# XIAOYANG CHENG, Ph.D.

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## EDUCATION

University of Tennessee Health Science Center, Memphis, TN, USA, Aug. 2000 – May 2006

**Ph.D.** in Physiology
Advisor: Jonathan H Jaggar, Ph.D.

Dissertation: Calcium signaling in cerebral artery smooth muscle cells

Awards:

- Daniel L. Gerwin Graduate Scholarship, Department of Physiology, University of Tennessee Health Science Center, 07/2005 – 06/2006
- American Heart Association Predoctoral Fellowship' 07/2002 – 06/2004
- J Paul Quigley Memorial Scholarship, Department of Physiology, University of Tennessee Health Science Center, 07/2001 – 06/2002

China Pharmaceutical University, Nanjing, Jiangsu, P.R.China,

**M.Sc.** in Pharmacology, Sept. 1994 – June 1997
Advisor: De-zai Dai, MD

Award:

Jiuhuang Scholarship, China Pharmaceutical University, Nanjing, P.R. China, 1995

**B.Sc.** in Pharmacology, Sept. 1989 – June 1994

Awards:

University Academic Scholarships, China Pharmaceutical University, 1989-1994

## RESEARCH EXPERIENCE

Yale University School of Medicine, New Haven, CT, USA

- Associate Research Scientist, July 2011 – present
- Postdoctoral associate, Apr. 2007 – June 2011

Advisor: Stephen G Waxman, MD, Ph.D.

Project:

Biophysical properties of voltage-gated sodium channels and their roles in neuropathic pain

Award:

Travel award, FASEB Summer Research Conference in Ion Channel Regulation, 06/2011

University of Tennessee Health Science Center, Memphis, TN, USA, May 2006 – Apr. 2007

Postdoctoral fellow

Advisor: Jonathan H Jaggar, Ph.D.

Project:

Molecular profile and electrophysiological properties of L-type calcium channel $Ca_V1.2$ splice variants in rat cerebral artery.

Shanghai Institute of Physiology, Chinese Academy of Science, Shanghai, P.R.China, July 1997 – June 2000

Research Associate, July 1999 – July 2000

Research Assistant, July 1997 – June 1999

Advisor: Pei-hong Zhu, Professor

**EXPERTISES:**

1) ***Electrophysiology:*** Whole-cell patch clamp (voltage-clamp and current clamp) on
   - cell lines (HEK 293, ND7/23)
   - primary cultures of neurons (Dorsal root ganglion neuron, Purkinje neuron, Hippocampal neuron)
   - acutely dissociated vascular smooth muscle cells.
2) ***Molecular biology:***
   - PCR, mutagenesis, 5'-RACE, real time PCR
   - Transient transfection using
     - Transfection reagent: Lipofectamine 2000, Optifect, Fugene 6
     - Electroporation
     - Biolistic transfection
   - Western Blot
3) ***Others:***

Confocal microscopy

**RESEARCH INTEREST**

I am interested in the biophysical properties of voltage-gated ion channels and associated channelopathies, with specific focus on voltage-gated sodium channels (VGSCs).

VGSCs are essential for action potential initiation and propagation in excitable cells, such as neuron, muscle, and neuroendocrine cells. Mutations of VGSCs have been linked to many clinical disorders, including epilepsy, periodic paralysis, cardiac disorders, and pain.

Using molecular biological and electrophysiological approaches, I study the biophysical properties of mutant VGSCs discovered from patients with pain disorders, aiming to explicate the relationship between the biophysical properties of mutant VGSCs and clinical symptoms of those pain disorders, and therefore, to explore new approaches for clinical pain treatment.

My future research will continue focusing on the properties and functions of VGSCs and their roles in human diseases.

## PUBLICATIONS

1. **Cheng XY**, Dib-Hajj SD, Tyrrell L, te Morsche RHM, Drenth JPH, Waxman SG. Deletion mutation of sodium channel $Na_V1.7$ in inherited erythromelalgia: enhanced slow-inactivation modulates dorsal root ganglion neuron hyperexcitability. *Brain* 2011; 134: 1972-1986

2. Samad OA, Tan AM, **Cheng X,** Foster E, Dib-Hajj SD, Waxman SG. Virus-mediated shRNA knockdown of $Na_V1.3$ in rat dorsal root ganglion attenuates nerve Injury-induced neuropathic pain. *Mol Ther* 2012; Aug 21. doi: 10.1038/mt.2012.169. *[Epub ahead of print]*

3. Shields SD, **Cheng XY**, Üçeyler N, Sommer C, Dib-Hajj SD, Waxman SG. Sodium channel $Na_v1.7$ is essential for lowering heat pain threshold after burn injury. *J Neurosci* 2012; 32: 10819-32

4. Gasser A, Szu-Yu Ho T, **Cheng XY**, Chang KJ, Waxman SG, Rasband M, Dib-Hajj SD. An ankyrinG-binding motif is necessary and sufficient for targeting $Na_V1.6$ sodium channels to axon initial segments and nodes of Ranvier. *J Neurosci* 2012; 32: 7232-43

5. Shields SD, **Cheng XY**, Gasser A, Saab C, Tyrrell L, Eastman EM, Iwata M, Zwinger PJ, Black JA, Dib-Hajj SD, Waxman SG. A channelopathy contributes to cerebellar dysfunction in a model of multiple sclerosis. *Ann Neurol* 2012; 71: 186-94

6. Veeramah KR, O'Brien JE, Meisler MH, **Cheng XY**, Dib-Hajj SD, Waxman SG, Talwar D, Girirajan S, Eichler EE, Restifo LL, Erickson RP, Hammer MF. *De novo* pathogenic mutation of *SCN8A* identified by whole genome sequencing of a family quartet with infantile epileptic encephalopathy and SUDEP. *Am J Hum Genet* 2012; 90: 502-510

7. Faber CG, Hoeijmakers JG, Ahn HS, **Cheng XY**, Han C, Choi JS, Estacion M, Lauria G, Vanhoutte EK, Gerrits MM, Dib-Hajj S, Drenth JP, Waxman SG, Merkies IS. Gain of function $Na_V1.7$ mutations in idiopathic small fiber neuropathy. *Ann Neurol* 2012; 71: 26-39

8. **Cheng XY**, Dib-Hajj SD, Tyrrell L, Wright DA, Fischer TZ, Waxman SG. Mutations at opposite ends of the DIII/S4-S5 linker of sodium channel $Na_V1.7$ produce distinct pain disorders. *Mol Pain* 2010, 6: 24

9. Persson AK, Black JA, Gasser A, **Cheng XY**, Fischer TZ, Waxman SG. Sodium-calcium exchanger and multiple sodium channel isoforms in intra-epidermal nerve terminals. *Mol Pain* 2010, 6: 84

10. Gasser A, **Cheng XY**, Gilmore ES, Tyrrell L, Waxman SG, Dib-Hajj SD. Two Nedd4-binding motifs underlie modulation of sodium channel $Na_V1.6$ by p38 MAPK. *J Biol Chem* 2010; 285: 26149-61

11. Choi JS, **Cheng XY**, Foster E, Leffler A, Tyrrell L, te Morsche RHM, Eastman EM, Jansen HJ, Huehne K, Nau C, Dib-Hajj SD, Drenth JPH, Waxman SG. Alternative splicing may contribute to time-dependent manifestation of inherited erythromelalgia. *Brain* 2010, 133:1823-35

12. Sharkey L, **Cheng XY**, Drews V, Buchner D, Jones J, Justice M, Waxman S, Dib-Hajj S, and Meisler M. Mutation of sodium channel Scn8a ($Na_V1.6$) in the ataxia 3 mouse demonstrates a role of the N-terminal region in trafficking to the cell membrane. *J Neurosci.* 2009, 29:2733-41

13. **Cheng XY,** Dib-Hajj SD, Tyrrell L, Waxman SG. Mutation I136V alters electrophysiological properties of the $Na_V1.7$ channel in a family with onset of erythromelalgia in the second decade. *Mol Pain* 2008, 4:1

14. Bannister JP, Thomas-Gatewood CM, Neeb ZP, Adebiyi A, **Cheng XY**, Jaggar JH. $Ca_V1.2$ channel N-terminal splice variants modulate functional surface expression in resistance size artery smooth muscle cells. *J Biol Chem* 2011; 286(17): 15058-66

15. **Cheng XY**, Pachiai J, Blaskova E, Asuncion-Chin M, Liu J, Dopico AM, Jaggar JH. Alternative splicing of $C_{aV}1.2$ channel exons in smooth muscle cells of resistance-size arteries generates currents with unique electrophysiological properties. *Am J Physiol Heart Circ Physiol* 2009, 297:H680-8

16. **Cheng XY**, Liu JX, Asuncion-Chin M, Blaskova E, Bannister JP, Dopico AM, and Jaggar JH. A novel $Ca_V1.2$ N terminus expressed in smooth muscle cells of resistance size arteries modifies channel regulation by auxiliary subunits. *J Biol Chem* 2007, 282:29211-21

17. **Cheng XY** and Jaggar JH. Genetic Ablation of Caveolin-1 Modifies $Ca^{2+}$ Spark Coupling in Murine Arterial Smooth Muscle Cells. *Am J Physiol Heart Circ Physiol* 2006, 290: H2309-19

18. Jaggar JH, Leffler CW, Cheranov SY, Tcheranova D, E SY, **Cheng XY**. Carbon monoxide dilates cerebral arterioles by enhancing the coupling of $Ca^{2+}$ sparks to $Ca^{2+}$-activated $K^+$ channels. *Circ Res* 2002, 91: 610-7

19. **Cheng XY**, Chen KY, Zhang XH, Zhu PH. Effect of zinc ions on caffeine-induced contracture in vascular smooth muscle and skeletal muscle of rat. *Cell Physiol Biochem* 2002, 12: 119-26

20. Wei QQ, **Cheng XY**, Chen KY, Hu J, Li MQ, Zhu PH. Atomic force microscopy study of the rabbit skeletal muscle ryanodine receptors in different functional states. *Sci China C Life Sci* 2002, 45: 225-36.

21. Wang H, Wei QQ, **Cheng XY**, Chen KY, Zhu PH. Inhibition of ryanodine binding to sarcoplasmic reticulum vesicles of cardiac muscle by $Zn^{2+}$ ions. *Cell Physiol Biochem* 2001, 11: 83-92

22. Wei QQ, Chen SF, **Cheng XY**, Yu XB, Hu J, Li MQ, Zhu PH. Topography of skeletal muscle ryanodine receptors studied by atomic force microscopy. *J Vac Sci & Technol B* 2000, 18: 636-638

23. Xia RH, **Cheng XY**, Chen KY, Wei QQ, Zhu PH. Biophasic modulation of ryanodine binding to skeletal muscle ryanodine receptors/calcium release channels by zinc ions. *Biochem J* 2000, 345: 279-86

**CONFERENCES:**

1. SFN 2011 (Annual meeting of Society of Neuroscience), Nov. 12-17, 2011, Washington, DC. **Poster** "$Na_V1.7$ IEM mutations exhibit different responses to low temperature"

2. FASEB Summer Research Conference in Ion Channel Regulation, June 12-17, 2011, Steamboat Springs, CO. **Selected Presentation** "Deletion mutation of sodium channel $Na_V1.7$ in inherited erythromelalgia: enhanced slow inactivation modulates dorsal root ganglion neuron hyperexcitability"

3. SFN 2010, Nov. 13-17, 2010, San Diego, CA. **Poster** "Deletion of Leu955 within the DII/S6 of $Na_V1.7$ channel causes delayed-onset inherited erythromelalgia"

4. SFN 2008, Nov. 15-19, 2008, Washington, DC. **Poster** "Mutations at opposite ends of the DIII/S4-S5 linker underlie different painful neuropathies"

5. Experimental biology meeting, April 28-May 2, 2007, Washington, DC. **Poster** "Myocytes of resistance-size arteries express $Ca_V1.2$ channels with a novel N-terminus"

6. FASEB Summer Research Conference in Smooth Muscle, July 29-August 3, 2006, Snowmass Village, CO. **Poster** "Electrophysiological properties of a novel arterial smooth muscle cell $Ca_V1.2$ $\alpha_1$ subunit N-terminus"

7. Experimental biology meeting, April 1-5, 2006, San Francisco, CA. **Poster** "Genetic ablation of caveolin-1 modifies $Ca^{2+}$ spark coupling in murine arterial smooth muscle cells" (UT student travel award)

8. EB2005/IUPS meeting, March 31-April 6, 2005, San Diego, CA. **Poster** "Genetic ablation of caveolin-1 modifies $Ca^{2+}$ spark coupling in murine arterial smooth muscle cells"

9. EB2005/IUPS meeting, March 31-April 6, 2005, San Diego, CA. **Poster** "Multiple splice variants of $Ca_V1.2$ are expressed in smooth muscle cells of resistance-size cerebral arteries"