BIOGRAPHICAL SKETCH

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NAME: Zhiying Zhang

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

POSITION TITLE: Research 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)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Zhengzhou University	BA	08/2014	07/2018	Bioengineering
Peking University	PHD	10/2018	07/2023	Biochemistry and Molecular Biology
Memorial Sloan Kettering Cancer Center	Postdoc	10/2023	present	Structural Biology

A. Personal Statement

My academic training has provided me with an excellent background in multiple disciplines such as molecular biology, biochemistry, structural biology, microbiology, and bioengineering. During my undergraduate years in the microbiology lab, I was involved in the research of antiviral drugs for HBV, which has been talented and marketed. During my PhD in the structural biology lab, I was responsible for researching potent broad-spectrum neutralizing antibody drugs against SARS-CoV-2. The SA55 neutralizing antibody drug, developed in collaboration with partners, is currently the only publicly reported antibody drug that has not been escaped by the novel coronavirus. SA55 has been patented and formulated into nasal spray and injectable forms, undergoing clinical trials. These experiences have allowed me to accumulate expertise in virology research and drug development. My postdoctoral training turned to bacterial anti-phage mechanisms and viral. My sponsor, a globally recognized expert in nucleic acid structure and in the field of innate immunity, has extensive experience in training postdoctoral researchers, and has successfully trained several outstanding independent scientists. Besides providing new technologies, I have had the opportunity to engage in public presentations, lectures, laboratory management, and student guidance. These activities aim to enhance my ability to become an independent researcher. Additionally, he has had many outstanding collaborators, expanding my professional network in the academic field. Currently, although I have only been engaged in three months of postdoctoral research, I have achieved promising results. I believe that with the current research environment and the research plan I have proposed, I am laying a solid foundation for my future as an excellent independent researcher in bacteriophage research and viral immunology.

1. Cao Y[#], Jian F[#], **Zhang Z[#]**, Yisimayi A[#], Hao X[#], Bao L[#], Yuan F, Yu Y, Du S, Wang J, Xiao T, Song W, Zhang Y, Liu P, An R, Wang P, Wang Y, Yang S, Niu X, Zhang Y, Gu Q, Shao F, Hu Y, Yin W, Zheng A, Wang Y, Qin C, Jin R, Xiao J, Xie XS. Rational identification of potent and broad sarbecovirus-neutralizing antibody cocktails from SARS convalescents. **Cell Reports**. 2022 Dec 20;41(12):111845.

2. Du S[#], Liu P[#], **Zhang Z[#]**, Xiao T, Yasimayi A, Huang W, Wang Y, Cao Y, Xie XS, Xiao J. Structures of SARS-CoV-2 B.1.351 neutralizing antibodies provide insights into cocktail design against concerning variants. **Cell Research**. 2021 Oct;31(10):1130-1133.

3. Cao Y[#], Yisimayi A[#], Bai Y[#], Huang W[#], Li X[#], **Zhang Z[#]**, Yuan T[#], An R, Wang J, Xiao T, Du S, Ma W, Song L, Li Y, Li X, Song W, Wu J, Liu S, Li X, Zhang Y, Su B, Guo X, Wei Y, Gao C, Zhang N, Zhang Y, Dou Y, Xu X, Shi R, Lu B, Jin R, Ma Y, Qin C, Wang Y, Feng Y, Xiao J, Xie XS. Humoral immune response to circulating SARS-CoV-2 variants elicited by inactivated and RBD-subunit vaccines. **Cell Research**. 2021 Jul;31(7):732-741.

4. Zhu S[#], Liu Y[#], Zhou Z[#], **Zhang Z[#]**, Xiao X, Liu Z, Chen A, Dong X, Tian F, Chen S, Xu Y, Wang C, Li Q, Niu X, Pan Q, Du S, Xiao J, Wang J, Wei W. Genome-wide CRISPR activation screen identifies candidate receptors for SARS-CoV-2 entry. **Science China Life Sciences**. 2022 Apr;65(4):701-717.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 – Present Research Scholar, Memorial Sloan Kettering Cancer Center
2018 – 2020 Class Monitor, Peking University.
2019 – 2020 Biochemistry Teaching Assistant, Peking University.
2019 – 2020 Laboratory Teaching Assistant, Peking University.

Honors

2014 – 2018 First-class scholarship, Zhengzhou University.
2020 – 2022 Merit Student, Peking University.
2018 – 2019& 2021 – 2022 Academic Excellence Award, Peking University.
2020 – 2021 Outstanding Poster Award, Peking University Biochemistry Academic Week
2021 – 2022 Gu Wenyu Scholarship, Peking University.

C. Contributions to Science

1. **Graduate Career: Molecular mechanisms of SARS-CoV-2 Nabs targeting NTD and RBD.** Prophylactic and therapeutic drugs are urgently needed to combat COVID-19 caused by SARS-CoV-2. Over the past years, SARS-CoV-2 neutralizing antibodies have been developed for preventive or therapeutic uses, especially targeting RBD and NTD. To investigate the molecular mechanisms of SARS-CoV-2 Nabs targeting NTD and RBD, I solved two NTD-specific antibodies using X-ray crystallography and cryo-EM, they all target a single supersite and can be easily escaped by Beta and Omicron variants (Cell research, PMID: PMC8138844). I also solved six RBD-specific antibodies using Cryo-EM, to study the group B, D, E, and F antibody-evasion mechanism of Omicron (Cell research, PMID: PMC8385480). Especially the antibody cocktail SA55+SA58 which can broadly and potently neutralize SARS-CoV-2 variants and sarbecoviruses, making it a valuable bsNAb drug candidate (Cell reports, PMID: PMC9712074).

a) Cao Y[#], Yisimayi A[#], Bai Y[#], Huang W[#], Li X[#], **Zhang Z[#]**, Yuan T[#], An R, Wang J, Xiao T, Du S, Ma W, Song L, Li Y, Li X, Song W, Wu J, Liu S, Li X, Zhang Y, Su B, Guo X, Wei Y, Gao C, Zhang N, Zhang Y, Dou Y, Xu X, Shi R, Lu B, Jin R, Ma Y, Qin C, Wang Y, Feng Y, Xiao J, Xie XS. Humoral immune response to circulating SARS-CoV-2 variants elicited by inactivated and RBD-subunit vaccines. **Cell Research**. 2021 Jul;31(7):732-741.
b) Du S[#], Liu P[#], **Zhang Z[#]**, Xiao T, Yasimayi A, Huang W, Wang Y, Cao Y, Xie XS, Xiao J. Structures of SARS-CoV-2 B.1.351 neutralizing antibodies provide insights into cocktail design against concerning variants. **Cell Research**. 2021 Oct;31(10):1130-1133.
c) Cao Y[#], Jian F[#], **Zhang Z[#]**, Yisimayi A[#], Hao X[#], Bao L[#], Yuan F, Yu Y, Du S, Wang J, Xiao T, Song W, Zhang Y, Liu P, An R, Wang P, Wang Y, Yang S, Niu X, Zhang Y, Gu Q, Shao F, Hu Y, Yin W, Zheng A, Wang Y, Qin C, Jin R, Xiao J, Xie XS. Rational identification of potent and broad sarbecovirus-neutralizing antibody cocktails from SARS convalescents. **Cell Reports**. 2022 Dec 20;41(12):111845.

2. **Postdoctoral Career:**

a) The common mechanism of CXCR4 for FIV and HIV entry.

Feline immunodeficiency virus (FIV) infection of the domestic cat induces a disease state characterized by a progressive depletion of CD4+ T lymphocytes. The CXC chemokine receptor 4 (CXCR4) on the host cell is recognized by HIV or FIV envelope glycoprotein gp120 during the viral entry process. To address the common mechanism of CXCR4-mediated HIV of FIV infection, I have gained a low-resolution model of hCXCR4-gp120-CD4, it is worth to push the resolution because of the high importance of this structure in HIV field. Beside this, I have determined the apo form CXCR4 tetramer with 2.6 A resolution, it seems to be the only tetrameric GPCR which is unique, and the interface is strikingly different from previous models of CXCR4 dimerization which have solved by crystallography. Why there are so many forms of CXCR4 is unclear and the function is also needed further explore.

b) Anti-phage defense system and innate immunity.

The arms race between bacteria and phages has led to the development of anti-phage defense systems. My postdoctoral work primarily revolves around the mechanistic study of prokaryotic defense systems against phages. This includes SMC-like family such as Lamassu, the membrane associated Kiwa anti-defense system, and the viral defense system named Brig, which involves DNA glycosylase in collaboration with the Rockefeller Laboratory's Marraffini. Currently, I have obtained some promising data, so far, I got the apo structure of the effector membrane protein KwaA in the Kwia system. The next step is to assemble the receptor protein KwaB to elucidate the anti-phage mechanism of the Kwia system. For the Brig system, I have also resolved the crystal structures of the apo form of the Brig2 protein and the complex with the substrate hmC base. This provides a reference for understanding the substrate specificity and anti-bacteriophage mechanism of the Brig system.

D. Scholastic Performance

YEAR	COURSE TITLE	GRADE
2018	The Standards of Scientific Research	P
2018	Revolution of Modern Science &Technology and Marxism	A+
2018	Principles of Biology	A-
2018	Progresses in Molecular and cellular Biology	A-
2018	The Mechanism and Application of Modern Biological Techniques	A
2018	Intensive literature reading and seminars(I)	P
2018	Academic English Listening and Speaking For Graduate Students	B+
2018	Progress in Genetic and Developmental Biology	B+
2019	Principles of Modern Biology(II)	B
2019	Current topics on molecular and cellular biology	B
2019	Current topics on Genetics and Developmental Biology	B
2019	Lab Rotation	P
2019	Three Dimensional Cryo-Electron Microscopy	B
2019	Teaching Practice	P
2019	Intensive literature reading and seminars(II)	P
2020	Basic Theory and Scientific Research Practice of Graduate Students	P
2021	Laboratory Techniques of Modern Biology	P
2021	Literature Readings and Topic Discussions	P
2022	The Writing Rules of Academic Thesis	A-

Except for the scientific ethics course, Peking University graduate courses are graded P (pass) or F (fail). Passing is D or better. The scientific ethics course is using the letter grade system, A-, A, A+: Excellent; B-, B, B+: Good; C-, C, C+: Average; D, D+: Pass; F: Fail. One course credit unit is usually equivalent to 16 hours of instruction.