## Luis Fernando Queme Cobar, M.D., Ph.D.

Instructor

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### **Research Interests**

Neurophysiology of pain, ischemic myalgia, peripheral and central mechanisms of pain, musculoskeletal and myofascial pain, animal models of pain, chronic pain models, role of neurotrophic factors in the development of muscular pain, peripheral mechanisms of cardiovascular reflexes regulation, role of ion channels on nociception, role of purinergic receptors in pain development, mechanisms of mechanotransduction, delayed onset muscle soreness

#### Education

2008-2013 Doctor of Philosophy, Ph D.

Cell Information Medicine, focus on "pain neurophysiology" Nagoya University, Graduate School of Medicine, (Nagoya, Japan)

Dissertation: "Muscular Mechanical and Heat Sensitivity in Humans and Rats After

Lengthening Contraction"

Advisor: Kazue Mizumura M.D., D.Sc.

1999-2007 Doctor of Medicine, MD

Francisco Marroquin University (Guatemala City, Guatemala)

Thesis: "Absolute and Relative Adrenal Insufficiency in Children with Septic Shock"

Bachelor of Science, BS (Joint degree with MD)

Francisco Marroquin University (Guatemala City, Guatemala)

#### Certifications

Educational Commission for Foreign Medical Graduates Certification (ECFMG)

## Work Experience

2019-	Instructor, Cincinnati Children's Hospital Medical Center, Department of Anesthesia, Division of Pain Management Research Lab
2018-2019	Research Associate, Cincinnati Children's Hospital Medical Center, Department of Anesthesia, Division of Pain Management Research Lab Principal Investigator: Michael P Jankowski, Ph.D.
2014-2018	Post-doctoral Fellow, Cincinnati Children's Hospital Medical Center, Department of Anesthesia, Division of Pain Management Research Lab Principal Investigator: Michael P Jankowski, Ph.D.

### Research Experience

2019- Cincinnati Children's Hospital Medical Center

Instructor, 2019 – present

My current research explores the role of repeated injuries and stress in the development of chronic muscle pain. My focus is in exploring the changes in gene expression in the peripheral nervous system in different models of repeated muscle tissue injuries and how background stressors can be potential modulators of the development of chronic pain.

2018-2019 Cincinnati Children's Hospital Medical Center

Research Associate, 2018 - 2019

I studied how repeated ischemia with reperfusion injuries in the development of chronic pain. And how primary muscle afferents show sex differences in dynamic gene regulation after repeated injuries.

2014-2018 Post-doctoral Research Fellow, 2014 - 2018

During my postdoctoral fellowship I studied the dual modulation of nociception and cardiovascular reflexes by primary muscle afferents during peripheral ischemia in a mouse brachial artery occlusion model. I used a multidisciplinary approach, involving behavioral assays, electrophysiology recordings of primary sensory neurons in an ex-vivo muscle nerve, DRG, spinal cord preparation and multiple molecular biology techniques.

2009 Aalborg University

Guest Researcher, Nov-Dec 2009

During this graduate fellowship, I contributed to the design and execution of a protocol to research on healthy human volunteers the effects of heat sensitization on muscle pain using delayed onset muscle soreness as a model.

2008-2013 Nagoya University

Ph. D. Student, 2009-2013

During my graduate training I studied the role of TRPV1 ion channels on mechanical hyperalgesia and the role of NGF in muscle pain using *in vitro* single fiber recordings and animal models of acute and chronic pain.

I also performed studies analyzing the expression of pERK in the DRGs of rats exposed to repeated cold stress (as a model of chronic myofascial pain), using immunohistochemistry.

Research Student, 2008-2009

My initial work as a graduate student focused on the effect of NGF in mechanical hyperalgesia using behavioral experiments and Delayed Onset Muscle Soreness (DOMS) as a model of muscle pain in rats.

## Mentoring and Teaching Experience

2020- University of Cincinnati. Instructor for the Fundamentals of Neuroscience course laboratory.

My responsibilities include teaching and supervising the gross anatomy laboratories for the course.

2016- University of Cincinnati/Cincinnati Children's Hospital Summer Undergraduate Research Fellowship (SURF) Program mentor

During the summer semester I mentored and trained undergraduate students in basic research techniques and in developing a short project for capstone presentations.

2016- University of Cincinnati Biomedical Research and Mentoring Program (RaMP)

I mentor and train undergraduate students and directly supervised their work in the laboratory. In this program students learn how to keep research records, perform basic molecular biology experiments and present their results at a capstone session.

## **Mentored Students**

Name	Affiliation	Dates	Current Affiliation
Jessica Ross PhD	University of Cincinnati	02/2014 - 06/2017	Stanford University
Bhavana Katragadda	University of Cincinnati	02/2015 - 05/2016	University of Cincinnati
Evan Purvis	Xavier University	05/2016 - 08/2016	Southern Illinois University School of Medicine
Alex Weyler	University of Cincinnati	01/2017 -08/2018	University of Cincinnati
Adam Dourson BS	University of Cincinnati	09/2017 - Present	University of Cincinnati
Ally Butterfield	University of Cincinnati	01/2019 - 03/2020	University of Cincinnati
Irati Mitxelena	University of Cincinnati	01/2019 - 03/2020	University of Cincinnati

### **Awards and Honors**

2018	American Pain Society Young Investigator Travel Award to attend the Annual Scientific
	Meeting
2018	International Association for the Study of Pain (IASP) travel award to attend the World
	Congress on Pain
2018	International Association for the Study of Pain (IASP) special interest group on non-
	human pain poster presentation award
2016	International Association for the Study of Pain (IASP) travel award to attend the World
	Congress on Pain
2016	North American Pain School (NAPS) 2016 selected trainee.
2015	American Pain Society Young Investigator Travel Award to attend the Annual Scientific
	Meeting

# Service

Ad hoc Referee/Reviewer

**PLoS ONE** 

Molecular Pain

**Neuroscience Letters** 

Life Sciences

Pain

**Journal of Pain** 

Journal of Neurophysiology

Neurochemical Research

Biology of Sex Differences

## **Professional Organizations**

2020- US Association for the Study of Pain (USASP)

2014- Society for Neuroscience (SFN)

2014- Society for Neuroscience (SFN) – Ohio-Miami Valley (OMV) Chapter member

2014- American Heart Association (AHA) 2014-2019 American Pain Society (APS)

2010- International Association for the Study of Pain (IASP)

2008-2013 The Physiological Society of Japan (PSJ)

## **Research Funding**

Science, Technology (MEXT) Scholarship Queme LF [PI] 04/2008 - 04/2013

Japan Ministry of Education. ¥12,600,000 (~\$118,000USD)

16POST29750004 Queme LF [PI] 07/2016 - 06/2018

American Heart Association

Role of GDNF in the Dual Modulation of Nociception and Cardiovascular Reflexes during Peripheral Ischemia

\$102,550

Anesthesia Innovation and Pilot (AIP) Award Queme LF [PI] 07/2020- 06/2021

Cincinnati Children's Hosp. Department of Anesthesiology

\$20,630

#### **Invited Talks**

Mechanisms of Ischemic Muscle Pain and How to Target Them for Treatment. - *International Association for the Study of Pain (IASP) Pain Research Forum (painresearchforum.org) Weekly Seminar Series* – August 2020 (Webinar format: <a href="https://www.painresearchforum.org/forums/webinar/148070-prf-seminar-mechanisms-ischemic-muscle-pain-and-how-target-them-treatment">https://www.painresearchforum.org/forums/webinar/148070-prf-seminar-mechanisms-ischemic-muscle-pain-and-how-target-them-treatment</a>).

## **Publications**

Nagaraja S, **Queme LF**, Hofmann M, Tewari SG, Jankowski MP, Reifman J. In silico Identification of Key Factors Driving the Response of Muscle Sensory Neurons to Noxious Stimuli. Front Neurosci. 2021, In press

**Queme LF**, Jankowski MP. Single unit Electrophysiological Recordings of Primary Muscle Sensory Neurons using a Novel Ex-vivo Preparation. In: *Contemporary approaches to the study of pain: from molecules to neural networks.* Seal RP editor. Springer Nature. (Book Chapter in press)

Yang L, Slone J, Li Z, Lou X, Hu YC, **Queme LF**, Jankowski MP, Huang T. Systemic Administration of AAV-Slc25a46 mitigates mitochondrial neuropathy in Slc25a46-/- mice. *Hum Mol Genet.* 2020 Jan, DOI: 10.1093/hmg/ddz277

**Queme LF**, Weyler AA, Cohen ER, Hudgins RC, Jankowski MP. A role for peripheral GDNF signaling in ischemic myalgia development. *Proc Natl Acad Sci.* 2020 Jan, 117 (1) 698-707; DOI: 10.1073/pnas.1910905116

**Queme LF**, Jankowski MP. Sex differences and mechanisms of muscle pain. *Curr Opin Physiol.* 2019 Oct; 11:1-6. DOI: 10.1016/j.cophys.2019.03.006 Epub 2019 Apr 2

Nasu T, Kubo A, **Queme LF**, Mizumura K. A single administration of Neurotropin reduced the elongated immobility time in the forced swimming test of rats exposed to repeated cold stress. *Behav Pharmacol.* 2019 Jun 10. DOI: 10.1097/FBP.0000000000000488

He X, Zhang L, **Queme LF**, Liu X, Lu A, Waclaw RR, Dong X, Zhou W, Kidd G, Yoon SO, Buonanno A, Rubin JB, Xin M, Nave KA, Trapp BD, Jankowski MP, Lu QR. A histone deacetylase 3-dependent pathway delimits peripheral myelin growth and functional regeneration. *Nat Med.* 2018 Mar;24(3):338-351. DOI: 10.1038/nm.4483

Ross JL, **Queme LF**, Lamb JE, Green KJ, Jankowski MP. Sex differences in primary muscle afferent sensitization following ischemia and reperfusion injury. *Biol Sex Differ*. 2018 Jan 3;9(1):2. DOI:10.1186/s13293-017-0163-5

Ross JL, **Queme LF**, Lamb JE, Green KJ, Ford ZK, Jankowski MP. Interleukin 1β inhibition contributes to the antinociceptive effects of voluntary exercise on ischemia/reperfusion-induced hypersensitivity. *Pain.* 2018 Feb;159(2):380-392. DOI:10.1097/j.pain.00000000001094

**Queme LF**, Ross JL, Jankowski MP. Peripheral Mechanisms of Ischemic Myalgia. *Front Cell Neurosci.* 2017 Dec 22;11:419. DOI: 10.3389/fncel.2017.00419

Li Z, Peng Y, Hufnagel RB, Hu YC, Zhao C, **Queme LF**, Khuchua Z, Driver AM, Dong F, Lu QR, Lindguist DM, Jankowski MP, Stottmann RW, Kao WWY, Huang T. Loss of SLC25A46 causes neurodegeneration by affecting mitochondrial dynamics and energy production in mice. *Hum Mol Genet.* 2017 Oct 1;26(19):3776-3791. 2. DOI: 10.1093/hmg/ddx262

Liu X, Green KJ, Ford ZK, **Queme LF**, Lu P, Ross JL, Lee FB, Shank AT, Hudgins RC and Jankowski MP. Growth hormone regulates the sensitization of developing peripheral nociceptors during cutaneous inflammation. *Pain.* 2017 Feb;158(2):333-346. DOI: 10.1097/j.pain.00000000000000770

Lu P, Hudgins RC, Liu X, Ford ZK, Hoffmann MC, **Queme LF**, Jankowski MP. Upregulation of P2Y1 in neonatal nociceptors regulates heat and mechanical sensitization during cutaneous inflammation. *Mol Pain.* 2017 Jan-Dec;13:1744806917730255. DOI: 10.1177/1744806917730255

Ross JL, **Queme LF**, Cohen ER, Green KJ, Lu P, Shank AT, An S, Hudgins RC and Jankowski MP. Muscle IL1β drives ischemic myalgia via ASIC3-mediated sensory neuron sensitization. *J Neurosci.* 2016; 36(26):6857-71. DOI: 10.1523/JNEUROSCI.4582-15.2016

**Queme LF**, Ross JL, Lu P, Hudgins RC and Jankowski MP. Dual modulation of nociception and cardiovascular reflexes during peripheral ischemia through P2Y1 receptor dependent sensitization of muscle afferents. *J Neurosci.* 2016; 36(1):19-30. DOI:10.1523/JNEUROSCI.2856-15.2016

Ross JL, **Queme LF**, Shank AT, Hudgins RC, Jankowski MP. Sensitization of group III and IV muscle afferents in the mouse after ischemia and reperfusion injury. *J Pain.* 2014; 15(12):1257-70. DOI: 10.1016/j.ipain.2014.09.003

## Published as Queme F:

**Queme F**, Taguchi T, Mizumura K, Graven-Nielsen T. Muscular Heat and Mechanical Pain Sensitivity After Lengthening Contractions in Humans and Animals. *J Pain.* 2013 Nov;14(11):1425-36. DOI: 10.1016/j.jpain.2013.07.010

Murase S, Terazawa E, Hirate K, Yamanaka H, Kanda H, Noguchi K, Ota H, **Queme F**, Taguchi T, Mizumura K. Upregulated Glial Cell Line-derived Neurotrophic Factor Through Cyclooxygenase-2 Activation in the Muscle is Required for Mechanical Hyperalgesia After Exercise in Rats. *J Physiol.* 2013 Jun 15;591(12):3035-48. DOI: 10.1113/jphysiol.2012.249235

Murase S, Terazawa E, **Queme F**, Ota H, Matsuda T, Hirate K, Kozaki Y, Katanosaka K, Taguchi T, Urai H, Mizumura K. Bradykinin and Nerve Growth Factor Play Pivotal Roles in Muscular Mechanical Hyperalgesia After Exercise (Delayed-onset Muscle Soreness). *J Neurosci.* 2010 Mar 10;30(10):3752-61.

10.1523/JNEUROSCI.3803-09.2010

## **Presentations**

**Queme LF,** Weyler AA, Jankowski MP. Muscle GDNF signaling to neurons modulates peripheral sensitization after ischemic injury through a CREB/CBP interaction. - *Society for Neuroscience Annual Meeting 2019* – Chicago, USA (Abstract/Poster)

**Queme LF**, Weyler AA, Hudgins RC, Jankowski MP. GDNF/GFRα1 mediated upregulation of acid sensing ion channels and P2X receptors modulates muscle pain-related behaviors and exercise pressor reflexes after ischemia-reperfusion injury. - *17th World Congress on Pain (IASP)* - Boston, USA, 2018 (Abstract/Poster)

**Queme LF**, Weyler AA, Ross JL, Jankowski MP. Ischemia and reperfusion injury induces acute and chronic muscle pain-related behaviors through increased expression of the GFRα1 receptor. – *American Pain Society annual meeting 2018* - Anaheim, CA PA, USA (Abstract/Poster)

**Queme LF**, Purvis EC, Weyler AA, Ross JL, Hudgins RC, Jankowski MP. Increased pain related behaviors and cardiovascular responses to exercise after ischemia and reperfusion injuries are regulated by enhanced GDNF dependent signaling in muscle afferents. - *Society for Neuroscience Annual Meeting 2017* – Washington DC, USA (Abstract/Poster)

**Queme LF**, Ross JL, Hudgins RC, Seal RP, Jankowski MP. VGLUT3 containing primary muscle afferents are a unique subpopulation that respond to innocuous metabolites. - *American Pain Society annual meeting 2017* – Pittsburgh, PA, USA (Abstract/Poster)

**Queme LF**, Ross JL, Ford AK, Katragadda BK, Green KJ, Hudgins RC, Jankowski MP. Upregulation of GDNF family receptor  $\alpha 1$  in the dorsal root ganglia regulates pain-related behaviors and the cardiovascular response to exercise after ischemia with reperfusion injury. - *16th World Congress on Pain (IASP)* - Yokohama, Japan, 2016 (Abstract/Poster)

**Queme LF**, Ross JL, Hudgins RC, Jankowski MP. The ADP-responsive P2Y1 receptor modulates phenotypic changes in muscle afferents during chronic ischemic injury. - *Society for Neuroscience Annual Meeting 2014* – Washington DC, USA (Abstract/Poster)

**Queme F**, Mizumura K. Muscular Nociceptor Heat Sensitivity in Rats After Lengthening Contraction and NGF. - *90th Physiological Society of Japan (PSJ) Meeting* - Tokyo, Japan, 2013 (Abstract/Poster)

**Queme F**, Nie H, Mizumura K, Graven-Nielsen T. Experimental Muscle Pain and Muscle Hyperalgesia After Intramuscular Injections of Heated Saline or Capsaicin. - *13th World Congress on Pain (IASP)* - Montreal, Canada, 2010 (Abstract/Poster)

Murase S, **Queme F**, Taguchi T, Mizumura K. COX-2-GDNF Pathway to Delayed Onset Muscle Soreness in Rats. - *The 13th World Congress on Pain (IASP)* - Montreal, Canada, 2010 (Abstract/Poster)