NEWS AND RESEARCH:
FERGUSON LABORATORY FOR ORTHOPAEDIC AND SPINE RESEARCH

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EXPANDING THE BOUNDARIES OF BASIC SCIENCE AND CLINICAL SPINE RESEARCH

Low Back Pain Research Study Renewed by NIH

Codirectors of the Ferguson Laboratory for Orthopaedic and Spine Research, **Gwendolyn A. Sowa, MD, PhD**, professor and chair of the Department of Physical Medicine and Rehabilitation at the University of Pittsburgh School of Medicine, and **Nam Vo, PhD**, professor of orthopaedic surgery and deputy vice chair of research in the Department of Orthopaedic Surgery at Pitt, have received a five-year, $20 million National Institutes of Health (NIH)/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) award to continue and expand a multidisciplinary investigation into the phenotype evolution and clinical trajectories of chronic low back pain (CLBP).

The award supports the next phase of the original **Low Back Pain Biological, Biomechanical, and Behavioral (LB^{3}P study**, now called the **Holistic Pain Phenotypes (H2P) LB^{3}P study**, building on work originally funded in 2020 through the NIH **Helping to End Addiction Long-Term (HEAL**) Initiative–funded **Back Pain Consortium (BACPAC)**. The renewed study brings together the prior multidisciplinary team from orthopaedics, rehabilitation, bioengineering, pain medicine, psychology, molecular biology, biostatistics, and related fields, along with a strategic group of new researchers to examine CLBP as part of a broader whole-person pain experience.

"The first phase of LB^{3}P focused on building the data foundation needed to understand how pain manifests across multiple domains and to determine whether distinct pain phenotypes exist," Dr. Sowa says. "This next phase allows us to ask how those features relate to what actually happens to patients over time."

Addressing the Heterogeneity in CLBP

CLBP remains one of the most common and costly causes of disability. Despite similar clinical presentations and treatments, patients often can experience very different outcomes. Some improve, others remain stable, and others worsen.

This variability highlights the underlying heterogeneity in the biological, biomechanical, and behavioral factors that contribute to CLBP that are not captured by traditional symptom-based classifications or imaging findings alone.

The original LB^{3}P study was designed to address this challenge by developing a comprehensively characterized cohort rather than just testing different kinds of treatments or interventions. By collecting patient data across multiple domains in the same individuals, the study aimed to determine whether patients could be grouped into distinct phenotypes.

"The goal was to collect the data needed to ask better questions about why patients with CLPB differ in the first place," Dr. Vo says. "

Building the LB^{3}P Dataset

The LB^{3}P study enrolled more than 1,000 participants with CLBP and followed them for one year. Control data was also collected from individuals without low back pain for comparative studies and analysis.

The project has gathered a wide range of data, including clinical assessments, biomechanical and movement analyses, quantitative sensory testing, psychosocial and behavioral evaluations, and biospecimens for molecular analyses to create a comprehensive dataset capable of supporting phenotype discovery and hypothesis generation.

"What LB^{3}P gave us was the ability to study low back pain as a system rather than as isolated variables," Dr. Vo says.

Analytic Progress and Early Findings

To date, the LB^{3}P research team has published multiple peer-reviewed studies examining individual domains within the dataset, including biological markers, biomechanical measures, behavioral characteristics, and sensory processing. More recently, the analysis has been focused on integrating these domains to examine whether patients cluster into distinct phenotypes with shared features.

"Our early analyses suggest that there are patient subgroups that differ in meaningful ways," Dr. Sowa says. "For example, we see groups with similar reports of pain that tend to have different

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Low Back Pain Research Study (*continued*)

levels of function, movement patterns, or different medical comorbidities, as well as different biological profiles. These findings are preliminary and do not yet incorporate the entirety of the available data, but they suggest that distinct phenotypes may be present."

However, the first phase of LB^{3}P was not designed to determine how these features change over time or how they are influenced by other pain conditions. Addressing those questions is the main purpose of the new grant funding.

Extending LB^{3}P to Longitudinal Outcomes

The new grant extends the original LB^{3}P project by allowing the team to follow the study's cohort for up to five years. This longitudinal examination will provide data on how early phenotypic features relate to longer-term clinical trajectories, including improvement, persistence, or progression of pain and disability.

"What we want to understand now is what happens to these patients over time," Dr. Vo says. "Do they get better, stay the same, or worsen, and which early characteristics are associated with those paths?"

The extended follow-up also allows investigators to assess whether phenotypic features remain stable or evolve alongside changes in symptoms and function.

Looking Beyond the Spine

A focus of the new phase of research is understanding how CLBP relates to other chronic, and at times, overlapping pain conditions and common musculoskeletal disorders, such as osteoarthritis. These conditions frequently coexist with low back pain and may significantly influence CLBP pain severity, disability, and treatment outcomes.

"Low back pain does not occur in isolation for many patients," Dr. Sowa says. "If we ignore other pain sites or disease processes, we risk misinterpreting what we are seeing in the data."

The renewed study continues to involve many investigators from the original LB^{3}P project while adding new collaborators to address these broader pain mechanisms and analytic challenges, for example with joint pain and myofascial pain.

Toward Phenotype-Informed Clinical Trials

A long-term objective of the H2P LB^{3}P study is translation. Using longitudinal outcome data and refined phenotypic profiles, the research team plans to design future clinical trials to test whether treatments can be matched to patient subgroups defined by underlying contributors

"The goal is to design trials that are informed by data rather than assumptions," Dr. Sowa says. "We want to determine whether matching treatments to patient characteristics actually improves outcomes."

Ongoing Value to the Ferguson Lab Community and Trainees

The renewed study continues to serve as a major resource for the Ferguson Laboratory, supporting secondary analyses, trainee-led projects, and methodological innovation. As longitudinal data accumulate, the dataset is expected to generate new scientific questions and guide future research directions.

"Following patients over time allows us to see which early characteristics actually matter for outcomes," Dr. Vo says.

The University of Pittsburgh Low Back Pain: Biological, Biomechanical, Behavioral Phenotypes (LB3P) Mechanistic Center of the Back Pain Consortium Research Program (BACPAC), part of the National Institutes of Health Helping to End Addiction Long-term Initiative administered by the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) of the National Institutes of Health (NIH).

BMRC Laboratory Naming Ceremony and Move into Renovated Space

The Orland Bethel Family Musculoskeletal Research Center (BMRC) was established in October 2023 at the University of Pittsburgh School of Medicine through a philanthropic gift from the Orland Bethel Family Foundation. The center supports research, education, and training covering the entire spectrum of musculoskeletal disorders.

In late 2025, BMRC held a laboratory naming ceremony in the Biomedical Science Tower at the University of Pittsburgh to recognize the Bethel family's support and the completion of a renovated laboratory space. University leadership, BMRC faculty, and members of the Bethel family attended the event, and a permanent nameplate was installed.

BMRC core laboratories are now moving into the renovated space, consolidating research groups and shared resources to support ongoing work, including projects within the Ferguson Lab.

BMRC supports core laboratories, research fellowships, and training programs for students and early-career investigators, with an emphasis on advancing basic, translational, and clinically relevant musculoskeletal research. The center also provides shared research infrastructure to support affiliated laboratories.

Ferguson Lab Trainee Spotlight:

Hiroki Kaneta, MD

In November 2025, the Ferguson Lab for Orthopaedic and Spine Research welcomed its newest international visiting research scholar, **Hiroki Kaneta, MD**.

Dr. Kaneta is an orthopaedic surgeon by training. He grew up in Hokkaido, Japan, and earned his medical degree in 2015 from Asahikawa Medical University. After completing medical school, Dr. Kaneta moved to Hiroshima, Japan, for his two-year general residency and worked in several hospitals for 10 years with a focus on orthopaedic trauma.

Medical education and training in Japan is structured differently than in the United States. Medical students enter medical school directly after high school and after a competitive national entrance exam process. Medical school in Japan lasts 6 years, after which there is usually a 2 year residency that is broad-based. After completion of the residency program, doctors can apply for further subspecialty training programs, typically at a university or hospital. Subspecialty training in orthopaedics is another 5 to 6 years, followed by opportunities for fellowship-type training.

In 2022, he joined the Department of Orthopedic Surgery at the Hiroshima University Graduate School under the supervision of Professor Adachi, where he focuses on hip surgery and arthroplasty using some of the latest robotic-assisted surgical platforms. Dr. Kaneta also began basic science research training under the supervision of Dr. Nakasa in the laboratory of Professor Miyaki, whose lab's focus is on miRNAs in cartilage and arthritis.

Dr. Kaneta's research at Hiroshima University Graduate School is focused on the anti-inflammatory effects of ginger-derived extracellular vesicles (GDEVs) in models of rheumatoid arthritis. Results from both in vitro and in vivo studies suggest that GDEVs possess anti-inflammatory properties. In small animal models of ankle arthritis, GDEVs were shown to decrease inflammation and mitigate cartilage damage, supporting their potential therapeutic relevance in arthritis.

This prior work required the development and validation of biologically relevant small-animal models of chronic, degenerative musculoskeletal disease, an approach that directly informs his current research focus in the Ferguson Lab.

Projects in the Ferguson Lab

Dr. Kaneta's research project in the Ferguson Lab focuses on developing a small animal model of age-related Achilles' tendinopathy using aged rats, a common condition in older adults that can lead to substantial morbidities, including chronic pain, functional impairment, and an overall reduction in quality of life measures.

By prioritizingslow progressive age-related degeneration rather than acute injury, the project aligns with the Ferguson Lab's broader interest in creating clinically relevant models to study musculoskeletal tissue degeneration and repair.

Dr. Kaneta's mentor for the project is Ferguson Lab investigator, Allison Bean, MD, PhD, assistant professor in the Department of Physical Medicine and Rehabilitation, whose research focus is on understanding the molecular mechanisms of musculoskeletal tissue injury and repair to guide the development of novel regenerative rehabilitation therapies to improve physical function.

"Most small animal models of Achille's tendinopathy are based on young animals," says Dr. Kaneta. "This is a limitation because these younger models do not fully recapitulate age-related degenerative changes at the tissue and cellular level."

Many of the age-related degenerative changes that occur in Achille's tendinopathy, including cellular senescence, collagen structure remodeling, and extra cellular matrix changes, are absent in younger animal model. These likely blur some of the mechanistic components of age-related tendinopathy.

"Working with an older model should allow us to better reproduce the degenerative physiologic changes occurring in the tendon as age increases," Dr. Kaneta says. "The goal is to develop a more accurate and reliable model for mechanistic studies and effective therapeutic development."

The aged model is intended to serve as a platform for mechanistic investigations and for evaluating potential therapeutic strategies in a setting that more closely reflects the biology of tendon degeneration in older patients.

Notes and Initial Impressions of Pittsburgh, UPMC, and the University of Pittsburgh

Since arriving in Pittsburgh, Dr. Kaneta has been adjusting to a new research environment and daily life in the United States. He relocated with his wife and four children, and the transition so far has been very positive, particularly for his family.

"Pittsburgh reminds me a little of Hokkaido, particularly the snow. We are hoping to do some skiing this winter in our free time," Dr. Kaneta says. "I was captain of our racing ski team in medical school and look forward to trying out some of the local mountains."

Within the Ferguson Lab, Dr. Kaneta's experience so far with the team has been welcoming and supportive as he gets started on his research.

"The lab environment here is highly collaborative and was an important factor in my decision to come to Pittsburgh. Dr Sowa, Dr. Vo, and Dr. Lee are tremendous assets to young investigators and scholars. "I am honored to join the Ferguson Lab and the University of Pittsburgh, contribute to its ongoing work, and enhance my skills and expertise in basic science research" Dr. Kaneta says.

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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. Another major endeavor of the Ferguson research program is studying the deep phenotype of chronic low back pain through collection and processing of large patient datasets. 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

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