

## Panpan Hou, Ph.D.

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### Education, Training, and Position:

- 2005-2009 B.S. (Biomedical Engineering),  
Huazhong University of Science and Technology, Wuhan, China.
- 2009-2014 PhD. (Biophysics),  
Huazhong University of Science and Technology, Wuhan, China.
- 2014-2020 Postdoc (Biomedical Engineering),  
Washington University in St. Louis, US
- 2021-present Assistant Professor,  
Macau University of Science and Technology, Macao, China

### Contribution to Science

#### 1. VSD-pore coupling mechanism of ion channel voltage-dependent activation.

Among the three major molecular steps in voltage-dependent activation of an ion channel (VSD activation, VSD-pore coupling, and pore opening), the VSD-pore coupling is much less understood than the other two, due to the lack of powerful tools. Using voltage clamp fluorometry, pharmacology, and kinetic modeling, I systematically studied the VSD-pore coupling mechanism of the Kv7.1 (KCNQ1) potassium channel, and proposed a “Hand-and-elbow” mechanism that is well conserved among both voltage- and ligand-gated ion channels. (*Hou, et al. Nature Communications. 2020; Hou, et al. eLife. 2019; Hou, et al. Nature Communications. 2017; Taylor#, Kang#, Hou#, et al. eLife. 2020*)

#### 2. Physiology and drug screening of ion channels.

Ion channels can be modulated by various molecules and messengers (Ca<sup>2+</sup>, cAMP, PIP<sub>2</sub>, exogenous compounds, etc.) as well as tissue-specific auxiliary subunits. All these modulations together shape and largely diversify the ion channel functions, meanwhile also provide possibilities to develop new drugs for treating major human disease. Using electrophysiological tools with clinical data analysis, I elucidated the cAMP/PKA-dependent phosphorylation of cardiac KCNQ1+KCNE1 (IKs) channels; Using Ca<sup>2+</sup> uncaging technique, I measured the Ca<sup>2+</sup> binding rate of BK channels; and we also identified new compounds that can effectively modulate ion channels (*Zhong, Yan et al. Circ Res. 2024; Yan et al. Pharmacol Res. 2023; Ma, Zhong et al. PNAS. 2022; Hou et al., Scientific Reports. 2013, 2016; Liu\*, Hou\*, Guo\* et al. J. Biol. Chem. 2014*)

### Selected Publications:

1. Ling Zhong#, Zhenzhen Yan#, Dexiang Jiang, Kuo-Chan Weng, Yue Ouyang, Hangyu Zhang, Xiaoqing Lin, Chenxin Xiao, Huaiyu Yang, Jing Yao, Xinjiang Kang, Changhe Wang, Chen Huang, Bing Shen, Sookja Kim Chung, Zhi-Hong Jiang, Wandi Zhu, Erwin Neher, Jonathan R Silva\*, **Panpan Hou\***. Targeting the IKs Channel PKA Phosphorylation Axis to Restore Its Function in High-Risk LQT1 Variants. *Circulation*

- Research.** 2024 Sep 13;135(7):722-738.
2. **Panpan Hou\***, Lu Zhao, Ling Zhong, Jingyi Shi, Hong Zhan Wang, Junyuan Gao, Huilin Liu, Joan Zuckerman, Ira S Cohen, Jianmin Cui\*. The fully activated open state of KCNQ1 controls the cardiac “fight-or-flight” response. **PNAS Nexus**. 2024 Oct 9;3(10).
3. Zhenzhen Yan#, Ling Zhong#, Wandu Zhu, Sookja Kim Chung, **Panpan Hou\***. Chinese herbal medicine for the treatment of cardiovascular diseases — targeting cardiac ion channels. **Pharmacological Research**. 2023. 106765.
4. Demin Ma#, Ling Zhong#, Zhenzhen Yan, Jing Yao, Yan Zhang, Fan Ye, Yuan Huang, Dongwu Lai, Wei Yang\*, **Panpan Hou\***, Jiangtao Guo\*. Structural mechanisms for the activation of human cardiac KCNQ1 channel by electro-mechanical coupling enhancers. **PNAS**. 2022. 119(45).
5. **Panpan Hou**, Po Wei Kang, Audrey Deyawe Kongmeneck, Nien-Du Yang, Yongfeng Liu, Jingyi Shi, Xianjin Xu, Kelli McFarland White, Mark A. Zaydman, Marina A. Kasimova, Guiscard Seeböhm, Ling Zhong, Xiaoqin Zou, Mounir Tarek\*, and Jianmin Cui\*. Two-stage electro-mechanical coupling of a Kv channel in voltage-dependent activation. **Nature Communications**. 2020; 11: 676.
6. **Panpan Hou**, Jodene Eldstrom, Jingyi Shi, Ling Zhong, Kelli McFarland, Yuan Gao, David Fedida, Jianmin Cui\*. Inactivation of KCNQ1 potassium channels reveals dynamic coupling between voltage sensing and pore opening. **Nature Communications**. 2017. 8(1):1730.
7. **Panpan Hou**, Jingyi Shi, Kelli McFarland White, Yuan Gao, Jianmin Cui\*. ML277 specifically enhances the fully activated open state of KCNQ1 by modulating VSD-pore coupling. **eLife**. 2019. Jul 22;8.
8. Keenan C. Taylor#, Po Wei Kang#, **Panpan Hou#**, Nien-Du Yang, Georg Kuenze, Jarrod A. Smith, Jingyi Shi, Hui Huang, Kelli McFarland White, Dungeng Peng, Alfred L. George Jr., Jens Meiler, Robert L. McFeeters, Jianmin Cui\*, and Charles R. Sanders\*. Structure and Physiological Function of the KCNQ1 Channel Voltage Sensor Intermediate State. **eLife**. 2020. Feb 24;2.
9. **Panpan Hou\***, Xiaona Du\*, Hailong An\*. Ion Channels: Therapeutic Targets for Neurological Disease. **Frontiers in Molecular Neuroscience**. 2021.
10. **Panpan Hou#**, Feng Xiao#, Haowen Liu#, Ming Yuchi#, Guohui Zhang, Ying Wu, Wei Wang, Wenping Zeng, Mingyue Ding, Jianmin Cui, Zhengxing Wu\*, Lu-Yang Wang\* and Jiuping Ding\*. Extrapolating microdomain  $\text{Ca}^{2+}$  dynamics using BK channels as a  $\text{Ca}^{2+}$  sensor. **Scientific Reports**. 2016. 6:17343.
11. Zhenzhen Yan#, Bin Hu#, Xiying Guo, Anxi Weng, Ling Zhong, Feng Xiao, Jiuping Ding\*, and **Panpan Hou\***. Single Channel Recordings Reveal Differential  $\beta 2$  Subunit Modulations Between Mammalian and *Drosophila* BK<sub>Ca</sub>( $\beta 2$ ) Channels. **PLoS ONE**. 2016: e0163308.
12. Haowen Liu#, **Panpan Hou#**, Xiying Guo#, Zhiwen Zhao, Bin Hu, Xia Li, Lu-Yang Wang, Jiuping Ding\*, Sheng Wang\*. Structural Basis for Calcium and Magnesium Regulation of a Large Conductance Calcium-Activated Potassium Channel with  $\beta 1$  Subunits. **J. Biol. Chem**. 2014. 289:16914-16923.
13. **Panpan Hou#**, Rong Zhang#, Yongfeng Liu#, Jing Feng, Wei Wang, Yingliang Wu\* and Jiuping Ding\*. Physiological role of Kv1.3 channel in T lymphocyte cell investigated quantitatively by kinetic modeling. **PLoS ONE**. 2014. e89975.
14. Wei Wang#, Jie Luo#, **Panpan Hou#**, Yimei Yang, Feng Xiao, Ming Yuchi, Anlian Qu, Lu-Yang Wang\*, Jiuping Ding\*. Native gating behavior of ion channels in neurons with null-deviation modeling. **PLoS ONE**. 2013. e77105.
15. **Panpan Hou#**, Wenping Zeng#, Geliang Gan#, Caixia Lv#, Xiying Guo, Zheng Zhang, Haowen Liu, Ying Wu, Jing Yao, Aguan D. Wei, Sheng Wang\*, Jiuping Ding\*. Inter- $\alpha/\beta$  subunits coupling mediating pre-inactivation and augmented activation of BKCa( $\beta 2$ ). **Scientific Reports**. 2013. 3:1666.

16. Junnan Li, Zhenni Yang, Shaoying Zhang, Yangliang Ye, Jiangnan He, Yan Zhang, Huayun Han, Wan Kong, Jiangru Liu, Yu Min, Juwen Shen, Lianghe Mei, Zongsheng Chen, Panpan Hou, Jiangtao Guo, Qiansen Zhang & Huaiyu Yang\*. Small molecule inhibits KCNQ channels with a non-blocking mechanism. **Nature Chemical Biology**. 2025.(5)3874.
17. Shaoying Zhang, Demin Ma, Kun Wang, Ya Li, Zhenni Yang, Xiaoxiao Li, Junnan Li, Jiangnan He, Lianghe Mei, Yangliang Ye, Zongsheng Chen, Juwen Shen, **Panpan Hou**, Jiangtao Guo, Qiansen Zhang, Huaiyu Yang\*. A small-molecule activation mechanism that directly opens the KCNQ2 channel. **Nature Chemical Biology**. 2024.(3)7265.
18. Demin Ma, Yueming Zheng, Xiaoxiao Li, Xiaoyu Zhou, Zhenni Yang, Yan Zhang, Long Wang, Wenbo Zhang, Jiajia Fang, Guohua Zhao, **Panpan Hou**, Fajun Nan, Wei Yang, Nannan Su, Zhaobing Gao, Jiangtao Guo. Ligand activation mechanisms of human KCNQ2 channel. **Nature Communications**. 2023 14:6632
19. Julian A. Schreiber, Melina Möller, Mark Zaydman, Lu Zhao, Zachary Beller, Sebastian Becker, Nadine Ritter, **Panpan Hou**, Jingyi Shi, Jon Silva, Eva Wrobel, Nathalie Strutz-Seeböhm, Niels Decher, Nicole Schmitt, Sven G. Meuth, Martina Düfer, Bernhard Wünsch, Jianmin Cui, and Guiscard Seeböhm. A benzodiazepine activator locks Kv7.1 channels open by electro-mechanical uncoupling. **Communications Biology**. 2022. 5:3
20. Yangyang Lin#, Sam Z. Grinter#, Zhongju Lu#, Xianjin Xu#, Hong Zhan Wang, Hongwu Liang, **Panpan Hou**, Junyuan Gao, Chris Clausen, Jingyi Shi, Wenshan Zhao, Zhiwei Ma, Yongfeng Liu, Kelli McFarland White, Lu Zhao, Po Wei Kang, Guohui Zhang, Ira S. Cohen\*, Xiaoqin Zou\* & Jianmin Cui\*. Modulating the voltage sensor of a cardiac potassium channel shows antiarrhythmic effects. **PNAS**. 2021 May 18;118(20).
21. Yongfeng Liu#, Xianjin Xu#, Junyuan Gao#, Moawiah M. Naffaa, Hongwu Liang, Jingyi Shi, Hong Zhan Wang, Nien-Du Yang, **Panpan Hou**, Wenshan Zhao, Ira S. Cohen\*, Xiaoqin Zou\*, Jianmin Cui\*. A PIP2 substitute mediates voltage sensor-pore coupling in KCNQ activation. **Communications Biology**. 2020 Jul 16;3(1):385.
22. Wandu Zhu, Andrea Mazzanti, Taylor L. Vwoelker, **Panpan Hou**, Jonathan D. Moreno, Paweorn Angsutrarux, Kristen M. Naegle, Silvia G. Priori, Jonathan R. Silva\*. Predicting Patient Response to the Antiarrhythmic Mexiletine Based on Genetic Variation: Personalized Medicine for Long QT Syndrome. **Circulation Research**. 2018. 124(4):539-552.
23. Mark Zaydman, Marina Kasimova, Kelli McFarland, Zachary Beller, **Panpan Hou**, Holly E Kinser, Hongwu Liang, Guohui Zhang, Jingyi Shi, Mounir Tarek, Jianmin Cui\*. Domain–domain interactions determine the gating, permeation, pharmacology, and subunit modulation of the IKs ion channel. **eLife**. 2014. 3:e03606.
24. Rui Liu#, Zheng Zhang#, Huan Liu#, **Panpan Hou**, Jun Lang, Sheng Wang, Hongli Yan, Pengcheng Li, Zhigang Huang, Hongbing Wu, Mingqiang Rong, Jian Huang, Hong Wang, Longbao Lv, Mingfeng Qiu, Jiuping Ding\*, Ren Lai\*. Human beta-defensin 2 is a novel opener of Ca<sup>2+</sup>-activated potassium channels and induces vasodilation and hypotension in monkeys. **Hypertension**. 2013. 62:415-425.
25. Jie Luo, **Panpan Hou**, Jiuping Ding, and Anlian Qu\*. Kernel Based Non-Iterative Automatic Fast Capacitance Compensation in Patch-Clamp Experiments. **Cellular and Molecular Bioengineering**. 2012. 5:440-449.

#### Awards:

- 2007 Outstanding Youth League in HUST
- 2008 Outstanding Student Leader scholarship in HUST
- 2010 Early Investigator Award, Calcium Signaling Conference (Biophysical Society).
- 2010 Merit Predoctoral Student, Huazhong University of Science and Technology, China.
- 2013 National Predoctoral Scholarship, Ministry of Education, China.
- 2014 Early Investigator Award, HUST, China.

2018 AHA Postdoctoral Fellowship Award (2018-2020)  
2018 Best Poster Award (The 2<sup>nd</sup> Membrane Protein Physiology and Drug Development)  
2018 Best Poster Award (The 12<sup>th</sup> International Symposium on Calcium Signaling)  
2025 Best Research Output award in Macau University of Science and Technology

**Membership and academic contribution:**

Committee Member of Neurobiology Branch of Chinese Biophysical Society,  
Committee Member of Ion Channel and Receptor Branch of Chinese Society of Neuroscience

*The Innovation* Youth Editor (IF=25.3, Q1),

*Pharmacological Research* Editor (IF=10.3, Q1)

*Frontiers in Molecular Neuroscience* Review Editor (IF=6.2, Q2),

Biophysical Society since 2010;

American Heart Association since 2015;

Society for Neuroscience 2019;

Member of the JGP postdoctoral training program.

Reviewer for *eLife*, *Journal of General Physiology*, *Journal of Molecular and Cellular Cardiology*, *Molecular Pharmacology*, *Scientific Reports*, *BBA Biomembranes*, *International Journal of Molecular Sciences*, *Computers in Biology and Medicine*, etc.

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- 3) 2023/01/01-2025/12/31  
FDCT-MOST project  
Funding #: 0006/2021/AMJ  
Role: Principal Investigator
- 4) 2023/01/01-2025/12/31  
FDCT project  
Funding #: 0074/2022/A2  
Role: Principal Investigator
- 5) 2023/08/01-2024/07/31  
MUST FRG project  
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Role: Principal Investigator
- 6) 2024/01/01-2026/12/31  
FDCT project  
Funding #: 0098/2023/RIA2  
Role: Principal Investigator