BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Jiang, Youxing	Associate Professor of Physiology
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EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
Peking University, Beijing, China	B.S.	07/92	Chemistry
Yale University, New Haven, CT	Ph.D.	05/97	Biophysics
Rockefeller University, New York, NY	Postdoctoral	04/03	Molecular Neurobiology & Biophysics

A. Research Interests

Ion Channels and Transporters

The research of our laboratory has been focusing on the structural and functional studies of ion channels and transporters which control the flow of ions across the cell membrane. These proteins regulate many biological processes such as the excitation of nerve and muscle cells, the secretion of hormones, and sensory transduction. Our research approach is a combination of membrane protein X-ray crystallography, aimed at determining the three dimensional structure of the ion transporting proteins, and channel electrophysiology, to study the physiological functions of these proteins.

Ion Channels

Ion channels are membrane proteins which, in a regulated fashion, open a hole in the lipid membrane and allow the free diffusion of ions down their electrochemical gradients. Two fundamental properties are central to ion channel function: ion selectivity, whereby only the passage of specific ions is allowed through the channel pore; and channel gating, where the opening and closing of the channel pore is regulated in response to a specific stimulus. The research in our lab aims to understand the molecular mechanisms of both channel selectivity and gating in tetrameric cation channels, which comprise the single largest family of ion channels. In these channels, four membrane-spanning subunits or domains form a central pore through which specific ions cross the cell membrane.

To study channel gating, the lab focuses on a group of ligand gated K^+ channels that are regulated by a conserved ligand binding domain, the RCK domain. This group includes the majority of prokaryotic K^+ channels and the eukaryotic high-conductance Ca^{2+}-gated K^+ channels (BK or maxiK). Three RCK-regulated K^+ channels are being used as model systems for studying ligand specificity and ligand-induced conformational changes in K^+ channels: MthK, a Ca^{2+}-gated K^+ channel from *Methanobacterium thermoautotrophicum*; GsuK, a nucleotide-gated Ca^{2+} inhibited K^+ channel from *Geobacter sulfurreducens*; and the human high conductance Ca^{2+}-gated BK channel (hSlo1).

The other goal of our research is to understand the structural basis of ion selectivity in tetrameric cation channels using the NaK channel, a non-selective prokaryotic cation channel from *Bacillus cereus*, as the model system. Taking advantage of the extremely high-resolution crystal structures of NaK and its mutants representing the ion conduction pores of both selective and non-selective cation channels, we aim to elucidate the basic principles of ion selectivity in two families of physiologically essential cation channels. One is the non-selective, Ca^{2+} permeable cyclic nucleotide-gated (CNG) channels, whose functions are central to signal transduction in the visual and olfactory sensory systems, using NaK from *Bacillus cereus* and its CNG-mimicking chimeras as model systems. The other is the K^+ selective channel family, using a K^+ selective NaK mutant (NaK2K) and the MthK K^+ channel from *Methanobacterium thermoautotrophicum* as model systems.

Ion Transporters

Different from ion channels, ion transporters can move ions across the plasma membrane against the electrochemical gradient. The study on ion transporters in the lab has been focused on Na^+/Ca^{2+} exchangers and will soon be expanded to other cation transporters.

Na^+/Ca^{2+} exchangers (NCX) are crucial membrane transporters in maintaining the homeostasis of cytosolic Ca^{2+} for cell signaling essential for many physiological processes including muscle contraction, cell mobility, fertilization, exocytosis, and apoptosis. NCX proteins extrude intracellular Ca^{2+} across the cell membrane against its chemical gradient by utilizing the downhill gradient of Na^+. Several functional features of NCX define its physiological roles: it can exchange Ca^{2+} and Na^+ with a high turnover rate; the ion exchange process is electrogenic with a stoichiometry of 3 Na^+ for 1 Ca^{2+}; and the exchange reaction is bi-directional depending on the membrane potential and the chemical gradient of Na^+ and Ca^{2+}. Despite a large body of functional data, the structural mechanism underlying these unique functional features remains elusive. With the determination of a high resolution structure of an NCX protein from *Methanococcus jannaschii* (NCX_Mj), we now have a working model system to elucidate the structural basis and mechanistic details of ion exchange in NCX proteins.

B. Positions and Honors.

Positions and Employment

1992-1994	Teaching Assistant, Department of Chemistry, Yale University
1994-1997	Research Assistant, Department of Molecular Biophysics & Biochemistry, Yale University Mentor: Paul B. Sigler
1997-2003	Research Associate, HHMI, Rockefeller University Mentor: Roderick MacKinnon
2003-2008	Assistant Professor, Department of Physiology, University of Texas Southwestern Medical Center at Dallas
2008 -	Associate Professor, Department of Physiology, University of Texas Southwestern Medical Center at Dallas
2008 -	Investigator, Howard Hughes Medical Institute

Honors

2003	W.W. Caruth, Jr. Scholar in Biomedical Research, University of Texas Southwestern Medical Center at Dallas, TX
2004	Searle Scholar
2004	David and Lucile Packard Fellowship
2006	McKnight Scholar Award for Neuroscience
2008	Investigator, Howard Hughes Medical Institute

C. Peer-reviewed publications (in chronological order).

1. Jiang Y, Nock S, Nesper M, Sprinzl M and Sigler PB (1996). Structure and importance of the dimerization domain in elongation factor Ts from *Thermus thermophilus.* ***Biochemistry*** 35:10269-78.

2. Wang Y, Jiang Y, Meyering-Voss M, Sprinzl M and Sigler PB (1997). Crystal structure of the EF-Tu·EF-Ts complex from *Thermus thermophilus.* ***Nature Structural Biology*** 4:650-6.

3. Jiang Y, and MacKinnon R (2000). The barium site in a potassium channel by X-ray crystallography. ***J Gen Physiol*** 115:269-72.

4. Jiang Y, Pico A, Cadene M, Chait BT and MacKinnon R (2001). Structure of the RCK domain from the *E.coli* K+ channel and demonstration of its presence in the human BK channel. ***Neuron*** 29:593-601.

5. Jiang Y, Lee A, Chen J, Cadene M, Chait BT and MacKinnon R (2002). Crystal structural and mechanism of a calcium-gated potassium channel ***Nature*** 417:515-22.

6. Jiang Y, Lee A, Chen J, Cadene M, Chait BT and MacKinnon R (2002). Open conformation of potassium channel.. ***Nature*** 417:523-6.

7. Ruta V, Jiang Y, Lee A, Chen J and MacKinnon R (2003). Functional analysis of an archaebacterial voltage-dependent K^+ channel. ***Nature*** 422:180-5.

8. Jiang Y, Lee A, Chen J, Ruta V, Cadene M, Chait BT and MacKinnon R (2003). X-ray structure of a voltage-dependent K^+ channel. ***Nature*** 423:33-41.

9. Jiang Y, Ruta V, Chen J, Lee A and MacKinnon R (2003). The principle of gating charge movement in a voltage-dependent K^+ channel. ***Nature*** 423:42-8.

10. Dong J, Shi N, Berke I, Chen L & Jiang Y (2005) "Structures of the MthK RCK Domain and the Effect of Ca^{2+} on Gating Ring Stability" ***J. Bio. Chem.*** 280: 41716-24.

11. Shi N, Ye S, Alam A, Chen L & Jiang Y (2006) "Atomic Structure of a Na^+ and K^+ Conducting Channel" ***Nature*** 440: 570-4.

12. Ye S, Li Y, Chen L & Jiang Y (2006) "Crystal Structures of a Ligand-free MthK Gating Ring: Insights into the Ligand Gating Mechanism of K^+ Channels" ***Cell*** 126, 1161-1173.

13. Li Y, Berke I, Chen L & Jiang Y(2007) "Gating and Inward Rectifying Properties of the MthK K^+ Channel with and without the Gating Ring" ***J. Gen Physiol***, 129:109-120.

14. Alam A, Shi N & Jiang Y (2007) "Structural Insight into Ca^{2+} Specificity in Tetrameric Cation Channels" ***Proc Natl Acad Sci U S A*** 104, 15334-15339.

15. Alam A & Jiang Y (2009) "High resolution structure of the open NaK channel" ***Nature Structural & Molecular Biology*** 16, 30-34. (Epub 2008 Dec 21.)

16. Alam A & Jiang Y (2009) "Structural Analysis of Ion Selectivity in the NaK Channel" ***Nature Structural & Molecular Biology*** 16, 35-41. (Epub 2008 Dec 21.)

17. Linn KM, Derebe MG, Jiang Y & Valiyaveetil FI (2010) "Semisynthesis of NaK, a Na^+ and K^+ Conducting Ion Channel" ***Biochemistry*** 49, 4450-4456. PMCID: PMC2889250 [Available on 2011/6/1]

18. Wu Y, Yang Y, Ye S & Jiang Y (2010) "Structure of the gating ring from the human large-conductance $Ca2^+$-gated K^+ channel" ***Nature*** 466, 393-7. Epub 2010 Jun 23.

19. Ye S, Li Y & Jiang Y (2010) "Novel insights into K^+ selectivity from high resolution structures of an open K^+ channel pore" ***Nature Structural & Molecular Biology*** 17, 1019-23. Epub 2010 Aug 1. PMCID: PMC2918291 [Available on 2011/2/1]

20. Dorwart MR, Wray R, Brautigam CA, Jiang Y & Blount P (2010) "S. aureus MscL Is a Pentamer In Vivo but of Variable Stoichiometries In Vitro: Implications for Detergent-Solubilized Membrane Proteins". ***PLoS Biol*** 8(12): e1000555. doi:10.1371/journal.pbio.1000555

21. Derebe MG, Sauer D, Zeng W, Alam A, Shi N and Jiang Y. (2011) "Tuning the Ion Selectivity of Tetrameric Cation Channels by Changing the Number of Ion Binding Sites". ***Proc Natl Acad Sci U S A.*** 108, 598-602. (Epub Dec. 27, 2010.)

22. Derebe MG, Zeng W, Li Y, Alam A and Jiang Y (2011) "Structural studies of ion permeation and Ca^{2+} blockage of a bacterial channel mimicking the cyclic nucleotide-gated channel pore". ***Proc Natl Acad Sci U S A.*** 108, 592-597. (Epub Dec. 27, 2010.)

23. Cao Y, Jin X, Huang H, Derebe MG, Levin EJ, Kabaleeswaran V, Pan Y, Punta M, Love J, Weng J, Quick M, Ye S, Kloss B, Bruni R, Martinez-Hackert E, Hendrickson WA, Rost B, Javitch J, Rajashankar KR, Jiang Y, & Zhou M. (2011) "Crystal structure of a potassium ion transporter TrkH". ***Nature*** 471, 336-340. (E.pub Feb 13, 2011)

24. Alam A & Jiang Y (2011) "Structural Studies of Ion Selectivity in Tetrameric Cation Channels" ***J. Gen Physiol***. 137, 397-403 (Perspectives)

25. Shi N, Zeng W, Ye S, Li Y & Jiang Y (2011) "Crucial Points within the Pore as Determinants of K+ Channel Conductance and Gating" ***J. Mol. Biol.*** 411, 27-35 (available online: 30-APR-2011 DOI information: 10.1016)

26. Sauer DB, Zeng W, Raghunathan S & Jiang Y (2011) "Protein Interactions Central to Stabilizing the K^+ Channel Selectivity Filter in a 4-sited Configuration for Selective K^+ Permeation" ***Proc Natl Acad Sci U S A*.** (Epub Sep. 20, 2011. doi:10.1073/pnas.1111688108)

D. Research Support

Ongoing Research Support

R01 GM079179 Jiang (PI) 9/1/2007 – 8/31/2012
NIH/NIGMS
Molecular Mechanism of Cation Channel Selectivity

Grant # I-1578 Jiang (PI) 6/1/2010 – 5/31/2013
The Welch Foundation
Structural and Functional Studies of RCK-regulated Potassium Channel

HHMI Investigator Jiang (PI) 7/1/2008 -
Howard Hughes Medical Institute

Completed Research Support

Endowed Scholar Jiang (PI) 5/1/2003 – 8/31/2006
UT Southwestern Medical Center

Searle Scholars 2004 Jiang (PI) 7/1/2004 – 6/30/2007
Searle Family Trust & Chicago Community Trust

McKnight Scholar Award for Neuroscience Jiang (PI) 7/1/2006 – 6/30/2008
The McKnight Foundation

David and Lucile Packard Fellowship Jiang (PI) 11/1/2004 – 10/31/2009
The David and Lucile Packard Foundation

1 R01 GM071621 Jiang (PI) 9/1/2004 – 8/31/2009
NIH/NIGMS
Mechanism of Ligand Gating in Potassium Channels

The Welch Foundation Jiang (PI) 6/1/2004 – 5/31/2010
The Welch Foundation
Structural and Functional Studies of the MthK Potassium Channel