

Curriculum Vitae

Dr. Wei-chen Chang

Department of Chemistry
North Carolina State University
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EDUCATION

2011 - 2014

Postdoctoral Research

Department of Chemistry, The Pennsylvania State University, University Park, PA, USA
Mentor: J. Martin Bollinger, Jr., Ph.D. and Carsten Krebs, Ph.D.

Research Projects:

1. Carbapenem biosynthesis
2. Enzymatic cyclization and desaturation reactions
3. Development of new enzyme activities emerging from C-H activation

2005.09 - 2011.07

Doctoral Research

Division of Medicinal Chemistry, College of Pharmacy, The University of Texas at Austin.
Austin, TX, USA

Mentor: Hung-wen Liu, Ph.D.

Research Projects:

1. Chemical Studies of Isopentenyl Pyrophosphate Isomerase Type II
2. Elucidating Mechanisms of 2-Hydroxypropylphosphonate Epoxidase
3. Investigation of the IspH Catalyzed Reductive Deoxygenation

1999 - 2003

Bachelor of Science (B.S)

Department of Agricultural Chemistry, National Taiwan University, Taipei, Taiwan
Undergraduate Research Training and Thesis (03. 2002-06.2003)

Mentor: Tien-Yau Luh, Ph.D.

Research Project:

Developing and Synthesizing Heteroatoms Containing Oligo Aryl
Systems-New Annulation Route to Highly Photoluminescent Oligoaryls

PRIMARY APPOINTMENTS

present

Assistant Professor

Department of Chemistry, North Carolina State University, Raleigh, NC, USA

2014 - 2015

Research Associate

Department of Chemistry, The Pennsylvania State University, University Park, PA, USA

2011 - 2014	Postdoctoral Fellow Department of Chemistry, The Pennsylvania State University, University Park, PA, USA
2007 - 2011	Research Assistant Division of Medicinal Chemistry, College of Pharmacy, The University of Texas at Austin, Austin, TX, USA
2005 - 2007	Teaching Assistant Division of Medicinal Chemistry, College of Pharmacy. Department of Chemistry and Biochemistry, The University of Texas at Austin
2003 - 2005	Sergeant (Obligatory Military Service) Kinmen Defensive Center, Taiwanese Army, Kinmen, Taiwan
2002 - 2003	Undergraduate Research Assistant Institute of Chemistry, Academia Sinica, Taipei, Taiwan

ACDEMIC AWARDS & HONORS

2015	Founders Award for the 2015 Enzyme Mechanisms Conference
2010 - 2011	Vice President of Pharmacy Graduate Student Association, College of Pharmacy, University of Texas at Austin
2009	Dr. Jerry and Joan Fineg Student Professional Development Endowment. Austin, TX.
2008 - 2010	Jaime N. Delgado Endowed Graduate Fellowship in Medicinal Chemistry (3 times), Austin, TX.
2003	National Science Council Undergraduate Fellowship, Taiwan
2000	Taiwan Petroleum Corporation Scholarship, Taiwan
1999 - 2003	President's Award in National Taiwan University (4 times), Taipei, Taiwan

SCIENTIFIC MEMBERSHIP

2010-present	American Chemical Society
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PUBLICATIONS

1. Thibodeaux, C. J.; Mansoorabadi, S. O.; Kittleman, W.; Chang, W.-c.; Liu, H.-w. "Evidence for the Involvement of Acid/Base Chemistry in the Reaction Catalyzed by the Type II Isopentenyl Diphosphate/Dimethylallyl Diphosphate Isomerase from *Staphylococcus aureus*" *Biochemistry*, **2008**, *47*, 2547-2558.
2. Munos, J. W.; Moon, S.-J.; Manssorabadi, S. O.; Chang, W.-c.; Hong, L.; Yan, F.; Liu, A.; Liu, H.-w. "Purification and Characterization of the Epoxidase Catalyzing the Formation of Fosfomycin from *Pseudomonas syringae*." *Biochemistry*, **2008**, *47*, 8726-35.
3. Thibodeaux, C. J.; Chang, W.-c.; Liu, H.-w. "Linear Free Energy Relationships Demonstrate a Catalytic Role for the Flavin Mononucleotide Coenzyme of the Type II Isopentenyl Diphosphate: Dimethylallyl Diphosphate Isomerase." *J. Am. Chem. Soc.* **2010**, *132*, 9994-9996.

4. Xiao, Y.; Chang, W.-c.; Liu, H.-w.; Liu, P. "An Examination of IspH, A Key Enzyme In the Deoxyxylulose Phosphate Pathway, with Fluorosubstituted Substrate Analogues: Insight into Substrate Binding and Catalysis." *Org. Lett.* **2011**, *13*, 5912-5915.
5. Chang, W.-c.; Xiao, Y.; Liu, H.-w.; Liu, P. "Mechanistic Studies of IspH-catalyzed Reaction: Elucidation of the Mode of Substrate Binding and Protonation." *Angew. Chem. Int. Ed.* **2011**, *50*, 12304-12307.
6. Sun, H. G.; Rusczycky, M. W.; Chang, W.-c.; Thibodeaux, C. J.; Liu, H.-w. "Nucleophilic Participation of the Reduced Flavin Cofactor in the Mechanism of UDP-Galactopyranose Mutase." *J. Biol. Chem.* **2012**, *287*, 4602-4608.
7. Thibodeaux, C. J.; Chang, W.-c.; Liu, H.-w. "Enzymatic Chemistry of Cyclopropane, Epoxide, and Aziridine Biosynthesis." *Chem. Rev.* **2012**, *112*, 1681-1709.
8. Huang, H.; Chang, W.-c.; Pai, P.-j.; Romo, A.; Manssorabadi, S. O.; Russell, D. H.; Liu, H.-w. "Evidence for Radical-Mediated Catalysis by HppE – A Study Using Cyclopropyl and Methylene-cyclopropyl Substrate Analogues." *J. Am. Chem. Soc.* **2012**, *134*, 16171-16174. (Huang, H. and Chang, W.-c. contribute equally)
9. Li, N.; Chang, W.-c.; Warui, D. M.; Booker, S. J.; Krebs, C.; Bollinger, J. M., Jr. "Evidence for Only Oxygenated Cleavage of Aldehyde to Alk(a/e)nes and Formate by Cyanobacterial Aldehyde Decarbonylase." *Biochemistry*, **2012**, *51*, 7908-7916.
10. Thibodeaux, C. J.; Chang, W.-c.; Liu, H.-w. "Determining the Role of the Reduced FMN Coenzyme in the Reaction Catalyzed by the Type II Isopentenyl Diphosphate:Dimethylallyl Diphosphate Isomerase (IDI-2)." *In Proceedings of the 17th International Symposium of Flavins and Flavoproteins*. Miller, S., Hille, R., Palfey, B., Cecchini, G. Eds.; Alan R. Liss: New York, **2013**, 21-32.
11. Chang, W.-c.; Liu, P.; Dey, M.; Manssorabadi, S. O.; Moon, S.-J.; Zhao, Z.; Drennan, C. L.; Liu, H.-w. "Mechanistic Studies of an Unprecedented Enzyme-Catalyzed 1,2-Phosphono Migration Reaction." *Nature*, **2013**, *496*, 114-118.
12. Chang, W.-c.; Manssorabadi, S. O.; Liu, H.-w. "Reaction of HppE with Substrate Analogues: Evidence for Carbon-Phosphorus Bond Cleavage by a Carbocation Rearrangement." *J. Am. Chem. Soc.* **2013**, *135*, 8153-8156.
13. Zhao, L.; *Chang, W.-c.; Xiao, Y.; Liu, H.-w.; Liu, P. "Methylerythritol Phosphate Pathway: Mechanism, Regulation, and Metabolic Engineering." *Annu. Rev. Biochem.* **2013**, *82*, 497-530.
14. Chang, W.-c.; Song, H.; Liu, H.-w.; Liu, P. "Current Development in Isoprenoid Precursor Biosynthesis and Regulation." *Curr. Opin. Chem. Biol.* **2013**, *17*, 571-579.
15. Wang, C.; Chang, W.-c.; Guo, Y.; Huang, H.; Peck, S. C.; Pandelia, M. E.; Lin, G.-M.; Liu, H.-w.; Krebs, C.; Bollinger, J. M., Jr. "Evidence that the Fosfomycin-Producing Epoxidase, HppE, Is a Non-Heme-Iron Peroxidase." *Science*, **2013**, *342*, 991-995.
16. Pandelia, M. E.; Li, N.; Nørgaard, H.; Warui, D. M.; Rajakovich, L. J.; Chang, W.-c.; Booker, S. J.; Krebs, C.; Bollinger, J. M., Jr. "Substrate-Triggered Addition of Dioxygen to the Diferrous Cofactor of Aldehyde-Deformylating Oxygenase to Form a Diferric-Peroxide Intermediate." *J. Am. Chem. Soc.* **2013**, *135*, 15801-15812.
17. Matthews, M. L.; Chang, W.-c.; Layne, A. P.; Miles, L.A.; Krebs, C.; Bollinger, J. M., Jr. "Direct Nitration and Azidation of Aliphatic Carbons by an Iron-Dependent Halogenase." *Nat. Chem. Biol.* **2014**, *10*,

- 209-215.
- 18 Huang, H.; Chang, W.-c.; Romo, A.; Pai, P.-j.; Russell, D. H.; Liu, H.-w. "Stereochemical Consequence of the Reaction of the Mononuclear Non-heme Iron Enzyme HppE with 2-Hydroxy-3-methylenecyclopropyl Radical Clock Substrates." *J. Am. Chem. Soc.* **2014**, *136*, 2944-2947. (Huang, H. and Chang, W.-c. contribute equally)
 - 19 *Chang, W.-c.; Guo, Y.; Wang, C.; Butch, S. E.; Rosenzweig, A.C.; Boal, A. K.; Krebs, C.; Bollinger, J. M., Jr. "Mechanism of C5 Stereoinversion Reaction in the Biosynthesis of Carbapenem Antibiotics." *Science*, **2014**, *343*, 1140-1114.
 - 20 Martinie, R. J., Livada, J., Chang, W.-c.; Green, M. T., Krebs, C., Bollinger, J. M., Jr.; Silakov, A. "Experimental correlation of substrate position with reaction outcome in the aliphatic halogenase, SyrB2." *J. Am. Chem. Soc.* **2015**, *137*, 6912-6919.
 - 21 Bollinger, J. M., Jr.; Chang, W.-c.; Matthews, M. L.; Martinie, R. J.; Boal, A. K.; Krebs, C. "Chapter 3 Mechanisms of 2-Oxoglutarate-Dependent Oxygenases: the Hydroxylation Paradigm and Beyond." *Royal Society of Chemistry*, **2015**, 95-122.
 - 22 Rajakovich, L.J.; Nørgaard, H.; Warui, D.M.; Chang, W.-c.; Li, N.; Booker, S.J.; Krebs, C.; Bollinger, J.M.; Pandelia, M.E. "Rapid Reduction of the Diferric-Peroxyhemiacetal Intermediate in Aldehyde-Deformylating Oxygenase by a Cyanobacterial Ferredoxin: Evidence for a Free-Radical Mechanism." *J. Am. Chem. Soc.* **2015**, *137*, 11695-11709.
 - 23 Boal, A. K.; Bollinger, J. M.; Chang, W.-c. "Assembly of the Unusual Oxacycles in the Orthosomycin Antibiotics." *Proc. Natl. Acad. Sci.* **2015**, *112*, 11989-11990.
 - 24 Tamanaha, E.; Zhang, B.; Guo, Y.; Chang, W.-c.; Barr, E. W.; Xing, G.; Clair, J. St.; Ye, S.; Neese, F.; Bollinger, J. M., Jr.; Krebs, C. "Spectroscopic Evidence for the Two C–H-Cleaving Intermediates of *Aspergillus nidulans* Isopenicillin N Synthase." *J. Am. Chem. Soc.* **2016**, *138*, 8862-8874.
 - 25 *Chang, W.-c.; Li, J.; Lee, J. L.; Cronican, A. A.; Guo, Y. "Mechanistic Investigation of a Non-Heme Iron Enzyme Catalyzed Epoxidation in (-)-4'-Methoxycyclophenin Biosynthesis." *J. Am. Chem. Soc.* ASAP (DOI: 10.1021/jacs.6b05400)

RESEARCH PRESENTATION

1. Chang, W.-c.; Liu, H.-w. Investigation of the HPP Epoxidase Mechanism Using Isotopically Labeled Substrates. Gordon Research Conference 2009. Enzyme, Coenzyme and Metabolic Pathway
2. Chang W.-c.; Liu P.; Moon S-J; Zhao Z.; Liu, H.-w. Mechanistic Study of An Usual Carbon-Phosphorus Bond Rearrangement Reaction Catalyzed by HPP Epoxidase. vith Annual Louis C. Littlefield Celebrating Pharmacy Research Excellence Day 2010
3. Chang W.-c.; Liu P.; Moon S-J; Zhao Z.; Liu, H.-w. An Unusual Carbon-Phosphorus Bond Rearrangement Reaction Catalyzed by HPP Epoxidase. Texas Enzyme Conference 2010
4. Chang, W.-c.; Xiao, Y.; Liu, H.-w.; Liu, P. Elucidating IspH-catalyzed Reductive Deoxygenation Mechanisms. ixth Annual Louis C. Littlefield Celebrating Pharmacy Research Excellence Day 2011
5. Chang, W.-c.; Wang, C.; Krebs, C.; Bollinger, J. M., Jr. Involvement of Tyrosyl Radicals in the

- Sequential Epimerization and Dehydrogenation Reactions Catalyzed by Carbapenem Synthase. Gordon Research Conference 2012. Protein cofactors, Radicals and Quinones
6. Xiao, Y.; Chang, W.-c.; Freel Meyers C. L.; Liu, H.-w.; Liu, P. Mechanism Studies of Two Reductive Dehydration Reactions in the Deoxyxylose Phosphate Pathway with the Approach of Isotopic Labeled Mechanistic Probes. Gordon Research Conference 2012. Protein cofactors, Radicals and Quinones
 7. Chang, W.-c.; Miles, L.A.; Layne, A. P.; Krebs, C.; Bollinger, J. M., Jr.; Matthews, M. L. Expanding the Repertoire of Ferryl-Initiated Radical Group Transfer Reactions in the Aliphatic Halogenase, SyrB2. Gordon Research Conference 2013. Metals in Biology
 8. Chang, W.-c.; Non-Haem Iron Enzymes in the Biosynthesis of Bioactive Natural Products. International Conference on Bioinorganic Chemistry (ICBIC) 2013
 9. Chang, W.-c.; The Essential Stereoinversion in Carbapenem Biosynthesis (2): Mechanistic Implications. Frontiers in Metallobiochemistry Summer Symposium 2014
 10. Chang, W.-c.; Guo, Y.; Wang, C.; Butch, S. E.; Rosenzweig, A.C.; Boal, A. K.; Krebs, C.; Bollinger, J. M., Jr. Mechanism of the C5 Stereoinversion Reaction in the Biosynthesis of Carbapenem Antibiotics. Gordon Research Conference 2014. Enzymes, Coenzymes and Metabolic Pathways
 11. American Chemical Society (ACS) Central Regional Meeting 2014, Invited Seminar, Stereoinversion Reaction Mechanism and Beyond in the Biosynthesis of Carbapenem Antibiotics.
 12. 24th Enzyme Mechanisms Conference (EMC-24) 2015, The Founder's Travel Award Presentation, Demystifying the Chemical Magic of Non-heme-iron Enzymes in Natural Product Biosynthesis.
 13. 10th ISCMC 2016, Invited Seminar, Reveal Stereoinversion Reaction Logic in the Biosynthesis of Carbapenem Antibiotics and Beyond.
 14. National Taiwan Normal University, Invited Seminar, Taipei, Taiwan, January 21, 2016
 15. National Taiwan University, Invited Seminar, Taipei, Taiwan, January 22, 2016
 16. Kaohsiung Medical University, Invited Seminar, Kaohsiung, Taiwan, May 24, 2016
 17. 14th ISCOG 2016, Invited Seminar, Elucidating Chemical Logic of Non-heme-iron Enzymes Catalyzed Non-canonical Oxidative Modification.

AD HOC REVIEWER

Bioorganic & Medicinal Chemistry

Journal of Taibah University for Science