

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Pan, Yaping

eRA COMMONS USER NAME (credential, e.g., agency login): yp2177

POSITION TITLE: Assistant Professor

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
School of Medicine, Fudan University, Shanghai, China	B.S.	06/1999	Pharmacology
Peking Union Medical College, Beijing, China	Ph.D.	06/2004	Neuropharmacology
Baylor College of Medicine, Houston, TX	Postdoc	09/2005	Neuroscience
Columbia University, New York, NY	Postdoc	04/2011	Physiology

A. Personal Statement

I am interested in structure and function of ion channels and transporters and seek to understand how these protein machines work at the molecular level. I have extensive trainings in physiology and biophysics, and I am proficient in various biochemical and biophysical approaches.

1. **Pan Y**, Weng J, Kabaleeswaran V, Li H, Cao Y, Bhosle R, Zhou M. Cortisone dissociates *Shaker* family K⁺ channels from their β subunits. **Nature Chemical Biology**, 4(11): 708-714. (2008)
2. **Pan Y**, Weng J, Levin EJ, Zhou M. Oxidation of NADPH inhibits ball-and-chain type inactivation by restraining the chain. **Proceedings of the National Academy of Sciences**, 108(14): 5885-5890. (2011)
3. Cao Y*, **Pan Y***, Huang H*, Jin X, Levin EJ, Kloss B, Zhou M. Gating of the TrkH ion channel by its associated RCK protein TrkA. **Nature**, 496(7445): 317-322. (2013) (* equal contribution)
4. Zhang H, **Pan Y**, Hu L, Hudson MA, Hofstetter KS, Xu Z, Rong M, Wang Z, Prasad BVV, Lockless SW, Chiu W, Zhou M. TrkA undergoes a tetramer-to-dimer conversion to open TrkH which enables changes in membrane potential. **Nature Communications**, 11(1):547. (2020)
5. **Pan Y**, Ren Z, Gao S, Shen J, Wang L, Xu Z, Yu Y, Bachina P, Zhang H, Fan X, Laganowsky A, Yan N, Zhou M. Structural basis of ion transport and inhibition in ferroportin. **Nature Communications**, 11(1):5686. (2020)

B. Positions and Honors**Positions and Employment**

04/2011-01/2013	Associate Research Scientist, Department of Physiology and Cellular Biophysics, Columbia University, New York, USA
02/2013-06/2014	Research Associate, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA
07/2014-05/2020	Instructor, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA
06/2020-present	Assistant Professor, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston, USA

Other Experience and Professional Memberships

2006- Member, Biophysical Society

C. Contributions to Science

1. I examined malfunction of K⁺ channels in the Alzheimer's disease during my graduate study. I discovered that the delayed rectifier K⁺ current from the Kv2.1 subtype increases significantly in the hippocampus neurons injected with A β protein, and I found that widely-used acetylcholinesterase inhibitors (rivastigmine and galantamine) inhibit K⁺ channels in hippocampal neurons. These studies indicate that K⁺ channels may play an important role in the pathogenesis of Alzheimer's disease, and that K⁺ channels could be a potential therapeutic target.

- a. **Pan Y**, Xu X, Wang X. Galantamine blocks delayed rectifier, but not transient outward potassium current in rat dissociated hippocampal pyramidal neurons, **Neuroscience Letters**, 336(1): 37-40. (2003)
- b. **Pan Y**, Xu X, Wang X. Rivastigmine blocks voltage-activated K⁺ currents in dissociated rat hippocampal neurons, **British Journal of Pharmacology**, 140(5): 907-912. (2003)
- c. **Pan Y**, Xu X, Tong X, Wang X. Messenger RNA and protein expression analysis of voltage-gated potassium channels in the brain of Abeta(25-35)-treated rats, **Journal of Neuroscience Research**, 77(1): 94-99. (2004)

2. As a postdoctoral fellow, I studied modulation of Kv1 channels by the associated Kv β subunit. I demonstrated that Kv β 1 is a functional aldo-keto reductase and that the enzymatic activity of Kv β modulates the N-type inactivation in Kv1 channels. These results demonstrated direct coupling between an oxidoreductase and ion channel activities and have important implications in cellular oxygen sensing and response to metabolic changes. I then showed that oxidation of a Kv β -bound cofactor NADPH potentiates channel activity, and that the potentiation comes from release of N-type inactivation. In a parallel project, I designed a high-throughput screen to identify molecules that bind to Kv β and I found that cortisone binds to Kv β and reduces channel inactivation. I then showed that cortisone and its analogs promote dissociation of Kv β from the channel, and providing a novel way of regulating Kv1 channels.

- a. **Pan Y**, Weng J, Cao Y, Bhosle R, Zhou M. Functional coupling between the Kv1.1 channel and an aldo-keto reductase Kv β 1. **Journal of Biological Chemistry**, 283(13): 8634-8642. (2008)
- b. **Pan Y**, Weng J, Kabaleeswaran V, Li H, Cao Y, Bhosle R, Zhou M. Cortisone dissociates *Shaker* family K⁺ channels from their β subunits. **Nature Chemical Biology**, 4(11): 708-714. (2008)
- c. **Pan Y**, Weng J, Levin EJ, Zhou M. Oxidation of NADPH inhibits ball-and-chain type inactivation by restraining the chain. **Proceedings of the National Academy of Sciences**, 108(14): 5885-5890. (2011)
- d. **Pan Y**, Levin EJ, Quick M, Zhou M. Potentiation of the Kv1 family K⁺ channel by cortisone analogues. **ACS Chemical Biology**, 7(10): 1641-1646. (2012)

3. When I finished the Kv1-Kv β project in 2011, the field of ion channel structure and function is transitioning rapidly towards solving structures of ion channels and using the structures as a starting point for developing further mechanistic studies. I started to learn membrane protein expression and purification and worked on a bacterial channel TrkH and a bacterial bile acid transporter. I worked on both the structural and functional aspects of the TrkH project, combining electrophysiology, X-ray crystallography, and more recently cryo-electron microscopy, to first demonstrate that TrkH is an ion channel gated by ATP and ADP, and that the gating is achieved by conformational changes in the attached TrkA protein.

- a. Cao Y*, **Pan Y***, Huang H*, Jin X, Levin EJ, Kloss B, Zhou M. Gating of the TrkH ion channel by its associated RCK protein TrkA. **Nature**, 496(7445): 317-322. (2013) (* equal contribution)
- b. Zhang H, **Pan Y**, Hu L, Hudson MA, Hofstetter KS, Xu Z, Rong M, Wang Z, Prasad BVV, Lockless SW, Chiu W, Zhou M. TrkA undergoes a tetramer-to-dimer conversion to open TrkH which enables changes in membrane potential. **Nature Communications**, 11(1):547. (2020)

4. I have participated in a number of membrane protein structure and function projects and made significant contributions.

- a. Zhou X*, Levin EJ*, **Pan Y**, McCoy JG, Sharma R, Kloss B, Bruni R, Quick M, Zhou M. Structural basis of the alternating-access mechanism in a bile acid transporter. **Nature**, 505(7484): 569-573. (2014) (* equal contribution)
- b. Huang S, Balgi A, **Pan Y**, Li M, Zhang X, Du L, Zhou M, Roberge M, Li X. Identification of methylosome components as negative regulators of plant immunity using chemical genetics. **Molecular Plant**, 9(12):1620-1633. (2016)
- c. Zhang H, **Pan Y**, Hu L, Hudson MA, Hofstetter KS, Xu Z, Rong M, Wang Z, Prasad BVV, Lockless SW, Chiu W, Zhou M. TrkA undergoes a tetramer-to-dimer conversion to open TrkH which enables changes in membrane potential. **Nature Communications**, 11(1):547. (2020)
- d. Zheng X, Fu Z, Su D, Zhang Y, Li M, **Pan Y**, Li H, Li S, Grassucci R, Ren Z, Hu Z, Li X, Zhou M, Li G, Frank, J, Yang J. Mechanism of ligand activation of a eukaryotic cyclic nucleotide-gated channel. **Nature Structural & Molecular Biology**, 27(7):625-634. (2020)
- e. **Pan Y**, Ren Z, Gao S, Shen J, Wang L, Xu Z, Yu Y, Bachina P, Zhang H, Fan X, Laganowsky A, Yan N, Zhou M. Structural basis of ion transport and inhibition in ferroportin. **Nature Communications**, 11(1):5686. (2020)

Complete List of Published Work in MyBibliography:

<https://pubmed.ncbi.nlm.nih.gov/collections/59665745/?sort=date&direction=ascending>

D. Additional Information: Research Support and/or Scholastic Performance

Complete Research Support

0826067D

Pan (PI)

07/01/2008-06/30/2010

AHA

Kvbeta subunit as a target for novel modulators of voltage-dependent Shaker family K channels

The goal of this project is to identify a discrete binding site on Kvbeta that can be targeted for modulation of Kv1 channels.

Role: PI

Current Research Support

1 R01 HL157473-01 Pan (PI)

05/01/2021 – 04/30/2025

NIH/NHLBI

Structure and Mechanism of Mammalian Ferroportin

The major goal of this project is to understand the mechanism of iron transport in ferroportin and its inhibition by hepcidin.

Role: PI