

**BIOGRAPHICAL SKETCH**

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NAME OF APPLICANT: Jianguo Cheng, M.D., Ph.D.

eRA COMMONS USER NAME (credential, e.g., agency login): j0chen03

POSITION TITLE: Professor of Anesthesiology  
Director, Cleveland Clinic Multidisciplinary Pain Medicine Fellowship Program  
Medical Director, Cleveland Clinic Consortium for Pain

**EDUCATION/TRAINING**

INSTITUTION AND LOCATION	DEGREE (if applicable)	Completion DATE MM/YYYY	FIELD OF STUDY
Qingdao Univ. Med College, Qingdao, China	M.D., M.Sc.	06/1986	Medicine
Univ. of Guelph, Guelph, Ontario, Canada	Ph.D.	03/1994	Biophysics/Neuroscience
Univ. of Manitoba, Winnipeg, Manitoba, Canada	PDF	04/1996	Neurophysiology
Univ. of Alberta, Edmonton, Alberta, Canada	PDF	10/1998	Spinal cord physiology
Univ. of Louisville, Louisville, Kentucky	Residency	12/2004	Anesthesiology
Harvard Medical School/Mass General Hospital, Boston, Massachusetts	Fellowship	01/2006	Pain Medicine

**A. Personal Statement.**

I am a **Professor** of Anesthesiology, holding the position of **Director** at the Cleveland Clinic Multidisciplinary Pain Medicine Fellowship Program, and serving as **Medical Director** of the Cleveland Clinic Consortium for Pain (C3P). The proposed research in this application is based on the groundwork of our basic, translational, and clinical investigations. My clinical expertise, recognized by Best Doctors and Top Doctors in America, focuses on novel therapeutic strategies for refractory pain conditions. My bench research focuses on *understanding the neuroimmune mechanisms underlying neuropathic pain and advancing the development of novel therapeutics and multimodal biomarkers for chronic pain and opioid tolerance*. My expertise extends to **neuromodulation**, spinal cord electrophysiology, and sensorimotor integration. Specifically, I explore the roles of *neuroimmune communications in the development of neuropathic pain* and opioid tolerance. We pioneered the *neuroimmune modulatory effects of mesenchymal stem cells (MSCs) and their potential therapeutic applications* to prevent or reverse acute-to-chronic pain transition, neuropathic pain, and opioid tolerance. We showed that both intrathecal and intravenous MSC transplantations profoundly and consistently mitigated pain behaviors induced by chronic constriction injury of the sciatic nerve in rats and mice. MSCs derived from bone marrow or adipose tissues are equally effective in producing long-term analgesic effects. We further discovered that MSC transplantation consistently prevented or reversed the development of opioid tolerance and opioid-induced hyperalgesia, likely through inhibition of microglia and astrocyte activation in the spinal cord. Additionally, we have differentiated MSCs into neuron-like cells with neuronal electrophysiological properties. Our work, continuously supported by grants from the NIH, DOD, and other agencies for more than 20 years, has led to the development of multiple new treatments, patented medical devices, and technology transfers. We have published more than 180 *journal articles and book chapters* and 3 *textbooks* (**Fundamentals of Pain Medicine**, Springer-Nature; **Neuropathic Pain: A Case-based Approach to Practical Management**, Oxford University Press; **Neuroimmune Interactions in Pain: Mechanisms and Therapeutics**, Springer-Nature). My contributions extend beyond research and academia, as I have held key leadership roles such as **President** of the American Academy of Pain Medicine and **Chairman** of the US Section of the World Institute of Pain. I am actively involved as a member/leader of the *Department of Health and Human Services (HHS) Pain Management Inter-Agency Task Force*, *NIH grant review panels/Data and Safety Monitoring Board*, and the *National Academy of Medicine Action Collaborative on Countering the US Opioid Epidemic*. Through extensive collaborations with colleagues across multiple institutions, we have strengthened our research capability and collectively worked toward our common goal of finding innovative, efficacious, and safe therapies for chronic pain and opioid tolerance.

## Ongoing projects to highlight:

NIH/NINDS/1UG3NS127258-01A1 (UG3/UH3), 09/23/2022 - 08/31/2027

A first-in-class, mechanism-guided, cell-based therapy for complex regional pain syndrome

**Jianguo Cheng (PI)**

NIH/NIAMS 3R01AR077452-04S1, 09/15/2013 - 04/30/2025

Multi-Vendor Multi-Site Novel Accelerated MRI Relaxometry.

**Xiaojuan Li (PI), Jianguo Cheng (co-I)**

NIH/NIDA/NINDS/ 1R24NS132283-01, 09/28/2022 – 08/31/2027

Positively Uniting Researchers of Pain to Opine, Synthesize, and Engage (PURPOSE)

**Jacob Coverstone (PI, Neuroventions), Jianguo Cheng (Governing Board)**

NIH/NCI/5K08CA228039-03, 03/2020-02/2027

**Jijun Xu (PI), Jianguo Cheng (Clinical Adviser)**

Complement in Paclitaxel-induced peripheral neuropathy.

Patient-Centered Outcomes Research Institute (**PCORI**) Grant, 09/01 2017- 10/31/2024

Comparative Effectiveness of Pain Cognitive Behavioral Therapy and Chronic Pain Self-Management within the Context of Opioid Reduction

**Beth Darnell, (PI, Stanford University); Jianguo Cheng (Scientific Advisor)**

Lisa Dean Moseley Foundation Grant# LDMF JC0920, 09/01/2020-08/31/2024

A Novel Therapeutic Target for Mesenchymal Stem Cells to Mitigate Opioid Tolerance

**Jianguo Cheng (PI)**

Pain Management Innovations Fund #T56629 (established at Cleveland Clinic through private donations), 2022-2028. Complex Regional Pain Syndrome Research

**Jianguo Cheng (PI)**

## Citations

1. Fox L, Shen J, Ma K, Liu Q, Shi G, Pappas GD, Qu T, **Cheng J.** Membrane properties of neuron-like cells generated from human bone marrow-derived mesenchymal stem cells. ***Stem Cells & Development***, 2010; 19:1831-1841. PMCID: PMC3128307
2. Hua Z, Liu LP, Shen J, Cheng K, Liu A, Yang J, Wang L, Qu TY, Yang HN, Li Y, Wu H, Narouze J, Yan Y, **Cheng J.** Mesenchymal stem cells reversed morphine tolerance and opioid-induced hyperalgesia. ***Scientific Reports***. 2016; **6:32096**; doi: 10.1038/srep32096. PMCID: PMC4995471
3. Fei Li, Liu LP, Cheng K, Chen ZB, **Cheng J.** The use of stem cell therapy to reverse opioid tolerance. ***Clinical Pharmacology and Therapeutics***, 2018;103:1-4. DOI:10.1002/cpt.959.
4. Buchheit T, Huh Y, Maixner W, **Cheng J**, Ji RR. Neuroimmune modulation of pain and Regenerative Pain Medicine. ***Journal of Clinical Investigation***. 2020;130(5):2164-2176. PMCID: PMC7190995
5. Xu J, Huang P, Bie B, Dai Y, Ben-Salem S, Borjini N, Zhang L, Chen J, Olman M, **Cheng J**, Lin F. Complement Receptor C3aR1 Contributes to Paclitaxel-Induced Peripheral Neuropathic Pain in Mice and Rats. ***Journal of Immunology***. 2023;211(11):1736-1746.

## B. Positions, Scientific Appointments, and Honors

### Positions

**Professor of Anesthesiology**, Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland, Ohio, 2011~

**Director**, Cleveland Clinic Multidisciplinary Pain Medicine Fellowship Program, Ohio, 2009~

**Medical Director, Cleveland Clinic Consortium for Pain Research (C3P)**

<http://stage.intranet.lerner.ccf.org/lri/C3P/>), 2021~

**Anesthesiologist/Pain Physician/Principal Investigator**, Departments of Pain Management and Neurosciences, Cleveland Clinic, Cleveland, Ohio, 2006~

**Assistant Professor of Research**, Department of Neurological Surgery, University of Louisville School of Medicine, Louisville, Kentucky, 1998-2001

### Scientific Appointments

National Institutes of Health (NIH), Small Business: *Drug Discovery Involving the Nervous System*, ZRG1 NV-S (14), 11/16-17, 2023.

National Institutes of Health (NIH), Small Business: *Drug Discovery Involving the Nervous System*, ZRG1 NV-S (14) B, 06/27-28, 2023.

National Institutes of Health (NIH)/National Institute of Diabetes and Digestive and Kidney Diseases

(NIDDK), RFA-DK-23-006 Advancing Research on Mechanisms and Management of Pain for Diseases and Conditions within NIDDK Mission Areas (R01 Clinical Trial Optional) 07/20-21, 2023.

National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), Safety Officer, Data and Safety Monitoring Board (DSMB) for “A Sequenced-Strategy for Improving Outcomes in Patients with Knee Osteoarthritis Pain” (UG3/UH3 AR077360), 2020-2023.

National Institutes of Health (NIH), Small Business Panel for Drug Discovery Involving the Nervous System (ETTN-S (14)). ZRG1 NV-S (14) B, March 14-15, 2023.

National Institutes of Health (NIH), Small Business Panel for Drug Discovery Involving the Nervous System (ETTN-S (14)). ZRG1 NV-S (14) B, November 15-16, 2022.

National Institutes of Health (NIH), Small Business Panel for Drug Discovery Involving the Nervous System (ETTN-S (14)). 6/21-22, 2022.

National Institutes of Health (NIH/NINDS) ZNS1 SRB G (37) Special Emphasis Panel, HEAL Initiative RFA-NS-21-010 (Non-addictive Analgesic Therapeutics Development [Small Molecules and Biologics] to Treat Pain).

National Institutes of Health (NIH/NINDS) ZNS1 SRB G (40) Special Emphasis Panel, HEAL Initiative RFA-NS-21-010 (Non-addictive Analgesic Therapeutics Development [Small Molecules and Biologics] to Treat Pain).

National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), Safety Officer, Data and Safety Monitoring Board for “A Sequenced-Strategy for Improving Outcomes in Patients with Knee Osteoarthritis Pain” (UG3/UH3 AR077360), 2020-2023.

US Army Medical Research and Materiel Command, Scientific Peer Advisory and Review Services division of the American Institute of Biological Sciences (AIBS), 2013~

National Institutes of Health Special Emphasis Panel/Scientific Review Group ZRG1 MOSS-D (02), 2010/01 Section; 2010/06 Section.

#### **National Leadership Positions**

**President, American Academy of Pain Medicine (AAPM)**, 2018– 2019

**Chairman, USA Section of World Institute of Pain (WIP)** 2013 – 2015

**Member and lead writer, Department of Health and Human Services (HHS) Pain Management Best Practices Inter-Agency Task Force (PMTF)**, 2018 – 2019

**Member, National Academy of Medicine Action Collaborative** on Countering the US Opioid Epidemic, 2018 – 2025

**Centers for Medicare & Medicaid Services (CMS) Expert Work Group (EWG)** on the development of measures evaluating potential opioid overuse 2016 – 2021.

**Agency for Healthcare Research and Quality (AHRQ) Effective Health Care (EHC) Program Technical Expert Panel (TEP)**, 2018 – 2021

**Scientific Advisory Board (SAB), Association of University Anesthesiologists (AUA)**. 2015– 2018

**American Society of Anesthesiologists (ASA) Committee on Pain Medicine** 2013 – 2016

**Board Examination Pain Medicine Question Author, American Board of Anesthesiology (ABA)**, the American Board of Physical Medicine and Rehabilitation, and the American Board of Psychiatry and Neurology. 2013 – 2017

**Board of Directors, American Academy of Regenerative Medicine**. 2016~

**Associate Editor, *Pharmaceuticals***, Impact Factor 5.215. 2022~

**Associate Editor, *Frontiers in Pain Research***, 2023~

**Associate Editor, *Pain Practice*** (Official Journal of the World Institute of Pain) 2013 – 2018

**Senior Editor/Section Editor, *Pain Medicine*** (Official Journal of the American Academy of Pain Medicine). 2018 – 2023

**New England Journal of Medicine Expert Panelist, NEJM Resident 360: Ask the Expert: Addiction and Pain Control** 2017 – 2019

#### **Honors** (from 89 awards/recognitions)

**Best Doctors in America**, 2016, 2017, 2018, 2020, 2023, Best Doctors, Inc.

**Top Doctors in America**, 2023

**Top Doctors**, International Association of Anesthesiologists. Featured in The Leading Physicians in the World. 2017. Cleveland Magazine 2018, 2019, 2020, 2021, 2022, 2023.

**Best in Medicine Award**, American Health Council. May 2017.

**Lifetime Achievement Award**, Marquis Who's Who, 2018, 2019, 2020.

**Henry Fok Ying Tung (霍英东) Medal of Honor of Distinguished World Chinese Doctor (CNY 10,000).**

*The highest honor of Doctors of Chinese Ethnicity in the World*, World Association of Chinese Doctors, 2017.

**The Staff of the Year and Best Teacher of the Year**, Pain Medicine, Cleveland Clinic. 2015

**Cleveland Clinic Innovator Awards**, Cleveland Clinic. 2007, 2013

**Clinical Achievement Award**, Cleveland Clinic Foundation. 2012

**America's Most Compassionate Doctor Award**, American Registry Recognize Excellence. 2012

**70 Best Pain Management Physicians in America**, *Becker's Review* 2011

**Expertise Recognized by multiple national media coverage:** The New York Times, CNN, CBS News, ABC News, NPR report, etc.

### Licensure and certificates

State Medical Board of Ohio #35.087420, 2006-2025

Commonwealth of Massachusetts Board of Registration in Medicine # 221800, 2004-2006

Commonwealth of Kentucky Board of Medical Licensure # 38238, 2001-2005

American Board of Anesthesiology, Anesthesiology 4/20/2007-12/30/2027, Certificate # 40627

American Board of Anesthesiology, Pain Medicine 9/13/2008-12/30/2028, Certificate # 40627

World Institute of Pain, Fellow of Interventional Pain Practice (FIPP) 5/25/2010, Certificate# 575

Diplomate, American Board of Regenerative Medicine (DABRM, 2015).

### **C. Contributions to Science**

**1. Translational research:** We pioneered the study of neurotoxicity of HIV proteins and demonstrated that *tat*, an HIV genome-encoded protein, caused neuronal excitotoxicity and cell death through direct action on specific cell member receptors/channels (a). This work elucidated one of the key mechanisms by which HIV causes neuropathy and dementia. We identified a signaling pathway from cannabinoid receptor 1 activation to the inhibition of NMDA-mediated excitotoxicity and cell death and uncovered a vital role of the endocannabinoid system in the pathogenesis of neurological disorders including neuropathic pain (b). We showed that peripheral application of QX-314 combined with capsaicin effectively reduced neuropathic pain. Neuraxial application of this combination, in contrast, was not therapeutic but caused neurotoxicity (c). We demonstrated the efficacy and safety of stem cell therapy for preventing and treating neuropathic pain and opioid tolerance in different species of animals (d,e).

- Cheng J**, Nath A, Knudsen B, Hochman S, Geiger JD, Ma M, Magnuson DSK. Neuronal excitatory properties of human immunodeficiency virus type 1 *tat* protein. *Neuroscience*, 1998; 82:97-106.
- Liu Q, Bhat M, Bowen WD, **Cheng J**. Signaling pathways from CB1 receptor activation to inhibition of NMDA-induced  $Ca^{2+}$  influx and neurotoxicity in dorsal root ganglion neurons, *Journal of Pharmacology and Experimental Therapeutics*, 2009;331:1062-1070. PMID: PMC2784707
- Shen J, Fox L, **Cheng J**. Differential effects of peripheral versus neuraxial co-administration of capsaicin and QX-314 on neuropathic pain in rats. *Anesthesiology*, 2012; 117:365-380.
- Hua Z, Liu LP, Shen J, Cheng K, Liu A, Yang J, Wang L, Qu TY, Yang HN, Li Y, Wu H, Narouze J, Yan Y, **Cheng J**. Mesenchymal stem cells reversed morphine tolerance and opioid-induced hyperalgesia. *Scientific Reports-Nature*, 2016;**6**, 32096; doi: 10.1038/srep32096.
- Li F, Liu LP, Cheng K, Chen ZB, **Cheng J**. The use of stem cell therapy to reverse opioid tolerance. *Clinical Pharmacology & Therapeutics*, 2018;103(6):971-4. DOI:10.1002/cpt.959.

**2. Clinical Research:** As PI, I have led investigations into the efficacy and safety of pharmacological agents, spinal cord stimulation, and radiofrequency treatments for neuropathic and other chronic pain conditions. We substantially contributed to the current practice guidelines for the management of neuropathic pain such as diabetic neuropathy, complex regional pain syndrome (a), and radicular pain (b). Our original work helped establish a standard of care for chronic pain of the knee joint, sacroiliac joint (c,d), facet joint, and intervertebral disc. We invented a new device and a new procedure to manage low back pain effectively and safely (d), which is utilized worldwide.

- Cheng J**, Salmasi V, You J, Yang, D, Mascha EJ, Grille M, Cheng OT, Zhao F, Rosenquist RW. Outcomes of sympathetic blocks in the management of complex regional pain syndrome: A retrospective cohort study. *Anesthesiology*, 2019; 131:883-893 (featured in ASA and the Anesthesiology journal).
- Wang F, Zhou Q, Xiao L, Xiong D, Yang J, Li D, Liu L, Ancha S, **Cheng J**. A randomized comparative study of pulsed radiofrequency treatment with or without selective nerve root block for chronic cervical radicular pain. *Pain Practice*, 2017;17:589-595.
- Cheng J**, Pope JE, Dalton JE, Cheng O, Bensitel A. Comparative outcomes of cooled versus



traditional radiofrequency ablation of the lateral branches for sacroiliac joint pain. *Clinical Journal of Pain*, 2013;29:132-137.

- d. **Cheng J**, Chin SL, Zimmerman N, Dalton JE, LaSalle G, Rosenquist RW. A new procedure of radiofrequency ablation to treat sacroiliac joint pain. *Pain Physician*, 2016;19:589-601 (invention of technology licensed and utilized worldwide).

**3. Sensory-motor neuroscience research:** My research on the control of movement uncovered critical mechanisms of reflex modulation, neural networks for locomotion, and spinal cord injury. We demonstrated a physiological mechanism, by which somatosensory afferent discharges from muscle mechanoreceptors activated by movements powerfully modulated the transmissibility of the group Ia afferent pathways to spinal motoneurons and to the somatosensory cortex (a). At a cellular level, we identified the arrhythmogenic flexor and extensor centers in the spinal cord for the control of locomotion. We proposed the new concept of independent flexor and extensor centers in the neural networks for locomotion and localized the flexor center and extensor centers in specific regions of the spinal cord. This work has fundamentally influenced the conceptual framework of neuronal networks for locomotion (b). We uncovered a brainstem descending pathway in the ventrolateral funiculus that is critical for the initiation of locomotion (c). We further discovered that the neural network for locomotion in the spinal cord is powerfully modulated by electronic coupling through gap junctions (d).

- a. Brooke JD, **Cheng J**, Collins DF, McIlroy WE, Misiaszek JE, Staines WR. Sensory-sensory afferent conditioning with leg movement: Gain control in spinal reflex and ascending paths. *Progress in Neurobiology*, 1997;51:393-421.
- b. **Cheng J**, Stein RB, Jovanovic K, Yoshida K, Bennett D, and Han Y. Identification, localization, and modulation of the neural networks for walking in the mudpuppy (*Necturus maculatus*) spinal cord. *Journal of Neuroscience*, 1998;18:4295-4304.
- c. **Cheng J**, Magnuson DSK. Initiation of segmental locomotor-like activities by stimulation of ventrolateral funiculus in the neonatal rat. *Experimental Brain Research*, 2011;214:151-161.
- d. Lavrov I, Fox L, Shen J, Han Y, **Cheng J**. Gap junctions contribute to the regulation of walking-like activity in the adult Mudpuppy (*Necturus Maculatus*), PLoS **ONE**. 2016;11(3):1-16.

**4. Invention, Innovation, and Technology Transfers.**

**U.S. PATENTS**

US 20150164519 A1. Cheng, Jianguo (Solon, OH, US). DEVICES AND METHODS FOR TREATING MEDICAL CONDITIONS ASSOCIATED WITH SACROILIAC JOINT ABNORMALITIES.

US10,849,708 B2 (Date of Patent: Dec. 1, 2020). Jianguo Cheng. Devices and methods for treating medical conditions associated with sacroiliac joint abnormalities.

US 20150246074 A1. Qu, Tingyu (Chicago, IL, US), Cheng, Jianguo (Solon, OH, US), Sun, Jinhua (Hangzhou, CN), Yang, Hongna (Jinan, CN), Cheng, Kathleen (Solon, OH, US), Shen, Jun (Newton, MA, US). METHODS OF ATTENUATING OPIOID TOLERANCE

U.S. provisional patent application Serial No. 63/196,499, Cheng, Jianguo (Solon, OH, US.)

Spill protection basin for surgeries, filed in the United States Patent and Trademark Office on June 3, 2021, through the Cleveland Clinic.

**5. TECHNOLOGY INVENTION AND TRANSFERS**

**Biomotion Inc.** is a company based in Edmonton, Canada, and owned by Richard Stein, Kelly James, Robert Rolf, and **Jianguo Cheng**. We developed and commercialized our WalkAide® technology to treat foot drops due to strokes, multiple sclerosis, and other neurological disorders. Our WalkAide device has been utilized worldwide since 2008.

**Invention: Jianguo Cheng.** Devices and methods for treating medical conditions associated with sacroiliac joint abnormalities. The technology is transferred from the Cleveland Clinic to Cosman Medical Inc. (Now Boston Scientific Med. Inc.) based in Boston, Massachusetts, USA (2015).

**Invention: (Jianguo Cheng, Richard Stein, and Kelly James).** A novel technology of a wheelchair powered by electrical stimulation of paralyzed leg muscles and designed for patients with spinal cord injury and the elderly. The technology was transferred from the University of Alberta to Biomotion, a technological company based in Edmonton, Alberta, Canada (1998).

Complete List of Published Work in MyBibliography:

<https://www.ncbi.nlm.nih.gov/myncbi/1JQ35jeXmedkgm/bibliography/public/>

I have not received any research grants from any foreign sources.