

## Timothy A. Wencewicz, PhD – CV – September 2017

Washington University in St. Louis  
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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 Teaching Appointments

July 2013 – present      Assistant Professor, Dept. of Chemistry, Washington University, St. Louis, MO  
Research Focus: Bioorganic & Medicinal 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

2017                      • Cottrell Scholars 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 Award for College of Science (SEMO's top research award)  
2006                      • Chem. Dept. Outstanding Graduating Senior Award (Dept's top research award)  
2005                      • Department of Chemistry Service Award (Dept's top teaching award)  
2004                      • ACS Polymer Education Committee Outstanding Performance in Org. Chem. Award

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| 2004 | • Undergraduate Sophomore Organic Chemistry Achievement Award |
| 2003 | • Department 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)
- Society for Industrial Microbiology and Biotechnology (2014 – 2015)
- Curator of the Christopher T. Walsh Strain Collection (2012 – present)
- Ad hoc 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*, *Chemistry & Biology*
- Member of the University of Notre Dame Graduate and Research Advisory Council (2014 – 2017)
- **Invited seminars:** UCLA (2017), University of Wisconsin-Madison (2017, Perlman Symposium on Antibiotics), Emory (2017), Wichita State (2017), Monsanto (2016), Virginia Tech (2016), University of Mississippi (2016), University of Missouri – Columbia (2016), University of Notre Dame (2016, 2013), University of Missouri – St. Louis (2015), Truman State University (2015), Christopher Newport University (2015), Southeast Missouri State University (2014), Washington University in St. Louis School of Medicine (2013, 2014, 2015)
- Courses taught: Chem262 (organic chem II), Chem451 (organic chem III), Chem453 (bioorganic chemistry)

## Publications

### Textbooks

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

### Book Chapters

1. **Wencewicz, T. A.**; Miller, M. J. “Sideromycins as Pathogen-Targeted Antibiotics.” in *Topics in Medicinal Chemistry*. **2017**, Springer, Berlin, Heidelberg. DOI: [https://doi.org/10.1007/7355\\_2017\\_19](https://doi.org/10.1007/7355_2017_19).

## Peer-Reviewed Articles in Professional Journals

### *During Time at WUSTL:*

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.
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. Reached #2 on list of most read articles for the journal. Media highlights in WUSTL Record, Science Daily, and The Pathologist.**
17. Hart, K. M.; Reck, M.; Bowman, G.; **Wencewicz, T. A.\*** "Tabtoxinine- $\beta$ -Lactam is a 'Stealth'  $\beta$ -Lactam Antibiotic that Evades  $\beta$ -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.; Llufrío, 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.**

*Prior to WUSTL:*

14. Walsh, C. T.; **Wencewicz, T. A.** "Prospects for new antibiotics: A molecule-centered perspective." *J. Antibiotics* **2014**, *67*, 7-22.
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- $\beta$ -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." *Biomaterials* **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

TITLE: Structural, Mechanistic, & Evolutionary Characterization of Tetracycline Destructases

ROLE: Wencewicz (Co-PI), Tolia (Co-PI), Dantas (Co-PI)

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

TITLE: CAREER: Siderophore Chemistry in Pathogenic Bacteria

ROLE: PI

The goal of this project is to elucidate the chemical principles of siderophore-mediated metal acquisition pathways in pathogenic bacteria to enable new metal chelation probes that can be used to study metal trafficking in cells, image cellular processes, and target the delivery of molecular cargo to bacteria.

CS-24056, Cottrell Scholars Award, Research Corporation for Science Advancement, 07/1/17–06/30/20

TITLE: Chemoenzymatic Synthesis of Strained Beta-Lactones

ROLE: PI

The goal of this project is to study biosynthetic pathways that produced beta-lactone natural products and elucidate the mechanisms of enzymes catalyzing the formation of beta-lactone rings.

### 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: Wencewicz (PI)

The goal of this project is to investigate the correlation between the iron(III)-binding affinities of siderophores from bacterial pathogens and the competitive ability of these siderophores to expedite the acquisition of iron(III)-nutrient during the course of an infection.