

MANYUN CHEN

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Research Interest

My overarching research goal is to combine bioinformatics, protein engineering, chemical biology, and synthetic biology tools to discover and develop novel bioactive small molecules for therapeutic purposes. Specifically, I am interested in the following directions: (1) bioinformatics guided discovery and elucidation of novel biosynthetic machineries for natural product synthesis; (2) discovery and mechanistic characterization of new enzymes and biocatalyst development; (3) microbial production or in-vitro biocatalytic synthesis of valuable natural products and analogs.

Education

Ph.D., Medicinal Chemistry, University of Florida, Gainesville, FL	2017-2022
M.S., Pharmaceutical Sciences, University of Southern California, Los Angeles, CA	2015-2017
B.S., Pharmaceutical Sciences, Tsinghua University, Beijing, China	2011-2015

Honors and Awards

Margaret O. James Top Graduating Student Award (College of Pharmacy, University of Florida)	2022
Outstanding International Student Award (University of Florida)	2021
Liberty fund for meeting travel (College of Pharmacy, University of Florida)	2021
First place in the Oral Competition, Basic Science Division (COP 34th Annual Research Showcase)	2021

Research Experience

Assistant Scientist, Center for Natural Products, Drug Discovery and Development Department of Medicinal Chemistry, University of Florida	03/2023-Present
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- ❖ *Genomics-guided discovery of the biosynthetic pathways of marine natural products*
- ❖ *Heterologous production of bioactive marine natural products in the cyanobacterium*

Postdoctoral Fellow, Department of Medicinal Chemistry, University of Florida Advisor: Dr. Yousong Ding	09/2022-02/2023
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- ❖ *Elucidation of the enzyme mechanisms of novel ATP-grasp ligases and enzyme engineering to expand their functionality*
- ❖ *Chemoenzymatic synthesis of novel anti-UV agents.*
- ❖ *Mechanistic study of a novel non-heme iron-dependent oxygenase.*

Graduate Research Assistant, Department of Medicinal Chemistry, University of Florida Advisor: Dr. Yousong Ding	08/2017-08/2022
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Doctoral Thesis: Genomics-Guided Discovery and Characterization of Natural Biosynthetic Machineries: A Study Focused on Novel Anti-UV Agents

- ❖ *Genomics-guided discovery of a novel non-heme iron-dependent oxygenase involved in the natural sunscreen mycosporine-amino acid (MAA) biosynthetic pathway.*
- ❖ *Biochemical characterization of the MAA biosynthetic enzymes and development of biocatalytic systems for the synthesis of >30 MAA analogs.*

- ❖ *Discovery and characterization of the nitropyrrole biosynthetic pathways.*
- ❖ *Gene cluster refactoring and strain engineering for enhanced production of herbicidal thaxtomins.*
- ❖ *Assembly of the partial gene cluster (~24 kb) of the cytotoxic marine natural product apratoxin.*

Graduate Research Assistant, School of Pharmacy, University of Southern California 01/2016-06/2017

Advisor: Dr. Jianming Xie

Master Thesis: Enhancing the Anti-HIV Potency of eCD4-Ig by Unnatural Amino Acid Mutagenesis

We aimed to enhance the potency of a novel HIV entry inhibitor eCD4-Ig through unnatural amino acid mutagenesis at the CD4 binding Phe43 site. Using an aminoacyl-tRNA synthetase and amber suppressor-tRNA pair, we were able to incorporate biphenylalanine or iodo-phenylalanine into CD4. We also expressed the IgG1 Fc fragment fused with CCR5 mimetic sulfopeptide in mammalian cells, which was ligated with CD4 mutants through sortase conjugation.

Undergraduate Researcher, College of Pharmacy, Tsinghua University, China 09/2014-06/2015

Advisor: Dr. Feng Qian

Bachelor Thesis: A Controlled Release Therapy for Glycogen Storage Disease

Publications

1. **Manyun Chen**, Yujia Jiang, Yousong Ding. "Recent progress in unraveling the biosynthesis of natural sunscreens mycosporine-like amino acids." *J. Ind. Microbiol. Biotechnol.*, 2023, 50(1), kuad038.
2. **Manyun Chen**, Vanisa Petriti, Amit Mondal, Yujia Jiang, Yousong Ding. "Direct aromatic nitration by bacterial P450 enzymes." *Methods Enzymol.*, 2023, 693, 307-337.
3. Blake Ushijima, Sarath P Gunasekera, Julie L Meyer, Jessica Tittl, Kelly A Pitts, Sharon Thompson, Jennifer M Sneed, Yousong Ding, **Manyun Chen**, L Jay Houk, Greta S Aeby, Claudia C Häse, Valerie J Paul. "Chemical and genomic characterization of a potential probiotic treatment for stony coral tissue loss disease." *Commun Biol.*, 2023, 6, 248.
4. Dhakal Dipesh, Dimitris Kallifidas, **Manyun Chen**, Sofia Kokkaliari, Qi-Yin Chen, Valerie J. Paul, Yousong Ding, and Hendrik Luesch. "Heterologous Production of the C33–C45 Polyketide Fragment of Anticancer Apratoxins in a Cyanobacterial Host." *Org. Lett.*, 2023, 25(13), 2238-2242.
5. Xiao Tao, Ke Liu, Qiwen Gao, **Manyun Chen**, Young S. Kim, Shouguang Jin, Yousong Ding, and Robert W. Huigens III. "Design, Synthesis, and Evaluation of Carbonate-Linked Halogenated Phenazine-Quinone Prodrugs with Improved Water-Solubility and Potent Antibacterial Profiles." *ACS Infect. Dis.*, 2023, 9(4), 899-915.
6. Ke Liu, Tao Xiao, Hongfen Yang, **Manyun Chen**, Qiwen Gao, Beau R Brummel, Yousong Ding, Robert W Huigens. "Design, synthesis and evaluation of halogenated phenazine antibacterial prodrugs targeting nitroreductase enzymes for activation." *RSC Med. Chem.*, 2023, 14(8), 1472-1481.
7. Oscar Vargas-Rodriguez, Ahmed H. Badran, Kyle S. Hoffman, **Manyun Chen**, Ana Crnković, Yousong Ding, Jonathan R. Krieger, Eric Westhof, Dieter Söll, and Sergey Melnikov. "Bacterial translation machinery for deliberate mistranslation of the genetic code." *PNAS*, 2021, 118(35), e2110797118.
8. Christopher P. Martin, **Manyun Chen**, Maria F. Martinez, Yousong Ding, and Jonathan D. Caranto. "The Ferric-Superoxo Intermediate of the TxtE Nitration Pathway Resists Reduction, Facilitating Its Reaction with Nitric Oxide". *Biochemistry*, 2021, 60 (31), 2436-2446.
9. **Manyun Chen**, Garret M. Rubin, Guangde Jiang, Zachary Raad, Yousong Ding. "Biosynthesis and Heterologous Production of Mycosporine-Like Amino Acid Palythines." *J. Org. Chem.*, 2021, 86(16), 11160–11168.
10. Dake Liu, Garret M. Rubin, Dipesh Dhakal, **Manyun Chen**, Yousong Ding, "Biocatalytic synthesis of peptidic natural products and related analogues." *iScience*, 2021, 24(5), 102512.

11. Dhakal, Dipesh, **Manyun Chen**, Hendrik Luesch, and Yousong Ding. "Heterologous production of cyanobacterial compounds." *J. Ind. Microbiol. Biotechnol.*, 2021, 48(3-4), kuab003.
12. Zhang Peilan, Brian S. MacTavish, Guang Yang, **Manyun Chen**, Jaehyeok Roh, Kevin R. Newsome, Steven D. Bruner, and Yousong Ding. "Cyanobacterial Dihydroxyacid Dehydratases Are a Promising Growth Inhibition Target." *ACS Chem. Biol.*, 2020, 15(8), 2281-2288.
13. Zhang Yi, **Manyun Chen**, Steven D. Bruner, and Yousong Ding. "Heterologous production of microbial ribosomally synthesized and post-translationally modified peptides." *Front. Microbiol.*, 2018, 9, 1801.

Research Presentations

1. Biosynthesis and heterologous production of mycosporine-like amino acid palythines. The 35th UF CoP Annual Research Showcase. Gainesville, FL. Feb 08, 2022. (poster)
2. Biocatalytic Synthesis of Natural Anti-UV Agents: Mycosporine-like Amino Acids. UF SynBio Student/Postdoc Seminar Series. Gainesville, FL. Oct 20, 2021. (virtual, oral)
3. Biosynthesis and heterologous production of mycosporine-like amino acid palythines. Society for Industrial Microbiology and Biotechnology-SIMB 71st Annual Meeting. Austin, TX. Aug 09, 2021. (poster)
4. Biocatalytic synthesis of natural anti-UV agents: mycosporine-like amino acids. The 3rd UF Drug Discovery Symposium. Gainesville, FL. Apr 22, 2021. (virtual, poster).
5. Biocatalytic synthesis of natural anti-UV agents: mycosporine-like amino acids. The 34th UF CoP Annual Research Showcase. Gainesville, FL. Apr 13, 2021. (oral)
6. Photosynthetic production of sunscreen shinorine by an engineered cyanobacterium. New Frontiers in Natural Product Discovery. Corteva Agriscience. Indianapolis, IN. Aug 07, 2019. (poster)

Key Technical Skills

- ❖ Basic and advanced techniques in molecular biology, microbiology, and genetic engineering
- ❖ Protein expression, purification [FPLC, affinity chromatography, size exclusion chromatography, and ion exchange chromatography], and protein engineering
- ❖ Biocatalysis (multienzyme one-pot catalysis, whole cell biocatalyst, enzyme kinetics, etc.)
- ❖ Isolation of microbial natural products and structural characterization using analytic techniques [HPLC and LC-MS]
- ❖ Assembly and heterologous expression of natural product biosynthetic gene clusters in microbes including *E. coli*, cyanobacteria, bacillus and streptomyces strains
- ❖ Mammalian cell culture and bioassays

Mentorship

Yujia Jiang, Graduate Student	Fall 2022 - Present
Matthew Meise, Lab technician	Spring 2022 – Spring 2023
Hens Laurent, Graduate Student	Fall 2021
Vanisa Petriti, Graduate Student	Summer 2021
Sarah M. Hylton, Undergraduate Student Volunteer	Fall 2019 - Spring 2020
Zachary Raad, Undergraduate Student Volunteer	Fall 2018 - Spring 2021
Caitlin Cain, REU of HMFL, Virginia Commonwealth University	Summer 2018
Olufunmilayo A Daudu, ReTOOL, Florida A&M University	Summer 2018
Destin Holland, Undergraduate Student Volunteer	Fall 2017 - Spring 2018
Monica A. Cozad, Graduate Student in Microbiology	Fall 2017 - Spring 2018