

BIOGRAPHICAL SKETCH

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NAME Zu-Hang Sheng, PhD		POSITION TITLE Tenured and Senior Principal Investigator Chief of Synaptic Function Section NINDS, NIH	
eRA COMMONS USER NAME (credential, e.g., agency login)			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
University of Pennsylvania, Philadelphia, PA	Ph.D.	1989-1992	Biochemistry and Neuroscience
University of Washington, Seattle	Postdoc	1993-1996	Neuroscience

A. Research Goals

Ongoing research is focused on the molecular mechanisms regulating neuronal organelle transport and membrane trafficking and their impact on synaptic function and axonal degeneration. We are addressing the following questions:

Specific Aim 1: What is the molecular mechanism that regulates mitochondrial transport and distribution in axons in response to neuronal activity and how does mitochondrial mobility impact synaptic plasticity and axonal degeneration?

Specific Aim 2: What is the role of the retrograde transport of late endocytic organelles in the maintenance of cellular homeostasis of axons and synapses?

Specific Aim 3: How does neuronal transport regulate autophagy-lysosomal function?

Specific Aim 4: How do the kinesin motor-adaptor complexes regulate the axonal transport for synaptic formation, maintenance, and neuronal circuits?

Our long-term goal is to identify the cellular pathways (1) proper turnover or recycling of dysfunctional mitochondria in axons through altering their mobility and by regulating mitophagy, (2) the clearance of aggregation-prone intracytosolic proteins by up-regulating the autophagy-lysosomal system, (3) the maintenance of brain development and neural circuits by regulating axonal transport and cellular homeostasis.

B. Positions and Honors.

Positions and Employment

1997-2007 Principal Investigator, NINDS, NIH
2007- Senior Principal Investigator, Chief of Synaptic Function Section,
National Institute of Neurological Disorders and Stroke (NINDS), National Institutes
of Health (NIH)

Other Experience and Professional Membership

Editorial Board

2006-2011 The Journal of Biological Chemistry (JBC)

Reviewer for Scientific Journals

BMC Neuroscience,
Cerebral Cortex,
EMBO J,
JBC,
JCB,

Journal of Neurobiology,
Journal of Neurochemistry,
Journal of Neuroscience,
Neuron,
Nature Cell Biology,
Nature Neuroscience,
PNAS

Reviewer for Grant

The Wellcome Trust, UK;
BBSRC UK
National Science Foundation, US

Administrative Activities at NIH

1997-2001 Co-chair, NIH Nerve-Muscle Special Interest Group
2000-2001 NINDS Tenure-track Search Committee
2002-2004 NIH Institutional Biosafety Committee
2002- Program Director, The Joint Ph.D. Program in Neuroscience of NIH-Shanghai JiaoTong University
2002-2006 NIH Neuroscience Seminar Committee
2000-2002 Co-chair, NINDS GS-9 Office Manager Promotion Panel
2006- The Committee of the NIH National Graduate Student Research Festival (NGSRF)
2008- HHMI-NIH Research Program Advisory Committee
2008- NINDS/NIDCD Animal Care and Use Committee
2010- NIH Earl Stadtman Tenure-track Investigator Search Committee

Teaching and Mentoring

FAES Graduate Course at NIH: Fundamental Neuroscience

Serving as a mentor for 5 graduate students, 5 HHMI-NIH fellows, 13 postdoctoral fellows.

- Five past postdoctoral fellows were appointed with tenured or tenure-track faculty positions;
- Two past fellows were appointed as clinical faculty positions;
- Two fellow was awarded K08 award;
- One fellow was awarded NIH Pathway to Independence award (K99/R00)

Memberships in Professional societies

American Society for Neuroscience,
American Society for Cell Biology,
American Society for Biochemistry and Molecular Biology

Selected Invited Symposium and Seminar Talks

1998 Invited speaker at Forum of European Neuroscience at Berlin
2000 Invited speaker at Gordon Research Conference on Cell Biology of Neuron
2001 Invited speaker at University des Saalands, Hamburg, Germany
2001 Invited speaker at Centre National De La Recherche Scientifique, Marseille, France
2002 Invited Neuroscience Semianr Speaker at Harvard Medical School
2002 Invited speaker at International Symposium on Exocytosis and Neurotransmitter Release
2002 Invited speaker at International Symposium on Molecular and Cellular Neuroscience in Valparaiso, Chile.
2003 Invited Neuroscience Seminar speaker at George Washington University
2004 Invited speaker at The Symposium of Synapse: Molecular Mechanisms of Plasticity
2005 Invited speaker at 28th Japanese Neuroscience Conference, Yokohama, Japan
2006 Invited Neuroscience Seminar speaker at University of Alabama at Birmingham
2006 Invited seminar speaker at University of Toronto, Toronto Western Research Institute, Canada

- 2006 Penn State University
- 2007 The 9th Symposium of Membrane Biology, Chinese Academy of Science, China
- 2007 NIH Research Festival, Co-chair of symposium
- 2007 Invited speaker at 3rd International Seattle Symposium on Membrane Signal Transduction
- 2007 Invited seminar speaker at Chinese Neuroscience Institute, Chinese Academy of Science
- 2007 Invited Neuroscience Seminar speaker at University of Michigan at Ann Arbor
- 2008 Invited Neuroscience Seminar speaker at Cornell University,
- 2008 Invited Neuroscience Seminar speaker at Case Western Reserve University,
- 2008 Speaker and symposium chair at the Biennial Meeting of European Neuroscience at Geneva
- 2008 Cleveland Clinic, Neuroscience Seminar
- 2008 Invited Speaker at 2nd International Symposium on Molecular and Cellular Mechanisms of Axonal Degeneration, Woods Hole
- 2008 Invited Neuroscience Seminar speaker at Indiana University School of Medicine,
- 2009 Osaka City University, Japan
- 2009 Chair and speaker at International Symposium on Channels and Synapses, Shanghai,
- 2009 University of Tokyo, Graduate School of Medicine, Japan
- 2009 The 1st International Symposium on Membrane Biology, Guilin, China
- 2009 Invited speaker at ISN (International Society for Neurochemistry), Japan
- 2009 Chair and speaker at International Symposium on Channels and Synapses, Shanghai.
- 2009 Plenary lecture speaker at biennial Meeting of the Chinese Society of Neuroscience, Guangzhou, China
- 2010 Invited seminar speaker at the University Paris Descartes, France
- 2010 Invited seminar speaker at the University College London, UK
- 2010 Invited seminar speaker at Saarland University, Germany
- 2010 Invited seminar speaker at American Society of Cell Biology
- 2010 Invited seminar speaker at Mount Sinai School of Medicine, Dept of Neurology and Neuroscience
- 2010 Invited seminar speaker at the New York State Institute for Basic Research
- 2010 Invited speaker at 2010 Japanese Neuroscience Conference
- 2011 Invited seminar speaker at Ohio State University

C. Selected publications (in chronological order).

Trimmer, J.S., Cooperman, S.S., Tomiko, S.A., Zhou, J., Crean, S.M., Boyle, M.B., Kallen, R.G., **Zu-Hang Sheng**, Barchi, R.L., Sigworth, F.J., Goodman, R.G., Agnew, S.A., and Mandel, G. (1989) Primary structure and functional expression of a mammalian skeletal muscle sodium channel. *Neuron* 3, 33-49.

Roland G. Kallen, **Zu-Hang Sheng**, Liquiong Chen, Jan Yang, Rogart, R.B., and Robert L. Barchi. (1990) Primary structure and differential expression of a sodium channel characteristic of immature and denervated rat skeletal muscle. *Neuron* 4, 233-242.

Zu-Hang Sheng, Jens Rettig, Masami Takahashi, and William A. Catterall. (1994). Identification of a syntaxin-binding site on N-type calcium channels. *Neuron* 13, 1303-1313.

Zu-Hang Sheng, Jens Rettig, Terry Cook, and William A. Catterall. (1996) Calcium dependent interaction of neuronal N-type calcium channels with presynaptic fusion proteins. *Nature* 379, 451-454.

Jens Rettig, **Zu-Hang Sheng**, D. Kyle Kim, Connie D. Hodson, Terry P. Snutch, and William A. Catterall. (1996). Isoform-specific interaction of α_1A subunits of brain calcium channels with the presynaptic proteins syntaxin and SNAP-25. *Proc. Natl. Acad. Sci. USA* 93, 7363-7368.

Sumiko Mochida, **Zu-Hang Sheng**, Carl Baker, Haruo Kobayashi, and William A. Catterall. (1996). Inhibition of neurotransmission by peptides containing the synaptic protein interaction site of N-type calcium channels. *Neuron* 17, 781-788.

Zu-Hang Sheng, Charles Yokoyama, and William A. Catterall. (1997). Interaction of the synprint site of N-type calcium channels with the C2B domain of synaptotagmin I. *Proc. Natl. Acad. Sci. USA* 94, 5405-5410.

Charles Yokoyama, **Zu-Hang Sheng**, and William A. Catterall. (1997) Phosphorylation of the synprint site on N-type calcium channels inhibits interactions with SNARE protein. *J Neuroscience* 17, 6929-6938.

Jens Rettig, Christian Heinemann, Uri Ashery, **Zu-Hang Sheng**, Charles T. Yokoyama, William A. Catterall, and Erwin Neher. (1997). Alteration of Ca^{2+} dependence of neurotransmitter release by disruption of Ca^{2+} channel/SNARE protein interaction. *J Neuroscience* 17, 6647-6656.

Jeffrey M. Ilardi, Sumiko Mochida, and **Zu-Hang Sheng** (1999). Snapin: a SNARE-associated protein implicated in synaptic transmission. *Nature Neuroscience* 2, 119-124. (*With News & Views*).

Lucas D. Pozzo-Miller, Wolfram Gottschalk, Li Zhang, Kathryn McDermott, Chikara Oho, **Zu-Hang Sheng**, and Bai Lu. (1999) The role of BDNF in Hippocampal synaptic plasticity: impairment in synaptic vesicle docking and synaptic protein distribution in BDNF knockout mice *J. Neuroscience* 19, 4972-4983.

Guifang Lao, Volker Scheuss, Claudia M. Gerwin, Qingning Su, Sumiko Mochida, Jens Rettig, and **Zu-Hang Sheng**. (2000). Syntaphilin: a syntaxin-1 clamp that controls SNARE assembly. *Neuron* 25, 191-201.

Milan G. Chheda, Uri Ashery, Pratima Thakur, Jens Rettig, and **Zu-Hang Sheng** (2001) PKA phosphorylation of Snapin: modulating its interaction with the SNARE complex. *Nature Cell Biology* 3, 331-338.

Qingning Su, Sumiko Mochida, Jin-Hua Tian, Rashi Mehta, and **Zu-Hang Sheng**. (2001) SNAP-29: a general SNARE protein that inhibits SNARE disassembly and is implicated in synaptic transmission. *Proc. Natl. Acad. Sci. USA* 98, 1438-1443.

Miriam Leenders, Arn M. J. M. van den Maagdenberg, Fernando H. Lopes da Silva, **Zu-Hang Sheng**, Peter C. Molenaar and Wim E.J.M. Ghijsen (2002) Neurotransmitter release from tottering mice nerve terminals with reduced expression of mutated P-, Q-type Ca^{2+} -channels, *Eur. J. Neuroscience* 15, 13-18.

Jin-Hua Tian, Sunit Das, and **Zu-Hang Sheng**. (2003) Ca-dependent phosphorylation of syntaxin-1A by DAP-kinase regulates its interaction with Munc-18. *The Journal of Biological Chemistry* 278, 262265-26274.

Sunit Das, Judit Boczan, Claudia Gerwin, Philip Zald, and **Zu-Hang Sheng**. (2003) Regional and developmental regulation of syntaphilin expression in the brain: a candidate molecular element of synaptic functional differentiation. *Molecular Brain Research* 116, 38-49.

Sunit Das, Claudia Gerwin, and **Zu-Hang Sheng** (2003) Syntaphilin binds to dynamin-1 and inhibits dynamin-dependent endocytosis, *The Journal of Biological Chemistry* 278, 41221-41226.

Brij B. Singh, Timothy P. Lockwich, Bidhan C. Bandyopadhyay, Xibao Liu, Sunitha Bollimuntha, So-ching Brazer, Christian Combs, Sunit Das, A.G. Miriam Leenders, **Zu-Hang Sheng**, Mark A. Knepper, Suresh V. Ambudkar, and Indu S. Ambudkar (2004) VAMP2-Dependent Exocytosis Regulates Plasma Membrane Insertion of TRPC3 Channels and Contributes to Agonist-Stimulated Ca²⁺ Influx, **Molecular Cell** 15, 635-646.

Pratima Thakur, David R. Stevens, **Zu-Hang Sheng** and Jens Rettig (2004) Effects of PKA-mediated phosphorylation of Snapin on synaptic transmission in cultured hippocampal neurons, **Journal of Neuroscience** 24, 6476-6481.

Judit Boczan, A. G. Miriam Leenders, and **Zu-Hang Sheng** (2004) Phosphorylation of syntaphilin by PKA modulates its interaction with syntaxin-1 and annuls its inhibitory effect on vesicle exocytosis, **The Journal of Biological Chemistry** 279, 18911-18919.

Qingning Su*, Qian Cai*(equal contributions), Claudia Gerwin, Carolyn L. Smith, **Zu-Hang Sheng** (2004) Syntabulin: a microtubule-associated protein implicated in syntaxin transport in neurons, **Nature Cell Biology** 6, 941-953 (*With News & Views and the journal cover image*).

Ping-Yue Pan, Qian Cai, Lin Lin, Pei-Hua Lu, Shu-Min Duan, and **Zu-Hang Sheng**. (2005) SNAP29-mediated modulation of synaptic transmission in cultured hippocampal neurons. **The Journal of Biological Chemistry** 280, 25769-25779.

Xiao-Ke Chen, Lie-Cheng Wang, Yang Zhou, Qian Cai, Murali Prakriya, Kai-Lai Duan, **Zu-Hang Sheng**, Christopher Lingle & Zhuan Zhou. (2005). Activation of GPCRs modulates quantal size in chromaffin cells through G(betagamma) and PKC. **Nature Neuroscience** 8,1160-1168.

Qian Cai, Claudia Gerwin, and **Zu-Hang Sheng**. (2005). Syntabulin-mediated anterograde transport of mitochondria along the neuronal processes. **Journal of Cell Biology** 170, 959-969.

Jin-Hua Tian, Zheng-Xing Wu, Michael Unzicker, Li Lu, Qian Cai, Cuiling Li, Claudia Schirra, Ulf Matti, David Stevens, Chuxia Deng, Jens Rettig, and **Zu-Hang Sheng**. (2005). The role of snapin in neurosecretion: *snapin* knockout mice exhibit impaired calcium-dependent exocytosis of large dense-core vesicles in chromaffin cells. **Journal of Neuroscience** 25, 10546-10555. (*Highlighted in J Neuroscience editorial news*).

Qian Cai, Pingyue Pan, and **Zu-Hang Sheng**. (2007). Syntabulin-kinesin-1 family 5B-mediated axonal transport contributes to activity-dependent presynaptic assembly. **Journal of Neuroscience** 27, 7284-7296. (*Highlighted in J Neuroscience editorial news and in Nature Reviews Neuroscience*).

Jian-Sheng Kang, Jin-Hua Tian, Philip Zald, Ping-Yue Pan, Cuiling Li, Chuxia Deng, and **Zu-Hang Sheng** (2008). Docking of axonal mitochondria by syntaphilin controls their mobility and affects short-term facilitation. **Cell** 132, 137-148 (*Highlighted in Nature Reviews Neuroscience*).

Miriam Leenders, Lin Lin, Claudia Gerwin, and **Zu-Hang Sheng**. (2008). The role of MAP1A light chain LC2 in surface expression and presynaptic targeting of Ca_v2.2 calcium channels. **Journal of Neuroscience** 28, 11333-11346.

Wenbo Lu, Huan Ma, **Zu-Hang Sheng**, and Sumiko Mochida. (2009). Dynamin and activity regulate synaptic vesicle recycling in sympathetic neurons. **The Journal of Biological Chemistry** 284, 1930-1937.

Ping-Yue Pan, Jin-Hua Tian and **Zu-Hang Sheng** (2009). Snapin Facilitates the Synchronization of Synaptic Vesicle Fusion. **Neuron** 61, 412-424.

Yan-Min Chen, Claudia Gerwin, and **Zu-Hang Sheng**. (2009). Dynein light chain LC8 regulates syntaphilin-mediated mitochondrial docking in axons. *Journal of Neuroscience* 29, 9428-9437.

Li Lu, Qian Cai, Jin-Hua Tian and **Zu-Hang Sheng**. (2009). Snapin associates with late endocytic compartments and interacts with late endosomal SNAREs. *Bioscience Report* 29, 261-269.

Huan Ma, Qian Cai, Wenbo Lu, **Zu-Hang Sheng** (co-corresponding author), and Sumiko Mochida. (2009). KIF5 motor adaptor syntabulin maintains synaptic transmission in sympathetic neurons. *Journal of Neuroscience* 29, 13019-13029.

Qian Cai, **Zu-Hang Sheng**. (2009). Moving or stopping mitochondria: Miro as a traffic cop by sensing calcium (Previews). *Neuron* 61, 493-496.

Qian Cai, Li Lu, Jin-Hua Tian, Yi-Bing Zhu, Haifa Qiao, **Zu-Hang Sheng**. (2010). Snapin-regulated late endosomal transport is critical for efficient autophagy-lysosomal function in neurons. *Neuron* 68, 73-86. (also see [Preview by M Yuzaki](#))

Qian Cai and **Zu-Hang Sheng**. Uncovering the role of Snapin in regulating autophagy-lysosomal Function. *Autophagy* (in press).

Bing Zhou, Yi-Bing Zhu, Lin Lin, Qian Cai, and **Zu-Hang Sheng**. Snapin deficiency is associated with developmental defects of the central nervous system *Bioscience Report* (in press).

Invited review articles in the past five years:

Zu-Hang Sheng, Ruth E. Westenbroek, and William A. Catterall. (1998). Physical link and functional coupling of presynaptic calcium channels and synaptic vesicle docking/fusion machinery. *J. Bioenergetics & Biomembranes* 30, 335-345.

Miriam Leenders and **Zu-Hang Sheng**, (2005). Modulation of neurotransmitter release by the second messenger-activated protein kinases: implications for presynaptic plasticity, *Pharmacology & Therapeutics* 105, 69-84.

Qian Cai, **Zu-Hang Sheng**. (2009). Molecular motors and Synaptic Assembly, *Neuroscientist* 15, 78-89.

Qian Cai, **Zu-Hang Sheng**. (2009). Mitochondrial Transport and Docking in Axons. *Experimental Neurology* 218, 257-267.

Invited book editor and chapters in the past five years:

Miriam Leenders, Claudia Gerwin, and **Zu-Hang Sheng**. "Multidisciplinary approaches for visualizing & identifying synaptic vesicle proteins". *The Current Protocols in Neuroscience*, Wiley Press. Inc. (2004).

Zu-Hang Sheng and Miriam Leenders. Calcium channels and neurotransmitter release: calcium channels and SNARE proteins. *New Encyclopedia of Neuroscience* (2008).

Zu-Hang Sheng. Modulation of neurotransmitter release and presynaptic plasticity by protein phosphorylation. *Molecular Mechanisms of Neurotransmitter Release*. The Humana Press Inc. (2008).

Zu-Hang Sheng, Amy Lee, and William Catterall. Initiation and regulation of synaptic transmission by presynaptic calcium channel signalling complexes. ***Structural and Functional Organization of the Synapse***. Springer Press. Inc. (2008).

Zu-Hang Sheng. Editor of the textbook ***Cellular and Molecular Mechanisms of Neurotransmission***. Shanghai Science and Technology Press Inc. (2008).