BIOGRAPHICAL SKETCH

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NAME: Tao, Yuan-Xiang

eRA COMMONS USER NAME (credential, e.g., agency login): YTAO01

POSITION TITLE: Professor of Anesthesiology and Vice Chair of Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Nanjing Medical University, Nanjing, China	B.A. & M.D.	07/1986	Medicine
Nanjing Medical University, Nanjing, China	M.Sc.	07/1992	Neurobiology and Pain
Shanghai Brain Research Institute, China	Ph.D.	07/1997	Neuroscience and Pain
University of Virginia, Charlottesville, VA, USA	Postdoctoral fellow	07/1999	Neuroscience and Pain

A. Personal Statement

The long-term goal of my lab is to investigate novel molecular and cellular mechanisms that underlie chronic pain (including neuropathic pain) and chronic opioid-associated disorders (e.g., tolerance and hyperalgesia) and to apply these findings to the prevention and/or treatment of these disorders. I have a broad background in neuroscience, with specific training and expertise in research related to physiological and pathological pain and chronic opioid tolerance/hyperalgesia. More than 170 original research articles and scientific reviews in the areas of neuroscience and pain have been published in top-rated scientific journals, such as *Nature Neurosci*, *Advanced Science*, *Neuron*, *JCI*, *J Exp Med* and *Nature Commun*. As PI or co-Investigator on several university-, private-, and NIH-funded grants, I laid the groundwork for the proposed research by accumulating substantial experience in and tools for conducting experiments that utilize techniques in molecular biology, biochemistry, cell biology, electrophysiology, morphology, and behavioral testing. In addition, I have successfully administered the projects (e.g. staffing, research protections, budget), and collaborated with other researchers. More importantly, the current application builds logically on our prior work. I have the expertise, the necessary facility, expertise, and motivation necessary to successfully accomplish the work in this proposed project.

Ongoing and recently completed projects that I would like to highlight include:

R01 NS094664
Tao (PI)
02/01/2016-01/31/2023 (non-cost extension)
Epigenetic regulation of neuropathic pain: Role of DRG histone methyltransferase G9a

R01 NS111553
Tao (PI)
7/15/2019-4/30/2024
Role of dorsal root ganglion FTO, a RNA demethylase, in neuropathic pain

RF NS113881
Davison and Tao (MPI)

9/30/2019-3/31/2024
Discovery and validation of a new long noncoding RNA as a novel target for neuropathic pain

R01 NS1174484
Hu and Tao (MPI)
4/15/2021-3/31/2026
Identification of a novel DRG-specifically enriched long noncoding RNA and its role in neuropathic pain

Citations:

1. Zhao X, Tang Z, Zhang H, Atianjoh FE, Zhao J, Liang L, Wang W, Guan X, Kao SC, Tiwari V, Hoffman PN, Cui H, Li M, Dong X, **Tao YX**. (2013) A native long noncoding RNA contributes to neuropathic pain by silencing Kcna2 in primary afferent neurons. Nat Neurosci 16:1024-31.
2. Zhao JY, Liang L, Gu X, Li Z, Wu S, Sun L, Atianjoh FE, Feng J, Mo K, Jia S, Lutz BM, Bekker A, Nestle EJ, **Tao YX**. (2017) DNA methyltransferase DNMT3a contributes to neuropathic pain by repressing Kcna2 in primary afferent neurons. Nat Commun 8:14712.
3. Du S, Wu S, Feng X, Wang B, Xia S, Liang L, Zhang L, Govindarajalu G, Bunk A, Kadakia F, Mao Q, Guo X, Zhao H, Berkman T, Liu T, Li H, Stillman J, Bekker A, Davidson S, **Tao YX.** (2022) A nerve injury-specific long noncoding RNA promotes neuropathic pain by increasing CCL2 expression. J Clin Invest 132 (13): e153563.
4. Li Y, Guo X, Sun L, Xiao J, Su S, Du S, Li Z, Wu S, Liu W, Xia S, Mo K, Chang Y-J, Denis D, **Tao YX**. (2020) N6-methyladenosine demethylase FTO contributes to neuropathic pain by stabilizing G9a expression in primary sensory neurons. Adv Sci (Weinh). 7:1902402.

B. Positions, Scientific Appointments, and Honors

Positions and Employment

2016.1-present Director, Center for Pain Medicine Research, Department of Anesthesiology, Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ
2013.10-present Professor, Departments of Cell Biology & Molecular Medicine, Pharmacology & Physiology, Neurology & Neuroscience, Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ
2013.7-present Vice Chair of Research, Department of Anesthesiology, Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ
2013.7-present Professor with tenure, Department of Anesthesiology, Rutgers, The State University of New Jersey, New Jersey Medical School, Newark, NJ
2005-2013.6 Associate Professor, Department of Anesthesiology, Johns Hopkins University
2001-2004: Assistant Professor, Department of Anesthesiology, Johns Hopkins University
1999-2000: Instructor, Department of Anesthesiology, Johns Hopkins University
1992-1994: Assistant Professor, Department of Anatomy and Neurobiology, Nanjing Medical University, Nanjing, China

Service on National Committees

2021.6,10 CDMRP Peer Reviewed Medical Research Program (PRMRP) Pain Medicine (PM) panel, Ad Hoc Reviewer
2020.6. NIH/ NIDCR Study Section, Ad Hoc Reviewer
2018-present Editorial Board, Molecular Pain
2017.6-2020.6 NIH/SPS study section, Member
2015-16, 2018 Chinese National Science Foundation, Advisory Council Panel
2015 Cancer TMOI of the French National Alliance for Life and Health Sciences, Ad Hoc Reviewer
2014-2017.2 NIH/SCS study section, Member
2014, 2016 UK Medical Research Council, Ad Hoc Reviewer
2014 NJMS Dean's Biomedical Research Awards, Ad Hoc Reviewer
2014-present Editor in Chief, Translational Perioperative and Pain Medicine
2014-present Member, Association of University of Anesthesiologists
2013 NIH CLHP study section, Ad Hoc Reviewer
2013 Austria Wings for Life Foundation, Ad Hoc Reviewer
2013-present: member in MD/PhD Oversight and Admission Committee, New Jersey Medical School, Rutgers, The State University of New Jersey.

2013-present: Core Faculty in Multidisciplinary Program in Biomedical Sciences at New Jersey Medical School, Rutgers, The State University of New Jersey
2013-present: Faculty in Center for Immunity and Inflammation at New Jersey Medical School, Rutgers, The State University of New Jersey
2012-present Board Member, International Chinese Academy of Anesthesiology (ICAA)
2012-2014 NIH SCS study section, Ad Hoc Reviewer
2012 NIH SAT study section, Ad Hoc Reviewer
2011-2020 Chinese National Science Foundation, Ad Hoc Reviewer
2009-2013.6 Junior Faculty Advisory Committee, Brain Science Institute at JHU
2009-2013.6 The Scholarship Oversight Committees for the Neonatology Fellows at JHU
2009-2013.6 Core Faculty in Interdisciplinary Training Program in Biobehavioral Pain Research at JHU
2009-2018 Editorial Board of Advisors, Journal of Medical Sciences
2003-present Member, American Society of Pain
2002-present Member, International Society for the Study of Pain
2000-present Member, Society of Neuroscience

Selected Honors

2021 Rutgers Chancellor Basic Science Researcher Award
2020 Rutgers Board of Trustees Award for Excellence in Research
2017 Excellence Research Award, New Jersey Health Foundation
2017 Faculty of the Year Award, Rutgers New Jersey Medical School
2011 Rita Allen Foundation Pain Scholar from the Rita Allen Foundation and the American Pain Society
1999 Outstanding contribution to Nature and Science, Chinese Academy of Sciences, China
1996 Beckman Outstanding Young Scientist Award, BECKMAN Instruments. Ins, Shanghai, China
1996 Outstanding Ph.D. Student, Chinese Academy of Sciences, China

C. Contributions to Science

1. **Dorsal horn postsynaptic density (PSD) proteins and their mediated glutamate receptor trafficking in chronic pain.** My early work first reported that PSD-95 and PSD-93 bound to NMDA receptor subunits NR2A/B and regulated their function and membrane surface expression in the superficial dorsal horn neurons and required for chronic pain genesis. We also demonstrated that dorsal horn PSD-95-cntrolled NMDA receptor activation and subsequent Ca2+ influx triggered PKC to phosphorylate AMPA receptor subunit GluR2, resulting in disruption between GluR2 and ABP/GRIP and GluR2 internalization in dorsal horn neurons after peripheral inflammation. The latter further increased Ca2+ influx and intracellular cascades that are associated with inflammatory pain maintenance. These early pioneer works have created recent pharmacological targets among glutamate receptors-PSD-95/93-nNOS complex for chronic pain treatments carried out by my lab and ones of others.
    a. Park JS, Voitenko N, Petralia RS, Guan X, Xu JT, Steinberg JP, Takamiya K, Sotnik A, Kopach O, Huganir RL, **Tao YX**. (2009) Persistent inflammation induces GluR2 internalization via NMDA receptor-triggered PKC activation in dorsal horn neurons. J Neurosci, 29:3206-3219.
    b. **Tao YX**, Rumbaugh G, Wang GD, Petralia RS, Zhao C, Kauer FW, Tao F, Zhuo M, Wenthold RJ, Raja SN, Huganir RL, Bredt DS, Johns RA. (2003) Impaired NMDA receptor-mediated postsynaptic function and blunted NMDA receptor-dependent persistent pain in mice lacking postsynaptic density-93 protein. J Neurosci, 23: 6703-6712.
    c. Wei Wi, Liu W, Du S, Govindarajalu G, Irungu A, Bekker A, **Tao YX**. A compound mitigates cancer pain and chemotherapy-induced neuropathic pain by dually targeting nNOS-PSD-95 interaction and $GABA_A$ receptor. Neurotherapeutics 2021 doi: 10.1007/s13311-021-01158-8.
    d. **Tao YX**, Raja SN. (2004) Are synaptic MAGUK proteins in chronic pain? TRENDS in Pharmacological Sci. 25:397-400,
2. **Role of Dorsal Horn RNA Translation in Chronic Opioid Tolerance/Hyperalgesia and cancer pain.** Mammalian target of rapamycin (mTOR) controls RNA translation in most cells. My laboratory identified a new mu receptor-triggered PI3K/Akt/mTOR pathway in dorsal horn neurons, which contributes to the promotion of morphine-induced spinal RNA translation and associated with induction and maintenance of morphine tolerance/hyperalgesia. We also demonstrated that spinal cord NMDAR-mediated activation of

mTOR and its downstream effectors was required for cancer pain development and maintenance. These preclinical observations have been verified/confirmed by later clinical case reports.

a. Xu JT, Zhao J, Zhao X, Ligons D, Tiwari V, Lee CY, Atianjoh FE, Liang L, Zang W, Njoku D, Raja SN, Yaster M, **Tao YX**. (2014) Opioid Receptor-triggered spinal mTORC1 activation contributes to morphine tolerance and hyperalgesia. J Clin Invest 124: 592-603.
b. Shih MH, Kao SC, Wang W, Yaster M, **Tao YX**. (2012) Spinal cord NMDA receptor-mediated activation of mTOR is required for the development and maintenance of bone cancer-induced pain hypersensitivities in rats. J Pain. 13: 338-349.

3. **Identification of long non-coding RNAs and their role in neuropathic pain**. Several novel pain-associated long noncoding RNAs (lncRNAs) have been identified in my lab. We first reported an endogenous lncRNA, which was named as *Kcna2* antisense RNA as most parts of its sequence are complementary to *Kcna2* mRNA. This lncRNA specifically and selectively targets *Kcna2* mRNA/protein and contributes to neuropathic pain through regulating Kv1.2-gated DRG neuronal excitability. This work was highlighted by several top-rated scientific Journals and received higher attentions in pain field. Recently, we reported two new lncRNAs, DS-lncRNA and NIS-lncRNA, which participated in neuropathic pain through negative regulation of *Ehmt2*-coding G9a and promotion of CCL2 expression, respectively. Our discovery provides novel insights into the mechanisms underlying neuropathic pain as well as potential new strategies for this disorder management.
    a. Zhao X, Tang Z, Zhang H, Atianjoh FE, Zhao J, Liang L, Wang W, Guan X, Kao SC, Tiwari V, Hoffman PN, Cui H, Li M, Dong X, **Tao YX**. (2013) A native long noncoding RNA contributes to neuropathic pain by silencing Kcna2 in primary afferent neurons. Nat Neurosci 16:1024-31.
    b. Pan Z, Du S, Wang K, Guo X, Mao Q, Feng X, Huang L, Wu S, Hou B, Chang YJ, Liu T, Chen T, Li H, Bachmann T, Bekker A, Hu H, **Tao YX**. (2021) Downregulation of a dorsal root ganglion-specifically enriched long noncoding RNA is required for neuropathic pain by negatively regulating RALY-triggered *Ehmt2* expression. Adv Sci 8: 2004515.
    c. Du S, Wu S, Feng X, Wang B, Xia S, Liang L, Zhang L, Govindarajalu G, Bunk A, Kadakia F, Mao Q, Guo X, Zhao H, Berkman T, Liu T, Li H, Stillman J, Bekker A, Davidson S, **Tao YX.** (2022) A nerve injury-specific long noncoding RNA promotes neuropathic pain by increasing CCL2 expression. J Clin Invest 132 (13): e153563.
    d. Wu S, Bono J, **Tao YX**. (2018) Long noncoding RNA (lncRNA): A target in neuropathic pain. Expert Opin Ther Targets. 23: 15-20.

4. **DNA/histone/RNA methylation-mediated epigenetic modifications contribute to neuropathic pain through participating in nerve injury-induced changes of pain-associated genes in sensory neurons**. Our recent work demonstrated that nerve injury-induced alternations in thousands of pain-associated genes were controlled likely by DNA methyltransferases DNMT3a/DNMT1, histone lysine methyltransferases G9a/SUV39H1, and /or RNA m6A demethylase FTO in inured DRG. Targeting these mechanisms revealed more efficiency in neuropathic pain treatment. Our studies may provide new avenues for this disorder management.
    a. Zhao JY, Liang L, Gu X, Li Z, Wu S, Sun L, Atianjoh FE, Feng J, Mo K, Jia S, Lutz BM, Bekker A, Nestle EJ, **Tao YX**. (2017) DNA methyltransferase DNMT3a contributes to neuropathic pain by repressing Kcna2 in primary afferent neurons. Nat Commun 8:14712.
    b. Li Y, Guo X, Sun L, Xiao J, Su S, Du S, Li Z, Wu S, Liu W, Xia S, Mo K, Chang Y-J, Denis D, **Tao Y-X**. (2020) N6-methyladenosine demethylase FTO contributes to neuropathic pain by stabilizing G9a expression in primary sensory neurons. Adv Sci (Weinh). 7:1902402.
    c. Mo K, Wu S, Gu X, Xiong M, Atianjoh FE, Jobe EE, Zhao X, Tu WF, **Tao YX**. (2018) MBD1 contributes to the genesis of acute pain and neuropathic pain by epigenetic silencing of *Oprm1* and *Kcna2* genes in primary sensory neurons. J Neurosic 38: 9883-9899.
    d. Zhang J, Liang L, Miao X, Wu S, Cao J, Tao B, Mao Q, Mo K, Xiong M, Lutz B, Bekker A, **Tao YX**. (2016) Contribution of the SUV39H1 in dorsal horn and spinal cord dorsal horn to nerve injury-induced nociceptive hypersensitivity. Anesthesiology. 125: 765-778.

5. **Role of transcription factors in neuropathic pain.** Our laboratory has identified several transcription factors that are critical for neuropathic pain genesis through regulating long-coding RNAs, DNA methylation, histone modifications and RNA methylation. These pain-associated transcription factors

include myeloid zinc finger protein 1, CCAAT/enhancer-binding protein-β, octamer transcription factor 1, runt-related transcription factor 1, zinc finger protein 382 and POU doman, class 4, transcription factor 3. They are endogenous initiators in neuropathic pain.

a. Ma L, Yu L, Jiang B-C, Wang J, Guo X, Huang Y, Ren J, Sun N, Gao DS, Ding H, Lu J, Zhou H, Gao Y, Wang L, Sun K, Ming Y, Meng Z, **Tao YX**, Yan M. ZNF382 controls neuropathic pain by silencer-based epigenetic inhibition of *Cxcl13* in DRG neurons. J Exp Med 2021, 218: e20210920.
b. Li Z, Mao Y, Liang L, Wu S, Yuan J, Mo K, Mao Q, Cao J, Bekker A, Zhang W, **Tao YX**. (2017) Contribution of dorsal root ganglion C/EBPβ to peripheral nerve trauma-induced nociceptive hypersensitivity. Sci Signal 10: eaam5345.
c. Yuan J, Wen J, Wu S, Mao Y, Mo K, Li Z, Ai Y, Bekker A, Zhang W, **Tao YX**. (2019) Contribution of dorsal root ganglion octamer transcription factor 1 to neuropathic pain after peripheral nerve injury. Pain 160:375-384.
d. Zhang Z, Zheng B, Du S, Han G, Zhao H, Wu S, Jia S, Bachmann T, Bekker A, **Tao YX**. (2020) Eukaryotic initiation factor 4 gamma 2 contributes to neuropathic pain through downregulation of Kv1.2 and mu opioid receptor in mouse primary sensory neurons. Br J Anaesth. 126: 706-719.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/myncbi/yuan-xiang.tao.1/bibliography/public/