in our bones. These cells balance metabolic and mechanical homeostasis through mechanisms that we are uncovering for the first time. A recent publication by Dr. Charles Schurman and coauthors describes his graduate work in the Alliston lab, in which they found that the loss of osteocytic TGF β

signaling is a major factor in age-related bone fragility. Supported by new grants from the NIH and the DOD, the research team is building on this discovery to identify new therapeutic strategies to promote healthy aging and improve skeletal repair.

Musculoskeletal tissues possess abundant extracellular matrix (ECM), the material that makes bone hard or cartilage shock absorbent. The ECM complicates the use of cutting-edge molecular methods for profiling, spatial, and single cell analysis of the musculoskeletal system. The Alliston lab embraces the creative adaptation and development of new strategies to apply these approaches to musculoskeletal tissues. Within the last year, their collaborations led to important technical advances, including a novel pipeline for deep proteomic profiling, among others. Their efforts advance the field with essential new tools to investigate musculoskeletal tissues. By applying these approaches to experimental models and tissues from patients undergoing orthopaedic surgery, the Alliston lab is driving discovery of new mechanisms responsible for osteoarthritis and bone fragility in humans – a key step to developing the next generation of therapies to improve musculoskeletal health.



Digital Orthopaedic Biomechanics Laboratory

Parnassus Heights

The Digital Orthopaedic Biomechanics Laboratory is directed by Jeannie Bailey, PhD.

Dr. Jeannie F. Bailey, PhD, directs UCSF's Digital Orthopaedic Biomechanics Laboratory. Her lab is part of the Musculoskeletal Research Consortium (METRICS), bridging musculoskeletal research across orthopaedic surgery, neurosurgery, and physical therapy. Dr. Bailey is also the director of the Physical Function and Biomechanics Research Core for an NIH Mechanistic Research Center for Phenotyping Chronic Low Back Pain in close collaboration with other UCSF orthopaedic surgery investigators. Her research develops advanced technology and data science approaches for creating and analyzing novel patient outcomes for predicting response to treatment. She has numerous studies tracking patient-specific biomechanical function and muscle health in various populations, including astronauts, low back pain patients, and orthopaedic surgery patients. Using these approaches, her research seeks to clarify the role of muscle health on predicting post-treatment biomechanical and pain-related outcomes for orthopaedic surgery patients. She is also actively developing and testing digital tools for enhancing patient-engagement with care and recovery, as well as safe and non-invasive digital therapeutics. While much of her basic science research is funded by the NIH, she also has had numerous grants through the UCSF Catalyst Program to develop novel devices and digital health applications for orthopaedic patient care.

Dr. Bailey is in the second year of her R01 project, teasing apart structure and function for paraspinal muscle health in chronic low back pain patients. She was also gifted a 1-million-dollar donation to support her digital health research in collaboration with Dr. Bobby Tay. In the next three to five years, she hopes to have established her research mobile platform OrthoCAP for capturing remote biomechanical tests. She also hopes to have learned more about tracking multi-domain patient recovery using real-world data from smartwatches and mobile devices. Her effort here is to create patient-specific, post-treatment recovery plans for improving long-term outcomes in many MSK patient populations.

We use markerless motion capture to examine video data of patients doing various movements, such as a sit-to-stand test. Then, using a novel approach to distill all the movements of each joint relative to each other, we can generate an overall "kinematic profile" (bottom left) for each subject during each movement. From the kinematic profiles, we can calculate the relative difference to a control population to generate a singular "movement quality" metric called the K-Score (bottom right). This work strives to create a singular metric for overall biomechanical impairment to track improvements during recovery.

UCSF medical student Aidan Foley conducts studies in the METRICS lab of Jeannie Bailey, PhD at 95 Kirkham in San Francisco. Dr. Bailey and her team concentrate on lumbar spinal conditions and low back pain, delving into innovative approaches for identifying clinically relevant biomechanical phenotypes and examining potential interactive mechanisms between distinct musculoskeletal pain phenotypes.





Musculoskeletal Crosstalk

Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research on Parnassus Heights

The laboratory for musculoskeletal crosstalk is directed by Kelsey Collins, PhD.

Dr. Kelsey Collins, PhD, directs the Laboratory for Musculoskeletal Crosstalk, which opened in the UCSF Department of Orthopaedic Surgery and Musculoskeletal Center in April 2023. Dr. Collins completed her postdoctoral in the Department of Orthopaedic Surgery at Washington University in St. Louis School of Medicine. Her work focuses on osteoarthritis (OA), the leading cause of musculoskeletal pain, which represents the primary driver for patient care-seeking behavior. There are presently no disease-modifying OA drugs, and existing pain management strategies are inadequate. Obesity is one of the leading co-morbidities in OA patients, and as such, our work has focused on better understanding this complicated relationship. Her work has shown that cartilage damage and pain with OA may originate from factors outside cartilage or outside the knee joint, such as signals from adipose tissue (fat). These findings have contributed to a paradigm shift in our understanding of OA as a systemic disease. These studies were motivated by clinical and preclinical data illustrating that changes in body mass with obesity and loading incompletely explain OA burden.

Organisms are comprised of complex, interconnected signaling networks of organs, tissues, and cells. With chronic disease, aging, and multimorbidity, this interorgan communication can break down, resulting in pathology. The goal of the Laboratory for Musculoskeletal Crosstalk is to disentangle and understand interorgan crosstalk, which may be the key to developing a first-in-class drug for OA. To this end, Dr. Collins and her team leverage their interdisciplinary skillset to characterize crosstalk from systemic contributors to musculoskeletal (MSK) damage, such as fat, the gut microbiome, and circulating factors in the blood. These interactions are critical to understanding the basic mechanisms of the disease and developing much-needed novel

therapeutic strategies. This approach is powerful at dissecting complex systemic mechanisms and interactions between age-related metabolic, biomechanical, and inflammatory factors in obesity and OA.

Using OA as a model system to understand these relationships, Dr. Collins and team can disentangle adipocyte interorgan crosstalk with effector tissues, like nerves and joint tissues in OA, obesity, diabetes, and aging. As pain is what drives OA patients to the clinic, the lab has developed a skillset in pain and behavioral testing, an outcome that is insufficiently addressed in OA. The team will harness these mechanisms to deliver novel cell-based therapeutics for arthritis, metabolic, and age-related diseases. We have developed a stem cell therapy-based platform to interchangeably and specifically delete signaling factors from fat to uncover the mechanism of fat-cartilage signaling using genome engineering tools. This approach can also be applied to leverage the cell's own regulatory mechanisms to guide therapeutic delivery in response to inflammatory signals. By endogenously delivering a variety of biologic drugs, this platform can be flexibly and readily expanded, establishing a novel approach and cell-based therapy using iPSCs that can be differentiated into designer fat or other tissues. Dr. Collins hopes to harness these mechanistic insights to create a first-in-class therapeutic strategy for OA with relevance to obesity, aging, and other chronic diseases.

This year, her leading-edge work was acknowledged with an NIH Director's New Innovator Award (DP2), the Basic Science Rising Star Award from the Osteoarthritis Society International (OARSI), and she was an invited participant in the 2024 Grainger Foundation Frontiers of Engineering Award by the National Academy of Engineering.

Grants

NIH DP2 Director's New Innovator Award 2024-2029

Arthritis National Research Foundation, 2023-2025

Lipedema Foundation, 2023-2025

NIH NIAMS R00 Pathway to Independence Award

Bakar Aging Institute Collaborative Award 2025
(with Dr. Emily Goldberg)

T32 Training for Research on Aging and Chronic Disease
Fellowship to Dr. Hope Welhaven

IRACDA K12 Fellowship to Dr. Priscilla Tjandra

Papers

Relationships between the infrapatellar fat pad and patellofemoral joint osteoarthritis differ with Body Mass Index and sex. *Journal of Orthopaedic Research*. Accepted December 2024, In press. Wagner JG*, Chen, L*, Jiang, F., Nedley, E, Akkaya, Z, Ngarmsrikan, C, Link TM, Majumdar, S, Collins KH#, Souza RB#. * annotates co-first author, #annotates co-senior author.

Engineered Self-Regulating Macrophages for Targeted Anti-inflammatory Drug Delivery. 2024 May 31. Klimak M, Cimino A, Lenz K, Springer L, Collins KH, Harasymowicz N, Xu N, Pham C, Guilak F.

Myofiber “Lipotoxicity” Does Not Disrupt Cellular Biophysical Properties. *Physiology*. 2024 May 21. Shen KC, Collins KH, Guilak F, Meyer G.

Excess Intramyocellular Lipid Does Not Affect Muscle Fiber Biophysical Properties in Mice or People With Metabolically Abnormal Obesity. *Diabetes*. 2024 Aug 1. Shen KC, Collins KH, Collins KH, Ferey JLA, Fappi A, McCormick JJ, Mittendorfer B, Guilak F, Meyer GA. PMID: 38701374. View in: PubMed

Infrapatellar fat pad synovitis morphology scores are negatively related to cartilage structure and pain. *Osteoarthritis and Cartilage*. 2024 Apr. Nedley E, Akkaya Z, Chen L, Link TM, Majumdar S, Collins KH, Souza R.

The role of sensory neurons in a hyperalgesia phenotype in Complement Factor D/Adipsin knockout mice challenged with post-traumatic osteoarthritis and obesity. *Osteoarthritis and Cartilage*. 2024 Apr. Collins KH, Braxton L, Lenz K, Oestreich A, Springer LE, Akk A, Hassan M, Scheller E, Yan H, Wu X, Atkinson J, Pham C, Guilak F.

Three decades of advancements in osteoarthritis research: insights from transcriptomic, proteomic, and metabolomic studies. *Osteoarthritis and Cartilage*. 2024 Apr. Rai MF, Collins KH, Lang A, Maerz T, Geurts J, Ruiz-Romero C, June RK, Ramos Y, Rice SJ, Ali SA, Pastrello C, Jurisica I, Appleton CT, Rockel JS, Kapoor M. PMID: 38049029. View in: PubMed

Independent and combined effects of obesity and traumatic joint injury to the structure and composition of rat knee cartilage. *Connective Tissue Res*. 2024 Mar 26. Karjalainen K, Tanska P, Collins KH, Herzog W, Korhonen RK, Moo EK. PMID: 38530304. View in: PubMed

Evolution and Advancements in Genomics and Epigenomics in OA Research: How Far We Have Come. *Osteoarthritis and Cartilage*. 2024 Feb 28. Ramos Y, Rice SJ, Ali SA, Pastrello C, Jurisica I, Rai MF, Collins KH, Lang A, Maerz T, Geurts J, Ruiz-Romero C, June RK, Appleton CT, Rockel JS, Kapoor M. PMID: 38428513. View in: PubMed

Chondrocyte-Specific Knockout of PIEZO Ion Channels Protects Against Post-Traumatic Osteoarthritis. *Orthopaedic Proceedings*. 2024 Jan 02. Ely EV, Collins KH, Lenz K, Paradi S, Liedtke W, Chen Y, Guilak F.

Fields Laboratory for Orthopaedic Biomechanics and Biotransport

UCSF Parnassus Heights

The Fields Laboratory for Orthopaedic Biomechanics and Biotransport is directed by Dr. Aaron J. Fields, PhD



Research in the Fields Laboratory for Orthopaedic Biomechanics and Biotransport, directed by Dr. Aaron J. Fields, PhD, broadly relates to structure-function relationships in musculoskeletal tissues. It has a particular focus on discovering the mechanisms of nutrient transport in cartilage and bone and harnessing nutrient transport for tissue repair and regeneration. We combine engineering and biology approaches to (1) understand the effects of aging and disease on structure-transport relationships and (2) develop translatable diagnostic and therapeutic strategies.

A primary focus of the lab's current research is the role of nutrient supply in spinal disc degeneration and regeneration. Disc degeneration is a chronic matrix remodeling process that causes back pain in many patients. Therapies to regenerate the disc — including cell, gene, or growth factor injections — have shown promise in pre-clinical studies. But clinical trials in humans indicate these therapies are largely ineffective. Poor disc nutrient supply may be the culprit. This is because increasing the number of cells inside the disc or enhancing the metabolism of native disc cells requires a rich nutrient supply, which may be inadequate in many patients. To address this issue, the Fields lab recently developed a new MRI biomarker for identifying patients with adequate nutrient supply to support regenerative therapies (Bonnheim et al.

2023. Quantitative Imaging Medical Surgery). This new MRI biomarker provides a more comprehensive assessment compared to legacy techniques, and the lab is currently leading an ongoing, NIH-funded study to test if the biomarker is predictive of patient response to intradiscal platelet-rich plasma (PRP) treatment.

While improving patient selection is critical, it doesn't address the needs of patients for whom disc nutrient supply is inadequate. Thus, the Fields lab also engineered the first treatment for enhancing disc nutrient supply (Habib et al. 2023. *Frontiers in Bioengineering and Biotechnology*) and is now conducting pre-clinical testing.

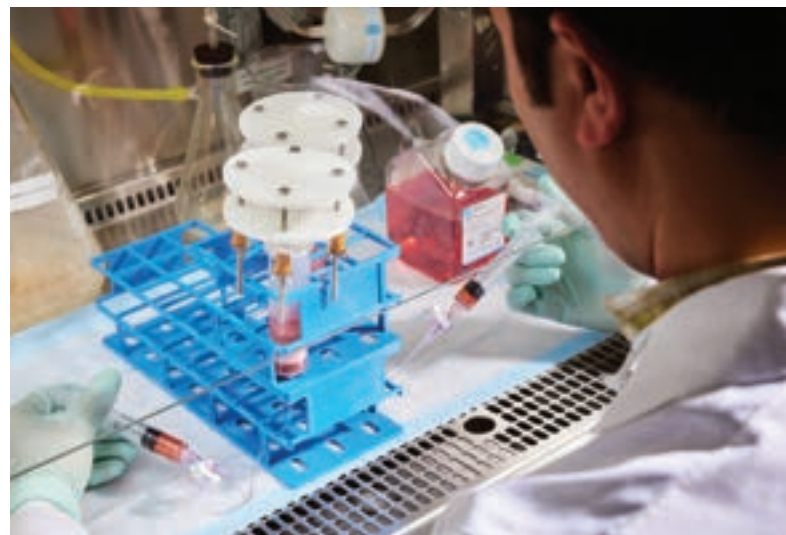
Finally, the lab is continuing its track record of pioneering discoveries into structure-function relationships in spinal cartilage. For example, the group recently found that nutrient transport in the spinal cartilage endplate is impaired by molecular cross-links, which accumulate in the disc due to aging, disease, and diet (Jung et al. 2023. *JOR Spine*). This finding complements other recent work by the group which demonstrates that excessive cross-linking impairs the biomechanical behavior of the disc (Rosenberg et al. 2023. *PNAS Nexus*).

Recent accomplishments

Jiamin Zhou's ISSLS abstract on the etiology of endplate bone marrow lesions was a finalist for the 2024 Best Paper Award at the annual meeting of the International Society for the Study of the Lumbar Spine (ISSLS)

Noah Bonnheim presented his research on sex differences in lumbar spine health at the International Spine Research Symposium

Noah Bonnheim was awarded a postdoctoral fellowship from the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS).





Hernandez Research Group

UCSF Parnassus Heights

The Hernandez Research Group is directed by
Christopher J. Hernandez, PhD.

The Hernandez Research Group, part of the Department of Orthopaedic Surgery and UCSF Health Innovations Via Engineering, studies interactions between microbes, musculoskeletal disease, orthopaedic surgery, and materials science. A primary research thrust of the lab is to understand how the gut microbiome regulates the initiation and progression of musculoskeletal diseases, including osteoporosis and osteoarthritis. Our long-term goal is to identify microbiome-based therapeutics (probiotics, fecal microbiota transplant, or molecules generated by beneficial gut microbes) to address musculoskeletal disease.

In the past year, our research group has shown that changes in the mechanical properties of bone tissue caused by the gut microbiome are reversible in the adult skeleton. This finding suggests the possibility that a microbiome-based therapeutic could be made to improve bone matrix material properties. This is a beneficial effect distinct from current therapies that focus on increasing the amount of bone matrix (for example, bone size and density). Our recent findings suggest that an adverse gut microbiome alters bone matrix in the same way as natural aging. With support from the Chan-Zuckerberg Biohub San Francisco Investigator Program, Dr. Hernandez has established collaborative relationships with CZ Biohub scientists to bring the newest genomics and metabolomics techniques to orthopaedic research.

In another arm of our research, we use micro- and nanofluidic devices manufactured with tools used in the semiconductor industry to isolate and compress individual bacteria. With support from the Center for Disruptive Musculoskeletal Innovation, our group has studied the ability of the pathogen *Staphylococcus*

aureus to squeeze into nanoscale channels within bone (similar in size to osteocyte canaliculi). Here, they are protected from neutrophils and other immune cells and may therefore contribute to the persistence of osteomyelitis. These findings have the potential to identify new strategies to address osteomyelitis and periprosthetic joint infection and to understand how bacteria colonize orthopaedic implants.

We have recently initiated several projects taking advantage of the collaborative environment at UCSF. These include efforts to understand the effects of the gut microbiome on the development of osteoarthritis (in collaboration with Kelsey Collins), and using high throughput gene editing to determine how the composition of bone and other extracellular matrices influences mechanical performance and the development of disease.

Sam Stephens, postdoctoral candidate, performs research in the Hernandez Research Group



High-impact Papers

1. Liu C., Cyphert E.L., Stephen S.J., Wang B., Morales A., Nixon J., Natsoulas N., Garcia M., Carmona PB, Vill A., Donnelly E., Brito I.L., Vashishth D., Hernandez C.J. (2024) "Microbiome-induced Increases and Decreases in Bone Tissue Strength can be Initiated After Skeletal Maturity. *J Bone Miner Res.* 39(11):1621-1632. doi: 10.1093/jbmr/zjae157

2. Heveran, C.M., Gerlach, R., Hernandez, C.J., Intemann, K., Meyer, A., Ajo-Franklin, C., Charrier, M., Srubar, W.V., Joshi, N., Nelson, A., Fields, M. (2024) "Unlocking the societal potential of engineered living materials" *Matter* 7(9): 2846-2858. doi: org/10.1016/j.matt.2024.07.011

3. Cyphert, E.L., Liu, C., Morales, A.L., Nixon, J.C., Blackford, E., Garcia, M., Cevallos, N., Turnbaugh, P.J., Brito, I.L., Booth, S.L., Hernandez, C.J. (2024) «Effects of high dose aspartame-based sweetener on the gut microbiota and bone strength in young and aged mice» *JBMR Plus.* ziae082, <https://doi.org/10.1093/jbmrpl/ziae082>

4. Lee, J., Jha, K., Harper, C.E., Zhang, W., Ramsukh, M., Bouklas, N., Chen, P., Hernandez, C.J. (2024) "Determining the Young's Modulus of the Bacterial Cell Envelope Using Microfluidic-based Extrusion Loading". *ACS Biomater Sci Eng.* 13;10(5):2956-66. 10.1021/acsbiomaterials.4c00105

Schneider Laboratory for Developmental and Evolutionary Skeletal Biology

Parnassus Heights

The Laboratory for Developmental and Evolutionary Skeletal Biology is directed by Richard A. Schneider, PhD

Dr. Richard A. Schneider, PhD, directs the Laboratory for Developmental and Evolutionary Skeletal Biology. Dr. Schneider and his lab investigate how the musculoskeletal system achieves its structural and functional integration during development. To do so, his lab created a unique surgical transplantation system that involves embryos from two distinct types of birds (quail and duck), which differ considerably in their evolutionary history, functional anatomy, and growth rates. Transplanting skeletal and other progenitor cells between these birds challenges the resulting chimeric “quack” and “duail” embryos to integrate two different species-specific developmental programs. By assaying for donor-versus-host-controlled changes to embryonic patterning and growth, this strategy has illuminated molecular and cellular mechanisms that regulate the musculoskeletal system and enable bones, cartilages, tendons, muscles, and other tissues to acquire their proper size, shape, orientation, and functional integration. A goal is use such information to devise novel molecular- and cell-based therapies for repairing and regenerating musculoskeletal tissues affected by birth defects, disease, and injury. For example, a recent publication and a current grant continue to identify genes involved in the formation and resorption of bone. DR. Schneider's research has important implications for understanding normal

Researchers in the Schneider Lab prepare chick embryos to test the role of various molecules in inducing bone formation, which has clinical implications for generating new bone in cases of injury, disease, and birth defects.

bone growth and homeostasis in the skeleton, as well as the etiologies of bone loss diseases, such as osteoporosis and osteonecrosis. Other ongoing projects focus on mechanisms that enable certain tendons to attain robust osteointegration, which has clinical implications for enhancing the capacity of torn muscle insertions to be re-attached to bone via molecular therapies. Discoveries from the Schneider Lab have also helped elucidate the role of development in evolution by revealing how genetic variation in programs for osteogenesis can drive species-specific changes in skeletal morphology.

Noteworthy Publications

Schneider RA. 2024. Cellular, Molecular, and Genetic Mechanisms of Avian Beak Development and Evolution. *Annual Reviews in Genetics*. Nov. 58(1):433-454.

Ongoing Awards and Grants

NIH Natl Inst Dental & Craniofacial Research: R01
DE016402 Mesenchymal Regulation of Osteogenesis

2/1/2022-3/31/2027

\$3,170,360



Laboratory of Muscle Injury and Translational Orthopedic Research (MITO LAB)

Directors: Xuhui Liu, MD, Michael Davies, MD, Brian Feeley, MD

What are you researching and why?

Muscle is the largest organ in the musculoskeletal system and is a dynamic organ that is critical in maintaining the health of athletes and weekend warriors. The focus of our research is to understand the cellular and molecular changes that occur within the muscle after different injuries, particularly rotator cuff tears. We have developed novel injury and repair models to study the acute and chronic effects of rotator cuff injury on the important signal transduction pathways that govern muscle cell size and stem cell fate within the muscle. We also focus on understanding how muscle injury patterns affect the stem cell populations within the muscle (satellite cells, fibroadipogenic progenitor, or FAP cells) in an effort to determine treatment strategies that would improve muscle function following orthopedic injuries.

Our past research identified FAP cells as the key cellular source of fatty infiltration, which we subsequently confirmed in patients with rotator cuff tears. Then, we started to look at how FAP cells decide to remain classic, white fat or differentiate to beige fat and aid in muscle regeneration. To do so, we developed a mouse model that simulates human cuff tears and involves tiny surgeries that mimic human rotator cuff repair. Now, we are transplanting different cells and administering pharmacologic agents (medicines created for other purposes) into the mice and watching what happens. We are also evaluating exactly how FAPs can be leveraged to muscle regeneration, from the direct expression of different proteins, to the production of exosomes, and the transfer of mitochondria from one cell to another. Everything we've found so far suggests that we can influence FAP stem cells and increase regeneration in animal rotator cuff muscle.

Over the last year, we have begun to explore what else FAPs could be regulating in muscle injuries. We have found that they may have an important role in the regulation of pain in the setting of chronic muscle injury, which could lead to novel treatment strategies to improve pain management in patients with myofascial pain.

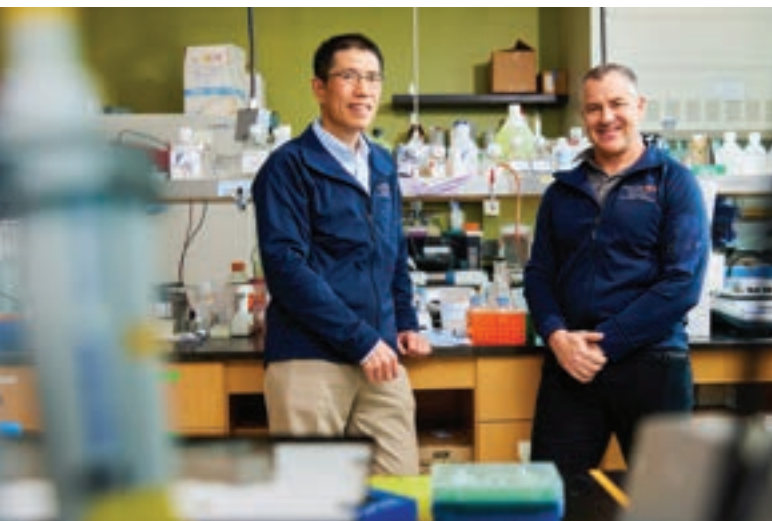
What have you accomplished over the last year?

In February of 2025, Brian Feeley and Xuhui Liu, along with Michael Davies, Steven Garcia, and Hubert Kim were awarded the AAOS/ORS Kappa Delta Award. Alex Brown, PhD, was a NIRA finalist at the ORS Annual Meeting. **Kevin Wang**, MD, our shoulder and sports medicine fellow, presented his abstract "The Influence of Age on Cellular Senescence in Injured versus Healthy Muscle and Its Implications on Rotator Cuff Injuries" at The American Shoulder and Elbow Surgeons (**ASES**) Fellows' Day Podium. At this symposium, Kevin received the Robert H. Cofield, MD, Award for Best Oral Presentation, which is awarded to the highest rated presentation.

Working with **Justin Lau**, he explored scRNAseq dataset to understand how age impacts the risk of rotator cuff tears and affects the success of repair surgery. We also had the largest number of learners in the lab over the prior summer (20+ people!)

What are the major goals for your group of the next 3-5 years?

Our goal over the next three to five years is to continue to expand our collaborations within the orthopedic surgery department, as well as across UCSF and nationally. We are excited to work with neuroscientists, aging experts, and surgeon scientists at UCSF to improve our understanding of how cellular interactions affect outcomes across the injury and degeneration spectrum. Our goal is to continue to improve the depth of our science, foster a continued diverse and inclusive environment in lab for all levels of scientists, and transition our translational research into clinical models.



Grants

NIH R01. Cell Transitions During Bone Fracture Healing. PI: Ralph Marcucio

NIH R01. The Role of Continuous Phenotypic Variation in Structural Birth Defects of the Face. PIs: Ralph Marcucio, Benedikt Hallgrimsson (U Calgary)

NIH R01. Transcriptional Regulatory Landscapes Underlying FEZ Formation. PIs: Ralph Marcucio, Licia Selleri (UCSF)

NIH, R01: Therapeutic Application of Painless Nerve Growth Factor to Accelerate Endochondral Fracture Repair. PI: Chelsea Bahney

Laboratory of Skeletal Regeneration

Orthopaedic Trauma Institute

The Laboratory of Skeletal Regeneration is directed by Ralph Marcucio, PhD and Theodore Miclau, MD

The Laboratory of Skeletal Regeneration located at the Orthopaedic Trauma Institute focuses on development and regeneration of the skeleton. Skeletal birth defects often present as a range of changes that fall along a spectrum from mild to severe. We have uncovered fundamental mechanisms by which this occurs. Genetic mutations often lead to decreased function of the proteins that are encoded. This decreased function leads to a deviation from normative skeletal outcomes, as well as an increase in the variance in the outcomes.

Our lab also studies skeletal trauma and regeneration. We have multiple ongoing studies that are aimed at understanding the cellular and molecular regulation of fracture healing and developing treatments for problematic fractures.

During fracture healing, a large cartilage template forms that is replaced by bone. Our studies have revealed that this cartilage directly transforms into the bone as the chondrocytes “transdifferentiate” into the osteoblasts that make the new bone. We have recently used an mRNA delivery system to activate a molecular pathway that increases the rate of conversion of cartilage to bone during fracture healing. This may serve as the basis for a new therapeutic approach to treat problematic fractures.



Ongoing Awards and Grants

Continuing:

NIH R01. Cell Transitions During Bone Fracture Healing. PI: Ralph Marcucio

NIH R01. The Role of Continuous Phenotypic Variation in Structural Birth Defects of the Face. PIs: Ralph Marcucio, Benedikt Hallgrímsson (U Calgary)

NIH R01. Transcriptional Regulatory Landscapes Underlying FEZ Formation. PIs: Ralph Marcucio, Licia Selleri (UCSF)

NIH, R01: Therapeutic Application of Painless Nerve Growth Factor to Accelerate Endochondral Fracture Repair. PI: Chelsea Bahney

Top 5 noteworthy publications

β -catenin mRNA encapsulated in SM-102 lipid nanoparticles enhances bone formation in a murine tibia fracture repair model. Nelson, AL, Mancino, C, Gao, X, Choe, JA, Chubb, Williams, K, Czachor, M, Marcucio, R, Taraballi, F, Cooke, JP, Huard, J, Bahney, C, Ehrhart, N. Bioactive Materials. Volume 39, September 2024, Pages 273-286

Age-related changes to macrophage subpopulations and TREM2 dysregulation characterize attenuated fracture healing in old mice. Clark D, Brazina S, Miclau T, Park S, Hsieh CL, Nakamura M, Marcucio R. Aging Cell. 2024 Sep;23(9):e14212.

Dosage-dependent effects of FGFR2W290R mutation on craniofacial shape and cellular dynamics of the basicranial synchondroses. Richbourg HA, Vidal-García M, Brakora KA, Devine J, Takenaka R, Young NM, Gong SG, Neves A, Hallgrímsson B, Marcucio RS. Anat Rec (Hoboken). 2024

Genetic architecture of trait variance in craniofacial morphology. Andrade F, Howell L, Percival CJ, Richtsmeier JT, Marcucio RS, Hallgrímsson B, Cheverud JM. Genetics. 2024 Apr 3;226(4)

Polytrauma impairs fracture healing accompanied by increased persistence of innate inflammatory stimuli and reduced adaptive response. Saiz AM, Rahmati M, Gresham RCH, Baldini TD, Burgan J, Lee MA, Osipov B, Christiansen BA, Khassawna TE, Wieland DCF, Marinho AL, Blanchet C, Czachor M, Working ZM, Bahney CS, Leach JK. J Orthop Res. 2024 Nov 17.



The Laboratory for Evolutionary Anatomy (LEA)

Zuckerberg San Francisco General Hospital

The Laboratory for Evolutionary Anatomy (LEA) is directed by Nathan M. Young, PhD.

The Laboratory for Evolutionary Anatomy (LEA), located in the Orthopaedic Trauma Institute (OTI) at Zuckerberg San Francisco General Hospital's Pride Hall, is directed by Dr. Nathan M. Young, PhD. The LEA utilizes genetic tools and methods for quantifying and comparing phenotypes at a range of scales, from embryo to adult, in a range of model (mouse, chicken) and non-model (e.g., human, turtle, alligator) systems. The LEA employs evolutionary principles such as variation, functional compromise, and historical constraint to address basic biomedical questions, and has three research foci: (1) characterizing phenomic variation in human evolution, health, and disease, including clinical and disease correlates of shape, predictive medicine, 3D medical imaging, and shape analysis; (2) the evolution and development of the skeleton; and (3) human and ape evolution, including adaptations of the face and shoulder.

Notable LEA collaborations include those with Queen's University (Ontario, Canada) to develop tools to better visualize and quantify range of motion in the shoulder of humans and closely related

living primates from in silico modelling. This has a proximate goal of better predicting function and behavior in fossil hominins, such as *Australopithecus*. Further refinement of this approach aims to not only illuminate the evolutionary history of the human shoulder and its relation to changes in locomotion, but how function has changed over time. This may lead to compromises that affect performance and disability in living humans (see figure). Additional collaborations are with the University of Calgary, with a focus on characterizing the role of the brain in orchestrating normal and abnormal outcomes in the development of the face and primary palate. A highlight of this research builds off of extensive developmental data generated from NIH R56DE029124 and in support of an R01 grant submission with Benedikt Hallgrímsson (Calgary) and Ralph Marcucio (OTI) entitled "Illuminating the Role of Brain-Face Interactions in Cranial Development".

Research Highlights

Richbourg HA, et al. 2024. Dosage-dependent effects of FGFR2W290R mutation on craniofacial shape and cellular dynamics of the basicranial synchondroses. *Anatomical Record*.

Lee ECS, et al. in review. The stabilizing potential of the supraspinatus is inhibited in tear-associated scapula shapes but can be modulated by kinematic adjustments. *Frontiers in Bioengineering and Biotechnology*.

Young NM. in review. Hominoid shoulder evolution inferred from ancestral state reconstruction of major lineages and radiations. *American Journal of Biological Anthropology*.

Zanin C, et al. 2024. Shape Variability in the Human Knee and Shoulder: Implications of Locomotor Constraints on Joint Morphology. Queen's Health Sciences Research Day.

Lee ECS, et al. 2024. Investigating the interactions among shape, kinematics, and the stabilizing potential of the supraspinatus. *Canadian Society of Biomechanics*.

Lee ECS, et al. 2024. Tear-associated scapular morphology alters the stabilizing role of supraspinatus. *International Shoulder Group*.

"Does the Brain Predict the Face? Modularity, Integration, and Developmental Orchestration in Craniofacial Morphogenesis". UCSF Program in Craniofacial Biology. Invited Speaker. June 14, 2024.

The Bahney Lab

The Bahney Lab is directed by **Chelsea Bahney, PhD**

The Bahney lab is focused on developing translationally relevant therapies or diagnostics that improve health. Our innovative therapeutic strategies are inspired from mechanistic research into normal tissue development and repair. We take a team science approach to solving unmet clinical needs, leading to collaborations within the Department of Orthopaedics, with other UCSF departments (cell and developmental biology, bioengineering, anesthesia, and anatomy), and across other research institutes. In 2024, these collaborations led to a diverse set of publications focused on studying the molecular mechanisms of delayed fracture healing to driving tissue regeneration with a first-in-class injectable mRNA therapeutic to activate the Wnt signaling pathway (see publications highlights below).



Nelson AL et al. b-catenin mRNA encapsulated in SM-102 lipid nanoparticles enhances bone formation in a murine tibia fracture repair model. *Bioactive Biomaterials*. 23 May 2024.

Duke VR et al. Murine Progeria Model Exhibits Delayed Fracture Healing with Dysregulated Local Immune Response. Preprint: <https://www.biorxiv.org/content/10.1101/2024.05.29.596277v1>

Hambright WE et al. Clinical validation of C12FDG as a marker associated with senescence and osteoarthritic phenotypes. *Aging Cell*. 06 May 2024.

Nishimura H et al. Losartan and Fisetin reduce senescence and enhance osteogenesis in human bone marrow derived mesenchymal stem cells. *Journal of Tissue Engineering and Regenerative Medicine* (Accepted)

Saiz AM et al. Polytrauma impairs fracture healing accompanied by increased persistence of innate inflammatory stimuli and reduced adaptive response. *Journal of orthopaedic research*. 2024.

Other highlights of 2024 include NIH and CIRM funded progress to support our UCSF-based start-up company Hydronovo (www.hydronovo.com), whose mission is to drive tissue regeneration through stem cell reactivation. Dr. Bahney, a co-founder of Hydronovo, has led two student groups interested in clinical translation to support this venture. This includes a capstone project for the UCSF/UC Berkeley Master of Translational Medicine (<https://mtm.berkeley.edu>) and a CU Boulder Bioengineering Senior Design team. Shout out to the MTM team who recently received 1st place in the 2024 MTM Winter Poster Symposium.

The Bahney Lab's research priorities in 2025 are to (1) engineer novel therapeutics to accelerate tissue repair, (2) define biomarkers of fracture healing to improve clinical outcomes in clinical trials, (3) measure and modulate pain during fracture repair, and (4) test novel antimicrobial approaches to treating fracture-related infection.

***Complete list of publications:**

<https://pubmed.ncbi.nlm.nih.gov/?term=Bahney%20CS%5BAuthor%5D&sort=date>



Laboratory for Digital and Computational Health Science

Multi-Campus Laboratory

The Laboratory for Digital and Computation Health Sciene is directed by **Thomas Peterson, PhD.**

Dr. Thomas Peterson, PhD, continues to be a prominent figure at the UCSF Bakar Computational Health Sciences Institute and the Director of the NIH HEAL BACPAC UCSF REACH Analytics Core. In 2024, Dr. Peterson's research has significantly advanced the understanding and management of chronic low back pain (cLBP) through innovative computational approaches. His team made substantial progress in several key areas:

1. **EHR Pain Chronicity Detection:** They developed an automated method for annotating pain chronicity in cLBP patients using electronic health records, enhancing the ability to identify and track long-term pain conditions [1].
2. **Social Determinants of Health:** Dr. Peterson's research explored the associations between social risks and healthcare utilization in cLBP patients, highlighting the importance of socioeconomic factors in orthopaedic care [2].
3. **Machine Learning Applications:** His team created machine learning models for predicting the development of low back pain detection and identified influential factors, utilizing data from a 6-year nationwide survey to improve diagnostic accuracy [3].

4. **Multimodal Data Analysis for UCSF REACH:** Dr. Peterson contributed to several projects with his cLBP collaborators at REACH including a systematic clustering analysis using multimodal data for advancing our understanding of pain subgroups [4], identifying predictors of response in PROMIS-global measures within a cLBP specialty clinic, incorporating tools like STarTBack and considering chronic overlapping pain conditions [5], and characterizing high-impact cLBP patients in a large digital cohort across the United States, providing insights into this challenging patient population [6].

These achievements underscore Dr. Peterson's commitment to leveraging computational methods and big data to improve patient care in orthopaedics and pain management. His work continues to bridge the gap between advanced technology and clinical practice, with a focus on enhancing outcomes for patients with chronic low back pain.

References

Kanal SA, Bailey JF, Lotz J, Scheffler A, Peterson TA. Decoding Pain Chronicity in Electronic Health Records: Feasibility of Automated Annotation of Pain Chronicity in Chronic Low Back Pain Patients. *The Journal of Pain*. 2024 Apr 1;25(4):50.

Pak SS, Jiang Y, Lituiev DS, De Marchis EH, Peterson TA. Evaluating associations between social risks and health care utilization in patients with chronic low back pain. *Pain Reports*. 2024 Dec 1;9(6):e1191

Bhak Y, Ahn TK, Peterson TA, Han HW, Nam SM. Machine Learning Models for Low Back Pain Detection and Factor Identification: Insights From a 6-Year Nationwide Survey. *The Journal of Pain*. 2024 Feb 10;104497.

Watanabe I, Fields AJ, Mehling W, Keller A, Matthew R, Bailey JF, Anderson P, Umrao S, Takegami N, Imagawa Y, Hue T.

4. Systematic clustering analysis using multimodal data in a chronic low back pain cohort: a preliminary baseline analysis in the ComeBACK Study. *North American Spine Society Journal (NASSJ)*. 2024 Jul 1;18:100342.

Zheng P, Ewing S, Tang A, Black D, Hue T, Lotz J, Peterson T, Torres-Espin A, O'Neill C. Predictors of response in PROMIS-global in a chronic low back pain specialty clinic: STarTBack and chronic overlapping pain conditions. *Journal of Back and Musculoskeletal Rehabilitation*. 2024 Feb 1(Preprint):1-2.

Zheng P, Scheffler A, Ewing S, Hue T, Jones S, Morshed S, Mehling W, Torres-Espin A, Galivanche A, Lotz J, Peterson T., O'Neill, C., Chronic Low Back Pain Causal Risk Factors Identified by Mendelian Randomization: a Cross-Sectional Cohort Analysis. *The Spine Journal*. 2024 Dec 04.

Orthopaedic Translational Research

Multi-campus Laboratory

The Laboratory for Orthopaedic Translational Research is directed by **Hubert Kim, MD, PhD**, and **Alfred Kuo, MD, PhD**, at the UCSF VA Research Facility at Mission Bay.

Drs. Hubert Kim, MD, PhD, and Alfred Kuo, MD, PhD, co-direct the Laboratory for Orthopaedic Translational Research. The focus of their team's research effort is to examine the molecular and cellular mechanisms responsible for secondary injury cascades that are set in motion after trauma. There is particular interest in tissues that have an extremely limited capacity for healing and regeneration, where preservation of existing cells and tissue may be of great clinical significance. The intention is to apply lessons learned in the laboratory to design better treatments for patients. In addition, the laboratory evaluates new diagnostics and therapeutics for musculoskeletal conditions, including the use of ultrasound and powered knee braces for patients with knee osteoarthritis, and a novel implant for hip arthroplasty.



Orthopaedic Tissue Engineering and Regeneration

UCSF Parnassus Heights

The Orthopaedic Tissue Engineering and Regeneration Laboratory is directed by **Jeffrey C. Lotz, PhD**.

Dr. Jeffrey C. Lotz, PhD, is the David S. Bradford M.D. Endowed Chair in Orthopaedic Surgery and Vice Chair of Orthopaedic Research at UCSF. Dr. Lotz has led the Orthopaedic Tissue Engineering Laboratory at UCSF since 1992, and his research focuses on identifying mechanisms of disc degeneration, developing novel diagnostics and therapies for low back pain, and the biomechanics of spinal instrumentation. He is bringing his multifaceted expertise to bear on the development of precision medicine approaches for chronic low back pain as principal investigator of one of the three Mechanistic Research Centers funded through the NIH Back Pain Consortium (BACPAC) Research Program (under NIH HEAL). BACPAC is a translational, patient-centered effort to combine state-of-the-art diagnostic tools and artificial intelligence approaches to personalize therapies for chronic low back pain. Dr. Lotz is also director of two other research centers, including the NIDCR-funded Center for Dental, Oral and Craniofacial Tissue and Organ Regeneration

(C-DOCTOR), and the NSF-funded Industry/University Cooperative Research Center (CDMI). Dr. Lotz earned a doctorate degree in Medical Engineering from the Harvard/MIT Division of Health Sciences and Technology, a Master of Science Degree in Mechanical Engineering Design from Stanford University, and Bachelor of Science Degree in Mechanical Engineering from UC Berkeley. (C-DOCTOR), and the NSF-funded Industry/University Cooperative Research Center (CDMI). Dr. Lotz earned a doctorate degree in Medical Engineering from the Harvard/MIT Division of Health Sciences and Technology, a Master of Science Degree in Mechanical Engineering Design from Stanford University, and Bachelor of Science Degree in Mechanical Engineering from UC Berkeley.



Clinical Research

In 2024, the UCSF Department of Orthopaedic Surgery continued to advance clinical research initiatives across our subspecialties. Our research endeavors yielded numerous publications, meeting presentations, and awarded grants. The following section will highlight programs from each of our subspecialty sections

Arthroplasty Research Group

This past year marked new objectives for the Arthroplasty research group. Their work has focused on evaluating strategies to address the growing volume of primary and revision joint arthroplasty—the most significant challenge facing our subspecialty over the next 20 years. We believe that the harmonious integration of technological advancements, innovative implant designs, refined surgical techniques, and comprehensive perioperative care is essential not only to meet this demand but also to reduce failure rates among patients with complex health conditions.

2024 Advances:

Research:

In the realm of innovation, our group has consolidated its advances in the combined use of robotics and kinematic knee alignment, notably through the work of Dr. Bini, current president of the Personalized Arthroplasty Society. Regarding innovative implant design, we have contributed to the understanding of the safety of dual mobility cups. In refining current surgical techniques, we have published research contributing to a better understanding of the behavior of antibiotics on PMMA in addressing periprosthetic joint infections. Concerning perioperative care, we have published on the rationale for intra-articular cortisone injections for the hip, clarifying their role and leading a consensus statement on the proper use of formal physical therapy post-surgery. Another remarkable publication by Dr Barry describe the perioperative results among patients who were referred for medical or surgical complexity. In the expanding field of abductor mechanism repair for the hip, our group has established itself as a leader, now with a systematic review publication.





Dr. Paul Toogood presents research on trauma and joint reconstruction at the 68th Annual LeRoy C. Abbott Visiting Scientific Program in 2024 and moderates a symposium on the future of orthopedic education. His research focuses on improving care for patients with traumatic injuries or arthritis, especially vulnerable populations.

Accomplishments

We are pleased to announce the publication of book chapters and participation as faculty in several prestigious meetings, furthering our mission to expand our international influence. Furthermore, we have been confirmed as key members, holding leadership positions, in the most significant undertaking of our subspecialty globally in 2025: the International Consensus Meeting on Periprosthetic Joint Infections. We are also proud to organize what we believe to be an influential regional annual course: “UCSF Arthroplasty for the Modern Surgeon: Hip, Knee, and Health Innovation Technology.”

Discoveries

We are using innovative point-of-care technologies, such as thermography, to evaluate the risk of postoperative wound complications. Our group has also participated in the evaluation of two recently introduced hip stems, which hold promise for amplifying the excellent results of THA.

Trainees

We are building strong foundations by working closely with our residents and remaining receptive to their research ideas and projects. We nurture their enthusiasm and strive to replicate our culture of excellent clinical care supported by research activities—a hallmark of our department and group. We are pleased to welcome a formal research fellow starting next April.

Looking Ahead (3-5 Years)

Our group’s major goals include:

Expanding Research (Quality and Quantity): We have applied for an AAHKS-supported grant with three projects. We are confident in the quality of the ideas and design, and we expect these projects to help us advance in areas where we believe greater effort is needed: access to quality care for individuals with limited English proficiency, obese patients, and patients with significant comorbidities impacting joint replacement, such as spinal conditions.

Translating Findings into Clinical Practice: We are committed to implementing all meaningful new ideas.

Mentoring Future Researchers: We will continue to prioritize training and developing young scientists in orthopedics.

Notable Publications

Ghanta RB, Tsay E, Zaid M, Ward D, Barry J. Intraarticular hip corticosteroid injections offer no meaningful benefit in delaying time to total hip arthroplasty in patients with hip osteoarthritis. *J Orthop Surg Res.* 2024;19(1):679. doi:10.1186/s13018-024-05115-x

Diaz-Ledezma, Apud DD, Martinez RD. Preoperative Considerations in Rheumatoid Arthritis and Other Inflammatory Arthritis. In: Kort NP, Hirschmann MT, Sierra RJ, Thaler MR, eds. *Fast Track Surgery in Hip and Knee Arthroplasty: New Standards.* Springer International Publishing; 2024:181-187. doi:10.1007/978-3-031-57220-3_22

Warwick H, Kwong JW, Namiri NK, Kayupov E, Maher P, Hansen EN. Revision Dual Mobility Constructs With Unmatched Acetabular and Femoral Components Do Not Increase Failure Rate. *J Arthroplasty.* 2024;39(4):1044-1047. doi:10.1016/j.arth.2023.10.044

Warwick HS, Tan TL, Rangwalla K, Shau DN, Barry JJ, Hansen EN. Effect of Antibiotic Spacer Dosing on Treatment Success in Two-Stage Exchange for Periprosthetic Joint Infection. *J Am Acad Orthop Surg Glob Res Rev.* 2024;8(2):e23.00103. doi:10.5435/JAAOSGlobal-D-23-00103

Bengoa F, López A, Rojas N, Dabed D, Diaz-Ledezma C. Total Hip Arthroplasty in Chile Is Characterized By Low Utilization Rates and Disparity in Access. *HSS J.* 2024;20(2):208-213. doi:10.1177/15563316231171865

Urrutia J, Camino-Willhuber G, Guerrero A, Diaz-Ledezma C, Bono CM. An international consensus based on the Delphi method to define failure of medical treatment in pyogenic spinal infections. *Spine J.* 2024;24(2):250-255. doi:10.1016/j.spinee.2023.09.018

Tsay EL, Nwachuku K, Bhullar PS, Kelly BJ, Ward DT, Barry JJ. Early Clinical Outcomes of “Lemon-Dropped” Complex Primary Total Joint Arthroplasty Patients to a Tertiary Care Center. *J Arthroplasty.* 2024;39(9S2):S76-S80.e2. doi:10.1016/j.arth.2024.01.058

Chi H, Woolley KA, Allahabadi S, et al. Sex-based Differences in Patient Perspectives and Experiences With Shoulder, Hip, and Knee Arthroplasty. *J Am Acad Orthop Surg Glob Res Rev.* 2024;8(4):e24.00083. doi:10.5435/JAAOSGlobal-D-24-00083

Howie CM, Cichos KH, Shoreibah MG, et al. Racial Disparities in Treatment and Outcomes of Patients With Hepatitis C Undergoing Elective Total Joint Arthroplasty. *J Arthroplasty.* 2024;39(7):1671-1678. doi:10.1016/j.arth.2024.01.054

Kwong JW, Abramowicz M, Kühn KD, Foelsch C, Hansen EN. High and Low Dosage of Vancomycin in Polymethylmethacrylate Cements: Efficacy and Mechanical Properties. *Antibiotics (Basel).* 2024;13(9):818. doi:10.3390/antibiotics13090818

Diaz-Ledezma C, Molloy I, Nelissen R, Mokete L, Costantini J. Is Prescribed Postoperative Physical Therapy Necessary after Routine Primary Total Knee or Total Hip Arthroplasty? *J Arthroplasty.* Published online October 28, 2024:S0883-5403(24)01145-8. doi:10.1016/j.arth.2024.10.105

Foot and Ankle

The Foot and Ankle is actively engaged in numerous past and ongoing projects, with a particular focus on post-traumatic arthritis and Achilles ruptures. Notably, Achilles ruptures have become more prevalent in the aging population, paralleling the rise in an increasingly active senior demographic. Research exploring clinical, functional, and cellular outcomes will play a pivotal role in determining optimal treatment strategies for these patients.

Upcoming Projects:

The foot and ankle service has started conducting database research to understand gender differences and trends in Achilles tendon ruptures.



Hand, Elbow, and Peripheral Nerve Research Group

What are you currently researching and why?

Studying social determinants of health and their association with access to and outcomes of care to inform interventions to improve disparities. Why: I strongly believe that all people, regardless of background, socioeconomic status, etc should receive timely, high-quality, and person-centered care, which currently doesn't occur.

– Lauren Shapiro, MD, MS

Researching the impact of socioeconomic disparities on hand surgical outcomes. Across many areas of medicine, social determinants of health have impacts on patient outcomes. Specifically, we are using a UC-wide database to study if there are associations between race and area deprivation index on time to surgery after distal radius fracture across the UC system. We are planning a similar study to assess for the impact of primary language on delays in time to surgery after distal radius fracture. We have similarly studied if there are associations between race/ethnicity and rates of fixation of distal radius fractures nationally in the National Surgery Quality Improvement Program (NSQIP) database, and we have found non-white patients are treated surgically at lower rates. We are planning a future study on if there are associations between non-surgical treatments tried for CMC arthritis prior to surgery and race/ethnicity, and we are planning future studies on the impact of language on treatment of these conditions.

I am also working on collaborations with other institutions. We are working with pediatric hand surgeons at Shriners' Hospital to help characterize maternal and patient risk factors for Constriction Band Sequence, using a statewide database. I am also working with hand surgeons at Brigham & Women's Hospital to help understand if bracing, injections, or surgery are more effective at treating nocturnal awakening symptoms for carpal tunnel syndrome.

Finally, in terms of prospective studies, we are looking at the impact of wide-awake versus MAC anesthesia on anxiety scores in patients before and after simple hand surgeries. We are also planning biomechanical studies on the use of an Internal Joint Stabilizer and ligament reconstruction in the setting of elbow instability.

– Gopal Lalchandani, MD

I'm trying to focus my current research interests on nerve. Nerve surgery is a special focus of my clinical practice, and nerve injuries represent a significant burden to our patients. To date, our ability to effectively diagnose and treat nerve injuries continues to be limited and therefore I feel that clinical research in this field can

be particularly impactful. For example, one ongoing project seeks to find a correlation between visual appearance and histology of the nerve intra-operatively after neuroma resection in an attempt to assist surgical decision making.

– Igor Immerman, MD

What have you accomplished over the last year?

NIH K23 Award, OREF Mentored Clinical Scientist Award, Gelberman Scholar Award, DEI NOVA Award, continued to build research lab and collaborations at UCSF, domestically, and internationally.

– Lauren Shapiro, MD, MS

We have two reviews accepted into JHS, multiple presentations accepted at our annual hand society meetings, and started our prospective study of anxiety scores in wide-awake versus MAC anesthesia before and after simple hand surgeries.

We also completed a study on the surgical treatments for proximal humerus fractures nationally, finding there is an association between race/ethnicity and treatment with newer interventions such as reverse total shoulder arthroplasty.

– Gopal Lalchandani, MD

This year I took on a role of a PI for UCSF site as part of a multi-center RCT of a novel nerve repair device. This study is currently awaiting IRB approval at UCSF to begin enrolling patients. A Comparison of NeuroSpan Bridge, NeuraGen Nerve Guide, and Nerve Autograft for Peripheral Nerve Repair (NeuroSpan-1)

Co-investigator on a NIH R01 grant application by Dr Daehyun Yoon, Dept of Radiology, entitled Advanced 3D MRI of peripheral nerves. Unfortunately the grant was not funded this year but we are re-submitting.

– Igor Immerman, MD

Publications:

Lalchandani GR, Dyer GSM, Schroeder NS. Resident Education in Hand Surgery: Barriers and Opportunities. *J Hand Surg Am* (accepted, pending publication)

Lalchandani GR, Shapiro LM, Schroeder NS. Shared Decision Making in Hand Surgery. *J Hand Surg Am*. 2024 Oct;49(10):1022-1026. doi: 10.1016/j.jhsa.2024.04.013. Epub 2024 Jul 19. PMID: 39033454.

Halvorson RT, Su F, Ghanta RB, Garcia-Lopez E, Lalchandani GR, Shapiro LM. Adoption of reverse total shoulder arthroplasty for surgical treatment of proximal humerus fractures differs by patient race. *J Shoulder Elbow Surg*. 2024 Aug 7:S1058-2746(24)00533-0. doi: 10.1016/j.jse.2024.06.003. Epub ahead of print. PMID: 39097137.

Lauren Shapiro, MD, MS:

Mulakaluri A, Julian KR, Fernandez A, Kamal RN, Shapiro LM. Are Clinical Practice Guidelines Representative of Patients with Distal Radius Fractures? A Review of Patient Demographics and PROMs Used to Inform Guidelines. *J Hand Surg Am*. 2024;10:S0363-5023(24)00148-5.

Julian K, Mulakaluri A, Truong N, Fernandez A, Kamal RN, Shapiro LM. Are Orthopaedic Clinical Trials Linguistically and Culturally Diverse? A Systematic Review. *JBJS Reviews*. 2024; 12(5):e24.00012.

Siu J, Garcia-Lopez E, Pandya N, Feeley B, Shapiro LM. Are Patient-Reported Outcome Measures for Anterior Cruciate Ligament Injuries Validated for Spanish Language and Culture? A Systematic Review. *Orthopaedic Journal of Sports Medicine*. 2024;12(8):23259671241256413.

SDOH are associated with worse access and outcomes:

Truong NM, Stroud SG, Zhuang T Fernandez A, Kamal RN, Shapiro LM. The Association Between Social Determinants of Health and Distal Radius Fracture Outcomes. *J Hand Surg Am*. 2024 Jun 24:S0363-5023(24)00201-6.

Grants, awards, pubs, trainee grants: NIH K23 Award, OREF Mentored Clinical Scientist Award, Gelberman Scholar Award, multiple Heiman awards, multiple Summer Explore awards

This paper was accepted at JHS-Eur: Luria S et al. Round table discussion. Malunion of the distal radius. *Journal of Hand Surgery: European Volume*. In press. JHSE-D-24-00523R2

Poster presented at ASSH:

Liu TC, Galivanche AR, Immerman I. Increased patient communication in the perioperative period is associated with worse patient reported outcomes following hand surgery. Scientific ePoster at the American Society for Surgery of the Hand Annual Meeting, September 19-21, 2024. Minneapolis, Minnesota. (Accepted 7/2/24)

Awards

Wong L, Lalchandani GR, Lee NH. "A Biomechanical Analysis of Elbow Instability Using IJS and Ligament Restoration." Accepted for the \$5,000 James O. Johnston (JOJ) Grant.

Rosanna Wustrack, M.D., performs osseointegration surgery, in which a metal device is implanted directly into the femur. An orthopedic surgeon specializing in the surgical treatment of musculoskeletal tumors and fragility fractures, Dr. Wustrack leads research focused on immunotherapy for sarcomas, functional outcomes in cancer patients, osseointegration, and treatment strategies for metastatic disease.



Orthopaedic Oncology

Oncology's main research focuses over the past year have been:

Long-term outcomes of endoprosthetic reconstruction using compressive osseointegration. We established a multicenter group to establish a shared database, including patients treated with compressive osseointegration, titled FORCE. The group includes UCSF, Stanford, UC Davis, OHSU and Kaiser. In the past year we published a joint paper with Kaiser highlighting the good functional outcomes with a proximal tibia hemiarthroplasty. We are in the process of publishing the group's work on outcomes of this implant at the proximal tibia. Our group also presented our results on differences in short versus long spindles at the MSTs annual meeting.

Sarcoma immunotherapy: Our most recent sarcoma immunotherapy project involves defining the role of tertiary lymphoid structures in osteosarcoma. We are working with a

current second year medical student, our adult medical oncology partners and pathology to identify the presence or absence of TLS in pre-treatment osteosarcoma samples and to determine if TLS influence the response to chemotherapy and could be a potential marker for a good response to immune checkpoint therapy. We continue to work with our resident, Camille Sullivan, and our thoracic oncology and surgery colleagues to explore the difference in TIME between primary extremity and metastatic chondrosarcoma.

Disparity research. We worked with an MS1 student through the Heiman grant to evaluate the experience of hijab-wearing medical students when they rotate in the operating room. Our abstract was presented at the Western Orthopedic Association's annual meeting in 2024 and at the American Surgical Educator's meeting. We are expanding this work to better understand what factors protect against exclusion and promote a surgical career for Hijab-wearing medical students.

Ongoing awards and grants

Camille Sullivan's OREF grant will be used to explore the difference in TIME between primary extremity and metastatic chondrosarcoma.

Heiman Summer Research awards: 2024 Mathilly Diaz

Publications of 2024

Pozner, Amir, et al. "ASPSR1-TFE3 reprograms transcription by organizing enhancer loops around hexameric VCP/p97." *Nature communications* 15.1 (2024): 1165. Jackson, Kristopher J., et al. Surgical site infection is not associated with 1-year progression-free survival after endoprosthetic reconstruction for lower-extremity osteosarcoma: a secondary analysis of PARITY Study data. *Journal of Bone and Joint Surgery*. 105.Suppl 1 (2023): 49-56.

Schott, Courtney R., et al. "Osteosarcoma PDX-Derived Cell Line Models for Preclinical Drug Evaluation Demonstrate Metastasis Inhibition by Dinaciclib through a Genome-Targeted Approach." *Clinical Cancer Research* 30.4 (2024): 849-864. Boone, Sean L., et al. Botryomycosis: a rare mimic of sarcoma as an initial presentation of acquired immunodeficiency syndrome. *Skeletal Radiology* (2023): 1-6.

Kelly, T., Morse, L. J., Wustrack, R., & Zimel, M. (2024). Proximal Tibia Hemiarthroplasty Reconstruction Following Resection of Malignant Bone Tumors in Skeletally Immature Patients. *Journal of the Pediatric Orthopaedic Society of North America*, 9, 100118.

Boone, S. L., Horvai, A. E., Zimel, M. N., Brown, R., Link, T. M., & McGill, K. C. (2024). Botryomycosis: a rare mimic of sarcoma as an initial presentation of acquired immunodeficiency syndrome. *Skeletal Radiology*, 53(10), 2315-2320.

Ongoing Clinical Trials:

Collaborative group FORCE, as mentioned above. We have quarterly meetings and continue to optimize data collection and cleaning.

Upcoming projects

This year we hope to begin data collection for the chondrosarcoma immunotherapy project. We have identified our primary extremity and metastatic cohorts and have identified the samples that we will test.

We have completed a pilot study evaluating whether tertiary lymphoid structures and B-cell expression are seen in osteosarcomas. Our pilot of 8 pre-treatment osteosarcoma patient samples confirmed that we are able to test for TLS in calcified and decalcified tissue and showed that some samples do have TLS present while others do not. This year we will expand to our full cohort of 60 patient samples.



Orthotics and Prosthetics

The UCSF Orthotics and Prosthetics research division seeks to develop stronger evidence for clinical decision-making in the treatment of orthotic and prosthetic patients around the globe. Our practitioners are dedicated to research questions that can be directly implemented into practice and highlight how our devices impact the daily lives of our patients.

The Orthotics and Prosthetics Center (OPC) currently has three research protocols approved by UCSF's Institutional Review Board (IRB), including pediatric and adult orthosis and prosthesis users. These studies include:

UCSF pectus carinatum orthosis (PCO) study – continuation of a prospective clinical study utilizing pressure and temperature sensors to determine which treatment criteria have the greatest impact on patient outcomes. Data collection is complete we are in intermediate stages of data analysis.

Biofeedback for gait training for above-knee prosthesis users - proof-of-concept clinical trial developing best-practices for incorporating biofeedback into gait retraining protocols for individuals with above-knee amputation to improve functional outcomes and decrease the prevalence of secondary injury. Currently in the recruitment and data collection phase.

Cranial remolding orthosis (CRO) study - retrospective chart review investigating the impact of treatment parameters, such as age and cranial deformity, on CRO efficacy. We are collaborating with UT Southwestern to validate a predictive equation for CRO outcomes. Currently in the data collection phase.

Top publications

“Experience with the OPRA Axor II External Prosthetic Connection Device.” The Academy TODAY, Spring, 2024, 13-15

“Prospective Cohort Study on Treatment Parameters for the UCSF Pectus Carinatum Orthosis” –

50th Academy Annual Meeting & Scientific Symposium, April 2024

Goals for 2025

We aim to revitalize Dr. Inman's investigative efforts in human locomotion and prosthetics and orthotics, with the goal of once again making UCSF a leader in O&P research. We aim to produce robust evidence in O&P to improve the quality of patient care in our clinics and to have a transformative impact across the profession. Historically, the O&P division has relied on full-time clinical practitioners to lead our research efforts. Due to the logistical challenges associate with this approach, we realize that an experienced researcher, with knowledge in securing grant funding and managing multiple research projects is vital to us achieving our goals. Consequently, our 2025 research goal is dedicated to the recruitment of an O&P-focused, PhD-equivalent researcher.





Pictured, from left to right: Donald Kephart, Nirav Pandya, Jaclyn Hill, Ishaan Swarup, Jason Jagodzinski, Eliana Delgado, Sanjeev Sabharwal, Mohamed Diab, Rhonda Watkins, Celina de Borja

Pediatric Orthopaedic Surgery Division

Pediatric Orthopaedic Clinical Research

The clinical research conducted by the UCSF pediatric orthopaedic faculty in 2024 encompassed a broad range of musculoskeletal conditions. Some of the research themes we focused on included- evaluating Patient- Reported Outcome Measures (PROMs) in children with sports injuries, and those with spinal and lower limb differences; effective pain management strategies for adolescents following surgical correction of spinal deformities; developing survey instruments for validating patient expectations and investigating clinical outcomes for young patients with osteonecrosis of the femoral head receiving core decompression.

Additionally, we researched disparities in access to orthopedic care and strategies to address language barriers and foster health equity for our pediatric patients. Internationally, we traveled to

low-and middle-income countries (LMICs) and conducted an in-depth study of certain pediatric musculoskeletal conditions such as clubfoot, gluteal fibrosis and limb differences. We also collaborated, both nationally and internationally, on several multicenter projects and prospective registries for a variety of pediatric disorders such as Perthes Disease, Slipped Capital Femoral Epiphysis, Neuromuscular Scoliosis and Limb Differences including growth plate disorders.

Over the past year, our pediatric faculty had 38 peer reviewed publications, actively participated in 11 multicenter studies and 8 other studies that were grant funded.

Recent Publications with multi-authored UCSF Orthopaedic Faculty:

Sabatini CS, Edmonds EW, Nepple JJ, Liotta ES, Hergott K, Quinn M, Perkins CA, Wilson PL, Li Y, Ellis HB, Pandya NK, Pennock AT, Spence DD, Willimon SC, Bae DS, Kocher MS, Busch MT, Williams DN, Heyworth BE. Nonoperative Versus Operative Treatment of Z-Type Comminuted Clavicle Fractures in Adolescents: A Prospective Substratified Cohort Analysis. *J Orthop Trauma*. 2024 Jul 1;38(7):351-357. doi: 10.1097/BOT.0000000000002821. PMID: 38837911.

Serna J, Furie K, Wong SE, Swarup I, Zhang AL, Diab M. The Use of Combined Hip Arthroscopy and Periacetabular Osteotomy for Hip Dysplasia Is Increasing and Has Low Complication Rates. *Arthrosc Sports Med Rehabil*. 2024 Mar 26;6(3):100929. doi: 10.1016/j.asmr.2024.100929. PMID: 39006788; PMCID: PMC11240039.

Bonsignore-Opp L, O'Donnell J, Agha O, Bach K, Metz L, Swarup I. Evaluation and Management of Thoracolumbar Spine Trauma in Pediatric Patients: A Critical Analysis Review. *JBJS Rev*. 2024 Jun 17;12(6). doi: 10.2106/JBJS.RVW.24.00045. PMID: 38885326.

Spence DD, Wilson PL, Pennock AT, Nepple JJ, Pandya NK, Perkins CA, Li Y, Ellis HB, Sabatini CS, Edmonds EW, Willimon SC, Bae DS, Busch MT, Kocher M; FACTS Study Group; Heyworth BE. Treatment of Severely Shortened or Comminuted Clavicular Fractures in Older Adolescent Athletes. *Am J Sports Med*. 2024 Feb;52(2):423-430. doi: 10.1177/03635465231219248. Epub 2024 Jan 18. PMID: 38238901.

Pediatric Orthopaedics

Polinsky SG, Edmonds EW, Bastrom TP, Manhard CE, Heyworth BE; FACTS Study Group; Bae DS, Busch MT, Ellis HB, Hergott K, Kocher MS, Li Y, Nepple JJ, Pandya NK, Perkins C, Sabatini CS, Spence DD, Willimon SC, Wilson PL, Pennock AT. 5-Year Radiographic and Functional Outcomes of Nonoperative Treatment of Completely Displaced Midshaft Clavicular Fractures in Teenagers. *Am J Sports Med.* 2024 Mar;52(4):1032-1039. doi: 10.1177/03635465241228818. Epub 2024 Mar 4. PMID: 38439558.

Perkins CA, Nepple JJ, Pang JH, Busch MT, Edmonds EW, Ellis HB, Kocher MS, Li Y, Pandya NK, Pennock AT, Sabatini CS, Spence DD, Willimon SC, Wilson PL, Heyworth BE. Changes in Fracture Shortening Occur in the First 2 Weeks Following Completely Displaced Adolescent Clavicle Fractures. *J Pediatr Orthop.* 2024 Sep 1;44(8):e686-e690. doi: 10.1097/BPO.0000000000002724. Epub 2024 May 7. PMID: 38712672.

Grants

Scoliosis Research Society Grant, Young Investigator Award: Preoperative Patient Expectations in Patients with Adolescent Idiopathic Scoliosis. Ishaan Swarup, MD

NOVA Grant: Osteonecrosis of the Femoral Head (ONFH) Outcomes After Core Decompression. Ishaan Swarup, MD

Orthopaedics Department DEI NOVA Grant: Understanding the Experience of Families and the Role of Social Stigma in Outcomes for Children with Clubfoot and Other Lower Limb Differences (co-leads) Coleen Sabatini, MD, MPH, Sanjeev Sabharwal, MD, MPH

PONSA Registry Grant: International Limb Differences Registry (ILDR). Dr. Anthony Philip Cooper (Lead, University of British Columbia) and Sanjeev Sabharwal, MD, MPH

Trainee Grants

Orthopaedic Research and Education Foundation (OREF) grant - Effect of erector spinae plane block (ESPB) on pain management in pediatric patients following PSF. PGY2 Dr. Sara Kiani with Ishaan Swarup, MD

James O Johnston Resident Research Grant – Short vs Long Leg Cast in Physeal ankle fractures PGY3 Dr. Kelly Bach and Ishaan Swarup, MD

Awards

POSNA Humanitarian Award – Dr. Sabatini

Dr. Sabatini's education and Service Volunteerism along with her global health research highlight neglected musculoskeletal conditions and raise awareness.

Dr. Chau's fellowship allowed him to travel the world and learn the latest in hip preservation techniques.

Ongoing Collaborative Studies (Intra- and Extra-mural)

Assessing the Prevalence of Bullying in Pediatric Orthopaedic Patients.

Investigators: Coleen Sabatini, MD, MPH, Celine de Borja, MD, Sanjeev Sabharwal, MD, MPH, Ishaan Swarup, MD, Mohammad Diab, MD

This study aims to determine the prevalence of bullying in a population of adolescents under the care of a pediatric orthopaedist. The focus is on children using orthopaedic devices or various assistive devices and children with chronic disabilities. We plan to determine if assistive devices (walkers/ wheelchairs/ crutches), braces, casts, or external fixators were associated with an increased risk of bullying as well as determine a link between bullying and musculoskeletal conditions.

Children's Orthopaedic Trauma and Infection Consortium for Evidence-based Studies (CORTICES).

Site Investigators: Ishaan Swarup, MD Jaclyn Hill, MD

CORTICES is a collaboration of pediatric orthopaedic surgeons dedicated to improving the quality, safety, and value in the management of emergent orthopaedic conditions (trauma and infection). This registry seeks to investigate the effects of pediatric orthopaedic trauma-related injuries and musculoskeletal infections, using the collaborative efforts of multi-center principal investigators, and to advance evidence-based pediatric orthopaedics.

COLP: Conditioning + Open-label Placebo for the Management of Pain in Children who Undergo Surgical Treatment of Idiopathic Scoliosis

Investigators: Mohammad Diab, MD, Lionel Metz, MD

This is a randomized controlled trial that focuses on administering or not administering several placebo pills along with standard postoperative care for patients with Adolescent Idiopathic Scoliosis who underwent surgery. The patients will knowingly receive the placebo which is known as "Open-Label". The primary aim of this study is to see if administration of the placebo may lower postoperative opioid consumption. It will also evaluate outcomes including pain, functional ability, and mental health scores.

International Legg-Calvé-Perthes Study Group (IPSG) add Site Investigator: Ishaan Swarup, MD

This registry study will establish a database of prospectively identified patients with Legg-Calvé-Perthes disease and collect information regarding their presentation, treatment, and outcomes while receiving currently available treatments.

ILDR: International Limb Difference Registry

Investigator: Sanjeev Sabharwal, MD, MPH

This is an international multi-center registry study dedicated to lower limb differences. The purpose is to better understand several lower limb conditions, along with their treatment plans and outcomes. It includes investigating both clinical information and Patient Reported Outcomes.

A Multi-center Study Group for Pediatric Limb Deformity (CHILD STUDY).

Site Investigator: Sanjeev Sabharwal, MD, MPH

This multi-center study will evaluate the long-term clinical, radiographic, and functional outcomes of pediatric patients with limb deformities. With prospective data collection, this study group aims to better define the appropriate indications and expected outcomes in children treated for pediatric limb deformity.

Osteonecrosis of the Femoral Head (ONFH) Outcomes after Core Decompression

Investigator: Ishaan Swarup, MD, Dr. Bamidele Kammen (Radiology)

ONFH can cause severe disability, pain and joint degeneration. There is limited research on the use and efficacy of core decompression and the use of autologous bone marrow aspirate concentrate (BMAC) in the pediatric population. This prospective pilot study aims to determine patient satisfaction, clinical and functional outcomes as well as changes on imaging seen after core decompression and use of BMAC.

The Pediatric ALL Evaluation and Trial (PALLET): A Randomized, Controlled Trial.

Investigator: Nirav Pandya, MD

This study is a multi-center, unblinded, randomized controlled trial with longitudinal data collection. The purpose is to investigate whether adding anterolateral ligament reconstruction to anterior cruciate ligament (ACL) reconstruction in children will result in a lower rate of ACL re-tear than just ACL reconstruction alone.

The Pediatric Spine Registry Study (PSSG)

Investigators: Ishaan Swarup, MD, Mohammad Diab, MD, Lionel Metz, MD

This registry will serve as a hypothesis-generating database of prospectively collected outcomes. It will facilitate the development of targeted, hypothesis-testing randomized controlled trials and observational studies that can be housed within the larger registry.

Preoperative patient expectations in patients with Adolescent Idiopathic Scoliosis (AIS) undergoing posterior spinal fusion.

Investigators: Ishaan Swarup, MD, Mohammad Diab, MD, Lionel Metz, MD

Patient expectations have been shown to affect outcomes and satisfaction following surgery. This study aims to create and validate a patient expectations questionnaire to assess the relationship between preoperative patient expectation, outcomes, and satisfaction after spinal deformity surgery. Quantifying patient expectations will allow surgeons to better counsel patients prior to spinal surgery, and subsequently, align patient and surgeon expectations.

Prospective, Multi-Center Adolescent Clavicle Shaft Fracture Registry (FACTS).

Investigators: Nirav Pandya, MD, Coleen Sabatini, MD, MPH

This study focuses on the long-term outcomes of surgical and non-surgical approaches to clavicle shaft fracture management and may help to establish guidelines and understand the best treatment options for adolescents with clavicle shaft fractures.

SCFE Longitudinal International Prospective Registry (SLIP)

Investigators: Ishaan Swarup, MD, Jason Jagodzinski, MD

The registry includes initiation of a study examining patients' conditions prior to surgery and their long-term outcomes across participating multiple centers. It will provide valuable insight into the treatment and management of this condition.

Short vs Long Leg Casting for Physeal Ankle Fractures

Investigator: Ishaan Swarup, MD, Kelly Bach, MD (PGY-3)

Currently it is standard of care for patients with physeal ankle fractures is to receive either a short or long cast. This randomized controlled trial aims to compare the two by evaluating clinical, radiographic, and satisfaction outcomes. The goal is to provide more education to physicians and to maximize healing and patient satisfaction.

Understanding the Experience of Families and the Role of Social Stigma in Outcomes for children with clubfoot and lower limb differences.

Investigators: Coleen Sabatini, MD, MPH, Sanjeev Sabharwal, MD, MPH

The aim of this study is to understand the experience and stigmas associated with a pediatric clubfoot or other lower limb difference diagnoses through interviews with parents and caretakers of pediatric patients. These interviews will help to better understand their experience in terms of how they are treated when they have a child with a lower limb disability, and what resources they would benefit from having.

Upcoming Studies

Burden Of Musculoskeletal Disease in the Children of Uganda

Investigator: Coleen Sabatini, MD, MPH

This study aims to determine the prevalence of common musculoskeletal conditions in the pediatric population of Uganda. These conditions include, clubfoot, post-injection paralysis, limb deformities and more. It will provide information to increase awareness among the medical community, the government ministries and the public about the scope and burden of musculoskeletal conditions in the pediatric population.

The effect of erector spinae plane block (ESPB) on Pediatric Pain Management following Posterior Spinal Fusion (PSF) Surgery. *OREF Grant*

Investigator: Ishaan Swarup, MD, Sara Kiani, MD (PGY-2), Jocelyn Wong, MD (Department of Anesthesiology)

This randomized controlled trial focuses on the Adolescent Idiopathic Scoliosis and Neuromuscular Scoliosis population undergoing spinal deformity surgery. The ESPB is a local anesthetic injected into the patient's back muscles before surgery. Patients will not know if they receive or do not receive the ESPB. This study aims to see if administration of the ESPB lowers postoperative opioid usage, lowers patients' pain levels and leads to earlier mobilization.

Global Pediatric Orthopaedic Implant Safety & Efficacy (Global POISE) Clinical Follow-up Program

Investigator Sanjeev Sabharwal, MD, MPH

This is an international multi-center study being conducted to evaluate the safety and efficacy of pediatric medical implants made by the medical device company OrthoPedictrics. Through Clinical and Patient Reported Outcomes, this study aims to verify the expected lifetime outcomes of individual OrthoPedictrics Devices and understand patient satisfaction with them.

Role of Diffusion Tensor Imaging MRI as a functional marker of the growth plate (Collaborating with Columbia University and Hospital for Special Surgery)

Site Investigators: Sanjeev Sabharwal, MD, MPH, Bamidolo Kammon (Department of Radiology)

This study will be the first to provide an in-vivo window into differential physal growth of the lower limb including growth plate injuries using Diffusion Tensor Imaging (DTI), an MRI technique. This innovative technique serves as a biomarker of growth plate activity and will allow for earlier and more targeted surgical therapies in children with growth plate disorders.

Dr. Coleen Sabatini and Dr. Sanjeev Sabharwal, center, participate in the annual Clubfoot Picnic in Walnut Creek, California. The program, dedicated to treating and supporting children with clubfoot, is part of their commitment to improving pediatric musculoskeletal care.





Dr. Bobby Tay presents his research on cervical myelopathy at the 67th Annual LeRoy C. Abbott Visiting Scientific Program on May 12, 2023.

Orthopaedic Spine Service

The UCSF Orthopaedic Spine Service had an exciting and highly productive research year in 2024. This year was marked by transformative and innovative research pursuits in the fields of adult and pediatric spinal deformity, degenerative cervical and lumbar pathologies, and spinal oncology. With the goal of advancing the field and improving care and outcomes of spine patients, the UCSF Orthopaedic Spine Service directed local, national, and international prospective and retrospective clinical research trials, designed and evaluated biomechanically novel surgical strategies, and guided cutting edge translational and personalized medicine initiatives. More than 40 peer-reviewed manuscripts, chapters, and review articles published in 2024 as well as funding support approaching \$4 million dollars from philanthropy, industry, and intramural and extramural grants obtained 2024 are testaments to the UCSF Orthopaedic Spine Service's expertise and commitment to advancing the field. These achievements underscore the group as a leading research center in the field of spine surgery.

Research Initiative Highlights

International Spine Study Group (ISSG)

Sponsor: ISSG (Vedat Deviren, MD, Alekos Theologis, MD)

The ISSG is the most pre-eminent group of spinal deformity spine surgeons in the world dedicated to the advancement of treatment for adults with spinal deformity. Questions regarding treatment approach and techniques to achieve the best possible outcomes are studied through comprehensive multicenter prospective research studies. The group is divided into working groups each of which focuses on particular interests within the treatment of adult spinal deformity (cervical, minimally invasive surgery, complications, health economics and health-related quality of life, proximal junctional kyphosis, pediatric collaboration, and international collaborations). Work from the ISSG study group is recognized yearly by numerous research awards from the major spine organizations (SRS, NASS, IMAST). Alekos Theologis, in 2024, was nominated to join Vedat Deviren as part of the ISSG.

Durability of supplementary rod constructs—SuppleMentArY Rod Technique (SMART)—for long-segment posterior instrumented spinal fusion procedures

Sponsor: AO Foundation (Sigurd Berven, MD, Alekos Theologis, MD)

Implant failure is a common complication of long-segment spinal fusions. Rod failure is associated with pain, worse function, and loss of deformity correction and is a leading cause for revision surgery. Supplementary rod constructs are utilized to mitigate rod fracture, as they increase construct stiffness and maintain deformity correction until fusion occurs. This study aims to provide quality evidence regarding the benefits of supplementary rod constructs in reducing the risk of rod failures and other mechanical complications. This study shall provide the first long-term clinical evidence on clinical outcome and benefit of supplementary rod constructs. Alekos Theologis was nominated in 2024 by the AO Spine Knowledge Forum Deformity to be the site director for the SMART study at UCSF.

Spine Service continued...

Pediatric Spine Study Group (PSSG)

Sponsor: PSSG (Lionel Metz, MD)

The Pediatric Spine Study Group (PSSG) is a global consortium of over 200 members from 88 institutions across 11 countries, dedicated to enhancing the quality of care and treatment outcomes for children with spine and chest wall disorders. Central to the PSSG's mission is the Pediatric Spine Registry, a comprehensive database that prospectively collects data on patients with various spinal and chest wall conditions, including early onset scoliosis, immature complex scoliosis, cervical spine disorders, spondylolisthesis, lower back pain, and tethered spinal cords. This registry facilitates longitudinal studies to monitor patient outcomes and inform best practices.

Scoliosis Research Society (SRS) Adult Spinal Deformity Task Force on Senescence

Sponsor: SRS (Alekos Theologis, MD)

Globally, many countries are confronting fundamental demographic shifts towards an aging population. These evolving epidemiologic changes have significant implications for public health, particularly in the context of musculoskeletal conditions, which are among the leading causes of disability worldwide. Navigating the complexities of musculoskeletal aging necessitates a clear understanding of key terms such as senescence, sarcopenia, osteoporosis, and frailty. As part of the SRS Adult Spinal Deformity Task Force, Alekos Theologis has contributed to developing state-of-the-art and comprehensive reviews on spinal sarcopenia, biomarkers in musculoskeletal health and disease, and imaging and artificial intelligence of osteosarcopenia in the aging spine.

Finite Element Analyses of Novel Surgical Strategies in Cervical and Thoracolumbar Spinal Degenerative Conditions and Deformities

Sponsor: industry (\$250,000 -Alekos Theologis, MD)

Surgical strategies to improve safety and outcomes in cervical and thoracolumbar degenerative and deformity spinal surgery continue to rapidly evolve. Biomechanical assessments remain paramount in defining feasibility and potential clinical utility of novel surgical strategies. In 2024, with support from numerous industry sponsors and in collaboration with the University of Toledo, Alekos Theologis has designed and conducted multiple (>5) finite element analyses assessing unique surgical instrumentation constructs for occipitocervical stabilization (Figure 1), lumbar pedicle subtraction osteotomies, and pelvic fixation for thoracolumbar spinal deformities.

Figure 1. Novel occipital plate designed by Alekos Theologis that allows for creation of multiple rods (up to 4) across the occipitocervical junction.

BRIDGE – Apex Clinical Outcomes

Sponsor: philanthropic funds (\$1,000,000 - Bobby Tay, MD)

Clinical outcomes lay at the core of understanding utility of treatment strategies for spine patients. BRIDGE is an Apex dashboard that allows assessment of collected outcomes measures and patient data at the point of care. It allows objective assessment of how patients are functioning pre- and post-operatively over time. Bobby Tay has led the pursuit of expansion of the BRIDGE application to all divisions in the Department of Orthopaedic Surgery at UCSF, which has been critical to the entire department's clinical research endeavors and patient management.

Motion Analysis of Patients with Spinal Disorders

Traditional methods to assess function rely on static data (i.e. standing radiographs). As life is a game of motion, modalities to evaluate function during different activities (i.e. walking, sitting, standing from a seated position, etc.) are necessary.

Sponsor: philanthropic funds (\$2,000,000 – Bobby Tay, MD)

Bobby Tay, in collaboration with Jeannie Baily, has worked to develop and validate a mobile motion analysis and outcomes measurement application.

Sponsor: NSF (\$30,000 - Shane Burch, MD)

Shane Burch has installed a 3D motion tracking analysis lab within the UCSF Spine Center that captures real-time motion analysis data. In a multi-year prospective study that targets to enroll 150 patients, this system is used to collect pre- and post-operative range of motion (thoracic spine, lumbar spine, pelvis, hips and knees) in patients undergoing spinal fusion surgery. The analysis also compares velocity and acceleration of motion segments during flexion and extension as well as sit-to-stand maneuvers. The data can then be correlated to clinical outcomes. This work has been instrumental in determining dynamic function of spinal fusion patients post-operatively and is being used to develop methods to mitigate risks of mechanical failures.

The Effect of Topical TXA on Post-Operative Bleeding in Multi-level Spinal Fusion Surgery

Sponsor: Department of Defense (\$250,000 - Shane Burch, MD)

Multi-level posterior thoracolumbar spine instrumented fusions are plagued by high blood loss. While intravenous anti-fibrinolytics have been demonstrated to decreased blood loss and associated blood transfusions, the utility of topical tranexamic acid (TXA) on mitigating blood loss in multi-level posterior instrumented fusions is poorly understood. In this randomized controlled trial, led at UCSF by Shane Burch, patients (target 30) undergoing >5 levels of posterior instrumented fusions receive either topical saline or topical TXA at the completion of the case. Blood loss is evaluated post-operatively to determine the effect of topical TXA on post-operative bleeding.

Publication Highlights

Effects of pelvic fixation strategies and multi-rod constructs on biomechanics of the proximal junction in long thoracolumbar posterior instrumented fusions: a finite-element analysis.

Mumtaz M, Collins AP, Shekouhi N, Varier K, Tripathi S, Ames CP, Deviren V, Clark AJ, Goel VK, Theologis AA. *Spine Deform.* 2024 Nov;12(6):1571-1582.

Evaluating the biomechanical effects of pedicle subtraction osteotomy at different lumbar levels: a finite element investigation.

Shekouhi N, Tripathi S, Theologis A, Mumtaz M, Serhan H, McGuire R, Goel VK, Zavatsky JM. *Spine J.* 2024 Nov;24(11):2191-2203.

Radiation Therapy for Primary and Metastatic Spine Tumors.

Boreta L, Chhabra A, Theologis AA. *J Am Acad Orthop Surg.* 2024 Sep 15;32(18):823-832.

Correction: Costs of revision operations for distal junctional kyphosis following thoracic posterior spinal fusion for adolescent idiopathic scoliosis.

Theologis AA, Wu HH, Oeding JF, Diab M. *Eur Spine J.* 2024 Jul;33(7):2931.

Biomechanical analysis of a trans-discal, multi-level stabilization screw (MLSS) at the upper instrumented vertebra (UIV) of long posterior thoracolumbar instrumentations.

Collins AP, Shah AA, Shekouhi N, Goel VK, Theologis AA. *Spine Deform.* 2024 Jul;12(4):953-959.

Timelines for Return to Different Sports Types After Eight Cervical Spine Fractures in Recreational and Elite Athletes: A Survey of the Association for Collaborative Spine Research.

Hung NJ, McClellan RT, Hsu W, Hu SS, Clark AJ, Theologis AA. *Clin Spine Surg.* 2024 Dec 1;37(10):E404-E414.

Lumbar fusion surgery in the era of an aging society: analysis of a nationwide population cohort with minimum 8-year follow-up.

Kwon WK, Theologis AA, Kim JH, Moon HJ. *Spine J.* 2024 Aug;24(8):1378-1387.

Comparative Analysis of Three Posterior-Only Surgical Techniques for Isthmic L5-S1 Spondylolisthesis.

Klawson B, Buchowski JM, Punyarat P, Singleton Q, Feger M, Theologis AA. *J Am Acad Orthop Surg.* 2024 May 15;32(10):456-463.

Costs of revision operations for distal junctional kyphosis following thoracic posterior spinal fusion for adolescent idiopathic scoliosis.

Theologis AA, Wu HH, Oeding JF, Diab M. *Eur Spine J.* 2024 Jun;33(6):2504-2511.

Resection of a Recurrent Lumbar Chordoma With Intradural Extension and Complex Dural Repair: 2-Dimensional Operative Video.

Dada A, Tawil ME, Dietz N, Ambati VS, Chryssikos T, Theologis AA, Mummaneni PV. *Oper Neurosurg (Hagerstown).* 2024 Aug 1;27(2):250-251.

Coronal Alignment in Adult Spine Surgery.

Sharfman ZT, Clark AJ, Gupta MC, Theologis AA. *J Am Acad Orthop Surg.* 2024 May 15;32(10):417-426.

Trans-Sternal Multilevel Corpectomy for Cervicothoracic Renal Cell Metastasis: 2-Dimensional Operative Video.

Tawil ME, Chryssikos T, Sorour O, Ambati VS, Jamieson A, Theologis AA, Kratz J, Mummaneni PV. *Oper Neurosurg (Hagerstown).* 2024 Jul 1;27(1):120.

Odontoid fractures above C2 to pelvis posterior instrumented fusions: a single center's 11-year experience.

Lim P, Clark AJ, Deviren V, Berven SH, Burch S, Ames CP, Theologis AA. *Spine Deform.* 2024 Mar;12(2):463-471.

Predictability in Achieving Target Intervertebral Lordosis Using Personalized Interbody Implants.

Sadrameli SS, Blaskiewicz DJ, Asghar J, Ames CP, Mundis GM, Osorio JA, Smith JS, Yen CP, Berven SH, Patel AI, Temple-Wong M, Nicolau RJ, Kent RS. *Int J Spine Surg.* 2024 Aug 30;18(S1):S16-S23.

Diagnosis of spine pseudoarthrosis based on the biomechanical properties of bone.

Hipp JA, Mikhael MM, Reitman CA, Buser Z, Patel VV, Chaput CD, Ghiselli G, DeVine J, Berven S, Nunley P, Grieco TF. *Spine J.* 2024 Dec;24(12):2407-2416.

Spinal cord injury in high-risk complex adult spinal deformity surgery: review of incidence and outcomes from the Scolio-RISK-1 study.

Jiang F, Joshi H, Badhiwala JH, Wilson JRF, Lenke LG, Shaffrey CI, Cheung KMC, Carreon LY, Dekutoski MB, Schwab FJ, Boachie-Adjei O, Kebaish KM, Ames CP, Berven SH, Qiu Y, Matsuyama Y, Dahl BT, Mehdian H, Pellisé F, Lewis SJ, Fehlings MG. *Spinal Cord Ser Cases.* 2024 Aug 17;10(1):59.

The influence of osteoporosis on mechanical complications in lumbar fusion surgery: a systematic review.

Filley A, Baldwin A, Ben-Natan AR, Hansen K, Arora A, Xiao A, Hammond D, Chen C, Tweedt I, Rohde J, Link T, Berven S, Sawyer A. *N Am Spine Soc J.* 2024 May 3;18:100327.

Effects of liposomal bupivacaine on opioid use and healthcare resource utilization after outpatient spine surgery: a real-world assessment.

Berven S, Wang MY, Lin JH, Kakoty S, Lavelle W. *Spine J.* 2024 Oct;24(10):1890-1899.

Opioid Use Prior to Adult Spine Deformity Correction Surgery is Associated With Worse Pre- and Postoperative Back Pain and Prolonged Opioid Demands.

Sardi JP, Smith JS, Gum JL, Rocos B, Charalampidis A, Lenke LG, Shaffrey CI, Cheung KMC, Qiu Y, Matsuyama Y, Pellisé F, Polly DW Jr, Sembrano JN, Dahl BT, Kelly MP, de Kleuver M, Spruit M, Alanay A, Berven SH, Lewis SJ; AO Spine Knowledge Forum Deformity. *Global Spine J.* 2024 Jun 4;21925682241261662.

Association between opioid utilization and patient-reported outcome measures following lumbar spine surgery.

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Tension Parameters of Junctional Tethers in Proximal Junction Kyphosis: A Cadaveric Biomechanical Study.

O'Hehir MM, O'Connor TE, Mariotti BL, Soliman MAR, Quiceno E, Gupta MC, Berven S, Pollina J, Polly DW, Mullin JP. *World Neurosurg.* 2024 Feb;182:e798-e806.

Preferences for risks and benefits of treatment outcomes for chronic low back pain: Choice-based conjoint measure development and discrete choice experiment.

Wilson L, Denham A, Ionova Y, O'Neill C, Greco CM, Hassett AL, Hanmer J, Shaikh S, Wolf M, Berven S, Williams D, Ma Y, Lotz J, Zheng P. *PM R.* 2024 Aug;16(8):836-847.

Evaluation and Management of Thoracolumbar Spine Trauma in Pediatric Patients: A Critical Analysis Review.

Bonsignore-Opp L, O'Donnell J, Agha O, Bach K, Metz L, Swarup I. *JBJS Rev.* 2024 Jun 17;12(6).

High-Dose TXA Is Associated with Less Blood Loss Than Low-Dose TXA without Increased Complications in Patients with Complex Adult Spinal Deformity.

Kim AH, Mo KC, Harris AB, Lafage R, Neuman BJ, Hostin RA, Soroceanu A, Kim HJ, Klineberg EO, Gum JL, Gupta MC, Hamilton DK, Schwab F, Burton D, Daniels A, Passias PG, Hart RA, Line BG, Ames C, Lafage V, Shaffrey CI, Smith JS, Bess S, Lenke L, Kebaish KM; on behalf of the International Spine Study Group. *J Bone Joint Surg Am.* 2024 Dec 4;106(23):2205-2214.

A retrospective analysis of 513 patients undergoing pedicle subtraction osteotomy for adult spinal deformity by a single surgical team: are elderly patients at an elevated risk for complications?

Chiu PY, Choy W, Mazur-Hart DJ, Lau D, Kim J, Nguyen TH, Clark AJ, Deviren V, Ames CP. *J Neurosurg Spine.* 2024 Sep 6;41(5):666-675.

Hip Osteoarthritis in Patients Undergoing Surgery for Severe Adult Spinal Deformity: Prevalence and Impact on Spine Surgery Outcomes.

Diebo BG, Alsoof D, Balmaceno-Criss M, Daher M, Lafage R, Passias PG, Ames CP, Shaffrey CI, Burton DC, Deviren V, Line BG, Soroceanu A, Hamilton DK, Klineberg EO, Mundis GM, Kim HJ, Gum JL, Smith JS, Uribe JS, Kebaish KM, Gupta MC, Nunley PD, Eastlack RK, Hostin R, Protosaltis TS, Lenke LG, Hart RA, Schwab FJ, Bess S, Lafage V, Daniels AH; International Spine Study Group. *J Bone Joint Surg Am.* 2024 Jul 3;106(13):1171-1180.

Impact of Self-Reported Loss of Balance and Gait Disturbance on Outcomes following Adult Spinal Deformity Surgery.

Diebo BG, Alsoof D, Lafage R, Daher M, Balmaceno-Criss M, Passias PG, Ames CP, Shaffrey CI, Burton DC, Deviren V, Line BG, Soroceanu A, Hamilton DK, Klineberg EO, Mundis GM, Kim HJ, Gum JL, Smith JS, Uribe JS, Kebaish KM, Gupta MC, Nunley PD, Eastlack RK, Hostin R, Protosaltis TS, Lenke LG, Hart RA, Schwab FJ, Bess S, Lafage V, Daniels AH; ISSG. *J Clin Med.* 2024 Apr 11;13(8):2202.

Reliability of a Novel Classification System for Thoracic Disc Herniations.

Farber SH, Walker CT, Zhou JJ, Godzik J, Gandhi SV, de Andrada Pereira B, Koffie RM, Xu DS, Sciubba DM, Shin JH, Steinmetz MP, Wang MY, Shaffrey CI, Kanter AS, Yen CP, Chou D, Blaskiewicz DJ, Phillips FM, Park P, Mummaneni PV, Fessler RD, Härtl R, Glassman SD, Koski T, Deviren V, Taylor WR, Kakarla UK, Turner JD, Uribe JS. *Spine (Phila Pa 1976)*. 2024 Mar 1;49(5):341-348.

Abdominal lymphocele following multi-level anterior lumbar interbody fusion (ALIF) managed with a laparoscopic peritoneal window: case report and review of the literature.

Collins AP, Freise CE, Hiramoto J, Clark AJ, Theologis AA. *Eur Spine J*. 2024 Jul;33(7):2858-2863.

Biomechanical evaluation of multi-rod constructs to stabilize an S1 pedicle subtraction osteotomy (PSO): a finite element analysis.

Shekouhi N, Tripathi S, Goel VK, Theologis AA. *Spine Deform*. 2024 Mar;12(2):313-322.

Bilateral dual iliac screw pelvic fixation for adult spinal deformity: a case report of a superior gluteal artery pseudoaneurysm secondary to aberrant iliac screw trajectory.

Khela M, Kasir R, Lokken RP, Clark AJ, Theologis AA. *Spine Deform*. 2024 Mar;12(2):501-505.

Proximal Junctional Fracture and Kyphosis: Correction With Posterior Vertebral Column Resection and the “Rail Technique”: 2-Dimensional Operative Video.

Collins AP, Clark AJ, Ames CP, Theologis AA. *Oper Neurosurg (Hagerstown)*. 2024 Feb 1;26(2):237.

Degenerative lumbar spondylolisthesis: review of current classifications and proposal of a novel classification system.

Rangwalla K, Filley A, El Naga A, Gendelberg D, Baldwin A, Maziad A, Arora A, Wague A, O'Donnell J, Chryssikos T, Kasir R, Shah J, Theologis A, Tan L, Mummaneni P, Alamin T, Berven SH. *Eur Spine J*. 2024 May;33(5):1762-1772.



Pictured from left to right: Sibel Deviren, Paolo Mimbella, Patricia Zheng, Conor O'Neill, Lyndly Tamura, Peter I-Kung Wu

Non-Operative Spine

The primary research focus of the non-operative spine service is to advance the understanding of the biopsychosocial mechanisms of low back pain in order to develop individualized treatment algorithms. Drs. Conor O'Neill, Patricia Zheng, Peter Wu and Sibel Demir-Deviren are investigators with the UCSF Core Center for Patient-centric, Mechanistic Phenotyping in Chronic Low Back Pain (REACH). Together, they have assembled two, ongoing longitudinal cohort studies, including an innovative digital cohort. Data from these cohorts will be used to answer important questions that can improve low back pain care. In addition to the two cohort studies, members of our group have collaborated on

a number of ancillary projects with other REACH investigators. These projects span a number of diverse areas, including clinical biomechanics, disc biology, imaging, patient preferences, patient education, and social determinants of health. In addition to her work with REACH, Dr. Deviren helping to lead a project which will improve access to tools for managing low back pain, including a digital intervention that combines exercise and cognitive behavioral therapy, which have been shown to be the most effective treatments for chronic pain.

Ongoing Awards and Grants

NIH Natl Inst Neurological Disord &Strok R61 A139754
(Satterfield, Jason)

Integrating Nonpharmacologic Strategies for Pain with Inclusion, Respect, and Equity (INSPIRE): Tailored digital tools, telehealth coaching, and primary care coordination

8/15/2022-7/31/2024

\$1,614,220

Dr. Sibel Deviren (Co-PI)

NIH Natl Inst Neurological Disord &Strok R33 A144403
(Satterfield,Jason)

Integrating Nonpharmacologic Strategies for Pain with Inclusion, Respect, and Equity (INSPIRE): Tailored digital tools, telehealth coaching, and primary care coordination

8/1/2024-7/31/2027

\$4,783,072

Dr. Sibel Deviren (Co-PI)

NIH Natl Inst Arthr, Musculoskel & Skin U19 A134160 (Lotz, Jeffrey)

UCSF Core Center for Patient-centric Mechanistic Phenotyping in Chronic Low Back Pain (UCSF REACH)

9/25/2019-8/31/2025

\$34,059,132

Dr. Conor O'Neill (Co-Investigator)

Dr. Sibel Deviren (Co-Investigator)

Dr. Peter Wu (Co-Investigator)

Dr. Patricia Zheng (Co-Investigator)

NIH Natl Inst Arthr, Musculoskel & Skin - Univ of North Carolina at Chapel Hill U24 A139467 (Lotz, Jeffrey)

BACPAC- Biomarkers for Evaluating Spine Treatments (BEST) Study

10/1/2021-05/31/2024

\$650,000

Dr. Conor O'Neill (Co-Investigator)

Dr. Peter Wu (Co-Investigator)

Dr. Patricia Zheng (Co-Investigator)

NIH Natl Inst Arthr, Musculoskel & Skin - Univ of North Carolina at Chapel Hill U24 A139450 (Lotz, Jeffrey)

BACPAC- Biomarkers for Evaluating Spine Treatments (BEST) Study

10/1/2021-5/31/2024

\$2,730,922

Dr. Conor O'Neill (Co-Investigator)

Dr. Peter Wu (Co-Investigator)

Dr. Patricia Zheng (Co-Investigator)

NIH Natl Inst Arthr, Musculoskel & Skin - University of North Carolina System U24 A138257 (Lotz, Jeffrey)

Back Pain Consortium (BACPAC) Research Program Data Integration, Algorithm Development and Operations Management Center

11/1/2020-5/31/2024

\$795,491

Dr. Conor O'Neill (Co-Investigator)

NIH Center for Scientific Review - UC San Diego A134678

(O'Neill, Conor)

California Clinical and Translational Pain Research Consortium

09/30/2019-3/31/2024

\$37,618

Dr. Conor O'Neill (Co-Investigator)

NIH Natl Inst Arthr, Musculoskel & Skin UH3 A138078 (Fields, Aaron)

Novel imaging of endplate biomarkers in chronic low back pain

9/1/2021-8/31/2024

\$1,931,981

Dr. Conor O'Neill (Co-Investigator)

NIH Natl Inst Arthr, Musculoskel & Skin R01 A141607 (Bailey, Jeannie)

Mechanistic structure-function relationships for paraspinal muscle fat infiltration in chronic low back pain patients

6/1/2023-3/31/2028

\$1,776,500

Dr. Conor O'Neill (Co-Investigator)

Top 5 noteworthy publications

Normality analysis of numeric rating scale scores in patients with chronic axial spine pain before and after medial branch blocks: a multicenter study. *Pain Med.* 2024 Oct 01; 25(10):591-599. Ehsanian R, Buttner JA, Rivers WE, Nagpal A, Patel J, Zheng P, McCormick Z, Schneider BJ. PMID: 38775642.

Chronic Low Back Pain Causal Risk Factors Identified by Mendelian Randomization: a Cross-Sectional Cohort Analysis. *Spine J.* 2025 Jan 14. Zheng P, Scheffler A, Ewing S, Hue T, Jones S, Morshed S, Mehling W, Torres-Espin A, Galivanche A, Lotz J, Peterson T, O'Neill C, REACH investigators. PMID: 39818276.

The Back Pain Consortium (BACPAC) Research Program Data Harmonization: Rationale for Data Elements and Standards. *Pain Med.* 2023 08 04. Batorsky A, Bowden AE, Darwin J, Fields AJ, Greco CM, Harris RE, Hue TF, Kakyomya J, Mehling W, O'Neill C, Patterson CG, Piva SR, Sollmann N, Toups V, Wasan AD,

Wasserman R, Williams DA, Vo NV, Psioda MA, McCumber M. PMID: 36721327. PMCID: PMC11288398.

Preferences for risks and benefits of treatment outcomes for chronic low back pain: Choice-based conjoint measure development and discrete choice experiment. *PM R.* 2024 Aug; 16(8):836-847. Wilson L, Denham A, Ionova Y, O'Neill C, Greco CM, Hassett AL, Hanmer J, Shaikh S, Wolf M, Berven S, Williams D, Ma Y, Lotz J, Zheng P. PMID: 38040670; PMCID: PMC11251494.

Predictors of response in PROMIS-global in a chronic low back pain specialty clinic: STarTBack and chronic overlapping pain conditions. *J Back Musculoskelet Rehabil.* 2024; 37(4):909-920. Zheng P, Ewing S, Tang A, Black D, Hue T, Lotz J, Peterson T, Torres-Espin A, O'Neill C. PMID: 38427463; PMCID: PMC11307069.

On going clinical trials, research studies, and/or registries

The REACH cohort studies (comeBACK and BACKHOME) will continue in 2025.

Special or new projects to highlight, and/or plans in the upcoming year.

Dr. Wu and Dr. Aaron Fields will continue their collaboration on identifying mechanistic biomarkers of intradiscal biologic therapy effectiveness. Dr. Zheng's plans include introducing a mental health application into the BACKHOME digital cohort and improving back pain educational materials for non-English speaking individuals. Dr. O'Neill will be collaborating with Dr. Abel Torres-Espin, a data scientist, on better understanding the underlying causes and mechanisms of low back pain by applying AI methods to analyze data from the REACH cohorts. He will also be leading a study of intra-discal stem cells for treatment of low back pain. Dr. Sibel Deviren will continue her work on the INSPIRE study, investigating a digital intervention for chronic pain patients which includes cognitive behavioral therapy for chronic pain, exercise and mindfulness meditation.



Resident, Ryan Halvorson, MD, left, and Dr. Alan Zhang, participate in UCSF's PlaySafe Cardiac Physicals, part of the PlaySafe Sports Medicine Program -- a year-round initiative that provides sports medicine care to 28 Bay Area high schools.

Sports Medicine and Shoulder Service

The UCSF Sports Medicine and Shoulder Service continues to lead the country in basic science, translational and clinical research. This group's research efforts are led by Dr. Brian Feeley, Dr. Alan Zhang, Dr. C. Benjamin Ma, Dr. Drew Lansdown, and Dr. Stephanie Wong. The team participates in numerous clinical research initiatives and collaborates with institutions from across the country.

In 2024, the group published 80 peer-reviewed studies and received over \$1,000,000 in grant funding and sponsored study funding.

The Sports Medicine and Shoulder Service group is focused on four main research areas: orthobiologics, sports-related concussion, minimally invasive sports medicine procedures, and health disparities in sports medicine. With respect to orthobiologics, we have started a large, randomized controlled trial evaluating PRP in knee osteoarthritis utilizing proteomics

and patient reported outcomes in a collaboration with Saul Villeda, PhD. We aim to learn more about the molecular pathways by which PRP may exert its effects and how age may affect outcomes. We are studying the types of evaluations and treatments that patients with these injuries are provided at the time of injury and up to one year post-injury.

Grants and Awards

PRP – Knee osteoarthritis biomarkers

UCSF Orthopedic Equipment Grant – (Brian Feeley/Xuhui Liu)

Ongoing clinical studies

In our sports concussion group, we have been performing a retrospective cohort analysis of a large database to evaluate utilization trends in concussion. This project has allowed us to describe the use of referrals, imaging, and prescription medication for patients who have suffered a concussion without loss of consciousness.

For orthobiologics, we have published several studies evaluating the importance of platelet count and outcomes of PRP injections. We continue to evaluate these and other promising techniques related to early knee arthritis and tendonopathies.

We have also began investigating health disparities in primary care sports medicine. Our first project explores the relationship between the Social Vulnerability Index on high school sports participation and access to athletic trainers. The study highlights the importance of the UCSF Playsafe program in providing access to care to all high school athletes in San Francisco.

In addition, we have started investigating the safety and efficacy of non-steroidal intra-articular hip injections in non-osteoarthritis hip conditions with the goal of offering safer injection alternatives to our patients.

Members of the Women's Sports Medicine Center are leading a collaborative project exploring pregnancy-related hip and pelvis musculoskeletal conditions and their management.

We continue to collaborate with our colleagues at University of California, Los Angeles, investigating the role of sleep and athletic performance, following up on a study published last year in the *Clinical Journal of Sports Medicine*.

Upcoming projects

Primary care sports medicine has started optimizing our collection of patient-reported outcomes following minimally invasive sports medicine procedures, such as joint and soft tissue injections. This will allow them to advance the study of these interventions across multiple clinical research projects. They hope to enroll the majority, if not all, of the PRP-KOBE trial in 2024.

Papers

Berrigan WA, Bailowitz Z, Park A, Reddy A, Liu R, Lansdown D. A Greater Platelet Dose May Yield Better Clinical Outcomes for Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Systematic Review. *Arthroscopy*. 2024 Mar 19:S0749-8063(24)00206-8. doi: 10.1016/j.arthro.2024.03.018. Epub ahead of print. PMID: 38513880.

Berrigan W, Tao F, Kopcow J, Park AL, Allen I, Tahir P, Reddy A, Bailowitz Z. The Effect of Platelet Dose on Outcomes after Platelet Rich Plasma Injections for Musculoskeletal Conditions: A Systematic Review and Meta-Analysis. *Curr Rev Musculoskelet Med*. 2024 Dec;17(12):570-588. doi: 10.1007/s12178-024-09922-x. Epub 2024 Sep 27. PMID: 39331322; PMCID: PMC11652557.

Asturias AM, Wague A, Feeley LA, Senter C, Pandya N, Feeley BT. Gender Disparities in Endowed Professorships Within Orthopaedic Surgery. *Cureus*. 2024 Feb 28;16(2):e55180. doi: 10.7759/cureus.55180. PMID: 38558644; PMCID: PMC10980600.

Goldman JT, Donohoe B, Hatamiya N, Boland NF, Vail J, Holmes KE, Presby D, Kim J, Duffaut C. Baseline Sleep Characteristics in NCAA Division I Collegiate Athletes. *Clin J Sport Med*. 2024 Jul 1;34(4):370-375. doi: 10.1097/JSM.0000000000001205. Epub 2024 Jan 4. PMID: 38174994.

Goldman JT, Donohoe B, Hatamiya N, Boland NF, Vail J, Holmes KE, Presby D, Kim J, Duffaut C. Baseline Sleep Characteristics in NCAA Division I Collegiate Athletes. *Clin J Sport Med*. 2024 Jul 1;34(4):370-375. doi: 10.1097/JSM.0000000000001205. Epub 2024 Jan 4. PMID: 38174994.

Sports Medicine Research Group

The sports medicine research group explores a diverse set of clinical and translational research to maximize a variety of outcomes across the sports medicine and shoulder arthroplasty spectrum of injury and recovery. During 2024, the group focused on highlighting translational research, with several studies examining the outcomes of hip arthroscopy, rotator cuff repair, ACL reconstruction, and shoulder replacement. They continue to receive funding from the NIH, VA, AOSSM, as well as private donations and industry funding.



Stephanie Wong, MD, continued her work from the AOSSM Young Investigator Grant in for her work in collaboration with the MITO lab evaluating the role of sex on the transcriptomic signature of patients undergoing hip arthroscopy. Brian Feeley MD, along with Xuhui Liu MD, with their co-authors Michael Davies, Steven Garcia and Hubert Kim were awarded the AAOS/ORS 2025 Kappa Delta Award. Dr. Ma is leading an international team of researchers investigating short socket ACL reconstruction outcomes.

Ongoing clinical studies

There are several ongoing research clinical trials ongoing in sports medicine. Drs. Alan Zhang and Stephanie Wong run a large prospective database on hip arthroscopy outcomes. Chairman C. Benjamin Ma, MD, runs one of the largest long-term outcomes of shoulder arthroplasty databases in the country. Drew Lansdown, MD, is currently evaluating the outcomes of ACL reconstruction and treatment with montelukast to prevent cartilage degeneration. He also is investigating how the shape of the knee contributes to meniscus tear and ACL risk.

Upcoming projects

In 2025, Michael Davies, MD, will continue to expand his work on musculoskeletal translational research, evaluating how mitochondrial transfer improves muscle regeneration capabilities in pre-clinical and clinical models. Dr. Wong and Dr. Zhang continue to evaluate strategies to improve peri-operative and post-operative outcomes of hip arthroscopy. Dr. Lansdown is evaluating how synovial markers at the time of ACL injury and surgery could be predictive of future ACL outcomes and arthritis risk.

Highlighted papers from the Sports Medicine group include

Venishetty N, Xiao AX, Ghanta R, Reddy R, Pandya NK, Feeley BT. Lower Extremity Injury Rates on Artificial Turf Versus Natural Grass Surfaces in the National Football League During the 2021 and 2022 Seasons. *Orthop J Sports Med.* 2024 Aug 29;12(8):23259671241265378. doi: 10.1177/23259671241265378. PMID: 39221040; PMCID: PMC11363235.

Bedi A, Bishop J, Keener J, Lansdown DA, Levy O, MacDonald P, Maffulli N, Oh JH, Sabesan VJ, Sanchez-Sotelo J, Williams RJ 3rd, Feeley BT. Rotator cuff tears. *Nat Rev Dis Primers.* 2024 Feb 8;10(1):8. doi: 10.1038/s41572-024-00492-3. PMID: 38332156.

Theismann JJ, Hartwell MJ, Moulton SG, Wong SE, Zhang AL. Spin Bias Is Common in the Abstracts and Main Body of Systematic Reviews and Meta-analyses of Hip Arthroscopy in the Setting of Borderline Hip Dysplasia. *Arthrosc Sports Med Rehabil.* 2024 Jul 2;6(5):100971. doi: 10.1016/j.asmr.2024.100971. PMID: 39534026; PMCID: PMC11551358.

Pepic L, Markes AR, Sampson H, Soriano KKJ, Wong SE, Zhang AL. Preoperative Hip Injection Response Does Not Reliably Predict 2-Year Postoperative Outcomes After Hip Arthroscopy for Femoroacetabular Impingement. *Arthroscopy.* 2024 Aug 14:S0749-8063(24)00553-X. doi: 10.1016/j.arthro.2024.07.025. Epub ahead of print. PMID: 39128685.

Diaz A, Sang L, Garcia S, Wague A, Davies M, Youn A, Liu X, Feeley BT. Age-dependent decline of B3AR agonist-mediated activation of FAP UCP-1 expression in murine models of chronic rotator cuff repair. *J Orthop Res.* 2024 Oct;42(10):2307-2317. doi: 10.1002/jor.25905. Epub 2024 May 26. PMID: 38796742.



Dr. Alan Zhang examines a patient at the UCSF Orthopaedic Institute in San Francisco. Leading clinical and translational research on athletic hip injuries, the UCSF Hip Preservation Center aims to evaluate molecular factors contributing to hip pain and osteoarthritis progression in athletes. With over 1,300 patients' clinical outcomes collected, the center focuses on hip arthroscopy surgery and other research initiatives, including hamstring tears and gluteus injuries.

UCSF Hip Preservation Center

The UCSF Hip Preservation Center continues to lead clinical and translation research in the realm of hip preservation and athletic injuries of the hip.

As Director of the UCSF Hip Preservation Center, Alan Zhang, MD leads clinical research- prospectively collecting outcomes measurements for over 1500 patients who have undergone hip arthroscopy at UCSF. Stephanie Wong, MD was awarded a highly competitive AOSSM Young Investigator Grant to correlate molecular factors with patient symptoms and treatment outcomes for femoroacetabular impingement.

The UCSF Hip Preservation Center has also continued to grow with specialists and research initiatives in numerous areas- Mohammad Diab MD specializes in open hip preservation surgery, Ishaan Swarup MD specializes in pediatric hip disorders, Michael Chau MD specializes in pediatric sports injuries and Faustine Ramirez MD specializes in primary care sports medicine including ultrasound-guided procedures.

Publications

Serna J, Furie K, Wong SE, Swarup I, Zhang AL, Diab M. The Use of Combined Hip Arthroscopy and Periacetabular Osteotomy for Hip Dysplasia Is Increasing and Has Low Complication Rates. *Arthrosc Sports Med Rehabil*. 2024 Mar 26;6(3):100929. doi: 10.1016/j.asmr.2024.100929. PMID: 39006788; PMCID: PMC11240039.

Serna J, Nosrat C, Wang KC, Su F, Wong SE, Zhang AL. Socioeconomic Factors Including Patient Income, Education Level, and Health Insurance Influence Postoperative Secondary Surgery and Hospitalization Rates Following Hip Arthroscopy. *Arthroscopy*. 2024 May 10:S0749-8063(24)00338-4. doi: 10.1016/j.arthro.2024.04.032. Epub ahead of print. PMID: 38735415.

Wong SE, Julian KR, Carpio JG, Zhang AL. Proximal Hamstring Repair With All-Suture Anchors and an Accelerated Rehabilitation and Bracing Protocol Demonstrates Good Outcomes at 1-Year Follow-Up. *Arthrosc Sports Med Rehabil*. 2024 Feb 10;6(2):100891. doi: 10.1016/j.asmr.2024.100891. PMID: 38362482; PMCID: PMC10867423.

Nosrat C, Hartwell MJ, Sadjadi R, Cevallos N, Lansdown DA, Ma CB, Zhang AL. Increasing Hip Arthroscopy Case Volume Is Associated With Increased Risk for Revision Surgery but Not Conversion to Total Hip Arthroplasty or 90-Day Hospitalizations: A Cross-Sectional Analysis of 468 Surgeons. *Arthroscopy*. 2024 Apr;40(4):1168-1176.e1. doi: 10.1016/j.arthro.2023.08.078. Epub 2023 Sep 15. PMID: 37716629.



Orthopaedic Trauma Institute Clinical Research Center

The Orthopaedic Trauma Institute Clinical Research Center (OTI CRC) led by Saam Morshed, MD, MPH, PhD, is dedicated to designing and implementing clinical and translational studies to answer the most important questions in the care of patients with musculoskeletal injuries. In collaboration with industry, government (Department of Defense and National Institutes of Health), and professional societies (Orthopaedic Trauma Association, AO Foundation), the OTI CRC develops and coordinates clinical trials to evaluate the latest technologies and innovative treatment approaches in orthopaedic trauma. We are interested in the treatment and management of lower extremity fractures, surgical site infections, lower-limb amputations and data science that will advance the practice of trauma care.

2024 Highlights

This year, the Orthopaedic Trauma Clinical Research Center would like to highlight the work done in partnership with The Major Extremity Trauma Research Consortium and UCSF Department of Epidemiology and Biostatistics.

The Major Extremity Trauma Research Consortium (METRC), started in 2008, has become the largest clinical trials network in orthopaedic trauma ever assembled. It has completed 35 trials, enrolling over 23,000 patients in carefully designed clinical research studies that seek to answer some of the most important questions in surgical care and rehabilitation after musculoskeletal trauma. Dr. Saam Morshed, has served as PI and Steering Committee member on several federally funded METRC trials, and currently serves on METRC's Executive Committee. Partnering with experts from the UCSF Department of Epidemiology and Biostatistics, Morshed and colleagues are conducting analyses

of these rich data sets to answer new questions with innovated methods. Working with Dr. Aaron Scheffler and Austin Thompson, they developed a new time-dependent limb viability assessment among patients treated with high-energy lower extremity trauma and demonstrated superiority over legacy assessments of mangled limbs. They have also completed analyses of functional outcomes and risk factors for adverse mental health sequelae after high-grade open tibial fractures treated with ring external fixators versus internal fixation. Some of the main beneficiaries of this partnership, funded in part by the new program initiatives from Research Program Management Office, have been orthopaedic surgery residents Chris Stewart and Justin Solarczyk, who have been able to learn new techniques as they complete and present their work at national meetings. This model of collaboration will promise to empower more trainees and faculty to work with UCSF methodologist to take advantage of high-quality datasets accessible to UCSF faculty such as METRC.

Publications

The global burden of fracture-related infection: can we do better?

Metsemakers WJ, Moriarty TF, Morgenstern M, Marais L, Onsea J, O'Toole RV, Depypere M, Obremsky WT, Verhofstad MHJ, McNally M, Morshed S, Wouthuyzen-Bakker M, Zalavras C.

Lancet Infect Dis. 2024 Jun;24(6):e386-e393. Doi: 10.1016/S1473-3099(23)00503-0. Epub 2023 Nov 29.

PMID: 38042164 Review.

PMID: 37851955 Free PMC article. Review.

Diagnostic Performance of a telephone questionnaire for fracture-related infections (FRIIs) in open tibia fracture patients in Tanzania.

Rodarte P, O'Marr J, Haonga B, Patrick D, Niknam K, Urva M, Cortez A, Metsemakers WJ, Shearer D, Morshed S.

Injury. 2024 Feb;55(2):111179. Doi: 10.1016/j.injury.2023.111179. Epub 2023 Nov 7

PMID: 37972489 Clinical Trial.

Characterizing Physical Intimate Partner Violence-Associated Injuries Among Adults in Low- and Middle-Income Countries: A Systematic Review.

Brown KE, Zeyl VG, Nadone H, Flores MJ, Shearer D, Morshed S. Violence Vict. 2024 Sep 3;39(4):409-424. Doi: 10.1891/VV-2022-0091.

PMID: 39227079

Chronic Low Back Pain Causal Risk Factors Identified by Mendelian Randomization: a Cross-Sectional Cohort Analysis.

Zheng P, Scheffler A, Ewing S, Hue T, Jones S, Morshed S, Mehling W, Torres-Espin A, Galivanche A, Lotz J, Peterson T, O'Neill C; REACH investigators.

medRxiv [Preprint]. 2024 Sep 27;2024.09.23.24314235. doi: 10.1101/2024.09.23.24314235.

Update in: Spine J. 2025 Jan 14:S1529-9430(25)00020-8. Doi:

10.1016/j.spinee.2024.12.029

PMID: 39399002 Free PMC article. Preprint.

Preclinical models of orthopaedic trauma: Orthopaedic Research Society (ORS) and Orthopaedic Trauma Association (OTA) symposium 2022.

Wise PM, Saiz AM, Haller J, Wenke JC, Schaer T, Schneider P, Morshed S, Bahney CS. OTA Int. 2024 Mar 11;7(2 Suppl):e303. Doi: 10.1097/OI9.000000000000303. eCollection 2024 Mar.

PMID: 38487400 Free PMC article.

Retrospective cohort study analyzing outcomes of the SIGN Fin Nail in adult femoral fractures using the retrograde approach.

Subramanian A, Adejuyigbe B, Niknam K, Gomez-Alvarado F, Morshed S, Shearer D.

J Orthop. 2024 Mar 13;54:103-107. Doi: 10.1016/j.jor.2024.03.020. eCollection 2024 Aug.

PMID: 38560590

Estimating the economic impact of complications after open tibial fracture: A secondary analysis of the pilot Gentamicin Open Tibia trial (pGO-Tibia).

Flores MJ, Brown KE, Haonga B, Morshed S, Shearer DW.

OTA Int. 2024 Jan 19;7(1):e290. Doi: 10.1097/OI9.0000000000000290. eCollection 2024 Mar.

PMID: 38249318 Free PMC article.

Predictors of quality of life, economic impact, and loss to follow-up after open tibial shaft fractures in Ghana.

Ativor V, Konadu-Yeboah D, O'Marr J, Brown K, Rodarte P, Kumah R, Quartey R, Awariyah D, Konadu P, Baidoo PK, Okike K, Morshed S, Shearer D, Roberts H.

OTA Int. 2024 Jul 12;7(3):e340. Doi: 10.1097/OI9.0000000000000340. eCollection 2024 Sep.

PMID: 39006124 Free PMC article.



Pictured here are some of our Basic Science Researchers based at the OTI (From left to right: Marika Rosenfeld, Jonathan Layne, Chelsea Bahney, Ted Miclau, Diane Hu, Nathan Young, Chan Hee Mok, Nicholas Hanne, Ralph Marcucio, Toi Masakazu, Kazu Morioka, Charles Lam. The Molecular and Cellular Biology Laboratory is directed by Ralph Marcucio, PhD

Still in Search of Better Help for Psychological and Physical Recovery After

Lower-Extremity Trauma: Commentary on an article by the Major Extremity Trauma Research Consortium (METRC): "Cognitive-Behavioral-Based Physical Therapy for Improving Recovery After a Traumatic Lower-Extremity Injury. The Results of a Randomized Controlled Trial".

Morshed S.

J Bone Joint Surg Am. 2024 Jul 17;106(14):e30. doi: 10.2106/JBJS.24.00432. Epub 2024 Jul 17.

PMID: 39017654 No abstract available.

Skin Antisepsis before Surgical Fixation of Extremity Fractures.

PREP-IT Investigators; Sprague S, Slobogean G, Wells JL, O'Hara NN, Thabane L, Mullins CD, Harris AD, Wood A, Viskontas D, Apostle KL, O'Toole RV, Joshi M, Johal H, Al-Asiri J, Hymes RA, Gaski GE, Pilon HT, Carroll EA, Babcock S, Halvorson JJ, Romeo NM, Matson CA, Higgins TF, Marchand LS, Bergin PF, Morellato J, Van Demark RE 3rd, Potter GD, Gitajn IL, Chang G, Phelps KD, Kempton LB, Karunakar M, Jaeblo T, Demyanovich HK, Domes CM, Kuhn GR, Reilly RM, Gage MJ, Weaver MJ, von Keudell AG, Heng M, McTague MF, Alnasser A, Mehta S, Donegan DJ, Natoli RM, Szatkowski J, Scott AN, Shannon SF, Jeray KJ, Tanner SL, Marmor MT, Matityahu A, Fowler JT, Pierrie SN, Beltran MJ, Thomson CG, Lin CA, Moon CN, Scolaro JA, Amirhekmata A, Leonard J, Pogorzelski D, Bzovsky S, Heels-Ansdell D, Szasz OP, Gallant JL, Della Rocca GJ, Zura RD, Hebden JN, Patterson JT, Lee C, O'Hara LM, Marvel D, Palmer JE, Friedrich J, D'Alleyrand JG, Rivera JC, Mossuto F, Schrank GM, Guyatt G, Devereaux PJ, Bhandari M; The PREP-IT Investigators. N Engl J Med. 2024 Feb 1;390(5):409-420. doi: 10.1056/NEJMoa2307679.PMID: 38294973 Clinical Trial.

OTA Podium presentations

Functional Outcomes After Modern Ring External Fixation or Internal Fixation for Severe Open Tibial Shaft Fractures

Presenting Author: Justin K. Solarczyk, MD – University of California, San Francisco

Adverse Mental Health Outcomes After Severe Open Tibia Fracture: A Secondary Analysis of the FIXIT Study

Presenting Author / Corresponding Author: Natasha M. Simske, MD – Texas Tech University Health Sciences Center - El Paso

Co-Author: Justin K. Solarczyk, MD – University of California, San Francisco

Current Projects

ADAPT

Do smart phone application-based guided mindfulness exercises improve patient-reported outcomes after musculoskeletal trauma?

Principal Investigator: Dr. Saam Morshed

PAAIN

The Pain Alleviation Project uses wearable devices to measure the response of orthopaedic patients to pain medications pre-operatively.

Principal Investigator: Dr. Meir Marmor

Weight Bearing

Effect of early weight bearing on rehabilitation outcomes in patients with traumatic ankle and tibial plateau fractures

Site Investigator: Dr. Saam Morshed

DIFFIR

Geriatric distal femur: Fixation versus replacement – A randomized controlled trial of acute open-reduction internal fixation (ORIF) versus distal femur replacement (DFR). Observational study.

Site Investigator: Dr. Saam Morshed

SEXTANT

Evaluation of a new strategy for protocolized antibiotic care for severe open fractures

Site Investigator: Dr. Saam Morshed

ULTRAPRESS

Development of a novel method for non-invasive diagnosis of compartment syndrome

Principal Investigator: Dr. Meir Marmor

GO-Tibia

A masked, randomized controlled trial to evaluate local gentamicin versus saline in open tibia fractures. Tanzania

Principal Co-Investigator: Dr. David Shearer



Masakazu Toi, MD, PhD works in The Molecular and Cellular Biology Laboratory. Their research focuses on understanding the molecular and cellular mechanisms underlying sensory neuron function in bone healing and neuropathic pain.

OTI Digital Science Lab (OTI-DSL)

The OTI Digital Science Lab (OTI-DSL) makes use of digital technology, such as wearable sensors, image analysis, computer simulation, artificial intelligence (AI), and data science, to research and develop new technologies in orthopaedic trauma.

Our primary focus areas are:

- Use of ultrasound-based technologies to diagnose acute compartment syndrome and limb perfusion compromise
- Use of AI and wearable devices to optimized post-operative pain alleviation
- Use of wearable devices and image capture to measure outcomes in trauma patients
- Data science and AI applications to improve fracture management in vulnerable populations

Using a collaborative cross-disciplinary approach, the lab offers expertise in engineering, clinical research, and data science in the following domains:

- Data: Predictive modeling and retrospective analysis of large clinical datasets and prospective collected longitudinal biometrics
- Imaging: MSK ultrasound, AI, computer vision
- Sensors: Implantable sensors and wearable technologies to monitor injury recovery
- Simulation and modeling: Experimental biomechanics, finite element analysis (FEA), machine learning

The lab has received funding from the Department of Defense (DOD), National Science Foundation (NSF), AO Foundation, Orthopaedic Trauma Association (OTA), Center for Disruptive Musculoskeletal Innovation (CDMI), and UCSF Human Performance Center (HPC).

Research Awards and Grants:

Department of Defense Grant: Development of a handheld ultrasound-based system to assist in clinical diagnosis of acute compartment syndrome.

UCSF Human Performance Center Grant: Validation of use of previously collected Apple health data to determine current performance level.

Noteworthy Publications:

Zhao X, Debopadhyaya S, Toogood P, Marmor MT. Worldwide research trends concerning operative competence in orthopaedics: A bibliometric and visualization study. *Asian J Surg*. 2024 Sep 10:S1015-9584(24)01872-4. doi: 10.1016/j.asjsur.2024.08.132. Epub ahead of print. PMID: 39261170.

Vogel C, Grimm B, Marmor MT, Sivananthan S, Richter PH, Yarburo S, Hanflik AM, Histing T, Braun BJ. Wearable Sensors in Other Medical Domains with Application Potential for Orthopedic Trauma Surgery-A Narrative Review. *J Clin Med*. 2024 May 27;13(11):3134. doi: 10.3390/jcm13113134. PMID: 38892844; PMCID: PMC11172495.

Debopadhyaya S, Toogood P, Ding A, Marmor MT. Nonphysician Evaluators and Recording-Based Tools in Surgical Skill Assessment: A Feasibility Study. *J Surg Educ*. 2024 Aug;81(8):1161-1176. doi: 10.1016/j.jsurg.2024.05.013. Epub 2024 Jun 5. PMID: 38845300.

Marmor MT, Hu S, Mahadevan V, Floren A, Solans BP, Savic R. Prolonged Opioid Use Is Associated With Poor Pain Alleviation After Orthopaedic Surgery. *J Am Acad Orthop Surg*. 2024 Jul 1;32(13):e661-e670. doi: 10.5435/JAAOS-D-24-00044. Epub 2024 Apr 30. PMID: 38696825.

Braun BJ, Histing T, Menger MM, Herath SC, Mueller-Franzes GA, Grimm B, Marmor MT, Truhn D; AO Smart Digital Solutions Task Force(Andrew M Hanflik, Peter H Richter, Sureshan Sivananthan, Seth R Yarburo). Wearable activity data can predict functional recovery after musculoskeletal injury: Feasibility of a machine learning approach. *Injury*. 2024 Feb;55(2):111254. doi: 10.1016/j.injury.2023.111254. Epub 2023 Nov 30. PMID: 38070329.

Ongoing Clinical Studies:

UltraPress: Use of ultrasound to detect early stages of acute compartment syndrome (ACS)

PDUS ACS/Swelling: Use of power doppler to detect early-stage ACS and assess tissue swelling

PAAIN: Use of wearables and AI to optimize post-operative pain management

BYODV-Performance: Validation of performance metrics routinely collected on smartphones by performance testing

Upcoming Projects:

ASSERT: Assessment of skill using intra-operative task-specific video image analysis

RadRep: Use of NLP and LLMs to classify fractures

Pain Recorder: Clinical testing of a device to continuously record subjective pain experience

BYODV-Survey: Validation of performance metrics routinely collected on smartphones by patient-reposted outcome surveys

Among the few academic centers in the United States designed for surgeons to practice and perform surgical procedures, the Surgical Training Facility opened in 2024 at Zuckerberg San Francisco General Hospital and Trauma Center in Pride Hall. The laboratory works with leading researchers, engineers, and physician to provide hands-on training in the latest technologies.





Dr. Karina Del Rosario, on the left, is the current ZSFG site investigator for the INVEST and PROTECT sub-studies, part of the NIH-funded REACH Participant Diversity Program Grant, with a focus on bolstering diversity in chronic low back pain research. Dr. Lisa Pascual, at right, continues her role as an investigator for the ZSFG-based TRACK-SCI research group, which has expanded to multiple centers.

Orthopaedic Trauma Institute Clinical Research Center

Dr. Karina Del Rosario served as the ZSFG site investigator for the INVEST and PROTECT sub-studies that are part of the NIH-funded REACH Participant Diversity Program Grant to increase diversity in chronic low back pain research. The goals of the studies are to increase enrollment and retention of underrepresented racial and ethnic minorities in low back pain research, attain additional insight into their back pain treatment and health care experience, and improve culturally and linguistically appropriate patient-facing materials for non-English speakers. Dr. Masato Nagao is also serving as investigator for these studies and assisting with patient recruitment.

Dr. Lisa Pascual continues as an investigator for the ZSFG-based TRACK-SCI research group that now extends to multiple centers. Multiple disciplines participate in this collaboration, which includes neuroscientists, data scientists, and subspecialists in the fields of PM&R, neurosurgery, orthopaedic surgery, anesthesiology, neurologic intensive care, emergency medicine and neuroradiology. The group seeks to identify factors that impact or may predict functional outcomes of patients sustaining spinal cord injury.

Research Awards and Grants

Noteworthy Publications

The correlation of neurosurgery motor examinations with ISNCSCI motor examinations in patients with spinal cord injury: a multicenter TRACK-SCI study. *J Neurosurg Spine*. 2024 Oct 04; 1-9. Lui A, Bonney PA, Burke J, Kanter JH, Yue JK, Takegami N, Tarapore PE, Huang M, Mummaneni PV, Dhall SS, Hemmerle DD, Ferguson AR, Torres-Espin A, Duong-Fernandez X, Lai N, Saigal R, Pan J, Singh V, Kyritsis N, Talbott JF, Pascual LU, Huie JR, Whetstone WD, Bresnahan JC, Beattie MS, Weinstein PR, Manley GT, O'Banion LA, Kuo YH, Viljoen S, Grandhi R, Shammassian BH, DiGiorgio AM. PMID: 39366011.

Rehabilitation after musculoskeletal injury: an overview of systems in the United States and Canada. *OTA Int*. 2024 Jul; 7(5 Suppl):e311. Miclau TA, Pascual L, Ndoja S, Frazer A, Beaupre L, Schemitsch EH. PMID: 39135904; PMCID: PMC11318513.

ATF3 is a neuron-specific biomarker for spinal cord injury and ischaemic stroke. *Clin Transl Med*. 2024 Apr; 14(4):e1650. Pan JZ, Wang Z, Sun W, Pan P, Li W, Sun Y, Chen S, Lin A, Tan W, He L, Greene J, Yao V, An L, Liang R, Li Q, Yu J, Zhang L, Kyritsis N, Fernandez XD, Moncivais S, Mendoza E, Fung P, Wang G, Niu X, Du Q, Xiao Z, Chang Y, Lv P, Huie JR, Torres-Espin A, Ferguson AR, Hemmerle DD, Talbott JF, Weinstein PR, Pascual LU, Singh V, DiGiorgio AM, Saigal R, Whetstone WD, Manley GT, Dhall SS, Bresnahan JC, Maze M, Jiang X, Singhal NS, Beattie MS, Su H, Guan Z. PMID: 38649772; PMCID: PMC11035380.

Ongoing Clinical Studies:

INVEST and PROTECT have completed recruitment and enrollment of patients in May 2024 and currently are in the phases of data analysis and manuscript preparation.

TRACK SCI continues recruiting patients and performing follow-up data collection from multi-center sites.



Pictured from left to right: Michael Terry, Richard Coughlin, Sanjeev Sabharwal, Coleen Sabatini, Dave Shearer, Madeline Mackechnie, Nicolas Lee, Theodore Miclau

UCSF Institute for Global Orthopaedics and Traumatology (IGOT)

The UCSF Institute for Global Orthopaedics and Traumatology (IGOT) is dedicated to improving bone and joint care in low-resource settings through academic partnering and high-quality research. Working with hospitals and universities in Tanzania, Malawi, Uganda, Ghana, and Latin America, the initiative helps surgeons in these countries find better ways to treat injuries and bone diseases using locally available resources. Recent studies have made important discoveries across several domains, including open fracture care, diagnosis of musculoskeletal

infection, pediatric orthopaedics, and methods of effective orthopaedic outreach. The GRI also supports capacity building by conducting research trainings. These trainings, which were conducted in the US, Nigeria, and Tanzania last year, provide the skills necessary for surgeons to independently conduct clinical research in their home countries. Through these efforts, GRI continues to advance research and training to create equity in musculoskeletal care in areas that need it most.

Recent Publications

- Oji NM, Sabatini CS. Osteomyelitis and Septic Arthritis of the Upper Extremity in Pediatric Patients. *Curr Rev Musculoskelet Med*. 2024 Dec 24.
- MacKechnie MC, Shearer DW, Verhofstad MHJ, Martin C, Graham SM, Pesantez R, Schuetz M, Hüttl T, Kojima K, Bernstein BP, Miclau T; the Delphi Study Group. Establishing Consensus on Essential Resources for Musculoskeletal Trauma Care Worldwide: A Modified Delphi Study. *J Bone Joint Surg Am*. 2024 Jan 3;106(1):47-55.
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Special Research Initiatives

The Center for Disruptive Musculoskeletal Innovations (CDMI)

The Center for Disruptive Musculoskeletal Innovations (CDMI) is a National Science Foundation (NSF)-funded Industry-University Cooperative Research Center (IUCRC). The CDMI is a Phase II IUCRC currently consisting of three university sites: University of California, San Francisco (UCSF), University of Toledo, and Ohio State University. Each CDMI site has faculty with unique technical and clinical strengths.

The CDMI addresses pressing societal needs associated with the growing burden of musculoskeletal disorders (MSDs), with the goal of generating data on incidence, pathomechanisms,

treatment outcomes, and costs associated with MSDs. Based on these data, it develops new technologies for MSD prevention, diagnosis, and treatment.

The CDMI sustains interactions between academic researchers, trainees, and member companies who comprise the CDMI's Industrial Advisory Board (IAB). It serves as a hub to match industry-inspired fundamental research questions to new, high-impact discoveries, which serve as a nucleus for transformative industry and university collaborations.

Core Center for Patient-centric, Mechanistic Phenotyping in Chronic Low Back Pain (REACH) Center

Expanding his innovative research into developing diagnostic tools, clarifying mechanisms, and testing biologic therapies for chronic low back pain (cLBP), Jeffrey Lotz, PhD, serves as the director and principal investigator of the Core Center for

Patient-centric, Mechanistic Phenotyping in Chronic Low Back Pain (REACH). REACH is an NIH U19 Back Pain Consortium (BACPAC) Mechanistic Research Center (MRC) focused on positively impacting the opioid epidemic through the discovery of cLBP mechanisms and phenotypes. This will ultimately lead to precision medicine for low back pain and reduced dependence on additive therapies.

2024 was a sixth and supplemental year for REACH and saw the completion of baseline enrollment for the comeBack cohort (n = 400). The longitudinal/virtual cohort BACKHOME continues with over 3000 participants enrolled to date. In both studies, data elements from psychological, biological, and social domains are measured in cLBP subjects. REACH continued to follow the comeBack cohort with light phenotyping questionnaires at 3-month intervals. The Clinical Core also supported access to electronic medical record (EMR) information for subjects in both cohorts, which will be incorporated into patient phenotyping algorithmic work being performed by the Analytics Core. Progress was also made on data migration, cleaning, and codebook refinement for all REACH-related cohorts: comeBack, BACKHOME, BEST, INVEST (diversity recruitment ancillary study) and the Control cohorts.

The Biobehavioral Core continued their work of feature extraction from fMRI and QST assessments performed in comeBack, and collaborated with the Analytics Core to determine which biobehavioral measures (questionnaires, fMRI, QST) were independently able to explain variance in subject pain severity and pain interference, and whether some or all of these measures contribute significantly to predicting treatment response.

The Physical Function and Biomechanics Core worked on feature extraction from the sit-to-stand (STS) biomechanical test performed by the comeBack, BEST, and Control participants

during deep phenotyping. Features were refined during analyses of multi-modal data in attempts to maximize the variance explained by the STS data in cross-sectional and longitudinal analyses of pain severity and pain interference. Core leaders also compared biomechanical insights gained from STS biomechanics versus activity tracking via the Actigraph 7-day assessment, and collaborated with BACPAC sites in comparing the various biomechanical assessments to determine best practice recommendations for future work.

The Pathophysiology Core continued to work on feature extraction from advanced imaging (IDEAL, UTE, T1-rho, MRS) collected from the comeBack, BEST, and Control participants during deep phenotyping. Extracted features were refined during analyses of multi-modal data in attempts to maximize the variance explained by imaging data in cross-sectional and longitudinal analyses of pain severity and pain interference. Core leaders also worked to develop machine learning methodologies for extracting important features observed in advanced imaging from routine MRI. The Core continues to analyze biosample data extracted from comeBACK, BEST, and Control samples (blood, stool, saliva) to integrate into multi-modal clustering analyses.

The Analytics Core coordinated with other REACH cores to conduct traditional and novel analyses including determining patient clusters that predict treatment response.

The Administrative Core continued to coordinate research activities, communications with NIH and other stakeholders, manage research dissemination, and track finances.

REACH investigators Jeannie Bailey, PhD, Patricia Zheng, MD, and Trisha Hue, PhD, MPH, continue to oversee the Apple Watch study in the BACKHOME cohort. 500 Apple Watches are being used to collect data on vital signs, such as heart rate variability, sleep, mobility, and activity data.

To date, REACH authors have published nearly 50 articles and presented more than 40 abstracts/posters.

Core Center for Musculoskeletal Biology and Medicine (CCMBM)

A cornerstone of UCSF's musculoskeletal (MSK) research is a prestigious grant from the NIH-National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) P30 Center, which funds the CCMBM under the visionary leadership of Dr. Tamara Alliston. This program propels the success of UCSF MSK investigators across basic, clinical, computational, and population research spectrums.

In 2024, the CCMBM celebrated the renewal of its NIH/NIAMS funding for another five-year cycle, ensuring continued access to its unique core services, technical workshops, visiting faculty seminars, and funding opportunities for the musculoskeletal community. The CCMBM has been instrumental in fostering and expanding a vibrant MSK research network at UCSF and throughout the UC system.

The UC Skeletal Research Enhancing Training Collaboration and Health (STRETCH) program welcomed its second cohort of scholars. This year's initiative advanced groundbreaking

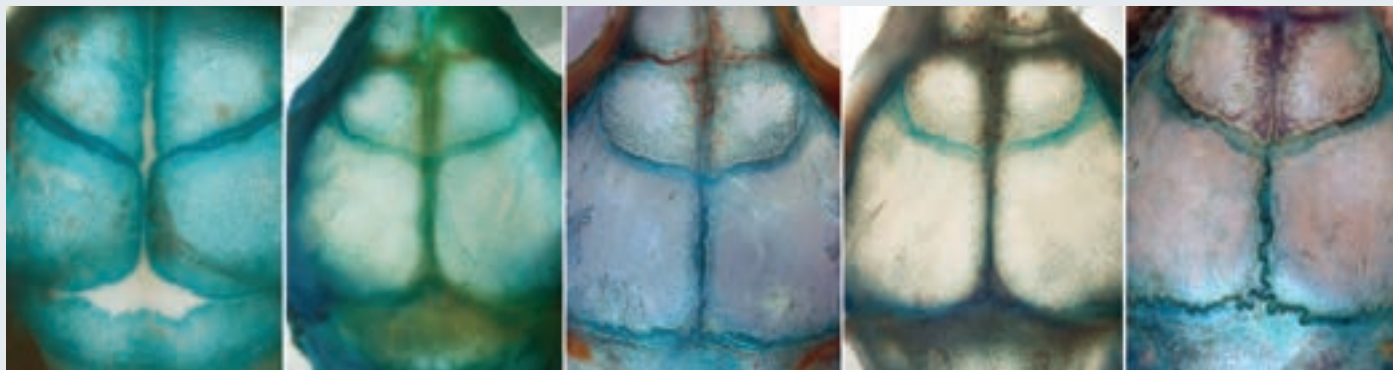
collaborative projects across three UC campuses, actively engaging and supporting a diverse group of undergraduate learners. Through mentored, collaborative musculoskeletal research, STRETCH is shaping the future of MSK science within the entire UC system.

Celebrating its tenth anniversary, CCMBM's annual spring scientific retreat, co-sponsored by the UCSF Department of Orthopaedic Surgery and five other distinguished groups, was an inspiring milestone. The event, titled "Fueling MSK Health & Discovery with Data Science, Technology, and Digital Health," attracted nearly all attendees in person, including special guest Chancellor Hawgood, who reflected on the impact of the Center on UCSF research and patients. This remarkable gathering united leading research scientists, clinicians, and patients, fostering groundbreaking discussions and exploration of the latest advancements and opportunities at the intersection of data science, technology, and digital health with musculoskeletal research and clinical practice.

The Center for Dental, Oral, and Craniofacial Tissue and Organ Regeneration (C-DOCTOR)

Realizing that few of the National Institutes of Health's investments in basic, discovery research ever directly results in tangible patient impacts, the National Institute of Dental and Craniofacial Research (NIDCR) established two national Tissue Regeneration Resource Centers. These are tasked with the specific goal of accelerating clinical translation of innovative regenerative technologies to replace dental, oral, and craniofacial (DOC) tissues or organs lost to congenital disorders, traumatic injuries, diseases, and medical procedures.

C-DOCTOR (c-doctor.org) is one of NIDCR's resource centers and is led by UCSF co-principal Dr. Jeffrey Lotz, PhD, and University of Southern California co-principal Dr. Yang Chai, DDS, PhD. C-DOCTOR is a public-private partnership, with the primary mission of providing full clinical, scientific, technical, regulatory, financial/industrial, and management resources to promote cost-effective translation and timely development of DOC tissue engineering/regenerative medicine (TE/RM) technologies.





Visiting students from across California universities and high schools participate in MSK Center's Summer Student Social at Genentech Hall in San Francisco.

The UCSF Musculoskeletal (MSK) Center

The UCSF Musculoskeletal (MSK) Center, under the visionary leadership of Dr. Tamara Alliston, PhD, serves as a hub for pioneering musculoskeletal research, education, and advocacy. This dynamic center unites a diverse community of investigators across the basic, translational, computational, and clinical research spectrum, fostering collaborative efforts that drive innovation in musculoskeletal health. By connecting leading UCSF researchers with cutting-edge projects, the MSK Center is at the forefront of transformative discoveries. From lab-grown tissue models to AI-driven solutions, the Center's innovative approaches are revolutionizing the fight against arthritis, osteoporosis, back pain, and other debilitating conditions, positioning us as leaders in advancing musculoskeletal health.

Funding by a \$1.2M T32 training grant from the National Institutes of Health, the Musculoskeletal (MSK) Training Program continued its comprehensive scientific education of basic, translational, and surgeon scientists in MSK research. Under the direction of Dr. Aaron Fields, PhD, the program fosters a dynamic and diverse community of PhD scientists, MD, and MD/PhD residents and fellows, equipping them for lifelong scholarly contributions that enhance our understanding and treatment of MSK diseases. During 2024, the program proudly awarded three grants to its second cohort of MSK training program scholars, underscoring its commitment to advancing research and improving patient care in the field of musculoskeletal health.



Eva González Díaz, PhD

Postdoctoral Scholar,
Orthopaedic Surgery

Project: Investigating the Role
of the Gut Microbiome in
Musculoskeletal Tissue Aging

Mentor: Christopher
Hernandez, PhD

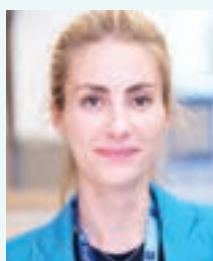


Ryan Halvorson, MD

Resident, Orthopaedic
Surgery

Project: Markerless Motion
Capture and Movement
Quality Algorithms to Predict
Injury Risk in High School
Sports

Mentors: Jeannie Bailey, PhD
and Brian Feeley, MD



Zsafia Torok, PhD

Postdoctoral Scholar, Cellular
and Molecular Pharmacology

Project: Identifying Sex-
Specific Pathways of
Hypothalamic-Ventricular
Crosstalk in Bone
Homeostasis

Mentor: Holly A. Ingraham,
PhD

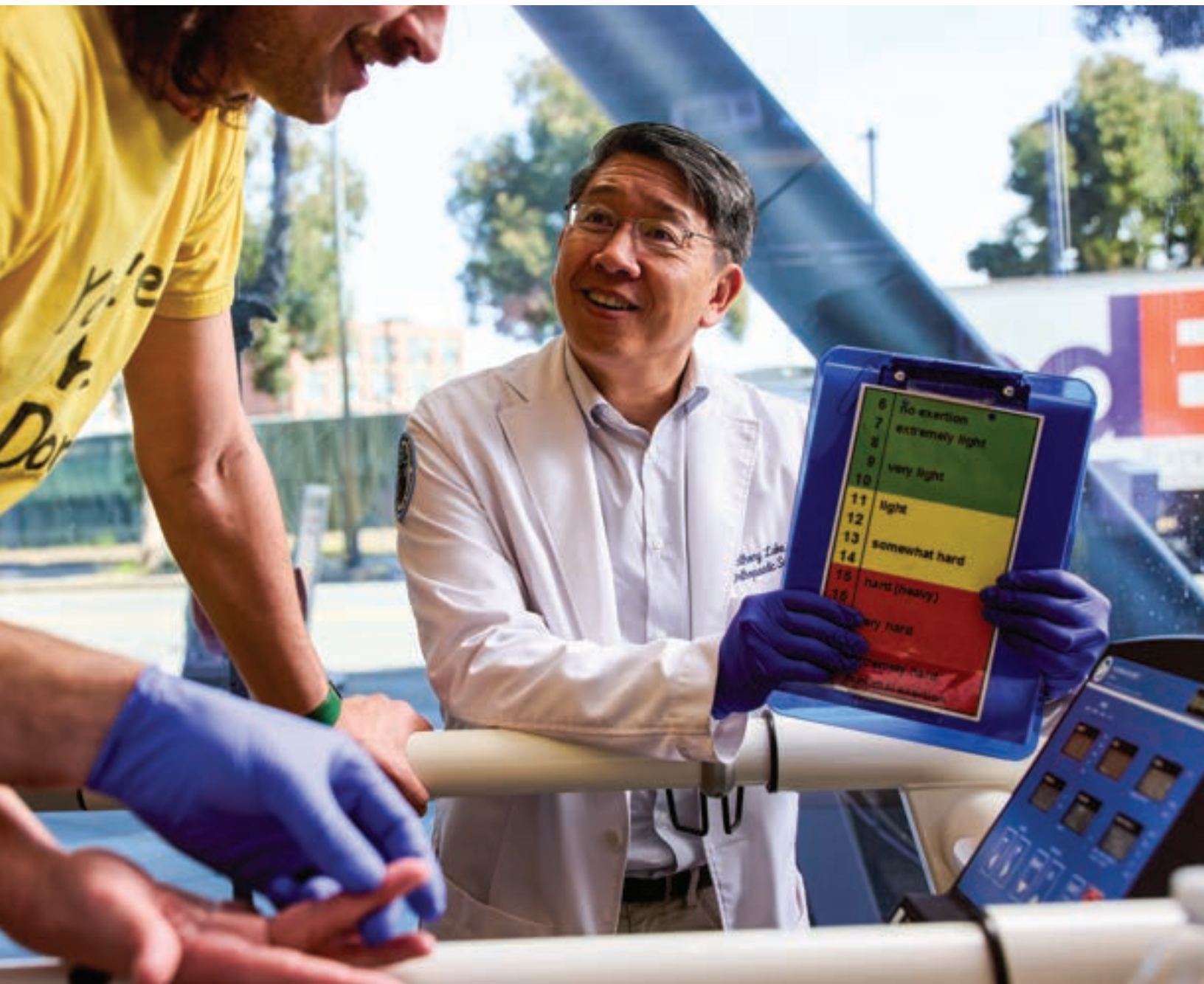
Recognizing the need to address disparities in representation and foster a passion for health sciences among underrepresented learners, the MSK Center hosted its annual Summer Social for high school and undergraduate students engaged in musculoskeletal research (Figure 2). This program, which includes researchers from musculoskeletal labs within the UCSF departments of Orthopaedic Surgery, Radiology and Biomedical Imaging, and Physical Therapy and Rehabilitation Science, equips students with invaluable professional skills, hands-on research experience, and essential networking opportunities that pave the way for success in STEM careers. Through these initiatives, the Center not only supports students' academic and professional growth but also strengthens the future of health sciences by cultivating a diverse and talented workforce.

The MSK Center produced “A Skeleton for Discovery, A Skeleton for Cures,” which is an inspiring video that captures the essence of the Center's groundbreaking research and innovation. The video highlights the extraordinary work being conducted at the UCSF Musculoskeletal Center, with the relentless dedication and pioneering efforts of our researchers, who are committed to transforming the landscape of musculoskeletal health, with cutting-edge research that is driving medical advancements at an unprecedented pace. Our team of world-class scientists and clinicians is making significant strides in understanding and treating conditions that affect millions of individuals worldwide.

The Center builds an integrated research community by helping to recruit talented new faculty. During 2024, the MSK Center contributed to the successful hiring of Michael Davies, MD, a distinguished orthopaedic surgeon, sports medicine specialist, and avid researcher on the role of mesenchymal stem cells in tissue regeneration, utilizing cutting-edge technology including single-cell RNA sequencing to characterize stem cell populations within tissues to leverage their regenerative properties.

The Core Center for Musculoskeletal Biology and Medicine (CCMBM) is an integral component of the MSK Center, serving as a vital campus resource for translational musculoskeletal research. In 2024, the MSK Center began integrating its operations and branding with the CCMBM, symbolizing a unified and interconnected research community.

Open MSK Integrated Knowledge Exchange (Open MIKE) continued to foster dynamic collaborations between MSK researchers and experts from other fields. By facilitating discussions on innovative projects, this initiative brought together investigators to explore and accelerate preclinical product development, including diagnostics and therapeutics, commercialization, and clinical adoption, ultimately invigorating the research community.



Dr. Anthony Luke, director of the UCSF Human Performance Center (HPC) works with a patient at the Orthopaedic Institute in San Francisco. The HPC conducts vital tests to further groundbreaking research endeavors.

UCSF Human Performance Center

The Human Performance Center (HPC) is the key center for exercise related science serving the UCSF community. The state-of-the-art equipment and expert staff enable the center to remain at the forefront of research involving human motion and exercise, investigating knee osteoarthritis, prostate cancer, Parkinson's Disease and other conditions that plague human function as people age.

Anthony Luke MD, MPH is the Director of the HPC, Brooke Schultz, MS is the manager and Biomechanist for the Center, Mathias Sorensen, MS is the exercise physiologist, and Richard Souza, PT, PhD, is the HPC Director of Research.

2024 Highlights

After installing a new Qualisys Motion Capture Camera System in 2023, seven funded projects used the new system for data collections in 2024. This included both a 10-camera Arqus A5 traditional marker-based system as well as a 10-camera Miquis Color Video system for Theia Markerless 3D motion analysis. Some of these projects used the two systems independently while others ran them simultaneously showcasing the versatility of motion capture at the Human Performance Center.

One such project initiated in 2024 that utilizes Theia3D is with Marta San Luciano Palenzuela, MD (Neurology). In this novel project, 10 children and young adults with dyskinetic cerebral palsy and disabling movement disorders undergo bilateral DBS in the dorsal dentate nucleus of the cerebellum, using Medtronic Percept, a bidirectional neurostimulator that can sense and store brain activity and deliver DBS therapy. The efficacy of cerebellar DBS in improving quality of life and motor outcomes will be tested by a series of N-of-1 clinical trials. We will characterize abnormal patterns of cerebellar oscillatory activity measured by local field potentials from the intracranial electrodes related to clinical assessments, wearable monitors and kinematic measures in the HCP.

The HPC has a long history of collaborating with Urology on exercise intervention related research for men with prostate cancer. In 2024, Stacey Kenfield, ScD, and Scott Bauer, MD, ScM, expanded this relationship via the PROUD study: evaluating the feasibility, acceptability, fidelity, and safety of a remote exercise intervention and health education control among physically inactive older men with LUTS/BPH. Fitness assessments are completed at the HPC pre- and post-exercise intervention.

The HPC welcomed new collaborator, Janet Y. Lee, MD, MPH, MAS, and the SEPSITY-EXT study in 2024. The objective of this study is to evaluate the trajectory of bone mass, architecture, and strength in transgender and gender diverse youth (TGD) who follow the peer-concordant puberty-timing model, and to assess the determinants of skeletal health in this population. The HPC team perform a longitudinal assessments of isometric knee extension muscle strength for the patient population. This is an observational extension study of TGD youth who participated in the original SEPSITY study.



Jeanie Bailey, PhD has been collaborating with the HPC on an R01 grant by using the new Theia 3D markerless motion capture system for full body biomechanical analysis. The project is focused on teasing apart the structure and functional relationship of the multifidus in chronic low back pain patients. Participant recruitment began in 2024 and reached 50% of it's goal by years end.

PhD student, Hector Carbajal Mendez, completed a \$5,000 HPC Seed Grant to validate the effectiveness and repeatability of markerless motion capture systems against traditional marked methods. The study's findings showed that markerless systems demonstrated comparable accuracy in sagittal and frontal plane joint angles, with notable improvements in inter-session reliability and reduced variability compared to traditional marked data. His findings were presented at the ASB 2024 conference in Wisconsin.

HPC Seed Grant recipient, Meir Marmor, MD FAAOS, FACS, completed the pilot "Bring Your Own Device" (BYOD) study, which involved 11 healthy participants, successfully demonstrated that app-derived metrics, such as step count, heart rate, and respiratory rate, correlated strongly with validated laboratory performance metrics. Based on various predictor regression models, app-derived metrics were able to predict all performance metrics assessed, with the exception of jump height. The abstract was presented at Inman Abbot Scientific Program 2024.

Ongoing Research in the Human Performance Center

The HPC continues to support Richard Souza, PT, PhD with his research on osteoarthritis progression in the lower extremities. His continued collaboration with the Department of Radiology on joint osteoarthritis currently has two active R01 research projects and completed one CCMBM Pilot/Feasibility grant in 2024: (1) evaluating the interconnectivity of the knee and hip joints and (2) investigating the interaction of bone and cartilage in the patellofemoral joint (3) evaluating changes in gait biomechanics from decline treadmill walking on patients with patellofemoral joint osteoarthritis. Both R01 studies are longitudinal tracking of participants, evaluate tissue health through X-ray and MRI, as well as use 3D Motion Capture and functional testing motion analysis. In addition, study participants wear the AX6 activity tracker for 7 days of continuous physical activity tracking in their home environment.

Drs. Anthony Luke, William Berrigan and Nicolas Hatamiya launched, in 2024, the Knee Osteoarthritis Biomarker Exploration Platelet Rich Plasma (PRP) study (KOB-PRP) Phase 3 study, a randomized controlled trial evaluating if similar protein changes occur in blood and synovial fluid following platelet rich plasma injection versus saline control in knee osteoarthritis patients. They aim to explore the biological pathways by which PRP acts, including mirroring the human study in mice. This research is supported by the Lynne and Marc Benioff Foundation and other philanthropic donors and is actively recruiting patients.

In the SPARX3 study (PI: Dr. Nijee Luthra, MD PhD, Neurology), the HPC team implements a treadmill-based exercise training program utilizing Heart Rate Zones for early-stage Parkinson's patients. A VO2peak fitness assessment is administered at multiple timepoints in addition to disease biomarkers and other functional movement tests. Dr. Luthra has a K23 award continuing her investigation of exercise for Parkinson's patients. The EXCEL-PD study includes a resistance training program in addition to treadmill-based aerobic exercise.

The EDGE Lab

UCSF Orthopaedic Surgery faculty continue to expand innovative deployment of Advanced Visualization and Manufacturing capabilities on the frontlines of healthcare.

The EDGE Lab was founded in 2018 by Aenor Sawyer, MD,MS, Alexis Dang, MD and Alan Dang, MD with a focus on Engineering, Designing, and Growth Enabling digital (EDGE) and manufacturing technologies.

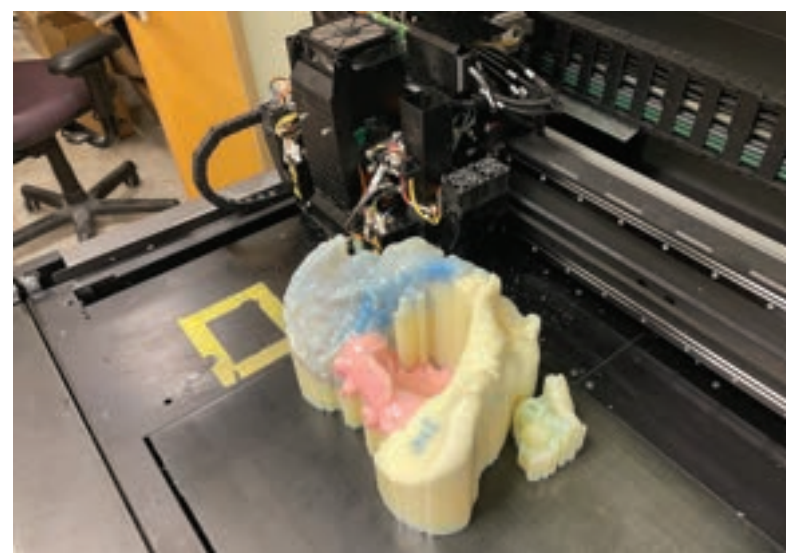
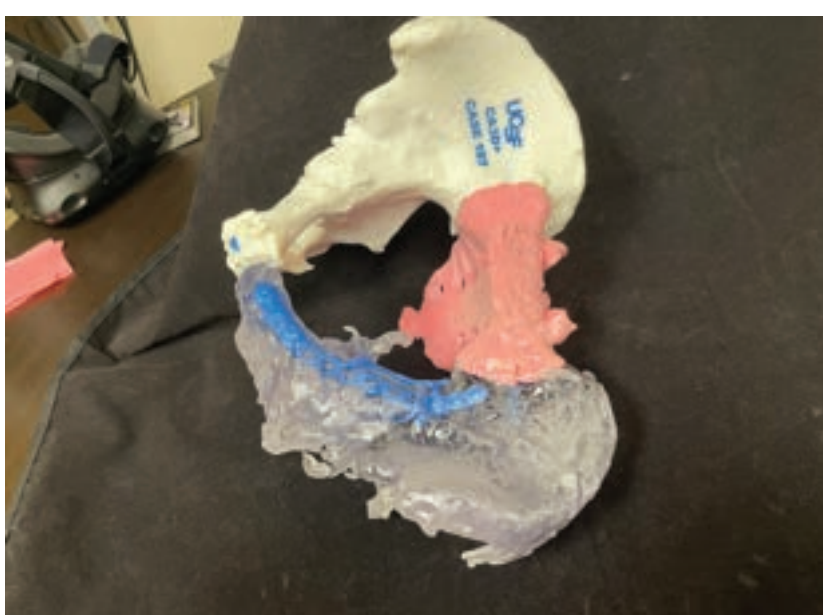
This initiative provided clinical 3D printing across the many campuses of the Department including UCSF Parnassus Heights, The Orthopaedic Institute at Mission Bay, ZSFGH, SF VAHC, UCSF Benioff Children's Hospital Mission Bay, and UCSF Benioff Children's Hospital Oakland. The EDGE team successfully enabled frontline 3D printing of Precision Anatomic Models for surgical pre-operative planning and continues to conduct research to assess the efficacy and economics of the technology.

This foundational initiative of EDGE served as the springboard for an exciting programs in advanced visualization and manufacturing technologies at UCSF that started this year.

At the San Francisco VA, Dr Alexis Dang and Dr Alan Dang successfully developed the TRST-3D (Translational Radiology and Surgical Technologies) program. This was initially funded through a 1.4 million dollar grant over 3 years starting in 2018. This was followed up with an additional 1.4million dollars starting fiscal year 2023. this is now considered the flagship medical 3D printing program within the Veterans Administration nationally.

As a result of their work in the 3D imaging arena, Alexis Dang, MD and Alan Dang, MD won the San Francisco Federal Executive Board "Federal Employee of the Year" award in Science & Technology related to 3D printing in orthopaedics

Models are created by TRST-3D (Translational radiology and surgical technologies), based at the VA with affiliation with EDGE Lab.





Stefano Bini, MD, Department's Chief Technology Officer, leads all aspects of the Department's technology vision and development. As the CTO, their primary focus is advancing the overall direction and development of the Department's technology infrastructure and ensuring operational excellence with the highest level of quality in the Department's digital endeavors.

Digital Health Team

After an initial trial with a digital scribe platform, our department has enthusiastically adopted Ambience, with 37 team members now using it. Dr. Jason Jagodzinski is leading an initiative to establish best practices, ensuring that users maximize its benefits. For most clinicians, Ambience has significantly simplified charting. However, the platform has the potential to do even more. We are hopeful that, in the near future, UCSF will allow us to trial additional features that could assist with accurately coding our clinical notes, further streamlining documentation.

Our patient engagement solution remains Get Well Loop, and our team has worked closely with the company to refine and update our protocols. Special thanks to Rachel Wynne, who

has championed this initiative, ensuring that over 1,000 patients annually receive comprehensive text-based education on what to expect for 6 weeks before and after surgery. Her efforts have played a crucial role in improving patient preparedness and overall experience as we have previously shown that its use lowers readmission rates and has excellent patient satisfaction scores.

On the operational side, Docspera has now fully replaced paper-based surgical scheduling for arthroplasty and is being adopted in select sports medicine, pediatrics and spine practices. This transition has enabled greater collaboration among schedulers and enhanced visibility across different surgical environments. Thanks to Erica Suk's leadership, Docspera has also begun to analyze surgical scheduling data, revealing key insights. We now know that how cancellation rates vary by practice as well as how many patients never reschedule thus providing insights to help improve workflows.

Looking ahead, we plan to leverage a closed-system generative AI platform within Docspera to further enhance scheduling. This system (a chat bot interface) will proactively engage patients scheduled for surgery, confirming their commitment to their date. If a patient expresses concerns or the need to reschedule, our team will be alerted early, reducing the likelihood of last-minute cancellations. Thanks to the data we have collected on our current status, we will be able to show the impact of this technology on cancellation rates.

We are excited about the future of expanding these and other digital tools across service lines, optimizing patient care pathways, and driving continued improvements in efficiency and patient outcomes.

Digital Orthopaedics Lab

Our research leveraging sensors and AI to better understand human mobility in post-surgical recovery, has reached a significant milestone with the submission of two intriguing papers.

The first paper demonstrates how we used recurrent neural networks to process data from wearable sensors and replicate, with remarkable accuracy, kinetic and kinematic data typically collected in the gait lab. While temporospatial metrics such as stride length and step count are easily captured by smartwatches, biomechanical data has traditionally been far more complex to measure outside of a controlled environment. Our findings suggest that two inexpensive wearable sensors can deliver gait lab-quality data in real-world settings, enabling more practical and scalable gait analysis.

In a related study, we revisited a motion capture dataset collected years ago from ACL reconstruction patients to determine if machine learning algorithms could predict recovery progression based on gait patterns. Our models identified a strong correlation between recovery time and gait biomechanics, reinforcing the idea that wearable sensor-derived kinematic metrics could be used as an objective biomarker for recovery. Taken together, these studies indicate that personalized, sensor-driven rehabilitation pathways could eventually replace standardized recovery protocols, optimizing outcomes for each patient.

Looking ahead, our Digital Orthopedics Lab is exploring the application of large foundation models trained to interpret the physical environment to human motion data. Our goal is to develop a unified biomarker for human mobility, one that could serve as a universal health metric applicable across healthcare research. We are also looking at measuring the impact of digital tools on our clinical practices. We are working on an IRB to allow us to quantify the accuracy and fidelity of digital scribes in orthopedic patient visits and, in a later stage, on AI powered chat bot interfaces.

In parallel, we continue to investigate the diagnosis, biomechanics, and management of gluteus medius tears, an under-recognized yet debilitating injury that primarily affects middle-aged and older women. This condition remains underreported and undertreated, despite its significant impact on function and quality of life. We now have one of the largest case series on this topic and are actively analyzing biomechanics, indications, and surgical outcomes of abductor tendon repairs. One goal of our research is to compare the accuracy of our manual data recovery efforts to the use of a generative AI and natural language processing as well as use the technology to identify patient phenotypes that are at highest risk of failure.

With each of these efforts, we aim to bridge the gap between technology and clinical practice, advancing the future of personalized orthopedic care.



UC Space Health

3 Key Updates for 2024

UCSF, NASA Launch Historic Collaboration to Advance Cancer Research

UC Space Health Hosts Academic Symposium Exploring Parallels Between Spaceflight Challenges and Cancer Treatment

Executive leaders and top scientists from NASA and UCSF gathered to discuss potential research collaborations aimed at advancing cancer research and cutting the nation's cancer death rate by at least 50 percent over the next 25 years, aligning with the goals of the White House Cancer Moonshot Initiative.

"This meeting highlighted the beneficial impact of space research on terrestrial healthcare and ignited new cross-sector collaborations to accelerate advances in cancer research. Our investment of time and expertise in Space Health research yields a substantial R.O.E. – that is a "Return On Earth". Aenor Sawyer, MD

UC Space Health, founded in the UCSF Department of Orthopaedic Surgery had the pleasure of hosting NASA at an academic symposium to kick off an exciting collaboration as part of the White House Cancer Moonshot Initiative. Organized and executed by Aenor Sawyer, MD, (Director of Skeletal Health), the symposium brought together Oncology experts as well as MSK thought leaders including Tamara Alliston, PhD (MSK Basic Science), Jeannie Bailey, PhD (MSK Basic Science), Rosie Wustrack, MD (Orthopaedic Oncology), Melissa Zimel, MD (Orthopaedic Oncology), and Kiauntee Murray, MD (Orthopaedic Oncology).

This event marked a first such collaboration between UCSF and NASA, paving the way for groundbreaking research at the intersection of space exploration and cancer care.

The event featured roundtable discussions that explored the five hazards of human spaceflight—space radiation, isolation and confinement, distance from Earth, gravity, and closed or hostile environments—and their direct parallels to a cancer patient's experience, such as the isolation of hospital rooms and long-term effects of radiation.

NASA astronaut Yvonne Cagle, MD, former astronaut Kenneth Cockrell and NASA Flight Surgeon Joe Schmidt, MD were also present, sharing their insights on human spaceflight and NASA's cancer research efforts with patients at the UCSF Benioff Children's Hospital San Francisco. Patients had the unique opportunity to meet the astronauts and even received a video message from NASA astronauts Suni Williams and Butch Wilmore from the International Space Station.

UC Space Health Launched a monthly "Out of this World Science Symposium" - focused on Space Health and Space Biology. This is a collaborative program jointly hosted by UC Space Health and NASA Ames Biological and Physical Sciences, presented by NASA scientists and UC researchers.



In a surprise personal greeting from 260 miles above Earth, astronauts aboard the International Space Station sent a recorded message describing the orbiting laboratory's experiments on protein crystal growth, nanoparticle drug delivery and tissue engineering. "We go to space not just to explore the stars but to improve life here on Earth." Sunita "Suni" Williams, NASA Astronaut.

UC Space Health has a multidisciplinary research program with numerous publications including:

Hughes-Fulford M, Carroll DJ, Allaway HCM, Dunbar BJ, & Sawyer AJ. Women in space: A review of known physiological adaptations and health perspectives. *Experimental Physiology*, 1–24. 2024 Nov 2. <https://doi.org/10.1113/EP091527>

Wong MC, Bennett JP, Leong LT, Liu YE, Kelly NN, Cherry J, Kloza K, Li B, Luliano S, Sibonga J, Sawyer AJ, Ayton J, Shepherd JA. Evaluation of body shape as a human body composition assessment in isolated conditions and remote environments. *npj Microgravity* 10, 72 (2024). <https://doi.org/10.1038/s41526-024-00412-5>

Hughes-Fulford M, Carroll DJ, Allaway HCM, Dunbar BJ, Sawyer AJ. Women in space: A review of known physiological adaptations and health perspectives. *Exp Physiol*. 2024 Nov 02. PMID: 39487998. <https://pubmed.ncbi.nlm.nih.gov/39487998/>

Meer E, Grob SR, Lehnhardt K, Sawyer AJ. Ocular complaints and diagnoses in spaceflight. *NPJ Microgravity*. 2024 Jan 02; 10(1):1. PMID: 38167407. PMCID: PMC10762130. <https://pubmed.ncbi.nlm.nih.gov/38167407/>

For more information about UC Space Health - [Spacehealth.ucsf.edu](https://spacehealth.ucsf.edu)

2024 Resident Research Highlights

OREF Resident Research Grant



Wyatt David, MD

Orthopaedic Research and Education Foundation

Generating Crosswalks Between Common Hip-Specific Patient Reported Outcomes Measurements Utilized for Assessment of Symptoms and Treatment in Femoroacetabular Impingement Syndrome

10/1/24 – 9/30/25

\$5,000



Michael Flores, MD

Orthopaedic Research and Education Foundation

Predictors of Quality-of-Life after Fracture-Related Infections in Latin America (FRILA): A Prospective Multicenter Observational Study 10/1/24 – 9/30/25

\$5,000



Sara Kiani, MD

Orthopaedic Research and Education Foundation

The Impact of Erector Spinae Blocks on Pain after Pediatric Spinal Deformity Surgery

10/1/24 – 9/30/25

\$5,000



Lacey Smith, MD

Orthopaedic Research and Education Foundation

Quantifying the Burden of Musculoskeletal Disease in Tanzania 10/1/24 – 9/30/25

\$5,000

James O. Johnson (JOJ) Resident Research Grants



Chloe Dlott, MD

What patient factors influence ACL graft choice for patients undergoing primary ACL reconstruction

\$5,000



Omair Khan, MD

Variations in surgical offerings for CMC osteoarthritis based on socioeconomic factors.

\$5,000



Justin Solarczyk, MD

Patient Factors that Lead to Racial Disparities in Postoperative Complication Rates in Veterans after TKA

\$5,000



Liam Wong, MD

A Biomechanical Analysis of Elbow Instability Requiring Internal Joint Stabilization and Lateral Ulnar Collateral Ligament Reconstruction in a Cadaver Model

\$5,000

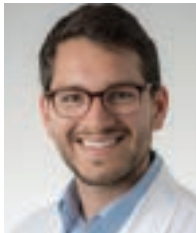
Manning Outstanding Paper Award



Ryan Halvorson, MD

Validation of a pretrained language model to predict need for musculoskeletal surgery and imaging

\$500



Steven Garcia, MD

Loss of DLK1 in Chronic Muscle Injury Results in Fatty Degeneration

\$500



Katherine Woolley, MD

Evaluation of spin bias in randomized controlled trials and clinical trials

\$500

Diversity, Equity, and Inclusion – Updates from our Faculty



I perform disparities research looking at access to care and impact of disparities on pediatric sports medicine conditions and youth sports participation. I have published eight disparity-related papers and have several ongoing projects looking at the impact of language on access to care. – **Nirav Pandya, MD, Pediatric Orthopaedics**



We have completed and are working on several studies looking at improving the readability and availability of patient educational materials in Spanish. We are also working to expand CODE to be more inclusive and applicable to non-English speaking patients. – **Ishaan Swarup, MD, Pediatric Orthopaedics**



The division of sports medicine has several ongoing research projects supporting DEI initiatives. This past year, we focused on transcriptomic differences in tissue, including ACL tissue and hip synovium. Drs. Wong, Feeley, O'Connell, and Garcia have shown transcriptomic-level sex-based differences in ACL injury, which may explain why women tear their ACL two to eight times more than men. Drs. Wong, in collaboration with the MITO Lab and Steven Garcia, MD, were recently awarded the AOSSM Young Investigator Award for their project on sex differences in hip synovium of femoroacetabular impingement syndrome leading to differences in clinical outcomes. Frances Tao, the primary care sports medicine fellow, is leading a study evaluating access to athletic training staff in high schools using several socioeconomic tools. The group, in collaboration with Kris Jones, MD, at University of California, Los Angeles, identified gender differences in medical and athletic training staffs in women's professional sports leagues. – **Stephanie Wong, MD, Sports Medicine**



We've done work on evaluating differences in periop outcomes following total joint arthroplasty between English-speaking and non-English speaking patients in our Asian and Latin X patient populations.

We've also looked at racial disparities in access and outcomes for our revision hip and knee arthroplasty patients. – **Erik Hansen, MD, Arthritis and Joint Replacement**



We are evaluating the factors that might lead to differences in outcomes across races after total knee arthroplasty. – **Alfred Kuo, MD, PhD, Arthritis and Joint Replacement**



Barber: I am doing a multi-institutional study (UCSF, Tufts University, Memorial Sloan Kettering Cancer Center, New York University, Providence hospitals, and a few others) on access to definitive cancer surgery for a subset of cancer surgery by race and socioeconomic status. We are looking at the difference from cancer identification to definitive surgery using the OMOP common data model. – **Tom Barber, MD, Arthritis and Joint Replacement**



We are conducting work evaluating the associations of socioeconomic, acculturation, language, and other variables on access and outcomes to those receiving hand and upper-extremity surgery. Specific examples include the association of insurance type, patient preferred language, and health literacy on time to surgery, complications, and patient-reported outcomes. – **Lauren Shapiro, MD, MS, Hand, Elbow, and Upper Extremity**



We are conducting two national database studies on association of race/ethnicity on types of surgical treatments for distal radius and proximal humerus fractures (Ramesh Ghanta, Ryan Halvorson, Lauren Shapiro, and me). We're also doing a similar study on UC-wide data across all UC campuses. – **Gopal Lalchandani, MD, Hand, Elbow, and Upper Extremity**



I am a mentor and co-principal on the ASBMR THRIVE mentorship program to enhance the success of scientists in underrepresented groups. I am also a leader within the Society of Hispanic Professional Engineers, organizing professional development programs for faculty and graduate students. Last May, I went to the White House to discuss ways to promote engineering within Hispanic populations within the US. – **Chris Hernandez, PhD, Basic Research**



Drs. Berrigan, Luke, and I are working with our primary care sports medicine fellow, Dr. Frances Tao, to evaluate the relationship of social vulnerability index scores (SVI) on access to high school athletic trainers in California based on census tracts and zip codes. – **Nicolas Hatamiya, MD, Sports Medicine**



Drs. Conor O'Neill, Karina Del Rosario, Masato Nagao, and I are working on PROTECT, a project to develop culturally and linguistically appropriate back pain self-help materials for non-English patients. We're focusing on the Spanish and Cantonese populations. Focus groups are being held at ZSFG, and we hope to eventually build a multimedia slew of contents to include print, web, and video. – **Patricia Zheng, MD, Spine**



Charles Park. I am involved in a NIH/NIDDK-funded research project looking at the social determinants of health in regard to diabetic foot ulcers and limb preservation. It is a multi-university group where we formed the Diabetic Foot Consortium and are collaborating together in many levels of diabetic foot research. – **Charles Park, MD, Podiatry**

New Faculty



Michael Davies, MD

Sports Medicine

Research Interests: Translating findings from mouse models to preclinical studies using the roles of mesenchymal stem cells in muscle degeneration and regeneration, including the role of mitochondrial transfer in the process of muscle healing after injury.

Research Goals: The role of exosomes derived from novel populations of human MSCs, the underlying mechanisms of mitochondrial transfer in muscle, and the underlying pathobiology of glenohumeral osteoarthritis



Camille Guzel, MD

Physical Medicine and Rehabilitation

Research Interests: Spasticity management, botulinum toxin for MSK disorders of the intrinsic chain: temporomandibular dysfunction, pelvic floor dysfunction, neurologic injury/polytrauma recovery and survivorship, electrodiagnostic (EMG/NCS) correlations in post-COVID myopathy

Research Goals: Improving lifespan transitions for adults with pediatric-onset disability, mobile health applications for movement disorders/neurorehabilitation, rehabilitation medicine integrated into disaster response for traumatic neurologic injury and amputation, rehabilitation in low-income settings



Andrew John, MD

Physical Medicine and Rehabilitation

Research Interests: Curricular development of fledgling rehabilitation training programs in a global health setting, ways to efficiently identify and address gaps in rehabilitative care in underdeveloped regions, utilizing longitudinal strategies such as local medical training programs

Research Goals: Establishing a good local network of medical professionals engaged or interested in global health as a starting point for future research projects



David Lowenberg, MD

Trauma

Research Interests: Basic Science of biofilm, maturation, growth, and its associated defense mechanisms, host factor optimization in musculoskeletal infections, host immune system markers for recurrent infection and index infections due to internal disruptions of host immune system mechanisms

Research Goals: Continue to participate in research in musculoskeletal infections



Paolo Mimbella, MD

Non-Op Spine

Research Interests:

Interventional pain procedures, regenerative medicine, and treatments for spine and peripheral joint pathology through a PM&R-centric lens.

Research Goals: Advance research in orthobiologics, minimally invasive interventions, and PM&R driven approaches to optimize function and improve outcomes for patients with spine and joint conditions



Jasmine Ng, MD

Physical Medicine and Rehabilitation

Research Interests: How a wide mix of national, ethnic, cultural and socioeconomic backgrounds affect patient and caregiver treatment choices, interactions with healthcare system, and understanding of high quality care

Research Goals: To help start an early referral pathway to Pediatric PM&R for early detection, diagnosis, and intervention of cerebral palsy in young infants, incorporate research in order to understand caregiver perspective related to how different factors affect understanding of cerebral palsy, and what caregivers perceive to be the biggest gap in care for children with CP in our health system



Kudret Usmani, MD

Arthroplasty and Trauma

Research Interests:

Eradicating health disparities, optimizing pain control in the trauma population, and research on post-operative care of mangled extremities

Research Goals: Continue studying the nuances of the development and treatment of post-traumatic arthritis, and the indications of primary arthroplasty in the treatment of fracture care. Begin an IRB on a retrospective study for treatment of post-traumatic arthritis and publish my book chapter on Pilon fractures in the AAOS Comprehensive Review Journal

News and Media



Scientist Tamara Alliston, PhD receives 2024 ORS Outstanding Achievement in Mentoring Award

SAN FRANCISCO (Jan. 10, 2024) – The **UCSF Department of Orthopaedic Surgery** is delighted to announce that **Tamara Alliston, PhD**, a Professor of Orthopaedic Surgery, has been honored with the prestigious 2024 Orthopaedic Research Society (ORS) **Outstanding Achievement in Mentoring Award**. This accolade celebrates Dr. Alliston's steadfast commitment to mentoring and fostering the success of emerging investigators dedicated to advancing orthopaedic research.

"Dr. Alliston is exceptional in nurturing the next generation of orthopaedic researchers," said **Dr. C. Benjamin Ma, Chair of the Department**. "She encourages innovation, collaboration, and excellence in orthopaedic research, and she instills a sense of curiosity and a commitment to pushing the boundaries of orthopaedic science. The Department is very proud of her."

The ORS Outstanding Achievement in Mentoring Award was created in 2014 to celebrate the commitment of the outstanding mentors who promote the success of new investigators in the pursuit of independent orthopaedic research careers.

"This award recognizes Dr. Alliston's vital role in shaping the future of orthopaedic research. Her influence reaches far and wide, and her legacy as a mentor will undoubtedly continue to inspire generations of researchers," Dr. Ma added.

About Tamara Alliston, PhD

Tamara N. Alliston, PhD, is a Professor in the UCSF Department of Orthopaedic Surgery. She directs the **UCSF Musculoskeletal Center** and the National Institutes of Health (NIH) P30-supported UCSF Core Center for Musculoskeletal Biology and Medicine. With a focus on TGF β signaling, her laboratory investigates the interaction between physical and biochemical signals in the control of skeletal cell differentiation and the role of these pathways in skeletal development and disease. Supported by the NIH, U.S. National Science Foundation (NSF), and the U.S. Department of Defense (DOD), her group employs approaches from molecular and cell biology, materials science, and engineering to identify mechanisms of skeletal disease to advance the development of new therapeutic strategies.

Dr. Alliston pursued her undergraduate education in Biology at Trinity University in San Antonio, Texas. She earned her doctoral degree in Cell Biology from Baylor College of Medicine in Houston, Texas in 1998, mentored by Dr. JoAnne Richards. After receiving her doctorate, Dr. Alliston was named an Arthritis Foundation Fellow and worked as a post-doctoral scientist mentored by Dr. Rik Derynck at UCSF. In 2002, she was appointed Assistant Adjunct Professor in the Department of Cell and Tissue Biology at UCSF, and in 2006, she started her laboratory in the UCSF Department of Orthopaedic Surgery.

Dr. Alliston is a faculty member in the **UC Berkeley/UCSF Graduate Program in Bioengineering** and the **UCSF Graduate Programs in Biomedical Sciences, Oral and Craniofacial Sciences, and Developmental and Stem Cell Biology**. She is also affiliated with the **UCSF HIVE: Health Innovations via Engineering**, the Program in Craniofacial Biology, and the **Eli and Edythe Broad Center for Regenerative Medicine and Stem Cell Research**.

Dr. Alliston serves widely as a reviewer for journals and funding agencies, including for the DOD and the NIH. She is also an Editorial Board Member at the *Journal of Bone and Mineral Research*. She chaired the AAOS/ORS Workshop on Joint Crosstalk and the 2022 Gordon Research Conference on Musculoskeletal Biology and Bioengineering. She currently serves as a Counselor for the American Society for Bone and Mineral Research.

Dr. Alliston is a Fellow of the American Institute for Medical and Biological Engineering (AIMBE). Dr. Alliston's honors include a Hulda Irene Duggan Arthritis Investigator Award, the ASBMR Harold M. Frost Young Investigator Award, the AIMM-ASBMR John Haddad Young Investigator Award, the ORS Women's Leadership Award, and the ASBMR Adele Boskey Esteemed Award.

Dr. Alliston's other service and leadership efforts focus on the development of the next generation of scientists and leaders.



Orthopaedic researcher Ralph Marcucio, PhD, receives prestigious award for contributions to and achievements in anatomical sciences

SAN FRANCISCO (January 26, 2024) – The UCSF Department of Orthopaedic Surgery is pleased to announce that Ralph Marcucio, PhD, a Professor of Orthopaedic Surgery, has been named the recipient of the Henry Gray Scientific Achievement Award by the American Association for Anatomy.

The American Association for Anatomy's highest scientific honor recognizes unique and meritorious contributions to and achievements in anatomical sciences by a distinguished American Association for Anatomy member.

"I have been an active member of AAA for almost 3 decades, and to be recognized by my colleagues in this organization is a huge honor," Dr. Marcucio said. "The award reflects the contributions of the many outstanding researchers--mentors, mentees, and collaborators--that I have had the honor and joy to work with throughout my career, as well as the incredible support provided to me by the Department of Orthopaedic Surgery and the Orthopaedic Trauma Institute."

"This is such a deserving award for Dr Marcucio in recognition of his dedication in understanding how our skeleton develops its form and heals after injury," said C. Benjamin Ma, MD, Chair, Department of Orthopaedic Surgery. "His work has contributed immensely to our field and has led to novel treatment directions for fracture care."

About Ralph Marcucio, PhD

Ralph Marcucio was born in and grew up in Amsterdam, N.Y. Dr. Marcucio began his research career as an intern at The Boyce Thompson Institute while he was an undergraduate at Cornell University in Ithaca, NY. After receiving his bachelor's degree from Cornell University in 1990, Dr. Marcucio was accepted into Cornell University's School of Agriculture PhD program. He completed his PhD in 1995. For his exemplary performance and dedication as a Graduate Teaching Assistant, Dr. Marcucio was recognized by the Dean of Cornell University's School of Agriculture for his outstanding contribution to undergraduate education. After receiving his PhD, Ralph was awarded a prestigious NIH training grant to study tissue interactions that control development of the musculoskeletal system. Dr. Marcucio spent 5 years in the New York State College of Veterinary Medicine studying the origins of the musculature responsible for moving the head and jaw skeleton.

In 2000, Dr. Marcucio joined the Molecular and Cellular Biology Laboratory at the University of California, San Francisco, (UCSF). In this position, he began studying how the skeleton of the face attains its shape and form. This work has resulted in the preparation of numerous manuscripts for publication in world-renowned research journals and has formed the basis for his independent research career.

In 2003, Dr. Marcucio was appointed to the faculty at UCSF as an Assistant Professor in Residence in the Department of Orthopaedic Surgery. His research program focuses on two basic science areas. First, he studies bone fracture healing focusing on the transformation of chondrocytes to osteoblasts and other cell types, as well as the inflammatory process during healing. Second, Dr. Marcucio is examining the role that the brain plays during normal development of the facial skeleton. Many facial birth defects have an underlying brain malformation, and the goal of the research is to generate novel therapeutic approaches that will allow correcting facial malformations prior to birth.



Department opens orthopaedic lab at 95 Kirkham on Parnassus campus

SAN FRANCISCO (March 26, 2024) -- The UCSF Department of Orthopaedic Surgery is delighted to announce the opening of the **METRiCS (Musculoskeletal Research Consortium)** lab space at **95 Kirkham Street**, located on the UCSF Parnassus campus in San Francisco. Led by **Jeannie Bailey, PhD**, the lab will focus on advancing sensor and motion capture related research, as well as fostering collaborations with other departments.

Originally constructed in the 1950s, the facility underwent a **full renovation**, which was completed at the end of 2023. The project included a seismic retrofit, modernized infrastructure, and the installation of a dry lab and support space suite; the building also houses upgraded offices, conference rooms, breakrooms, and an outdoor public garden.

Located at the intersection of Fifth Avenue and Kirkham Street in the Inner Sunset neighborhood, the lab conducts innovative research focused on identifying clinically relevant biomechanical phenotypes and probing potential interactive mechanisms among various musculoskeletal pain phenotypes. Dr. Bailey, an assistant professor, and her lab actively develop, test, and implement precision-based digital health technology to enhance engagement in treatment and recovery for clinicians and patients alike.

Examples of current collaborative efforts include: the development of in-clinic biomechanical assessments and smartwatch-based flare episode prediction for chronic low back pain patients, as part of the **REACH** initiative; and the creation of a biomechanical assessment mobile app called **OrthoCap**, developed in collaboration with spine surgeon **Bobby Tay, MD**.

"Through initiatives like **OrthoCap**, Dr. Bailey is pioneering the remote assessment of patient motion quality and constructing models to forecast long-term surgical outcomes during preoperative and early recovery stages," said Dr. Tay, who also serves as the Department's vice chair of quality and safety.

The **METRiCS** space also accommodates **Robert Matthew, PhD**, an assistant professor in the Department of Physical Therapy and Rehabilitation Sciences, who is involved in developing biomechanical assessment tools for the **REACH project**. Dr. Matthew is also spearheading a research program aimed at creating motion assessment tools for neurorehabilitation in stroke and spinal cord injury patients.

"We are excited to support both Dr. Bailey and Dr. Matthew, who have established a longstanding collaboration in advancing in-clinic biomechanical assessments for orthopedic surgery patients," said **Jeffrey Lotz, PhD**, who serves as the Department's vice chair of research. "Their ongoing research efforts have been recognized with NIH funding for the **REACH Physical Function and Biomechanics Research Core**."

"This initiative aligns with our mission to provide a secure and conducive environment for cutting-edge research and innovation within the UCSF community," said **C. Benjamin Ma, MD**, Chair of the Department. "Its development marks a significant stride forward in UCSF's commitment to advancing orthopaedic research and innovation as well as fostering a dynamic environment for scientific exploration and discovery."



Department receives funding to further research on rare hereditary neuromuscular disease, Duchenne muscular dystrophy

SAN FRANCISCO (April 3, 2024) — The UCSF Department of Orthopaedic Surgery is pleased to announce that Xuhui Liu, MD, was awarded a Translational Research Grant from the Duchenne Muscular Dystrophy Research Program from the Congressionally Directed Medical Research Programs (CDMRP) of the Department of Defense. This \$700,000 grant aims to explore the effectiveness of a beta-3 adrenergic receptor agonist in improving cardiac and respiratory function in Duchenne muscular dystrophy (DMD) using a mouse model.



Xuhui Liu, MD

“In confronting Duchenne muscular dystrophy (DMD), we face not only one of the most severe forms of inherited muscular dystrophies but also the most prevalent hereditary neuromuscular disease,” said Dr. Liu. “Regrettably, there exists no known treatment modality that halts disease progression, with the only options for patients at this time being palliative care options.”

The standard of care for DMD patients are glucocorticoid treatments and physiotherapy aimed at preventing orthopedic complications. In the forthcoming study, Dr. Liu will investigate the role of Mirabegron, an FDA-approved beta3 adrenergic receptor agonist, in treating cardiac and respiratory dysfunction and evaluate the combined effects of Mirabegron and the existing standard-of-care glucocorticoid treatment.

“Individuals who are affected by DMD often face respiratory muscle weakness or cardiomyopathy, which can lead to premature mortality in their early twenties. Through our ongoing research, we are committed to changing this narrative and uncovering effective treatments that offer hope and longevity to those battling this devastating condition.”

The safety profile of Mirabegron, coupled with its FDA approval, suggests that pivotal preclinical data from this study could expedite the transition to clinical trials, potentially benefiting DMD patients soon.

About the Congressionally Directed Medical Research Programs (CDMRP)

Founded in 1992, the CDMRP fosters novel approaches to biomedical research and fills research gaps by funding high impact, high risk, and high gain projects that other agencies may not venture to fund. While individual programs are unique in their focus, they all share the common goal of advancing paradigm shifting research, solutions that will lead to cures or improvements in patient care, or breakthrough technologies and resources for clinical benefit.

About the UCSF Muscle Injury and Translational Orthopedic (MITO) Research Lab

The UCSF MITO Research Lab is committed to improving patient care through high-quality translational lab research. Dr. Liu and Dr. Feeley have discovered novel mechanisms of muscle stem cell differentiation and are utilizing these mechanisms to enhance muscle regeneration across various pathophysiologies. These include both direct and indirect muscle injuries, as well as genetic musculoskeletal diseases such as DMD and Amyotrophic Lateral Sclerosis (ALS).



Lauren Shapiro, MD, MS secures research funding to tackle Spanish-speaking patient care disparities

A federal research grant awarded to Dr. Shapiro, above, will address treatment gaps in broken wrists among Spanish-speaking populations, spotlighting critical efforts to bridge healthcare divides. (Photo: UCSF Department of Orthopaedic Surgery)

SAN FRANCISCO (April 19, 2024) — UCSF Department of Orthopaedic Surgery is pleased to announce that Lauren Shapiro, MD MS, an orthopaedic hand surgeon and medical researcher, has been awarded a prestigious K23 grant to address a significant gap in healthcare provision for Spanish-speaking patients with distal radius fractures, commonly known as broken wrists. This injury is prevalent both in the United States and globally, contributing significantly to the overall burden of morbidity.

“This research represents a crucial step toward addressing the disparities in healthcare faced by Spanish-speaking patients with distal radius fractures,” said Dr. Shapiro. “By developing culturally adapted outcome measures, we aim to ensure that these patients receive more accurate assessments and tailored treatments, ultimately improving their overall care and outcomes.”

The crux of the issue lies in the assessment of treatment outcomes using Patient Reported Outcome Measures (PROMs), which evaluate the physical function and symptom burden of patients. However, many current PROMs lack cultural and linguistic relevance for Spanish-speaking patients, leading to potential inaccuracies in measuring their physical function and consequently influencing treatment decisions and patient outcomes.

To bridge this gap, Dr. Shapiro’s research aims to develop and validate culturally adapted PROMs tailored specifically for Spanish-speaking patients with distal radius fractures. Collaborating with esteemed experts including Dr. Patricia Katz, Dr. Alicia Fernandez, and Dr. Theodore Miclau, the project will undertake a comprehensive approach. It includes assessing the suitability of existing PROMs, adapting them to fit the cultural context of Spanish-speaking populations, and rigorously testing the efficacy of the newly developed measures. The knowledge gained from this work is not limited to Spanish-speaking patients with wrist fractures; it will inform the adaptation of PROMs for patients of other backgrounds and those with other injuries, contributing generally to the improvement of PROMs and disparities in healthcare.

“This groundbreaking research will not only shed light on the influence of language and culture on healthcare outcomes, but it will also pave the way for improved treatment strategies for Spanish-speaking patients with broken wrists, not only in the United States but worldwide,” said Dr. C. Benjamin Ma, MD, Department Chair.

Administered by the NIH/NIAMS, the purpose of the K23 award is to provide individuals who have a clinical doctoral degree with an intensive, supervised, patient-oriented research experience. The K23 provides support and ‘protected time’ for these individuals considered to be on the path to a productive, independent clinical research career. Dr. Shapiro’s K23 grant funding is \$841,140 over a five-year period.

Dr. Brian Feeley receives 2023-24 Long-Term Mentor Award

San Francisco, May 30, 2024 — The UCSF Department of Orthopaedic Surgery is pleased to announce that Dr. Brian Feeley, an orthopaedic surgeon and co-director of the UCSF Muscle Injury and Translational Orthopedic (MITO) Research Lab, has been awarded the 2023-24 Long-Term Mentor Award by the UCSF School of Medicine.

Nominated by students, the award honors faculty mentors who have shown dedication to nurturing leaders, innovators, advocates, and researchers and have partnered with students to complete long-term research projects, between 12 weeks to 12 months or longer.

This year's honor recognizes Dr. Feeley's exceptional mentorship, as highlighted by his mentee, Aboubacar Wague, BA, who is currently a UCSF medical student and member of the UCSF MITO Lab.

"Dr. Feeley empowers his mentees to develop their hypotheses and grow as independent researchers, while his commitment to diversity has created an inclusive and supportive lab environment," Wague said.

Wague, who was awarded the 2024 Long-Term Dean's Prize for a yearlong research project titled "Novel Machine Learning Approach to Assess Function in Musculoskeletal Mice Models," seeks to apply a novel data acquisition system to reveal clinical data in upper and lower extremity musculoskeletal injury models in mice.

UCSF Medical School student Aboubacar Wague, center at left, performs translational research at the UCSF MITO Research Lab



on the Mission Bay campus in San Francisco. (Photo: UCSF Department of Orthopaedic Surgery)

"Dr. Feeley represents the diversity of scientific inquiry and exemplifies a commitment to student scholarship, advocacy, and scientific rigor," said Dr. C. Benjamin Ma, chair of the UCSF Department of Orthopaedic Surgery. "His mentorship has guided many students -- contributing to their successful careers in research and clinical medicine."

"Aboubacar Wague's nomination letter praised Dr. Feeley's passion for stem cell research and his ability to create a culture of encouragement and innovation," Dr. Ma added.

The award was formally presented at the 2024 Inquiry Symposium and Dean's Prize Awards held on May 15, 2024, at Millberry Union on the Parnassus campus.



Kelsey Collins, PhD, recognized for excellence in Osteoarthritis Research and Regenerative Medicine

San Francisco, CA – October 9, 2024 – The UCSF Department of Orthopaedic Surgery is pleased to announce that Kelsey H. Collins, PhD, has been honored for her exceptional contributions to the fields of osteoarthritis research and regenerative medicine. Over the past year, Dr. Collins has received several prestigious recognitions that highlight her significant impact on advancing scientific knowledge and enhancing patient care.

\$1.5M funding for osteoarthritis, regenerative medicine research

Among her recent accomplishments, Dr. Collins has been awarded the NIH Director's New Innovator DP2 Award, providing over \$1.5 million in funding to support researchers engaged in high-risk, high-reward studies. This funding will support her groundbreaking work in regenerative therapies aimed at addressing musculoskeletal pain, a significant contributor to the opioid crisis.

"Our research indicates that body fat contributes to systemic inflammation, which plays a significant role in cartilage loss and pain in osteoarthritis," Dr. Collins said. "We believe that understanding the complex interactions between factors secreted by fat and musculoskeletal tissues is critical for developing innovative osteoarthritis therapeutics aimed at improving overall health. The exciting part about this work is that fat likely plays a role in many pathologies associated with obesity and aging, so we can use the tools we are building to understand interorgan crosstalk relationships that are broadly applicable to aging and obesity."

Academic recognition from OARSI, Grainger Foundation

Additionally, Dr. Collins was recognized as a 2024 Rising Star in Basic Science by the Osteoarthritis Research Society International (OARSI), an honor presented at the recent OARSI meeting in Vienna, Austria. This recognition is underscored by her three impactful papers, which have significantly contributed to the field, and is typically awarded to mid-career researchers. For a deeper dive into her research contributions, readers can



access her papers here: Adipose tissue is a critical regulator of osteoarthritis (PNAS), A genome-engineered bioartificial implant for autoregulated anticytokine drug delivery (Science Advances), and Leptin mediates the regulation of muscle mass and strength by adipose tissue (Journal of Physiology).

Dr. Collins was also invited to participate in the highly selective Grainger Foundation Frontiers of Education Meeting, co-sponsored by the National Academy of Engineering, which took place from September 11 to 14, 2024, at the Beckham Center in Irvine, California. This prestigious event honors trailblazers across diverse fields—not solely scientists—inviting them to showcase groundbreaking research and educational advancements.

"We are immensely proud of her achievements and the promise she holds for the future of orthopaedic research," Dr. C. Benjamin Ma, chair of the UCSF Department of Orthopaedic Surgery, said. "Dr. Collins embodies the PRIDE values of UCSF—Professionalism, Respect, Integrity, Diversity, and Excellence. As a champion of these principles, she not only drives innovation in her own research but also actively recruits and mentors researchers in her lab, fostering a collaborative environment that yields remarkable results that could shift paradigms in the treatment of osteoarthritis, obesity and aging."



Philanthropy

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To learn more about how to make a gift for the Department of Orthopaedic Surgery, please contact Darrel Young, Senior Director of Development & Alumni Relations, at (415)-502-8389 or send an email to darrel.young@ucsf.edu.

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