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: XU, PEIYU

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

POSITION TITLE: Postdoctoral scholar

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
Jilin University, Changchun, China	BS	07/2015	Pharmaceutical Engineering
Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, Shanghai, China	PHD	05/2021	Pharmacology
Broad Institute of MIT and Harvard	Postdoctoral		Gene Engineering and Structural Biology

A. Personal Statement

As a postdoctoral scholar at the Broad Institute of MIT and Harvard, my focus is on advancing structural biology and genetic engineering through innovative research. My academic journey began with a solid foundation in Pharmaceutical Engineering at Jilin University, followed by a Ph.D. in Pharmacology from the Shanghai Institute of Materia Medica, University of Chinese Academy of Sciences, under the guidance of H. Eric Xu. During my doctoral studies, I made significant contributions to elucidating the structural basis of G protein-coupled receptors (GPCRs) and their interactions with ligands, contributing to our understanding of serotonin and dopamine receptor signaling complexes. In my current postdoctoral research at the McGovern Institute for Brain Research at MIT and the Broad Institute, I integrate structural biology with neuroscience to uncover new insights into brain function and therapeutic targets. Under the mentorship of Feng Zhang, I combine my expertise in structural biology with genetic engineering to investigate complex biological systems, including eukaryotic RNA-guided endonuclease systems. Beyond research, I am passionate about scientific communication and mentorship, as demonstrated by my recognition as an Outstanding Lecturer at the East China Structural Biology Conference and my involvement in mentoring graduate students and young researchers. Looking ahead, I am committed to leveraging my expertise in structural biology and bioengineering to address fundamental questions in science. My goal is to contribute to transformative research that bridges basic science with clinical applications, thereby improving human health and advancing our understanding of biological systems.

B. Positions, Scientific Appointments, and Honors

Positions and Scientific Appointments

2022 – Postdoctoral Scholar, Broad Institute of MIT and Harvard and McGovern Institute for Brain Research at MIT, Supervisor: Feng Zhang
2021 – 2022 Special Research Assistant, Shanghai Institute of Materia Medica, Chinese Academy of Sciences

Honors

2021 Member of the Youth Innovation Promotion Association, Chinese Academy of Sciences
2021 Presidential Award from the Chinese Academy of Science (Award to 1/1000 graduates)
2021 Shanghai Outstanding Graduate Award
2021 Outstanding Lecturer Award of the 8th East China Structural Biology Conference
2019 Merit Student of the University of Chinese Academy of Sciences
2015 Scholarship of Jilin University
2014 Silver Medal of International Genetically Engineered Machine (iGEM)
2014 Silver Award in the Biomedical Entrepreneurship Competition for College Students in Jilin Province
2013 Outstanding Student of the School of Life Sciences, Jilin University
2013 Scholarship of Jilin University

C. Contributions to Science

In the field of G-protein coupled receptor and drug development, I have made significant contributions by elucidating the structures of over 30 GPCRs, with extensive focus on serotonin and dopamine receptor families. This research is pivotal for advancing drug development for conditions such as schizophrenia, depression, and Parkinson's disease. Additionally, I pioneered the structural elucidation of various glycoprotein hormone receptor signaling complexes, guiding drug development efforts targeting reproductive system disorders. These achievements are highlighted in several impactful publications: (* denote co-first authors)

1. **Xu P***, Huang S*, Zhang H*, Mao C*, Zhou XE*, Cheng X*, Simon IA, Shen DD, Yen HY, Robinson CV, Harpsøe K, Svensson B, Guo J, Jiang H, Gloriam DE, Melcher K, Jiang Y, Zhang Y, and Xu HE. Structural insights into the lipid and ligand regulation of serotonin receptors. *Nature* (2021).
2. **Xu P***, Huang S*, Mao C*, Krumm BE*, Zhou XE*, Tan Y, Huang XP, Liu Y, Shen DD, Jiang Y, Yu X, Jiang H, Melcher K, Roth BL, Cheng X, Zhang Y, and Xu HE. Structures of the human dopamine D3 receptor-Gi complexes. *Molecular Cell* (2021).
3. **Xu P***, Huang S*, Guo S*, Yun Y*, Cheng X, He X, Cai P, Lan Y, Zhou H, Jiang H, Jiang Y, Xie Xin, and Xu HE. Structural identification of lysophosphatidylcholines as activating ligands for orphan receptor GPR119. *Nature Structural & Molecular Biology* (2022).
4. **Xu P***, Huang S*, Krumm BE*, Zhuang Y*, Mao C*, Zhang Y, Wang Y, Huang XP, Liu YF, He X, Li H, Yin W, Jiang Y, Zhang Y, Roth BL, Xu HE. Structural Genomics of the Human Dopamine Receptor System. *BioRxiv* (2022).
5. Duan J*, **Xu P***, Luan X*, Ji Y, He X, Song N, Yuan Q, Jin Y, Cheng X, Jiang H, Zheng J, Zhang S, Jiang Y, and Xu HE. Hormone-and antibody-mediated activation of the thyrotropin receptor. *Nature* (2022).
6. Yin W*, Xu Y*, **Xu P***, Cao X*, Wu C*, Gu C*, He X, Wang X, Huang S, Yuan Q, Wu K, Hu W, Huang Z, Liu J, Wang Z, Jia F, Xia K, Liu P, Wang X, Song B, Zheng J, Jiang H, Cheng X, Jiang Y, Deng SJ, and Xu HE. Structures of the Omicron Spike trimer with ACE2 and an anti-Omicron antibody. *Science* (2022).
7. Duan J*, **Xu P***, Cheng X*, Mao C*, Croll T, He X, Shi J, Luan X, Yin W, You E, Liu Q, Zhang S, Jiang H, Zhang Y, and Xu HE. Structures of full-length glycoprotein hormone receptor signaling complexes. *Nature* (2021).
8. Zhuang Y*, **Xu P***, Mao C*, Wang L*, Krumm B*, Zhou XE*, Huang S, Liu H, Cheng X, Huang XP, Shen DD, Xu T, Liu YF, Wang Y, Guo J, Jiang Y, Jiang H, Melcher K, Roth BL, Zhang Y, Zhang C, and Xu HE. Structural insights into the human D1 and D2 dopamine receptor signaling complexes. *Cell* (2021).
9. Huang S*, **Xu P***, Shen DD*, Simon IA*, Mao C, Tan Y, Zhang H, Harpsøe K, Li H, Zhang Y, You C, Yu X, Jiang Y, Zhang Y, Gloriam DE, Xu HE. GPCRs steer Gi and Gs selectivity via TM5-TM6 switches. *Molecular Cell* (2022).
10. Huang S*, **Xu P***, Tan Y*, You C, Zhang Y, Jiang Y, and Xu HE Structural basis for recognition of anti-migraine drug lasmiditan by the serotonin receptor 5-HT1F–G protein complex. *Cell Research* (2021).
11. Tan Y*, **Xu P***, Huang S*, Yang G, Zhou F, He X, Ma H, Xu HE, and Jiang Y. Structural insights into the ligand binding and Gi coupling of serotonin receptor 5-HT5A. *Cell Discovery* (2022).
12. You C*, Zhang Y*, **Xu P***, Huang S, Yin W, Xu HE, Jiang Y. Structural insights into the peptide selectivity and activation of human Neuromedin U Receptors. *Nature Communications* (2022).
13. Wang Y*, Guo S*, Zhuang Y*, Yun Y*, **Xu P***, He X, Guo J, Yin W, Xu HE, Xie X, and Jiang Y. Molecular recognition of an acyl-peptide hormone and activation of ghrelin receptor. *Nature Communications* (2021).

14. Cong Z, Chen LN, Ma H, Zhou Q, Zou X, Ye C, Dai A, Liu Q, Huang W, Sun X, Wang X, **Xu P**, Zhao L, Xia T, Zhong W, Yang D, Xu HE, Zhang Y, and Wang MW. Molecular insights into ago-allosteric modulation of the human glucagon-like peptide-1 receptor. *Nature Communications* (2021).
15. Duan J, Shen DD, Zhou XE, Bi P, Liu Q, Tan Y, Zhuang Y, Zhang H, **Xu P**, Huang S, Ma S, He X, Melcher K, Zhang Y, Xu HE, and Jiang Y. Cryo-EM structure of an activated VIP1 receptor-G protein complex revealed by a NanoBiT tethering strategy. *Nature Communications* (2020).
16. Zhao F, Zhou Q, Cong Z, Hang K, Zou X, Zhang C, Chen Y, Dai A, Liang A, Ming Q, Wang M, Chen L, **Xu P**, Chang R, Feng W, Xia T, Zhang Y, Wu B, Yang D, Zhao L, Xu HE, and Wang MW. Structural insights into multiplexed pharmacological actions of tirzepatide and peptide 20 at the GIP, GLP-1 or glucagon receptors. *Nature Communications* (2022).
17. Shao Z, Tan Y, Shen Q, Yao B, Hou L, Qin J, **Xu P**, Mao C, Chen L, Zhang H, Shen DD, Zhang C, Li W, Du X, Li F, Chen Z, Jiang Y, Xu HE, Ying S, Ma H, Zhang Y, and Shen H. Molecular insights into ligand recognition and activation of chemokine receptors CCR2 and CCR3. *Cell Discovery* (2022).
18. Duan J, Shen DD, Zhao T, Guo S, He X, Yin W, **Xu P**, Ji Y, Chen LN, Liu J, Zhang H, Liu Q, Shi Y, Cheng X, Jiang H, Xu HE, Zhang Y, Xie X, Jiang Y. Molecular basis for allosteric agonism and G protein subtype selectivity of galanin receptors. *Nature Communications* (2022).

In addition to significant contributions in GPCR structural biology and drug development, I have made substantial advancements in the field of gene editing during my postdoctoral tenure. Recently, we reported on Fanzor, a eukaryotic RNA-guided endonuclease. Through structural engineering of Fanzor proteins, we achieved a significant increase in gene editing efficiency in human cells. I have deciphered the structural insights of Fanzor, revealing its mechanism of DNA targeting and cleavage. Moreover, I have elucidated a series of Fanzor structures, further elucidating the diversity and DNA cleavage mechanisms within this family.

19. Saito M*, **Xu P***, Faure G, Maguire S, Kannan S, Altae-Tran H, Vo S, Desimone A, Macrae RK, Zhang F. Fanzor is a eukaryotic programmable RNA-guided endonuclease. *Nature* (2023).
20. **Xu P***, Saito M*, Faure G, Maguire S, Vo S, Wilkinson M, Kuang H, Wang B, Rice WJ, Macrae RK, Zhang F. Structural insight into the diversity and DNA cleavage mechanism of Fanzor. *Cell (accepted in principle).*