

# Zehua Wang (Zack Wang)

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## Education

<b>The University of Auckland</b> PhD Candidate in Pharmacology	<b>Grafton, Auckland</b> Expected enrollment in Oct 2025
<b>China Pharmaceutical University (CPU)</b> Master's Degree in Pharmacokinetics GPA: 3.84/4.0      IELTS: 6.5      PTE: 62      CET-6: 567	<b>Nanjing, Jiangsu</b> Sep 2022 - Jun 2025
<b>Shandong First Medical University (Shandong Academy of Medical Sciences, SDFMU)</b> Bachelor of Engineering in Pharmaceutical Engineering Overall Arithmetic average: 83.5/100      CET-4: 592	<b>Jinan, Shandong</b> Sep 2018 - Jun 2022

## Research

**1. Clinical Antibody Therapy for Alzheimer's Disease: Pop-PKPD Modeling and Application** 06/2024- Present  
*Collaboration with Prof. Jacqueline Hannam and Prof. Nick Holford, FMHS, University of Auckland, and Dr. Xuhui Chen, Neurology Cognitive Impairment Clinic, Peking University Shenzhen Hospital*

**Project Overview:** Focused on developing population pharmacokinetic-pharmacodynamic (Pop-PKPD) models for Alzheimer's disease (AD) patients receiving antibody therapies (e.g., lecanemab and donanemab), characterizing PKPD behaviors, and discerning drug effects on disease progression, specifically differentiating between transient symptomatic relief and sustained disease modification. We identify key covariates (e.g., body weight, age, ApoE  $\epsilon$ 4 genotype, blood-brain barrier permeability) to elucidate drug mechanisms, optimize dosing, predict outcomes, and advance personalized AD treatments for enhanced patient quality of life. The project includes a prospective clinical study analyzing drug exposure-clinical outcome relationships, currently in the data collection phase.

**2. PBPK-PD Modeling for Predicting PK, PD, and Toxicity Risks of ADCs in Mice and Humans** 03/2023- 07/2025

*Supervised by Prof. Kun Hao in Guangji Wang's lab, State Key Laboratory of Natural Medicines, CPU*

**Project Overview:** Developed a comprehensive physiologically based pharmacokinetic (PBPK) and pharmacodynamic (PD) model for cleavable ADCs, such as Trastuzumab deruxtecan (T-DXd) and Sacituzumab govitecan (SG), aimed at predicting PK, PD, therapeutic efficacy, and the risk of interstitial lung disease (ILD). The model innovatively integrates components including antibodies, linkers, and payloads, and was validated in tumor-bearing mouse models. Furthermore, the model successfully extrapolated findings to human patients, demonstrating accurate predictions of plasma and tissue concentrations, progression-free survival (PFS), and hazard ratios (HR). Additionally, Sobol' global sensitivity analysis (GSA) was employed to identify critical factors influencing drug disposition in key organs. Simulations further quantified age- and dose-dependent ILD risks through lung payload thresholds, thereby informing optimized dosing strategies and risk mitigation approaches in pharmacometrics.

**3. Study on Transporters, Enzymes, Signaling Pathways, and CNS Disorders** 09/2022-06/2025  
*Supervised by Prof. Li Liu and Prof. Xiaodong Liu, Jiangsu Provincial Key Laboratory of Drug Metabolism and Pharmacokinetics*

**Project Overview:** (1) Developed a whole-body PBPK model for the neuroprotective candidate SPT-07A, predicting its interspecies pharmacokinetics by quantifying UGT-driven metabolism in liver, kidney, and intestine, and validating key clearance mechanisms (hepatic and renal) across rats, dogs, and humans. (2) Uncovered how chronic liver injury downregulates organic cation transporters (OCT1/2, OCTN2) at the blood-brain barrier via estrogen receptor- $\alpha$  (ER- $\alpha$ ) and farnesoid X receptor (FXR) pathways, leading to cerebral carnitine deficiency and disrupted energy metabolism in hepatic encephalopathy. (3) Revealed renal OCT2/MATE1 suppression in liver failure via estrogen/TNF- $\alpha$  signaling, explaining elevated metformin exposure and clinical toxicity risks. (4) Deciphered venlafaxine-induced psychiatric disorders via PI3K/AKT/mTOR-mediated COMT upregulation, which depleted methyl-donor S-adenosylmethionine (SAM) and reduced histone methylation (H3K4me3/H3K27me3), linking kinase signaling to epigenetic dysregulation in the CNS.

**4. School-Enterprise Cooperation: Phase I Clinical Study of New NSAI Drugs** 10/2023-03/2024

**Project Overview:** Executed comprehensive modeling and simulation studies to investigate modifications in administration routes, dosages, and dosing frequencies to align with specific clinical requirements derived from empirical data. Led efforts in data preprocessing, model development, parameter estimation, simulation, evaluation, and optimization using tools such as WinNonlin and R. Additionally, authored the project report, detailing methodologies and findings.

**5. Preparation and Performance Testing of Antibacterial MOF-Derived Carbon Materials** 09/2021-07/2022

*Supervised by Prof. Jiahui Yu and Prof. Chenwei Li, Medical Science and Technology Innovation Center, SDFMU*

**Project Overview:** Focused on synthesizing and evaluating metal-organic framework (MOF)-derived carbon materials, such as UiO-66, and their applications in water purification and antibacterial solutions. The developed gradient graphene spiral sponge (GGS) demonstrated excellent durability and stability, enabling efficient freshwater production.

## Publication

1. Wang Z, Zhu J, Sang L, et al. PBPK-PD Model for Predicting Pharmacokinetics, Tumor Growth Inhibition, and Toxicity Risks of Topoisomerase Inhibitor ADCs in Mice and Humans [J]. Awarded the Excellent Poster Presentation Award at the “14th Academic Conference on Drug and Chemical Foreign Metabolism of the Drug Metabolism Professional Committee of the Chinese Pharmacological Society”. Manuscript under revision (R1) at *European Journal of Pharmaceutical Sciences* (Manuscript ID: PHASCI-D-25-00583R1).
2. Zhu X, Kong W, Wang Z, et al. Prediction of SPT-07A Pharmacokinetics in Rats, Dogs, and Humans Using a Physiologically-Based Pharmacokinetic Model and In Vitro Data [J]. *Pharmaceutics*, 2024, 16(12): 1596. <https://doi.org/10.3390/pharmaceutics16121596>.
3. Zhi H, Wang Z, Zhu X, et al. Chronic liver injury decreases levels of cerebral carnitine and acetylcarnitine in rats partly due to the downregulation of organic cation transporters OCT1/2 and OCTN2 at the blood-brain barrier[J]. *Drug Metabolism and Disposition*, 2025, 53(5): 100072. <https://doi.org/10.1016/j.dmd.2025.100072>.
4. Zhi H, Dai Y, Su L, et al. Thioacetamide-Induced Acute Liver Injury Increases Metformin Plasma Exposure by Downregulating Renal OCT2 and MATE1 Expression and Function [J]. *Biomedicines*, 2023, 11(23): 3314. <https://doi.org/10.3390/biomedicines11123314>.
5. Qian L, Yang H, Ye Q, et al. Venlafaxine Induces Psychiatric Disorders Due to Upregulation of Cerebral Catechol-O-Methyltransferase via the PI3K/AKT/mTOR Pathway [J]. Preprint available at *Research Square*, 2023. <https://doi.org/10.21203/rs.3.rs-3206277/v1>.

## Interdisciplinary Online Course

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|---|-----------------|
| (1) Artificial Intelligence and Cloud Computing by Prof. Maheswaran and Prof. Franchitti    | 07/2023-09/2023 |
| (2) Emerging Biotechnology Development and Global Governance by Prof. Liu and Prof. Wang    | 10/2023-12/2023 |
| (3) Big Data and Public Health; Artificial Intelligence in Public Health by Prof. Ramezani  | 10/2023-03/2024 |
| (4) Exploration and Application: Probability and Statistical Theory in Games by Prof. Iozzi | 07/2024-09/2024 |
| (5) Data Science and Business Analytics by Prof. Zhang Foutz                                | 07/2024-09/2024 |

## Honors and Awards

- (1) Outstanding Graduate, CPU, 2025
- (2) Exploring the World Scholarship, CPU, 2024
- (3) Outstanding League Member, awarded three times, CPU, 2022-2025
- (4) Scholarship of Academic Excellence, awarded three times, CPU, 2022-2025
- (5) Outstanding Graduate, SDFMU, 2022
- (6) Scholarship of Academic Excellence, awarded two times, SDFMU, 2020-2021
- (7) Work-study Exemplary Student, 2018-2019

## Skills & Hobbies

Computer Skills	Proficient in pharmacometrics software like Monolix, R, SPSS, Berkeley Madonna, NONMEM, and Phoenix WinNonlin. Experienced with Adobe Suite, including Photoshop, Premiere and After Effects.
Experiment Skills	Expertise in animal and cell culture, Western Blot, PCR, ELISA, HPLC-MS, laser confocal microscopy, high-content imaging, SPR, MST, BLI, and biomolecular interaction analysis.
Hobbies	Engaged in photography and filmmaking with provincial and school-level awards. Over ten years of chess experience with provincial awards. Active in swimming, table tennis, and badminton.