Zengtao Wang

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Work Experience

Eli Lilly and Company, Indianapolis, IN **June.2024 Present**

Title: Advisor-Pharmacometrician

Supervisor: Nieves Velez de Mendizabal, PhD

Education

University of Minnesota-Twin Cities, Minneapolis, MN **Sep.2019 May. 2024**

Major: Ph.D. in Pharmaceutics (GPA: 4.00/4.00)

Thesis: "Anomalous Aβ exposure and blood-brain barrier insulin resistance induce cerebrovascular dysfunction in Alzheimer's disease"

Shanghai Jiao Tong University, Shanghai, China **Sep.2015 Jun.2019**

Major: B.S. in Pharmacy (GPA: 3.88/4.00)

Thesis: "Design, synthesis and biological evaluation of molecular imaging probe targeting cytochrome P450 1B1"

Research Experience

Anomalous amyloid beta exposure and blood-brain barrier insulin resistance induce cerebrovascular dysfunction in Alzheimer's Disease **Nov.2019 May.2024**

Graduate Research Assistant, Advisor: Karunya K. Kandimalla, PhD

Department of Pharmaceutics, University of Minnesota-Twin Cities, Minneapolis, MN

- Developed a population pharmacokinetic model and conducted mechanistic studies to investigate the trafficking and accumulation kinetics of Aβ isoforms at the BBB endothelium. *(Published in Mol Pharm.)*
- Conducted flow cytometry, western blot and cellular imaging studies to investigate molecular mechanisms of cellular uptake and intracellular trafficking of Aβ in the BBB endothelial cells (*Published in Mol Pharmacol.*)
- Established a compartmental PK model to deconvolve plasma PK of various macromolecular tracers from their dynamic heart imaging data obtained by SPECT/CT imaging. *(Published in J Pharmacol Exp Ther.)*
- Performed graphical analysis of in vivo SPECT/CT dynamic brain imaging data and in vitro intracellular trafficking studies to investigate the effect of high-density lipoprotein (HDL) mimetic peptide and gut microbiome metabolite on Aβ accumulation in the BBB endothelium. *(Published in Mol Pharm.)*
- Interpreted results of time-series transcriptomic analysis of BBB endothelial cells after insulin exposure and drafted the manuscript. (*Published in NPJ Syst Biol Appl.*)
- Developed a quantitative systems pharmacology model to characterize the dynamics of insulin signaling transduction and VCAM1 expression in BBB endothelial cells and combined it with proteomics/transcriptomics data to simulate cerebrovascular inflammation in AD patients. *(Published in CPT Pharmacometrics Syst Pharmacol.)*

Research Experience (continued)

Model-based meta-analysis (MBMA) of MDS-UPDRS scores to inform trial design in early Parkinson's disease (PD) **Jan. 2023 Jun. 2023**

Modeling and Simulation Co-op, Supervisor: Jingxian (JC) Chen, PhD
Clinical Pharmacology and Pharmacometrics, Biogen Inc., Cambridge, MA

- Summarized, tabulated and visualized aggregated clinical data of PD from multiple contemporaneous studies in R.
- Developed a non-linear mixed effect model to characterize the PD disease progression as measured by MDS-UPDRS score in NONMEM.
- Developed a non-linear mixed effect model to describe a time-to-event (TTE) type endpoint in Monolix.
- Simulated longitudinal profiles of different endpoints to inform trial design in R.
- Presented key model assumptions, findings and applications to various internal groups and stakeholders. (*Poster presentation in the ACoP14*)

Population pharmacokinetics-pharmacodynamics (PK-PD) modeling of an antisense oligonucleotide (ASO) for treatment of Parkinson's disease **Jan. 2023 Jun. 2023**

Modeling and Simulation Co-op, Supervisor: Jingxian (JC) Chen, PhD
Clinical Pharmacology and Pharmacometrics, Biogen Inc., Cambridge, MA

- Developed a pop-PK/PD model to describe the PK/PD data of an ASO drug from its phase I study.
- Simulated PK/PD profile with new dosing regimen using the established pop-PK/PD model to inform dose optimization.

Development of molecular imaging probes targeting cytochrome P450 (CYP) 1B1 for early tumor detection **Oct. 2016 Jun. 2019**

Undergraduate Research Assistant, Advisor: Qingqing Meng, PhD
School of Pharmacy, Shanghai Jiao Tong University, Shanghai, China

- Synthesized and characterized near infrared (NIR) and NIR-positron emission tomography (PET) bimodal imaging probes targeting CYP1B1.
- Evaluated probes' binding affinity and selectivity towards CYP1B1-overexpressed cancer cell lines with flow cytometry and confocal microscopy studies.
- Assessed tumor visualization ability and biodistribution of NIR probes with *in vivo* and *ex vivo* imaging. *(Published in J Med Chem. and Chembiochem.)*

Anti-Aβ antibody delivery across the BBB for treatment of Alzheimer's disease **Summer 2018**

Summer Research Intern, Supervisor: Kazunori Kataoka, PhD
University of Tokyo/Innovation Center of Nanomedicine, Kawasaki, Japan

- Prepared and characterized the PEGylated antibody with gel permeation chromatography (GPC) and dynamic light scattering (DLS).
- Investigated the pharmacokinetics profile and brain accumulation of PEGylated antibodies.

Honors & Awards

- Lilly Innovator Award (H2, 2024)-Eli Lilly and Company ATPLV-HSE, 2024
- Doctoral Dissertation Fellowship-University of Minnesota, 2023
- Bighley Graduate Fellowship-University of Minnesota College of Pharmacy, 2023
- Highlighted Trainee Author-Molecular Pharmacology, 2023
- Highlighted Trainee Author-The Journal of Pharmacology and Experimental Therapeutics, 2023
- Research Award-American Association of Indian Pharmaceutical Scientists (AAiPS), 2023
- Ronald J. Sawchuk Fellowship in Pharmacokinetics-University of Minnesota College of Pharmacy, 2022
- Registration, Selected by faculty to be the GPEN-Sponsored participant to attend GPEN 2022, Sponsored by Upsher-Smith, 2022
- UMII-MnDRIVE PhD Graduate Assistantship Award-University of Minnesota Informatics Institute, 2021
- Runner-up, 3-Minute Thesis (3MT)-University of Minnesota College of Pharmacy, 2021
- Edward G Rippie Fellowship in Pharmaceutics-University of Minnesota College of Pharmacy, 2021
- Certificate of Excellent Bachelor Thesis (top 1%)-Shanghai Jiao Tong University, 2019
- China National Scholarship-Ministry of Education of China, 2018
- Shanghai Municipal Government Scholarship-Shanghai Municipal People's Government, 2017

Publication

After joining the Pharmaceutics Ph.D. program

- **Wang Z**, Veerareddy V, Eberts P, Azarin SM, Kandimalla KK. "Endothelial-pericyte interactions activate insulin signaling and its implications for blood-brain barrier dysfunction in Alzheimer's disease." (In preparation) **(2025)**
- Salian V, **Wang Z**, Wengenack T, Curran GL, Jack CR, Podulso JF, Kandimalla KK. "Estimation of various physiological parameters affecting amyloid plaque distribution of a novel MRI contrast agent in the brain of Alzheimer's disease transgenic mice" (In preparation) **(2025)**
- **Wang Z**, Veerareddy V, Tang X, Thompson KJ, Krishnan S, Kalari KR, Kandimalla KK. "QSP Modeling Shows Pathological Synergism Between Insulin Resistance and Amyloid-Beta Exposure in Upregulating VCAM1 Expression at the BBB Endothelium." **CPT Pharmacometrics Syst Pharmacol.** 2025 Mar;14(3):561-571. **(2024)**
- **Wang Z**, Zhong R, Curran GL, Min P, Lowe VJ, Li L, Kandimalla KK. "High-Density Lipoprotein Mimetic Peptide 4F Reduces Toxic Amyloid-Beta Exposure to the Blood-Brain Barrier Endothelium in Alzheimer's Disease Transgenic Mice." **Mol Pharm.** 2024 Nov 4;21(11):5661-5671. **(2024)**
- Nelson D, Thompson KJ, Wang L, **Wang Z**, Eberts P, Azarin SM, Kalari KR, Kandimalla KK. "Pericyte Control of Gene Expression in the Blood-Brain Barrier Endothelium: Implications for Alzheimer's Disease." **J Alzheimers Dis.** 2024;99(s2):S281-S297. **(2024)**
- **Wang Z**, Sharda N, Omtri RS, Li L, Kandimalla KK. "Amyloid-beta proteins 40 and 42 employ distinct molecular pathways for cell entry and intracellular transit at the BBB endothelium." **Mol Pharmacol.** 2023 Nov;104(5):203-213. **(2023)**
- **Wang Z**, Wang L, Ebbini M, Curran GL, Vernon CJ, Min HK, Siegel RA, Lowe VJ, Kandimalla KK. "Deconvolution of plasma pharmacokinetics from dynamic heart imaging data obtained by SPECT/CT imaging." **J Pharmacol Exp Ther.** 2023 Jul;386(1):102-110. **(2023)**

Publication (continued)

- **Wang Z**, Tang X, Swaminathan SK, Kalari KR, Kandimalla KK. "Mapping the Dynamics of Insulin-responsive Pathways in the Blood Brain Barrier Endothelium using Time-series Transcriptomics Data." **NPJ Syst Biol Appl.** 2022 Aug 16;8(1):29. **(2022)**
- **Wang Z**, Chen D, Fan Q, Wu Z, Dong J, Cui J, Wang J, Xu T, Meng Q, Li S. "Design, Synthesis and In Vivo Fluorescence Imaging Study of a Cytochrome P450 1B1 Targeted NIR Probe Containing a Chelator Moiety." **Chembiochem.** 2022 May 14:e202200268. **(2022)**
- Taubel JC, Nelson NR, Bansal A, Curran GL, Wang L, **Wang Z**, Berg HM, Vernon CJ, Min HK, Larson NB, DeGrado TR, Kandimalla KK, Lowe VJ, Pandey MK. "Design, Synthesis, and Preliminary Evaluation of [68Ga]Ga-NOTA-Insulin as a PET Probe in an Alzheimer's Disease Mouse Model." **Bioconjug Chem.** 2022 May 18;33(5):892-906. **(2022)**
- Chen D, Fan Q, Xu T, Dong J, Cui J, **Wang Z**, Wang J, Meng Q, Li S. "Design, Synthesis and Binding Affinity Evaluation of Cytochrome P450 1B1 Targeted Chelators." **Anticancer Agents Med Chem.** 2022;22(2):261-269. **(2022)**
- **Wang Z**, Sharda N, Curran GL, Li L, Lowe VJ, Kandimalla KK. "Semimechanistic Population Pharmacokinetic Modeling to Investigate Amyloid Beta Trafficking and Accumulation at the BBB Endothelium." **Mol Pharm.** 2021 Nov 1;18(11):4148-4161. **(2021)**
- Sharda N, Pengo T, **Wang Z**, Kandimalla KK. "Amyloid-β Peptides Disrupt Interactions Between VAMP-2 and SNAP-25 in Neuronal Cells as Determined by FRET/FLIM." **J Alzheimers Dis.** 2020;77(1):423-435. **(2020)**
- Xie J, Gonzalez-Carter D, Tockary TA, Nakamura N, Xue Y, Nakakido M, Akiba H, Dirisala A, Liu X, Toh K, Yang T, **Wang Z**, et al. "Dual-sensitive nanomicelles enhancing systemic delivery of therapeutically active antibodies specifically into the brain." **ACS Nano.** 2020 Jun 23;14(6):6729-6742. **(2020)**
- Dong J, **Wang Z**, Cui J, Meng Q, Li S. "Synthesis and structure-activity relationship studies of α-naphthoflavone derivatives as CYP1B1 inhibitors." **Eur J Med Chem.** 2020 Feb 1;187:111938. **(2020)**
- **Wang Z**, Meng Q, Li S. "The Role of NIR Fluorescence in MDR Cancer Treatment: From Targeted Imaging to Phototherapy." **Curr Med Chem.** 2020;27(33):5510-5529. **(2020)**

Before joining the Pharmaceutics Ph.D. program

- Dong J, Huang G, Zhang Q, **Wang Z**, Cui J, Wu Y, Meng Q, Li S. "Development of benzochalcone derivatives as selective CYP1B1 inhibitors and anticancer agents." **Medchemcomm.** 2019 Jul 2;10(9):1606-1614. **(2019)**
- Meng Q, **Wang Z**, Cui J, Cui Q, Dong J, Zhang Q, Li S. "Design, Synthesis, and Biological Evaluation of Cytochrome P450 1B1 Targeted Molecular Imaging Probes for Colorectal Tumor Detection." **J Med Chem.** 2018 Dec 13;61(23):10901-10909. **(2018)**
- Dong J, **Wang Z**, Meng Q, Zhang Q, Huang G, Cui J, Li S. "Development of 2-arylbenzo[h]quinolone analogs as selective CYP1B1 inhibitors." **RSC Adv.** 2018 Apr 20;8(27):15009-15020. **(2018)**
- Dong J, Zhang Q, Meng Q, **Wang Z**, Li S, Cui J. "The Chemistry and Biological Effects of Thioflavones." **Mini Rev Med Chem.** 2018;18(20):1714-1732. **(2018)**
- Dong J, Zhang Q, **Wang Z**, Huang G, Li S. "Recent Advances in the Development of Indazole-based Anticancer Agents." **ChemMedChem.** 2018 Aug 10;13(15):1490-1507. **(2018)**

Conference Presentation

- **Wang Z**, Tang X, Thompson KJ, Kalari KR, Kandimalla KK. "Systems biology modeling of the insulin signaling network in the blood-brain barrier endothelium predicts cerebrovascular inflammation in Alzheimer's disease." Special poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Boston, MA, 2022
- **Wang Z**, Wang L, Curran GL, Vernon CJ, Min PH, Lowe VJ, Kandimalla KK. "Prediction of plasma pharmacokinetics from dynamic heart imaging data." Special poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Philadelphia, PA, 2021
- **Wang Z**, Chen J, Yang M, Hirst WD, Dam T, Burton J. "Model-based meta-analysis of the MDS-UPDRS scores to improve clinical trial efficiency for Parkinson's disease." Poster presentation, the 14th American Conference of Pharmacometrics, National Harbor, MD, 2023
- **Wang Z**, Curran GL, Zhong R, Lowe VJ, Li L, Kandimalla KK. "High-density lipoprotein mimetic peptide 4F reduces amyloid beta peptide accumulation in the blood-brain barrier endothelium in Alzheimer's disease." Poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Orlando, FL, 2023
- **Wang Z**, Tang X, Thompson KJ, Kalari KR, Kandimalla KK. "Systems biology modeling of the insulin signaling network in the blood-brain barrier endothelium predicts cerebrovascular inflammation in Alzheimer's disease." Poster presentation, *GPEN 2022*, University of Minnesota, MN, 2022
- **Wang Z,** Veerareddy V (presenting author), Kandimalla KK. "Gut microbial metabolites regulate bidirectional transport and accumulation of Alzheimer's disease amyloid beta peptides at the blood-brain barrier endothelium." Poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Boston, MA, 2022
- **Wang Z**, Tang X, Swaminathan SK, Kalari KR, Kandimalla KK. "Mapping the dynamics of insulin-responsive pathways in the blood-brain barrier endothelium and impact of amyloid beta exposure." Poster presentation, *Barriers of the CNS Gordon Research Conference,* New London, NH, 2022
- **Wang Z**, Kalari KR, Tang X, Swaminathan SK, Kandimalla KK. "Mapping the dynamics of insulin-responsive pathways in the blood-brain barrier endothelium using time-series transcriptomics data." Poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Philadelphia, PA, 2021
- **Wang Z**, Zhou AL, Sharda N, Curran GL, Lowe VJ, Kandimalla KK. Semi-mechanistic Pharmacokinetic Model to Predict the Impact of Age and Insulin Exposure on Alzheimer's Disease Amyloid Beta Peptide Kinetics at the Blood-Brain Barrier. Poster presentation, *American Association of Pharmaceutical Scientists Annual Meeting*, Virtual, 2020

Continued Education

Monoclonal Antibody PK/PD Workshop, SUNY Buffalo **May, 2022**

MonolixSuite Pharmacometrics Spring School, Lixoft **March, 2022**

Skills

- *Technical:* chemical synthesis, cell culture, permeability assays, ELISA, flow cytometry, confocal microscopy, western blot, HPLC, PK/PD modeling
- *Computer/software:* NONMEM, Monolix, MATLAB-SimBiology, R Studio, mrgsolve, Phoenix WinNonlin, SAAM II, Stella Architect, FlowJo, ImageJ, Graphpad Prism

Teaching Experience

Graduate Teaching Assistant

PHAR6738 Pharmacokinetics	**Fall, 2019 2**
PHAR6748 Biopharmaceutics	**Spring, 2020 2**
PHAR6797 Advanced Pharmacy Practice Learning Experience	**Summer, 2020 2**

Service

Journal Reviewer, AAPS Journal	**2024**
Journal Reviewer, Pharmaceutical Research	**2024**
Abstract Reviewer, AAPS 2023 Annual Meeting	**2023**
Secretary, AAPS Student Chapter at UMN	**2021-2022**
Scientific Planning Committee Head, GPEN 2022	**2022**