Wenqian Kelly Chen

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EDUCATION

The Scripps Research Institute (TSRI) June 2019-Current
GPA: 3.67; Doctor of Philosophy in Biological Sciences
University of California, Berkeley (UCB) May 2017
GPA: 3.45; Bachelor of Arts in Molecular and Cell Biology
City College of San Francisco (CCSF) May 2015
GPA: 3.58; Associate of Sciences in Biological Sciences

SCHOLARSHIPS, FELLOWSHIPS, AND AWARDS

National Science Foundation Graduate Research Fellowship, TSRI 2022-2025
David C. Fairchild Endowed Fellowship, TSRI 2019-2022
Dean's Fellowship, TSRI 2019-2020
Biology Scholars Program Research Fellowship, UCB 2016-2017
George A. Miller Scholars Program, UCB 2015-2017
Berkeley Undergraduate Scholarship, UCB 2015-2017
Carl and Brigetta Beetz Scholarship, CCSF 2015-2016
Asian and Pacific Islander American Scholarship, CCSF 2014-2015

RESEARCH EXPERIENCE

National Science Foundation (NSF) Graduate Research Fellow March 2022-Current
Department of Integrative Structural and Computational Biology, TSRI, Laboratory of Gabriel C. Lander, PhD
Project: Structural insights into human ClpXP mechanism of activation

- Solved the first cryo-EM structures of human ClpP and human ClpXP complex at ~ 3 Å and 4 Å, respectively (manuscript in preparation)
- Worked with a senior scientist to establish a protocol for the fabrication cryo-EM grids with a monolayer graphene and published the protocol in the *Journal of Visualized Experiments*
- Collaborated with other researchers on their projects, resulting in a publication of a co-authorship publication in *Nature Structural and Molecular Biology*
- Successfully overcame major challenges in cryo-EM sample preparation through optimization of proteins constructs using AlphaFold, troubleshooting of protein purification, and detergent screening to over preferred orientation of protein in vitreous ice
- Regularly performed cryo-EM techniques including negative staining, freezing of cryo-EM grids using manual "blot-and-plunge" and Vitrobot, clipping grids and transferring of the clipped grids to the autoloader cassette for data collection

Skaggs Research Fellow June 2019-March 2022
Department of Molecular Medicine, TSRI, Laboratory of Xiang-lei Yang, PhD
Project 1: Clinical and molecular characterization of novel FARS2 variants causing neonatal mitochondrial disease

- Worked with other researchers as a team to characterize the molecular mechanism underlying neonatal mitochondrial disease caused by mutations in mitochondrial phenylalanyl-tRNA

(mtPheRS), leading to a first-author publication in *Molecular Genetics and Metabolism*

- Performed biochemical assays including *in vitro* aminoacylation assay to test the enzymatic activities of mtPheRS and tested the thermal stability of mtPheRS using a fluorescence-based thermal shift assay

Project 2: Defining a novel signaling complex involving extracellular tRNA and tRNA synthetase

- Examined the interactions between aminoacyl-tRNA synthetases (aaRSs) and neuropilin1 in the context of Charcot Marie Tooth (CMT) disease and investigated a novel role of tRNA in the glycyl-tRNA synthase (GlyRS) linked to CMT
- Performed various biochemical assays to probe protein-protein and protein-tRNA interactions, including co-immunoprecipitation, biolayer interferometry (Octet), electrophoretic mobility shift assay, mass photometry, and filter binding assay
- Utilized my expertise in co-immunoprecipitation and contributed to a collaborative project, resulting in a co-authorship publication in *Nature Communications*
- Wrote and published a first-author review paper on anti-aminoacyl-tRNA synthetase syndrome in *Trends in Biochemical Sciences*

Post-baccalaureate Research Fellow June 2017-May 2019
National Institute on Deafness and Other Communication Disorders, National Institute of Health (NIH)
Advisor: Thomas B. Friedman, PhD

Project 1: The phenotypic landscape of a Tbc1d24 mutant mouse includes convulsive seizures resembling human early infantile epileptic encephalopathy

- Investigated molecular functions of the TBC1D24 protein, which is associated with deafness and/or epilepsy in humans by studying protein-protein interactions and conducting behavioral tests on mouse models for phenotypic characterizations
- Published the research findings (second author) in *Human Molecular Genetics*

Project 2: Transcriptional profiling of mouse Cdc14a

- Characterized the functions of human and mouse *Cdc14a* isoforms that are associated deafness and/or male infertility by studying protein expression and quantifying mRNA expression
- Studied Cdc14a protein localizations using confocal fluorescent microscopy
- Maintained mice colonies and performed mouse handling and restraint for anesthesia

Biology Scholars Program Research Fellow February 2016-May 2017
Department of Public Health, University of California, Berkeley
Advisor: Fenyong Liu, PhD

Project: Functional profiling of Open Reading Frame (ORF) 11 of Kaposi's Sarcoma-Associated Herpesvirus

- Examined the functional role of the open reading frame (ORF) 11 on the viral life cycle of Kaposi's sarcoma-associated herpesvirus
- Constructed ORF11-deficient viruses using a two-step homologous recombination technique
- Made careful observations of viral growth in the transfected cell line under a fluorescent microscope

PROFESSIONAL SKILLS

- **Structural Biology (Single-Particle cryo-EM):** sample optimization and grid screening; data acquisition on Talos Arctica and Titan Krios; cryo-EM data processing using Appion, CryoSPARC, and Relion; molecular modeling and visualization using Coot, ChimeraX ISOLDE,

and Phenix; HPC (high-performance computing)

- **Biochemistry:** protein purification using Ni-NTA and GST column; FPLC based ion exchange and gel filtration chromatography; SDS-PAGE analysis; Western blotting; ELISA; thermal shift assay; mass photometry
- **Molecular Biology**: molecular cloning, reverse-transcription polymerase chain reaction (RT-PCR), site-directed mutagenesis, DNA library construction, primer design, PCR genotyping, DNA purification and extraction
- **Cell Biology**: maintenance of adherent HeLa and HEK293T cell lines; transfection; use of CRISPR-Cas9 and flow cytometry to generate gene knockout cell lines; small-interferon RNA silencing to generate gene knockdown cell lines; confocal fluorescent imaging
- **Computer/software skills**: MS Office; Excel; GrapPad Prism; ChimeraX; Phenix; Coot; Pymol; ImageJ; Biorender; Adobe Photoshop and Illustrator

TEACHING/MENTORING EXPERIENCE

Teaching Assistant Jan 2021-March 2021

Introduction to Biostatistics Course, TSRI

- Helped professor Jill Waalen coordinate a class of 52 students
- Graded exams, answered student questions regarding statistical analysis and the use of R package

SAT Tutor/Mentor January 2017-May 2017

CollegeSpring, California

- Tutored SAT Writing to a group of 5 middle school students weekly for one hour
- Advised students on college and financial aid application processes

Supplementary Instruction Facilitator January 2015-May 2015

General Chemistry Course, CCSF

- Facilitated a weekly one-hour study session consisting of 5 to 10 General Chemistry students
- Prepared weekly study sheets and problem-sets based on chemistry lectures
- Assisted students with learning difficult chemistry concepts

PUBLICATIONS

1. **Chen, W.**, Yang J., Lander, G. C. (2023). Structural Insights into the Functions of Human ClpXP. *Manuscript in preparation*
2. **Chen, W.***, Rehsi, P.*, Thompson, K., Yeo, M., Stals, K., He, L., Schimmel, P., Chrzanowska-lightowelers, Z., Wakeling, E., Taylor, R.W., & Kuhle, B. (**2023**). Clinical and molecular characterization of novel FARS2 variants causing neonatal mitochondrial disease. *Molecular Genetics and Metabolism* ***denotes co-first author publication**
3. Basanta, B.*, **Chen, W. ***, Pride, D. E., & Lander, G. C. (**2023**). *Fabrication of Monolayer Graphene-coated Grids for Cryoelectron Microscopy*. *July*, 1–15. https://doi.org/10.3791/65702
4. Yang, J., Baron, K. R., Pride, D. E., Schneemann, A., Guo, X., **Chen, W.**, Song, A. S., Aviles, G., Kampmann, M., Wiseman, R. L., & Lander, G. C. (**2022**). DELE1 oligomerization promotes integrated stress response activation. *Nature Structural and Molecular Biology* **30**, 1295–1302 (2023). https://doi.org/10.1038/s41594-023-01061-0
5. Kanaji, S.*, **Chen, W.***, Morodomi, Y., Shapiro, R., Kanaji, T., & Yang, X. L. (**2023**). Mechanistic perspectives on anti-aminoacyl-tRNA synthetase syndrome. *Trends in Biochemical Sciences*, *48*(3), 288–302. https://doi.org/10.1016/j.tibs.2022.09.011
6. Gioelli, N., Neilson, L. J., Wei, N., Villari, G., **Chen, W.**, Kuhle, B., Ehling, M., Maione, F.,

Willox, S., Brundu, S., Avanzato, D., Koulouras, G., Mazzone, M., Giraudo, E., Yang, X. L., Valdembri, D., Zanivan, S., & Serini, G. (**2022**). Neuropilin 1 and its inhibitory ligand mini-tryptophanyl-tRNA synthetase inversely regulate VE-cadherin turnover and vascular permeability. *Nature Communications*, *13*(1), 1–16. https://doi.org/10.1038/s41467-022-31904-1

7. Tona, R., **Chen, W.**, Nakano, Y., Reyes, L. D., Petralia, R. S., Wang, Y. X., Starost, M. F., Wafa, T. T., Morell, R. J., Cravedi, K. D., Du Hoffmann, J., Miyoshi, T., Munasinghe, J. P., Fitzgerald, T. S., Chudasama, Y., Omori, K., Pierpaoli, C., Banfi, B., Dong, L., … Friedman, T. B. (**2019**). The phenotypic landscape of a Tbc1d24 mutant mouse includes convulsive seizures resembling human early infantile epileptic encephalopathy. *Human Molecular Genetics*, *28*(9), 1530–1547. https://doi.org/10.1093/hmg/ddy445

PRESENTATIONS

1. **Structural Insights into Human ClpXP Functions**, March 2024, the American Society for Biochemistry and Molecular Biology Conference 2024
2. **Structural Insights into Human ClpXP Functions**, March 2024, ER Stress Club, TSRI
3. **Structural Insights into Human ClpXP Functions**, March 2024, Cryo-EM Supergroup, TSRI
4. **Defining a novel signaling complex involving extracellular tRNA and tRNA synthease**, March 2021, Gradaute Student Symposium, TSRI
5. **Mutations of Mouse Tbc1d24 Recapitulate the Epilepsy of Pathogenic Variants of Human TBC1D24***,* May 2018, Summer Poster Day, NIH
6. **Mutations of Mouse Tbc1d24 Recapitulate the Epilepsy of Pathogenic Variants of Human TBC1D24***,* October 2018, Monthly Trainee Talk, NIH