FALL 2023

NEWS AND RESEARCH:
FERGUSON LABORATORY FOR ORTHOPAEDIC AND SPINE RESEARCH

EXPANDING THE BOUNDARIES OF BASIC SCIENCE AND CLINICAL SPINE RESEARCH

LB³P Mechanistic Research Center Probes Phenotypes and Mechanisms Driving Low Back Pain in Search for Personalized Treatment Advances

In 2019, the National Institutes of Health (NIH) awarded a total of $21.3 million U19 grant through its Helping to End Addiction Long-Term (HEAL) initiative to University of Pittsburgh and UPMC researchers to establish the Low Back Pain: Biological, Biomechanical, Behavioral Phenotypes (LB³P) Mechanistic Research Center. The award is a testament to the world-class expertise and cutting-edge research facilities at UPMC and the University of Pittsburgh, including the multidisciplinary Ferguson Laboratory for Spine Research.

LB³P is led by Ferguson Laboratory co-directors and study principal investigators Gwendolyn A. Sowa, MD, PhD, chair of the Department of Physical Medicine and Rehabilitation, and Nam V. Vo, PhD, professor of Orthopaedic Surgery. They are joined in the project by numerous research collaborators f rom the University of Pittsburgh (see complete list at FergusonLab.Pitt.edu).

The Widespread Prevalence and Consequences of Low Back Pain

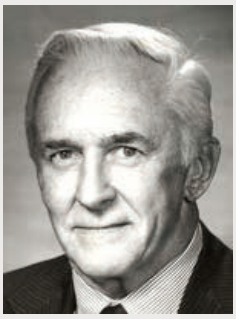
Low back pain affects millions of people of all ages and backgrounds worldwide. It is a major public health concern, invariably leading to reduced quality of life, lost productivity, and increased health care costs. Despite its prevalence, there is still a limited understanding of the underlying mechanisms contributing to low back pain, making it difficult to develop targeted and effective treatments.

About the LB³P Low Back Pain Research Study

The LB³P study aims to revolutionize the treatment of low back pain, a complex and heterogeneous condition attributed by various biological, biomechanical, behavioral, and environmental factors. The study aims to systematically identify and analyze these factors, their interactions, and the underlying mechanisms that contribute to low back pain through biomechanical assessments,

Contined >

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.

sociopsychological and behavioral characteristics, and biological features such as blood genetic and protein biomarkers.

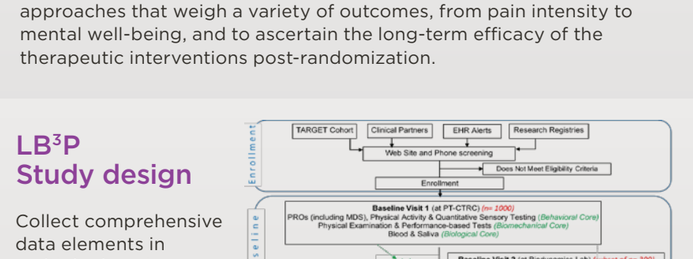
Insights from the study should help to clarify how things like disc degeneration, inflammation, muscle imbalances, and psychosocial factors cause or influence the experience of low back pain and response to treatments. By categorizing patients into different phenotypic groups based on these factors, the work from LB³P may lead to more personalized treatment approaches designed for individuals or subpopulations and mark a significant departure from the current assessments and standards of care for treating and managing low back pain.

Recent Publications and Abstracts from the LB³P Team

Below is a small selection of recent publication highlights for further reading. The first seven papers were coauthored by Ferguson lab or University of Pittsburgh faculty for a special supplement in the journal Pain Medicine, outlining aspects of the LB³P study, its composition, and the larger BACPAC group and its research program. UPMC/Pitt/Ferguson Lab faculty coauthors are listed for each paper.

- Vo N, Piva SR, Patterson CG, McKernan GP, Zhou L, Bell KM, Anderst W, Greco CM, Schneider MJ, Delitto A, Dicianno BE, Darwin J, Sowa GA. Toward the Identification of Distinct Phenotypes: Research Protocol for the Low Back Pain Biological, Biomechanical, and Behavioral (LB³P) Cohort Study and the BACPAC Mechanistic Research Center at the University of Pittsburgh. Pain Med. 2023. Aug 4; 24 (Suppl 1): S36-S47.
- Batorsky A, Bowden AE, Darwin J, et al. The BACPAC Research Program Data Harmonization: Rationale for Data Elements and Standards. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthors: Jessa Darwin, Carol Greco, Charity Patterson, Sara Piva, Nam Vo.
- Mauck MC, Lotz J, Psioda MA, et al. The Back Pain Consortium (BACPAC) Research Program: Structure, Research Priorities, and Methods. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthors: Nam Vo, Gwendolyn Sowa.
- Fields AJ, Dudii S, Schrepf A, et al. Protocol for Biospecimen Collection and Analysis within the BACPAC Research Program. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthors: Jessa Darwin, Gwendolyn Sowa, Nam Vo.
- Grego CM, Wasan AD, Schneider MJ et al. Biobehavioral Assessments in BACPAC: Recommendations, Rationale, and Methods. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthors: Carol Greco, Michael Schneider, Jessa Darwin.
- Sollman N, Fields AJ, O'Neill C, et al. Magnetic resonance imaging of the lumbar spine—recommendations for acquisition and image evaluation from the BACPAC Spine Imaging Working Group. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthor: William Anderst.
- Quirk DA, Johnson ME, Anderson DE. Biomechanical Phenotyping of Chronic Low Back Pain: Protocol for BACPAC. Pain Med. 2023. Aug 4; 24 (Suppl 1): Coauthors: Kevin Bell, Jessa Darwin.
- Tonelli Enrico V, Vo N, Methe B, Morris A, Sowa G. An unexpected connection: A narrative review of the associations between Gut Microbiome and Musculoskeletal Pain. Euro Spine J. 2022; 31: 3603-3615.

LB³P: deep phenotyping cLBP-mountains of data



Multicenter Biomarkers Study Tests Treatment Efficacy

In the fall of 2022, the Back Pain Consortium, part of the NIH's HEAL Initiative, of which the Ferguson Lab and LB³P is a member, launched a collaborative clinical trial, with the University of Pittsburgh as one of 12 nationwide sites studying the effectiveness of treatments for chronic low back pain. The Biomarkers for Evaluating Spine Treatments (BEST) seeks to refine therapeutic strategies for chronic low-back pain through a precision medicine approach. The study focuses on discerning optimal treatments predicated on individual phenotypic markers and their subsequent therapeutic responses. The BEST trial randomizes study participants into one of four treatment approaches:

- **Acceptance and Commitment Therapy**
- **Duloxetine**
- **Enhanced self-care**
- **Evidence-based Exercise and Manual Therapy**

The BEST trial also aims to develop and refine dynamic treatment approaches that weigh a variety of outcomes, from pain intensity to mental well-being, and to ascertain the long-term efficacy of the therapeutic interventions post-randomization.

LB³P Study design

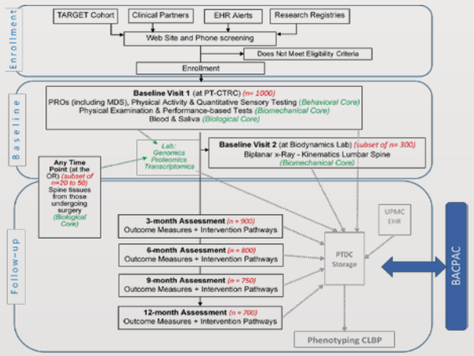
Collect comprehensive data elements in multiple domains for 1000 subjects

↓

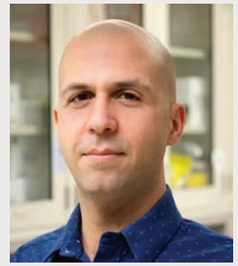
Deep phenotyping

↓

Distinct types of cLBP



Ferguson Lab Trainee Spotlight: *Valerio Tonelli Enrico, PT, MSCE*



Valerio Tonelli Enrico, PT, MSCE, is a Rehabilitation Science PhD candidate at the University of Pittsburgh's School of Health and Rehabilitation Sciences. He joined the Ferguson Laboratory for Spine Research in June 2020, and will be completing his doctoral studies in summer 2024.

Valerio's initial education was a Bachelor of Science in Physiotherapy from Universitá Degli Studi di Torino, Italy. His thesis focused on neural mobilization treatment in post-thoracotomy pain. He worked as a physical therapist in Italy until 2013.

He subsequently earned a Master's degree in clinical epidemiology from Memorial University, Newfoundland, Canada. His thesis explored the dietary inflammatory index's role in chronic musculoskeletal pain.

Valerio's research and clinical endeavors primarily revolve around chronic pain and pain syndromes, particularly low back pain. "After my PT training, my interactions with fellow professionals amplified my interest in research, especially about chronic pain and its myriad facets," says Valerio.

After completing his epidemiology studies, Valerio moved to the US with his family and sought programs in the U.S. to continue his research on chronic pain while also continuing to practice as a therapist. "I was keen to explore research on biomarkers of systemic contributors to chronic pain " says Valerio.

His search culminated at the University of Pittsburgh and the Ferguson Lab, particularly due to the lab's LB³P NIH-funded project on chronic low-back pain.

"The sub-classification concept for pain was something that greatly influenced my clinical perspective. The idea that similar pain symptoms can stem from varied factors is what we're exploring in the LB³P study at the Ferguson Lab," he says.

An interesting facet of chronic pain, and in particular low back pain, is how and to what degree a patient's existing comorbidities may play into its manifestation and influence not only the trajectory of the condition or its severity, but also how these factors may influence an individual's response to a specific therapy. Psychological factors like depression or anxiety, genetic and epigenetic variables, environmental factors, trauma or injury, diseases like diabetes or obesity – all likely can and do have a profound influence on chronic pain – but in who, why, and to what degree is the clinical challenge to solve.

"This whole concept of the modulatory factors that can contribute to chronic pain - like low back pain – who's susceptible, what predispositions may influence it, how to screen for these, is largely a mystery," says Valerio. "But it's exactly the mystery that LB³P is trying to solve and that I hope to continue to study into the future."

One aspect or possible factor gaining more attention, and something Valerio has been working on during his time in the Ferguson Lab contributing to LB³P research is the potential role of the gut microbiome in chronic low back pain.

As Valerio explains, by looking into the specific taxa, species, and overall diversity of gut bacteria, the aim of this work is to establish an initial baseline for future studies probing correlations and metrics related to pain syndromes.

"The microbiome significantly influences our overall health, from our nervous system to hormone production and immune regulation," says Valerio. "Its role in conditions like chronic low back pain is still speculative, but it's a direction we're keen to explore."

Valerio's doctoral research is centered on the microbiome and targeted proteomics, aiming to find correlations between individuals' microbiome baselines, pain, and post-physical therapy outcomes.

What I've been interested in my entire career so far is what LB³P is designed to study and understand – how and what constitutes a specific phenotype of chronic pain – in this instance low back pain," says Valerio. "Once we know that, we can better screen for the condition, predict what trajectory an individual will follow, and how to optimally treat a person given all their underlying factors and predispositions. That's a big challenge but definitely one worth pursuing."

** The Back Pain Consortium Research Program is administered by the National Institute of Arthritis and Musculoskeletal and Skin Diseases. This research was supported by the National Institutes of Health through the NIH HEAL Initiative under award number U19AR076725-01. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or its NIH HEAL Initiative.*

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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.

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