RUSH

Anne-Marie Malfait, MD, PhD

The Klaus E. Kuettner, PhD, Professorship of Osteoarthritis Research

Advancement of Medicine and Research

Chronic pain is a major health problem worldwide, and the musculoskeletal system is its predominant source. Our research is focused on pain in musculoskeletal and rheumatic diseases. Our team uses animal models and human tissues to explore the relationship between joint damage and the neurobiological processes that underlie pain associated with rheumatic diseases.

I am the director of the recently established Chicago Center for Musculoskeletal Pain, or C-COMP, which is funded by a P30 from the National Institute of Arthritis and Musculoskeletal and Skin Diseases. C-COMP aims to foster and support research and training aimed at understanding mechanisms of pain in rheumatic and musculoskeletal diseases. As part of the Center's activities, we have awarded pilot funding to 13 early-career researchers throughout the U.S., including Rush; organized a hybrid seminar speaker series attended by approximately 50-80 people worldwide; organized a quarterly journal club attended by 50-70 scientists globally; and provided resources and training to more than 30 groups in the country and around the world. In addition, I am the principal investigator of a UC2 consortium grant, called RE-JOIN, from the National Institutes of Health, which is aimed at mapping the innervation of the knee joint, and how this may relate to pain and identifying new targets for drug development.

These large grants provide a framework for our R-funded research that is focused on the neurobiology of the joint and the musculoskeletal system. We were recently awarded an R21 innovation grant to explore mechanisms of pain in patients with Ehlers Danlos Syndromes, an inheritable connective tissue disease characterized by skin fragility, joint hypermobility and chronic pain.

Importantly, the Kuettner Professorship has contributed to my salary, and this has enabled us to purchase an autostainer. This critical piece of equipment has allowed us to triple the number of

tissue samples that we can process per week, which has allowed us to expand our analysis of the innervation of human tissues.

I am grateful to be the recipient of the 2024 Rush Faculty Excellence Award for Research, which is an institute-wide recognition of our team's work.

Mentoring and Education

My educational and scholarly activities and recognition include:

- Advisory board of a T32 that provides postdoctoral training in joint health.
- Serve as faculty on the U.S. Bone and Joint Young Investigator Initiative, as well as on the Scientific Advisory Board of the Arthritis National Research Foundation. I am strongly committed to motivating young researchers to study osteoarthritis and joint pain.
- NIH study sections in the past year.
- Editor-in-Chief of Osteoarthritis and Cartilage, the premier multidisciplinary journal in the field.
- HEAL Pain Strategic Planning: Non-Addictive Pain Therapeutics Development virtual session, panelist, "Osteoarthritis targets," Nov 15.

Speaking Engagements

- Invited to lecture worldwide as a speaker or keynote in conferences and universities around the world. Some examples include:
    - "Pain, plasticity, and peripheral nerves in osteoarthritis" 44 the European Workshop for Rheumatology Research, Budapest, Hungary (keynote);
    - "The future of artificial intelligence in OA publishing OARSI World Congress on Osteoarthritis", Incheon, S. Korea, April 24-27;
    - "Joint innervation, neuroplasticity, and osteoarthritis" 14th Annual GCC Pain Translational Research Conference, Houston TX (keynote);
    - "Update on Osteoarthritis" Winter Rheumatology Symposium, ACR, Snowmass CO;
    - "Neurobiological Processes and Pain in Osteoarthritis" 4th Kock Foundation International Symposium on Osteoarthritis and Alzheimer's Disease, Trelleborg, Sweden;

  - "Chronic joint pain: Insights from Osteoarthritis" 7th Annual Biopharmaceutics Research and Development Symposium, University of Nebraska Medical Center, Omaha, NE;
  - "The biology of pain" 14th International Congress on Spondyloarthritides, Ghent, Belgium;

- Grand Rounds:
  - Osteoarthritis joint pain: The quest for new targets
    Johns Hopkins Blaustein Pain Grand Rounds, virtual (April 11)
  - The neurobiology of joint pain: Lessons learnt from osteoarthritis.
    NIAMS/NIH Grand Rounds, virtual (Jan 17)

Publication Highlights — Abbreviated

- Ishihara S, Miller RE, **Malfait AM.** Assessment of Knee Hyperalgesia in Mice using Pressure Application Measurement. *Journal of Visual Experimentation (Jove)* **2025,** in press.
- Ko F, Fullam S, Lee H, Ishihara S, Adamczyk N, Obeidat AM, Soorya S, Miller RJ, **Malfait AM**, Miller RE. Clearing-enabled light sheet microscopy as a novel method for three-dimensional mapping of the sensory innervation of the mouse knee. *J Orthopedic Res* **2025;** 43(3):632-639. doi: 10.1002/jor.26016. (on the cover)
- Geraghty T, Ishihara S, Obeidat AM, Adamczyk NS, Hunter RS, Li J, Wang L, Lee H, Ko FC, **Malfait AM**, Miller RE. Acute systemic macrophage depletion in osteoarthritic mice alleviates pain-related behaviors and does not affect joint damage. *Arth Res Ther* **2024**; 26(1):224.
- Obeidat AM, Ishihara S, Li J, Lammlin L, Junginger L, Maerz T, Miller RJ, Miller RE, **Malfait AM**. Intra-Articular Sprouting Of Nociceptors Accompanies Progressive Osteoarthritis: Comparative Evidence In Four Murine Models. *Frontiers in Neuroanatomy* **2024**; 15, 18:1429124.
- Schmukler J, **Malfait AM**, Block J, Pincus T. 36-40% of routine care osteoarthritis or rheumatoid arthritis patients screen positive for anxiety, depression and/or fibromyalgia. *ACR Open Rheumatology* **2024**; 6(10):641-647.

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- Obeidat AM, Kim SY, Burt KG, Hu B, Li J, Ishihara S, Xiao R, Miller RE, Little CB, **Malfait AM**, Scanzello CR. Recommendations For a Standardized Approach to Histopathologic Evaluation of Synovial Membrane in Murine Models of Experimental Osteoarthritis. *Osteoarthritis and Cartilage* **2024**;32(10):1273-1282.
- Vroman R, Ishihara S, Fullam S, Wood, MJ, Adamczyk NS, Lomeli N, Malfait, F **Malfait AM**, Miller RE, Markovics A. Reduced Capsaicin-Induced Mechanical Allodynia and Neuronal Responses in the DRG in the Presence of Shp1 Overexpression. *Molecular Pain* **2024;** 20:17448069241258106.
- Frank MO, Jiang JS, Zhang H, Lewis MJ, Sikandar S, Pitzalis C, Lesnak J, Price T, **Malfait AM**, Miller RE, Zhang F, Goodman S, Darnell R, Wang F, Orange DE. Machine Learning Reveals Fibroblast-Neuronal Crosstalk as a Source of Peripheral Sensitization in Rheumatoid Arthritis Synovium. *Science Translational Medicine* **2024**;16(742).
- George DS, Jayaraj ND, Ren D, Miller RE, **Malfait AM**, Miller RJ, Menichella DM. A subpopulation of peripheral sensory neurons expressing the Mas-related G Protein-Coupled Receptor d (Mrgprd) generates pain hypersensitivity in painful diabetic neuropathy. *Pain* **2024**;165(5):1154-1168 (selected as editor's highlight)

The Year Ahead: 2025 and Beyond

We will continue to grow our new center, C-COMP, with an increased focus on other diseases such as Ehlers Danlos Syndromes and spondyloarthritis (grant in preparation). In addition, we are planning a pain symposium in Dec 2025.

With Gratitude

I am grateful for your generosity that continues to provide invaluable support in our ongoing quest to ease the pain for those suffering from musculoskeletal and rheumatic diseases.