FERGUSON LABORATORY EDITION

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MARCH 2023

DEPARTMENT OF ORTHOPAEDIC SURGERY

Message from Ferguson Laboratory Directors

Welcome to the inaugural Ferguson Laboratory for Orthopaedic and Spine Research newsletter. In this and future issues, we will share the latest news and research progress from our faculty and students, upcoming conferences and lectures, and in-depth profiles of the individuals working and training in our facility.

From L to R: Gwendolyn A. Sowa, MD, PhD, Nam V. Vo, PhD, Joon Y. Lee, MD, FAOA

Our multidisciplinary lab works at the intersection of physical medicine and rehabilitation and orthopaedic surgery to uncover the complex and interrelated biological and mechanical processes that lead to or exacerbate intervertebral disc degeneration (IDD) and low-back pain, conditions that affect vast numbers of individuals world-wide, often with severe impacts to health and quality of life.

By sharing our accomplishments, training endeavors, and research findings, we hope other researchers and clinicians investigating the mysteries of spinal conditions will benefit from our learnings, spark conversations and collaborations with colleagues around the country, and inspire students at all levels to join the search for effective therapies and a thorough understanding of the processes that drive IDD and its downstream consequences. To learn more about the Ferguson Laboratory, please visit **www.fergusonlab.pitt.edu**.

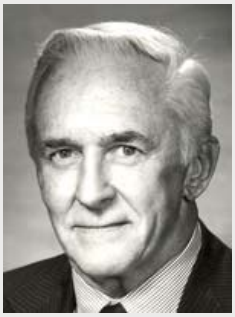
Respectfully,

Joon Y. Lee, MD, FAOA
Medical Director, Ferguson Laboratory
Orland Bethal Endowed Professor in Spine Surgery
Associate Program Director
Department of Orthopaedic Surgery
University of Pittsburgh School of Medicine

Gwendolyn A. Sowa, MD, PhD
Co-Director, Ferguson Laboratory
Professor of Physical Medicine and Rehabilitation, Orthopaedic Surgery, and Bioengineering
Chair, Department of Physical Medicine and Rehabilitation
University of Pittsburgh School of Medicine

Nam V. Vo, PhD
Co-Director, Ferguson Laboratory
Deputy Vice Chair of Research
Associate Professor of Orthopaedic Surgery
Department of Orthopaedic Surgery
University of Pittsburgh School of Medicine

The Ferguson Laboratory Legacy



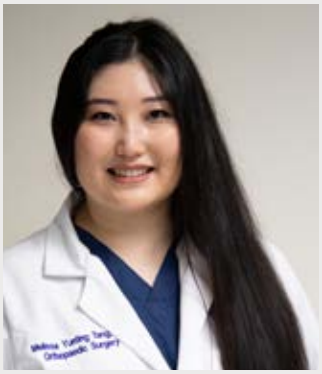
Former Department of Orthopaedic Surgery chair, Albert B. Ferguson, Jr., MD, spent more than three illustrious decades at the University of Pittsburgh building the Department into an internationally renowned program built upon exceptional clinical care, excellence in research, and a dedication to training the best orthopaedic surgeons anywhere.

Research was of critical importance to Dr. Ferguson, and one of his first acts after assuming leadership of the Department was to create the Orthopaedic Surgery Research Lab, now called the Ferguson Laboratory for Orthopaedic and Spine Research.

Through its ongoing basic science, translational, and clinical studies, including the in progress LB3P Low Back Pain Research Study funded by a National Institutes of Health U19 grant, the lab continues to conduct innovative research while fostering the creativity and independence of students, residents, and fellows that Dr. Ferguson was known for during his time in the Department.

UPMC LIFE CHANGING MEDICINE

Ferguson Laboratory Feature: *Melissa Yunting Tang, MD*



Melissa Yunting Tang, MD, is a second-year resident in the University of Pittsburgh Department of Orthopaedic Surgery and a current research fellow in the Ferguson Laboratory for Orthopaedic and Spine Research.

Dr. Tang is pursuing the research track of the residency program and is on the path toward becoming an academic spine surgeon. She came to the University of Pittsburgh after earning her medical degree from the University of Arizona College of Medicine in 2021. While becoming a doctor and scientist was a long-standing ambition, she developed an interest in orthopaedic surgery during her first semester of medical school.

"One of my first classes was on the musculoskeletal system, and my professor was a female orthopaedic surgeon who allowed me to shadow her in the operating room," says Dr. Tang. "The first time I held a drill and a hammer, I knew orthopaedic surgery was my calling. I also knew that I not only wanted to do surgery, but I wanted to make treatments better by becoming a physician scientist."

Dr. Tang matched at her first choice for orthopaedic residency at the University of Pittsburgh.

"I ranked Pitt #1 because of the legacy in producing academic surgeons and leaders in the field," she says. "Freddie Fu personally trained more chairmen than any other orthopaedic chair in the country."

Dr. Tang was overjoyed when she received a phone call from the world-renowned Freddie Fu, MD, the department's former longtime chairman who sadly passed away much too soon in 2021.

"In his usual passionate and energetic voice, he said, 'You come to Pittsburgh okay? You do six year, okay?' and he hung up. So, we were on the same page," says Dr. Tang. "I wanted to come here and continue his legacy. He was my personal hero and I was so honored to have been the last class that he chose before he passed. This is one of the foremost training programs for orthopaedic surgeons in the world, built by Dr. Fu, his predecessor Dr. Ferguson, and everyone else that's come before them."

Research in the Ferguson Laboratory

Dr. Tang chose to pursue her dedicated research year of residency in the Ferguson Laboratory for a number of reasons. As she explains, there is not only the opportunity to work in a multidisciplinary basic science lab studying spine pathologies, but she also has the ability to work with other research groups in the department, including the Biodynamics Laboratory and the Pittsburgh Orthopaedic Spine Research Group (POSR). Dr. Tang also talks about the leadership of the Ferguson Lab – Nam Vo, PhD; Gwendolyn Sowa, MD, PhD; Joon Lee, MD, and William Anderst, PhD, from the Biodynamics Lab, and the incredible mentorship and training opportunities she has received under their guidance.

"You have, at once, an incredibly accomplished, multidisciplinary group of leaders to train under who are working to better understand the pathophysiology of, and develop effective treatments for, common spine conditions, such as adjacent segment disease and intervertebral disc degeneration, which will make a significant clinical impact. We are using cutting edge technologies, such as biplane radiology and targeted gene therapy," says Dr. Tang.

Since beginning work in the lab, Dr. Tang has been involved in studies investigating ligamentum flavum hypertrophy and the potential for targeting the condition through a novel microRNA, miR-29a. This is a continuation of concept developed by

her predecessor, Dr. Richard Wawrose, also a resident research fellow of the Department of Orthopaedics.

"The lab will have a new paper coming out soon about this work and how miR-29a controls gene expression in several important fibrotic pathways important to ligamentum flavum hypertrophy and lumbar spinal stenosis," says Dr. Tang.

These studies are now progressing with additional work that will develop 3D ligament models that can be used to study the effects of static and cyclic loading on ligament remodeling. She is also developing a small animal model of ligamentum flavum hypertrophy for in vivo testing of miR-29a with guidance from Drs. Joon Lee, Peter Alexander, and Prashanta Silwal.

Dr. Tang also has been studying gene therapy approaches to treat intervertebral disc degeneration and is the lead author of a new forthcoming review paper that discusses current and emerging gene therapy approaches for delivering potential therapeutic options targeting the intervertebral disc.

"Gene editing, through methods such as CRISPR, are beginning to open a lot of new pathways to investigate disease-modifying therapies," says Dr. Tang. "The Ferguson Lab continues to be a leading center for these kinds of studies, building upon the work of former lab director James Kang, MD. There's a rich history to tap into from a learning perspective."

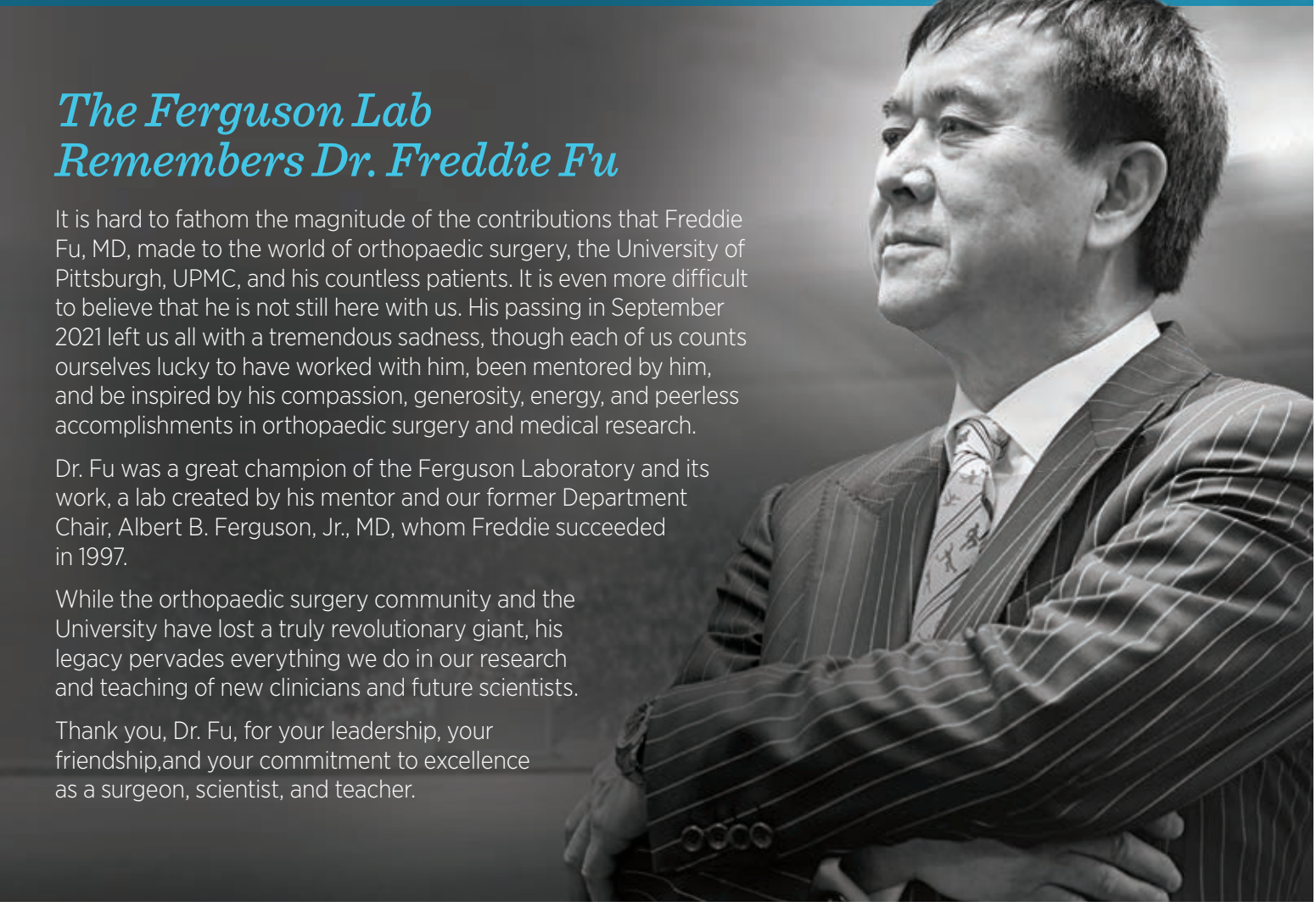
Recent Presentations at the Orthopaedic Research Society 2023 Annual Meeting

Numerous faculty from the Department of Orthopaedic Surgery, the Spine Research Team, and the Ferguson Laboratory presented research at the annual meeting of the Orthopaedic Research Society (ORS) in mid-February.

Dr. Tang is the author of 11 abstracts. For more information on the abstracts and posters, visit **UPMCPhysicianResources.com/Ortho**.

*The Ferguson Lab embodies the spirit of UPMC and Pitt Orthopaedics. **R**especting the past by embracing our future; **R**esidents and trainees as the bearers of our legacy; **R**esearch as a core element of our identity; and fostered **R**elationships as the conduit for success in the days ahead.*

MaCalus V. Hogan, MD, MBA
David Silver Professor and Chair Department of Orthopaedic Surgery/Chief, UPMC Orthopaedic Service Line



The Ferguson Lab Remembers Dr. Freddie Fu

It is hard to fathom the magnitude of the contributions that Freddie Fu, MD, made to the world of orthopaedic surgery, the University of Pittsburgh, UPMC, and his countless patients. It is even more difficult to believe that he is not still here with us. His passing in September 2021 left us all with a tremendous sadness, though each of us counts ourselves lucky to have worked with him, been mentored by him, and be inspired by his compassion, generosity, energy, and peerless accomplishments in orthopaedic surgery and medical research.

Dr. Fu was a great champion of the Ferguson Laboratory and its work, a lab created by his mentor and our former Department Chair, Albert B. Ferguson, Jr., MD, whom Freddie succeeded in 1997.

While the orthopaedic surgery community and the University have lost a truly revolutionary giant, his legacy pervades everything we do in our research and teaching of new clinicians and future scientists.

Thank you, Dr. Fu, for your leadership, your friendship,and your commitment to excellence as a surgeon, scientist, and teacher.

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ABOUT THE FERGUSON LABORATORY FOR ORTHOPAEDIC AND SPINE RESEARCH

The Ferguson Laboratory for Orthopaedic and Spine Research at the University of Pittsburgh studies the complex developmental mechanisms, etiologies, and basic biology behind intervertebral disc degeneration (IDD), and it works to develop biological, biomechanical, and cell-based therapies for IDD. Leading the laboratory's multidisciplinary research efforts are co-directors Joon Y. Lee, MD, FAOA; Gwendolyn A. Sowa, MD, PhD; and Nam V. Vo, PhD.

The Ferguson Laboratory explores distinct but complementary research areas to dissect and clarify the physiological processes that lead to disc degeneration. Dr. Vo leads the lab's efforts studying the contribution of aging on IDD and loss of disc extracellular matrix (ECM) proteoglycans, with a special focus on cellular senescence and autophagy in regulating aggrecan homeostasis. Dr. Sowa oversees investigations involving the mechanisms of mechanical strain on disc cell metabolism, with an emphasis on how mechanical strain-induced inflammation controls ECM collagen expression and breakdown. As a practicing orthopaedic surgeon, Dr. Lee explores minimally invasive treatment of trauma and conditions in the spine.

The lab is named in honor of Albert B. Ferguson Jr., who held the Silver Chair of Orthopaedic Surgery at the University of Pittsburgh from 1953 until his retirement in 1986. Dr. Ferguson was a visionary force behind the evolution and growth of the clinical, research, and training programs of the University of Pittsburgh Department of Orthopaedic Surgery into the internationally respected program of excellence it is today.

To learn more about the UPMC Department of Orthopaedic Surgery, please visit **UPMCPhysicianResources.com/Ortho.**

UPMC PHYSICIAN RESOURCES

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