Timothy A. Wencewicz, PhD – CV – March 2019

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Education

September 2011	PhD, Chemistry, University of Notre Dame, South Bend, IN
May 2006	BS, Chemistry & Mathematics, Southeast Missouri State Univ., Cape Girardeau, MO

Research and Academic Appointments

July 2013 – present	Assistant Professor, Dept. of Chemistry, Washington University, St. Louis, MO Research Focus: Bioorganic Chemistry
Sept 2011 – July 2013	Postdoctoral Research Assistant, Dept. of Biological Chemistry & Molecular Pharmacology, Harvard Medical School, Boston, MA Laboratory of Prof. Christopher T. Walsh (biosynthetic enzymology)
July 2006 – Sept 2011	Graduate Student, Chem & Biochem Dept., University of Notre Dame, South Bend, IN Laboratory of Prof. Marvin J. Miller (synthetic organic chemistry)
April 2008 – July 2008	Research Intern, Dept. of Microbiology, Hans Knöll Institute, Jena, Germany Laboratory of Dr. Ute Möllmann (evaluation of new antibiotic scaffolds)
Sept. 2004 – July 2006	Undergraduate Research, Dept. of Chemistry, Southeast Missouri State University Laboratory of Prof. Mohammed Hashmat Ali (green oxidation chemistry)

Awards, Scholarships, and Fellowships

Washington University in St. Louis St. Louis, MO

2018	• Sloan Research Fellowship
2017	• Cottrell Scholar Award
2017	• NSF CAREER Award
2016	• NIH Mentoring Workshop for New Faculty in Organic and Biological Chemistry
2016	• American Chemical Society Infectious Diseases Young Investigator Award
2015	• American Chemical Society Division of Biological Chemistry Travel Award
2014	• Oak Ridge Associated Universities Ralph E. Powe Junior Faculty Enhancement Award

University of Notre Dame Notre Dame, IN

2012	• Eli J. and Helen Shaheen Graduate School Award in Science (ND's top research award)
2010 – 2011	• Rohm & Haas Outstanding Graduate Student Award (Dept.'s top research award)
	• Jeremiah Freeman Award for Teaching in Organic Chemistry (Dept.'s top teaching award)
2007 – 2010	• Chemistry-Biochemistry-Biology Interface Program Fellow (NIH T32GM075762)
2006	• KANEB Outstanding Teaching Assistant Award; Brother Columba Curran Fellowship

Southeast Missouri State University Cape Girardeau, MO

2006 • Provost's Award for College of Science (SEMO's top research award)
2006 • Dept. of Chemistry Outstanding Graduating Senior Award (Dept.'s top research award)
2005 • Dept. of Chemistry Service Award (Dept.'s top teaching award)
2004 • ACS Polymer Education Committee Outstanding Performance in Org. Chem. Award
2004 • Undergraduate Sophomore Organic Chemistry Achievement Award
2003 • Dept. of Chemistry Outstanding Freshman Award
2002 • Regents Scholarship; Missouri Bright Flight Scholarship

Professional Activities

- WUSTL Division of Biology & Biomedical Sciences (DBBS) Faculty Member (2013 – present)
- WUSTL Siteman Cancer Center Faculty Member (2014 – present)
- American Chemical Society Member (2004 – present)
- American Society of Microbiology Member (2011 – present)
- American Society for Biochemistry and Molecular Biology (2017 – present)
- Society for Industrial Microbiology and Biotechnology (2014 – 2015)
- ExxonMobil Partners in Academic Laboratory Safety (PALS) Faculty Member (2013 – present)
- Curator of the Christopher T. Walsh Strain Collection (2012 – present)
- Editorial Board Member, *Journal of Biological Chemistry* (2019 – present)
- Reviewer: *Proceedings of the National Academy of Sciences, Journal of the American Chemical Society, Journal of Organic Chemistry, FEBS Letters, Bioorganic & Medicinal Chemistry, Journal of Medicinal Chemistry, ACS Medicinal Chemistry Letters, Cell Chemical Biology, Biochemistry, Nature Chemical Biology, RSC Advances, Chemical Science, ACS Chemical Biology, Natural Product Reports, ACS Infectious Diseases, Journal of Biological Chemistry, Journal of Biological Inorganic Chemistry, Frontiers in Microbiology*, *eLIFE*, *Nature Communications*, *ChemBioChem*
- Grant proposal reviewer: National Science Foundation (panelist), Research Corporation for Science Advancement, North Carolina Biotechnology Center
- Member of the University of Notre Dame Graduate and Research Advisory Council (2014 – 2017)
- Spotlight Session Organizer on "Emerging Antibiotics from Nature": 2018 ASBMB National Meeting
- **Courses taught:** Chem262 (organic chem II), Chem451 (organic chem III), Chem453 (bioorganic chemistry)
- **Mentees:** 3 postdocs (2 female), 14 graduate students (8 female), 14 undergraduate students (7 female)

Patent Applications

1. **Wencewicz, T. A.**; Schaffer, J. E.; Reck, M. R. "Chemoenzymatic Synthesis of Peptide Beta-Lactones." WU 016508-PRO1, patent application #62/471,183, filing date 03/14/2017.

2. **Wencewicz, T. A.**; Markley, J. L.; Tolia, N.; Dantas, G.; Park, J.; Gasparrini, A.; Forsberg, K.; Vogel, J. "Inhibition and Diagnostics of Emerging Tetracycline Resistance Enzymes." WU 016593-PRO1, patent application #15/633,254, filing date 03/18/2018.

Publications

Textbooks and Book Chapters

1. Walsh, C. T.; **Wencewicz, T. A.** "Antibiotics: Challenges, Mechanisms, Opportunities." January **2016**, ASM Press, Washington DC, USA. ISBN 9781555819309

2. **Wencewicz, T. A.***; Miller, M. J. "Sideromycins as Pathogen-Targeted Antibiotics." in *Topics in Medicinal Chemistry*, *26*, *Antibacterials, Volume II*, **2017**, edited by Fisher, J. F.; Mobashery, S.; Miller, M. J.; Springer, Berlin, Heidelberg. DOI: https://doi.org/10.1007/7355_2017_19. ISBN 978-3-319-70838-6.

Peer-Reviewed Articles in Professional Journals *(undergraduates are underlined):*

32. Bohac, T. J.; Fang, L.; Giblin, D. E.; **Wencewicz, T. A.*** "Fimsbactin and Acinetobactin Compete for the Periplasmic Siderophore Binding Protein BauB in Pathogenic *Acinetobacter baumannii*" *ACS Chemical Biology*, **2019** *ASAP*, DOI: 10.1021/acschembio.8b01051
31. Markley, J. L.; Fang, L.; Gasparrini, A. J.; Symister, C. T.; Kumar, H.; Kong, A.; Tolia, N. H.*; Dantas, G.*; **Wencewicz, T. A.*** "Semisynthetic Analogues of Anhydrotetracycline as Inhibitors of Tetracycline Destructase." *ACS Infectious Diseases*, **2019** *ASAP*, DOI: 10.1021/acsinfecdis.8b00349
30. Gasparrini, A. J.; Markley, J. L.; Kumar, H.; Wang, B.; Fang, L.; Irum, S.; Wallace, M.; Burnham, C.-A. D.; Tolia, N. H.*; **Wencewicz, T. A.***; Dantas, G.* "Tetracycline resistance by inactivation across environmental, human commensal, and pathogenic microbes." *Nature Chem. Biol.* **2019** *submitted* 2/1/19.
29. Bailey, D. C.; Bohac, T. J.; Shapiro J. A.; Giblin, D. E.; **Wencewicz, T. A.***; Gulick, A. M.* "Crystal Structure of the Siderophore Binding Protein BauB Bound to an Unusual 2:1 Complex Between Acinetobactin and Ferric Iron." *Biochemistry* **2018**, *57*, 6653–6661.
28. Markley, J. L.; Morse, T. L.; Rath, N. P.; **Wencewicz, T. A.*** "Photocyclization of Beta-Ketoformamides to 3-Hydroxy-Beta-Lactams" *Tetrahedron* **2018**, *74*, 2743-2753.
27. Markley, J. L.; **Wencewicz, T. A.*** "Tetracycline Inactivating Enzymes" *Frontiers in Microbiology*, **2018**, *9*, article 1058. DOI: https:doi.org/10.3389/fmicb.2018.01058 invited by Dr. Graeme Conn for a special issue entitled "Bacterial Mechanisms of Antibiotic Resistance: A Structural Perspective".
26. Sann Rivera, G. M.; Beamish, C. R.; **Wencewicz, T. A.*** "Immobilized FhuD2 Siderophore-Binding Protein Enables Purification of Salmycin Sideromycins from *Streptomyces violaceus* DSM 8286" *ACS Infectious Diseases* **2018**, *4*, 845-859.
25. Patrick, G. J.; Fang, L.; Schaefer, J.; Singh, S.; Bowman, G. R.; **Wencewicz, T. A.*** "Mechanistic basis for ATP-dependent inhibition of glutamine synthetase by tabtoxinine-β-lactam." *Biochemistry* **2018**, *57*, 117-135. **Invited for special issue entitled "Future of Biochemistry".**
24. Bohac, T. J.; Shapiro, J. A.; **Wencewicz, T. A.*** "Rigid oxazole acinetobactin analog blocks siderophore cycling in *Acinetobacter baumannii*." *ACS Infectious Diseases* **2017**, *3*, 802-806.
23. Schaffer, J. E.; Reck, M. R.; Prasad, N. K.; **Wencewicz, T. A.*** "Beta-Lactone formation during antibiotic cleavage from a non-ribosomal peptide synthetase." *Nature Chemical Biology* **2017**, *13*, 737-744. ***F1000 highlighted article.**
22. Park, J.; Gasparrini, A. J.; Reck, M. R.; Symister, C.; Elliott, J. L.; Vogel, J. P.; **Wencewicz, T. A.***; Dantas, G.*; Tolia, N. H.* "Plasticity, dynamics, and inhibition of emerging tetracycline-resistance enzymes." *Nature Chemical Biology* **2017**, *13*, 730-736. ***Co-corresponding authors.**
21. Shapiro, J. A.; **Wencewicz, T. A.*** "Structure-function studies of acinetobactin analogs." *Metallomics* **2017**, *9*, 463-470. **Featured on inside journal cover. *Editor's choice as "HOT ARTICLE".***
20. Endicott, N. P.; Lee, E.; **Wencewicz, T. A.*** "Structural basis for xenosiderophore utilization by the human pathogen *Staphylococcus aureus*." *ACS Infectious Diseases* **2017**, *3*, 542-553.
19. **Wencewicz, T. A.*** "New antibiotics from nature's chemical inventory." *Bioorganic & Medicinal Chemistry*, **2016**, *24*, 6227-6252. ***Invited article for antibiotics special issue featuring world leaders in the field.***
18. Shapiro, J. A.; **Wencewicz, T. A.*** "Acinetobactin Isomerization Enables Adaptive Iron Acquisition in *Acinetobacter baumannii* through pH-Triggered Siderophore Swapping." *ACS Infectious Diseases* **2016**, *2*, 157-168. ***Featured as cover article for Feb 2016 issue.***
17. Hart, K. M.; Reck, M.; Bowman, G.; **Wencewicz. T. A.*** "Tabtoxinine-β-Lactam is a 'Stealth' β-Lactam Antibiotic that Evades β-Lactamase-Mediated Antibiotic Resistance." *Med. Chem. Commun.* **2016**, *7*, 118-127. ***Invited article for antibiotics special issue featuring world leaders in the field.***
16. Gelman, S. J.; Mahieu, N. G.; Cho, K.; Llufrio, E. M.; **Wencewicz, T. A.**; Patti, G. J.* "Evidence that 2-Hydroxyglutarate is Not Readily Metabolized in Colorectal Carcinoma Cells." *Cancer Metabolism* **2015**, *3:13*, doi: 10.1186/s40170-015-0139-z, eCollection 2015.
15. Forsberg, K. J.; Patel, S.; **Wencewicz, T. A.***; Dantas, G.* "The Tetracycline Destructases: A Novel Family of Tetracycline-Inactivating Enzymes." *Chemistry & Biology*, **2015**, *22*, 888-897. ***Co-corresponding authors.**

Published Prior to WUSTL (undergraduate coauthors are underlined):

14. Walsh, C. T.; **Wencewicz, T. A.** "Prospects for new antibiotics: A molecule-centered perspective." *J. Antibiotics* **2014**, *67*, 7-22. ***Winner of JA Medal for Excellence.***
13. **Wencewicz, T. A.**; Miller, M. J. ""Biscatecholate-monohydroxamate mixed ligand siderophore-carbacephalosporin conjugates are selective sideromycin antibiotics that target *Acinetobacter baumannii*." *J. Med. Chem.* **2013**, *56*, 4044-4052.
12. **Wencewicz, T. A.**; Long, T. E.; Möllmann, U.; Miller, M. J. "Trihydroxamate siderophore-fluoroquinolone conjugates are selective sideromycin antibiotics that target *Staphylococcus aureus*." *Bioconjugate Chemistry* **2013**, *24*, 473-486.
11. **Wencewicz, T. A.**; Walsh, C. T. "*P. syringae* self protection from tabtoxinine-β-lactam by ligase TblF and acetylase Ttr." *Biochemistry* **2012**, *51*, 7712-7725.
10. Walsh, C. T.; **Wencewicz, T. A.** "Flavoenzymes: Versatile catalysts in biosynthetic pathways." *Nat. Prod. Rep.* **2012**, *30*, 175-200.
9. **Wencewicz, T. A.**; Oliver, A. G.; Miller, M. J. "Iron(III)-templated macrolactonization of trihydroxamate siderophores." *Org. Lett.* **2012**, *14*, 4390-4393.
8. **Wencewicz, T. A.**; Yang, B.; Rudloff, J. R.; Oliver, A. G.; Miller, M. J. "N-O chemistry for antibiotics: Discovery of *N*-alkyl-*N*-(pyridin-2-yl)hydroxylamine scaffolds as selective antibacterial agents using nitroso Diels-Alder and ene chemistry." *J. Med. Chem.* **2011**, *54*, 6843-6858.
7. Mayfield, J. A.; Frederick, R. E.; Streit, B. R.; **Wencewicz, T. A.**; Ballou, D. P.; DuBois, J. L. "Comprehensive spectroscopic, steady state, and transient kinetic studies of a representative siderophore-associated flavin monooxygenase." *J. Biol. Chem.* **2010**, *285*, 30375-30388.
6. Yan, S.; Miller, M. J.; **Wencewicz, T. A.**; Möllmann, U. "Syntheses and biological evaluation of new cephalosporin-oxazolidinone conjugates." *Med. Chem. Comm.* **2010**, *1*, 145-148.
5. Yan, S.; Miller, M. J.; **Wencewicz, T. A.**; Möllmann, U. "Syntheses and antibacterial activity studies of new oxazolidinones from nitroso Diels-Alder chemistry." *Bioorg. & Med. Chem. Lett.* **2010**, *20*, 1302-1305.
4. **Wencewicz, T. A.**; Möllmann, U.; Long, T. E.; Miller, M. J. "Is drug release necessary for antimicrobial activity of siderophore-drug conjugates? Syntheses and biological studies of the naturally occurring salmycin 'Trojan Horse' antibiotics and synthetic desferridanoxamine-antibiotic conjugates." *Biometals* **2009**, *22*, 633-648.
3. Ali, M. H.; Hedell, J.; **Wencewicz, T.** "Oxidation of sulfides to sulfoxides with 1,3-dibromo-5,5-dimethylhydantoin in the presence of hydrated silica gel." *Journal of Sulfur Chemistry* **2009**, *30*, 160-166.
2. Ali, M. H.; Kriedelbaugh, D.; **Wencewicz, T.** "Ceric ammonium nitrate (CAN) catalyzed oxidation of sulfides to sulfoxides." *Synthesis* **2007**, *22*, 3507-3511.
1. Ali, M. H.; Hartman, M.; Lamp, K.; Schmitz, C.; **Wencewicz, T.** "Oxidation of sulfides with *N*-bromosuccinimide in the presence of hydrated silica gel." *Synthetic Commun.* **2006**, *36*, 1769-1777.

Research Support

Active

1R01AI123394-01, NIH/NIAID, 02/11/16 – 01/31/21, Wencewicz (Co-PI), Tolia (Co-PI), Dantas (Co-PI)
TITLE: Structural, Mechanistic, & Evolutionary Characterization of Tetracycline Destructases
The goal of this project is to investigate the genetic origins, dissemination, and molecular mechanisms of tetracycline destructase resistance enzymes and develop inhibitors for combination antibiotic therapies.

CHE-1654611, NSF-CAREER, 06/01/17 – 05/31/22, Wencewicz (PI)
TITLE: CAREER: Siderophore Chemistry in Pathogenic Bacteria
The goal of this project is to study mechanisms of siderophore-mediated metal acquisition in bacteria.

CS-24056, Cottrell Scholar Award, Res. Corp. for Science Advancement, 07/1/17–06/30/20, Wencewicz (PI)
TITLE: Chemoenzymatic Synthesis of Strained Beta-Lactones
The goal of this project is to study biosynthetic pathways that produce beta-lactone natural products and elucidate the mechanisms of enzymes catalyzing the formation of beta-lactone rings.

Sloan Research Fellowship, 04/01/18–03/31/20, Wencewicz (PI)
This award provides funds to support all research activities in my laboratory.

MI-PD-II-2018-748, Interdisciplinary Research Initiative, Children's Discovery Institute, St. Louis Children's Hospital, Washington University School of Medicine, 02/01/18 – 01/31/21, Wencewicz (PI)
TITLE: Blocking Nitrogen Metabolism in TB
The goal of this project is to develop novel glutamine synthetase inhibitors as anti-TB agents.

W. M. Keck Fellowship, 07/01/18–06/30/19, Wencewicz (PI)
This award provides funds to support one postdoctoral researcher (Dr. Jana L. Markley) in my laboratory.

Completed

Oak Ridge Associated Universities Ralph E. Powe Jr Faculty Enhancement Award, 06/01/2014–05/31/2015
TITLE: Rusting Out Bacteria in the Host-Pathogen Battle for Iron
ROLE: PI
TOTAL AWARD AMOUNT: $10,000
The goal of this project was to study the chemistry and biology of hydroxamate siderophores.

Invited Seminars

(**32**) Xiamen University (China, chemistry 2019), (**31**) University of Florida (chemistry 2018), (**30**) Auburn University (chemistry/biochemistry 2018), (**29**) Duke University (chemistry 2018), (**28**) International Biometals Conference (Ottawa 2018), (**27**) Southeast Regional ACS Meeting (biochemical mechanisms 2018), (**26**) ASBMB National Conference (spotlight session organizer, Emerging Antibiotics from Nature 2018), (**25**) SUNY Buffalo (chemistry 2018), (**24**) Vanderbilt University (chemistry 2018), (**23**) University of Kentucky (pharmacy 2018), (**22**) Southern Illinois University (pharmacy 2018), (**21**) University of Illinois-Urbana Champaign (Mining Microbial Genomes Keynote 2018), (**20**) University of California-Los Angeles (chemistry/biochemistry 2017), (**19**) Emory (chemistry 2017), (**18**) Murray State (chemistry 2017), (**17**) GRC (Enzymes, Coenzymes, and Metabolic Pathways, 2017), (**16**) University of Wisconsin-Madison (Perlman Antibiotic Symposium Keynote 2017), (**15**) Wichita State (chemistry 2017), (**14**) GRC (Metals in Medicine 2016), (**13**) Monsanto (2016), (**12**) Virginia Tech (biochemistry 2016), (**11**) University of Mississippi (pharmacy 2016), (**10**) University of Missouri–Columbia (organic chemistry day 2016), (**8–9**) University of Notre Dame (chemistry/biochemistry 2016, NIH T32 2013), (**7**) University of Missouri–St. Louis (chemistry 2015), (**6**) Truman State University (chemistry 2015), (**5**) Christopher Newport University (chemistry 2015), (**4**) Southeast Missouri State University (chemistry 2014), (**1–3**) Washington University School of Medicine (micro 2013, biochem retreat Keynote 2014, pediatrics 2015)

Contributed Presentations (*During Time at WUSTL*)

(**14**) 9th Annual American Society of Pharmacognosy Conference (biosynthesis session, 2018), (**13**) 255th American Chemical Society National Meeting (med chem, 2018), (**12**) 255th American Chemical Society National Meeting (biological chemistry early investigators, 2018), (**11**) Gordon Research Conference (natural products and bioactive compounds, 2017), (**10**) Gordon Research Conference (enzymes, coenzymes, and metabolic pathways, 2016), (**9**) 50th Midwest Regional ACS Meeting (drug discovery, 2015), (**8**) 22nd Annual Biochemistry Retreat (WUSTL, 2015), (**7**) 22nd Midwest Microbial Pathogenesis Conference (Indiana University School of Medicine, 2015), (**6**) Gordon Research Conference (enzymes, coenzymes, and metabolic pathways, 2015), (**5**) 249th American Chemical Society National Meeting (biological chemistry young investigator symposium, 2015), (**4**) 24th Enzyme Mechanisms Conference (Galveston, TX, 2015), (**3**) 49th Midwest Regional ACS Meeting (organic & med chem, 2014), (**2**) Gordon Research Conference (enzymes, coenzymes, and metabolic pathways, 2014), (**1**) 20th Annual Biochemistry Retreat (WUSTL, 2013)

University Service

- Safety Committee
- Graduate Admissions Committee
- Website Committee
- Awards Committee

Outreach

- Catalysts for Change Faculty Sponsor
- Young Scientists Program Faculty Sponsor
- ExxonMobil Partners in Laboratory Safety (PALS) Faculty Sponsor