Welcome to the McKay Orthopaedic Research Laboratory at the University of Pennsylvania

Annually, musculoskeletal-related conditions in the United States account for 132 million doctor visits, 29 million emergency department visits, 15 million hospital stays and cost over $850 billion. Musculoskeletal injuries represent a critical health concern, which must be better understood and better treated.

In 1960, a program in orthopaedic research was established at the University of Pennsylvania. In 1979, the McKay Orthopaedic Research Laboratory was created to house all orthopaedic research laboratories in a single location. Currently, the McKay Lab is a thriving, multidisciplinary facility that occupies more than 15,000 square-feet on the University of Pennsylvania campus. Our multi-faceted research programs have more than 100 research personnel, including 10 primary faculty members. Research expenditures at McKay total more than $8.5 million per annum, supported primarily by grants from the National Institutes of Health (NIH), other governmental agencies, private foundations and industry. We are continually ranked among the top-five Orthopaedic Research Departments nationally in terms of NIH funding.

The McKay Lab serves as the focal point for the NIH-supported Penn Center for Musculoskeletal Disorders, a university-wide Center that provides resources and a forum for scientific exchange through annual symposia, year-long seminar series, pilot grant program and other activities. It also serves as the home of our NIH-supported training grant for students, which has been continually funded since the 1970s!

Our overall mission is to conduct the highest quality fundamental and translational research to improve patient lives and to train the next generation of leaders in our field. We appreciate your interest in our programs and hope you enjoy learning about our efforts to advance orthopaedic care.

Sincerely,

Louis J. Soslowsky, PhD
Fairhill Professor of Orthopaedic Surgery
Director, Orthopaedic Research and McKay Orthopaedic Research Laboratory

A MESSAGE FROM LOUIS J. SOSLOWSKY, PHD

TO LEARN MORE ABOUT THE MCKAY ORTHOPAEDIC RESEARCH LABORATORY, VISIT PENNMEDICINE.ORG/MCKAY.
The Dodge Lab addresses the translational area of degenerative joint diseases with a focus on extracellular matrix, cartilage cell biology, cartilage tissue engineering and cartilage response to injury. As part of our research, we have developed model systems to both generate cartilage analogs and study the control of cell phenotype, as well as a bioreactor to assess function in a mechanically loaded environment. In addition, we have designed testing platforms to deliver clinically-relevant impact injuries and test mechanical properties in a high throughput manner. Our research areas of expertise and interest include:

- Extracellular matrix (cartilage, tendon, disc)
- Chondrocyte cell biology
- Regulation of chondrocyte function in degenerative joint diseases and post-traumatic osteoarthritis
- Tissue engineering biological cartilage replacement materials
- Novel cartilage imaging, soluble cartilage biomarkers and nutraceuticals

KAPLAN LAB

The Center for Research in FOP and Related Disorders, under the direction of Frederick S. Kaplan, MD, and Eileen M. Shore, PhD, is the world’s premier research effort in two rare and disabling genetic disorders of heterotopic (extraskeletal) bone formation, fibrodysplasia ossificans progressiva (FOP) and progressive osseous heteroplasia (POH). The Center conducts research on the biology of FOP and POH and pursues treatments for these disorders based on our discovery of the mutations, triggers and dysregulated signaling pathways that cause these disorders. Our pioneering research will advance understanding of FOP and POH, and will stimulate more effective prevention and treatment for common disorders of heterotopic ossification that affect millions of individuals worldwide.

LIU LAB

In the Liu Lab, our research program focuses on the biological processes within bone and on how they influence bone material, microstructural and biomechanical properties with aging, disease and therapies.

Our research team utilizes state-of-the-art imaging, image analysis and mechanical modeling techniques to explore the mechanisms affecting the mechanical functions of the skeleton at different length scales in both animal models and clinical investigations. The ultimate goal of our lab is to translate the technologies and research findings from bench-side to bedside to improve the diagnostic and therapeutic strategies for osteoporosis and other serious bone diseases that affect the growing population.
The Mauck Lab develops novel tissue engineering and regenerative medicine (TERM) approaches for the restoration of musculoskeletal soft tissues, with a particular interest in articular cartilage, the knee meniscus and the intervertebral disc. Our team uses rigorous mechanical and molecular analyses to characterize native tissue structure and function, and employs this information to enhance the functional properties of engineered constructs through focused technology development. This includes optimization of the differentiation potential of adult progenitor/stem cells and the development of micro-mechanical measurement tools, custom mechanobiologic culture conditions and novel cell scaffolding technologies. Ongoing studies range from basic science inquires focused on understanding how differentiation alters stem cell apperception of mechanical signaling cues to translational large animal studies evaluating the efficacy of implanted engineered constructs. The Mauck Lab is focused on regenerative biology and explores the processes that restore the architecture of damaged or diseased muscle by employing mouse genetics, stem cell biology and bioengineering approaches. A major goal of our future research is to dissect the fine coordination of key cell populations and signaling pathways involved in skeletal muscle and cardiac repair upon injury. In addition, we aim to expand our recent findings on the crosstalk between oxidative DNA damage, uncapped telomeres and mitochondrial biogenesis in the regulation of regeneration mechanisms. Ultimately our hope is to use the knowledge gained from our studies to overcome existing challenges in mammalian regeneration and to advance the development of therapeutics in patients afflicted by muscle injuries.

The Pignolo Lab focuses on age-related bone loss and disorders of extraskeletal ossification, conditions linked by the common thread of dysregulated osteoblast differentiation. Using human tissue, animal models and in vitro cell systems, we investigate the following areas:

- Characterization of aging bone phenotypes in mouse models of physiological and accelerated aging
- Mechanisms of senescence in mesenchymal stem cells (MSCs)
- Effects of MSC transplantation on life span and bone phenotype
- In vivo telomere dysfunction in bone tissue
- Development of senescence-associated secretory phenotype in response to mechanical signals with aging
- Pre-clinical drug testing and biomarker development for genetic conditions of heterotopic bone formation
- Roles of hypoxia in formation of extra-skeletal ossification
- Roles of circulating osteogenic progenitor cells in heterotopic ossification
- New methods for analysis of bone and fat tissue

The Qin Lab uses a combination of molecular, biochemical, imaging and animal techniques to understand the downstream signaling pathways of growth factors and hormones that regulate the biology of bone formation. The adult skeleton continuously undergoes remodeling, namely, being resorbed by osteoclasts and renewed by osteoblasts. A shift in the balance toward resorption leads to osteoporosis, a silent disease causing bone fragility and fractures.
Our on-going projects in this area of research include:

- Studying the role of epidermal growth factor receptor (EGFR) in regulating bone marrow mesenchymal progenitors and mediating the action of parathyroid hormone (PTH) on bone formation
- Investigating molecular mechanisms by which anabolic treatment rescues bone damage induced by radiotherapy
- Characterizing endosteal mesenchymal progenitors within bone marrow
- Delineating the role of EGFR in endochondral ossification and osteoarthritis development

**SHORE LAB**

The Shore Lab investigates human genetic diseases of heterotopic (extra-skeletal) bone formation, mainly fibrodysplasia ossificans progressiva (FOP) and progressive osseous heteroplasia (POH)—two rare and severely debilitating disorders characterized by de novo formation of bone that begin in childhood and progress throughout life. Following our identification of the mutated genes for POH and FOP, we are now focused on determining the critical roles of these genes and their pathways in regulating cell fate decisions and the formation of bone and cartilage tissues. We apply a wide range of approaches to in vitro and in vivo model systems, including molecular and cell biology, genetics, and stem cell biology. Our goals are to use the information we learn to identify strategies and develop treatments for these and other disorders of bone.

**SOSLOWSKY LAB**

The Soslowsky Lab is focused on orthopaedic biomechanics, structure-function relationships and functional tissue engineering. More specifically, our lab goals are to determine fundamental relationships and mechanisms governing tendon and ligament injury, healing, repair and regeneration and to use this information to develop and evaluate potential treatment modalities. Our studies examine the rotator cuff, biceps, Achilles, flexors, patellar and other tendons, as well as the anterior cruciate ligament. We use a variety of sophisticated and rigorous model systems to address both basic and applied research questions in these tissues and in associated joint structures. Our multidisciplinary research team includes bioengineers, orthopaedic surgeons, therapists, as well as imaging and biologic experts.

**SMITH/MALHOTRA LAB**

The Translational Spine Research Lab is a jointly-run lab between the departments of orthopaedics and neurosurgery for spine research including:

- Development of bioactive injectable therapeutics for treatment of intervertebral disc degeneration

Our research goals are to develop synergistic, minimally invasive therapeutics that incorporate a structural implant to normalize mechanics, anti-inflammatory agents to prevent further degeneration, and stem cells to potentiate tissue regeneration to treat degeneration of the intervertebral discs of the lumbar spine.

- Pathogenesis and treatment of spine disease in mucopolysaccharidosis (MPS) disorders

MPS disorders are genetic disorders that affect children, which are associated with severe musculoskeletal manifestations. In the spine, vertebral dysplasia and accelerated disc degeneration lead to spinal cord compression and airway obstruction. Our research goals are to understand the molecular mechanisms underlying spine disease in MPS and develop new therapeutic strategies.
For more information about supporting the McKay Laboratory with a tax deductible contribution, please contact Penn Medicine Development and Alumni Relations at 215.898.0578 or email uphsgift@upenn.edu.

To make a donation online, visit PennMedicine.org/orthofund.