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Education and Training:

2005.09-2009.06 B.S. (Biomedical Engineering),
Huazhong University of Science and Technology (HUST), Wuhan, China.

2009.06-2014.06 PhD. (Biophysics), Supervisor: Prof. Jiuping Ding
Huazhong University of Science and Technology (HUST), Wuhan, China.

2014.08-2020.12 Postdoc (Biomedical Engineering), Supervisor: Prof. Jianmin Cui
Washington University in St. Louis, US

Contribution to Science

1. **VSD-pore coupling mechanism of 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 less understood than the other two despite decades of intensive studies, due to the lack of powerful tools. Using voltage clamp fluorometry, pharmacology, and kinetic modeling, I systematically study the VSD-pore coupling mechanism of KCNQ1 potassium channels during voltage-dependent activation. The studies determined a new pharmacological tool and revealed a two-stage VSD-pore coupling, which we named as Hand-and-elbow mechanism. This fundamental gating mechanism advances the understanding of how ion channel works, and it 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 pathology of ion channels.** Ion channels can be modulated by varies molecules and messengers (Ca2+, cAMP, PIP2 etc.) as well as tissue-specific auxiliary subunits. All these modulations together shape and largely diverse the ion channel functions. Problems with any of these modulations can lead to serious diseases. My studies on BK potassium channels answered several long-standing but fundamental gating and modulation questions: Using Ca2+ uncaging technique, our studies experimentally measured the Ca2+ binding rate and demonstrated that BK channel can serve as a Ca2+ sensor to probe the local calcium signaling during neuron firing; We also systematically studied inter- / subunits coupling of BK channels, and determined mechanisms of pre-inactivation and augmented-activation, which has puzzled the field for decades. (*Ma and Zhong et al.* ***PNAS.*** *2022;* ***Hou*** *et al.,* ***Scientific Reports.*** *2013;* ***Hou*** *et al.* ***Scientific Reports****. 2016; Liu*,* ***Hou*****, Guo* et al.* ***J. Biol. Chem.*** *2014; Yan et al. Ding[#], and* ***Hou[#]****.* ***PLoS ONE.*** *2016*)

3. **Ion channel drug screening and precision medicine.** Ion channel is becoming the most important drug target. My solid training in ion channel biophysics facilitates drug development targeting ion channels. I systematically investigate the pathology of ion channel associated diseases in native cells including human T- Lymphocyte, DRG neuron, ventricular myocyte, and patient-specific iPSC derived cardiomyocyte: We built up a cell

model of human T-lymphocyte, which provides a simple platform for studying Ca^{2+} signaling during T cell activation; We found that TRPV1 channels are functionally coupled with BK channels in DRG neurons, forming a negative feedback for pain processing; We also identified new modulators targeting BK potassium and Nav1.5 sodium channels for hypertension and arrhythmia. My new strategy for manipulating the KCNQ1 channel as a target for arrhythmia was funded by AHA. (***Hou*** *et al.. **PLoS ONE.** 2014; Wu*, Liu*,* ***Hou***** et al. **PLoS ONE.** 2013; Wang*, Luo*,* ***Hou***** et al. **PLoS ONE.** 2013; Liu et al. **Hypertension.** 2013*)

Publications:

1. 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).
2. **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 Seebohm, Ling Zhong, Xiaoqin Zou, Mounir Tarek*, and Jianmin Cui*. Two-stage electro-mechanical coupling of a K_V channel in voltage-dependent activation. ***Nature Communications*****.** 2020; 11: 676.
3. **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.
4. **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.
5. 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.
6. **Panpan Hou*,** Xiaona Du*, Hailong An*. Ion Channels: Therapeutic Targets for Neurological Disease. ***Frontiers in Molecular Neuroscience.*** 2021.
7. **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 Ca^{2+} dynamics using BK channels as a Ca^{2+} sensor. ***Scientific Reports***. 2016. 6:17343.
8. Zhenzhen Yan#, Bin Hu#, Xiying Guo, Anxi Weng, Ling Zhong, Feng Xiao, Jiuping Ding*, and **Panpan Hou***. Single Channel Recordings Reveal Diffe Subunit Modulations Between Mammalian and *Drosophila* BK_{Ca} . ***PLoS ONE.*** 2016: e0163308.
9. 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 1 Subunits. ***J. Biol. Chem.*** 2014. 289:16914-16923.
10. **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.
11. Ying Wu#, Yongfeng Liu#, **Panpan Hou**#**,** Zonghe Yan, Wenjuan Kong，Beiying Liu, Xia Li, Jing Yao, Yuexuan Zhang, Feng Qin* and Jiuping Ding*. TRPV1 channels are functionally coupled with BK(mSlo1) channels in rat dorsal root ganglion (DRG) neurons. ***PLoS ONE.*** 2013. e78203.
12. 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.

13. **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- / subunits coupling mediating pre-inactivation and augmented activation of BKCa(2). ***Scientific Reports.*** 2013. 3:1666.
14. 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-Seebohm, Niels Decher, Nicole Schmitt, Sven G. Meuth, Martina Düfer, Bernhard Wünsch, Jianmin Cui, and Guiscard Seebohm. A benzodiazepine activator locks Kv7.1 channels open by electro-mechanical uncoupling. ***Communications Biology***. 2022. 5:301.
15. 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).
16. 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):385.0 g0( )-41(Jian)4(m)]TJETQq0.0

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 2nd Membrane Protein Physiology and Drug Development)
2018 Best Poster Award (The 12th International Symposium on Calcium Signaling)
2019 Co-Chai tory mec or the Biophysical Society 63th annual meeting at Baltimore.
2021 Member of the Neurobiophysics of the Chinese Biophysical Society
2022 Co-Chai International Ion channel conference at Wuhan, China.

Membership and academic contribution:

Biophysical Society since 2010;
American Heart Association since 2015;
Society for Neuroscience 2019;
Member of the JGP postdoctoral training program.
Review Editor of *Frontiers in Molecular Neuroscience* (IF=6.2),
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.

Research Funding Support

2018/07/01-2020/06/30 Hou, Panpan Total: $111,636
American Heart Association Postdoctoral Fellowship
Funding #: 18POST34030203
Title: The AO state of KCNQ1 potassium channel can be a new anti-arrhythmic drug target.
Role: Principal Investigator.

2022/01/01-2025/12/31 Hou, Panpan Total: ￥580,000
National Natural Science Foundation of China (General Program)
Funding #: 3217110103
Title: Molecular mechanism underlying the phosphorylation of IKs channels.
Role: Principal Investigator.

2023/01/01-2025/12/31 Hou, Panpan Total: MOP 2,119,000
FDCT-MOST project
Funding #: 0006/2021/AMJ
Title: Discovery of KCNQ5 channel selective modulators and their function in the treatment of epilepsy and other neuropsychiatric diseases.
Role: Principal Investigator.

2023/01/01-2025/12/31 Hou, Panpan Total: MOP 1,600,000
FDCT project
Funding #: 0074/2022/A2
Title: Investigating the molecular mechanism of KCNQ1 mutants-induced high-risk heart disease and developing new therapeutics from Traditional Chinese Medicine.
Role: Principal Investigator.