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# MICHAEL F. FREEMAN

## EDUCATION

*Johns Hopkins University*, Baltimore, Maryland, USA
Ph.D. Biology, 2008

*University of Massachusetts*, Amherst, Massachusetts, USA
B.S. Biochemistry and Molecular Biology, 2001
*GPA: 3.9/4.0*

## RESEARCH EXPERIENCE

2016-present **Assistant Professor at the University of Minnesota**
Department of Biochemistry, Molecular Biology, and Biophysics & The Biotechnology Institute

2010-2015 **Post-doctoral Research with Professor Jörn Piel**
Eidgenössische Technische Hochschule (ETH) Zurich, Zurich, Switzerland
University of Bonn, Bonn, Germany
*Discovery and Elucidation of Marine Natural Products*

2008-2010 **Post-doctoral Research with Professor Craig A. Townsend**
Johns Hopkins University, Baltimore, Maryland, USA
*Regulation of β-Lactam Antibiotics in Streptomyces*

2001-2008 **Graduate Research with Professor Craig A. Townsend**
Johns Hopkins University, Baltimore, Maryland, USA
*Characterization of Enzymes Involved in Thienamycin Biosynthesis*

1999-2001 **Undergraduate Research with Professor Craig T. Martin**
University of Massachusetts, Amherst, Massachusetts, USA
*Directed Evolution of T7 RNA Polymerase Promoters*

*Publications* ** Equal contribution of authors, § Co-corresponding authors, † Corresponding author*

23. Bhushan, A, Egli, PJ, Peters, EE, **Freeman, MF**, Piel, J (**2019**) A genome mining and synthetic biology-enabled production platform for highly complex polytheonamide-type cytotoxins. *Nat. Chem., Online Sept 9,* DOI: 10.1038/s41557-019-0323-9.
[Concentrates: *Chem. Eng. News* **2019** 97(36)]

22. Quijano, MR*, Zach, C*, Miller, FS, Lee, AR, Imani, AS, Künzler, M§, **Freeman, MF§** (**2019**) Distinct autocatalytic α-*N*-methylating precursors expand the borosin RiPP family of peptide natural products. *J. Am. Chem. Soc.,* 141(24): 9637-9644. DOI: 10.1021/jacs.9b03690.

21. Helf, MJ, **Freeman, MF**, Piel, J (**2019**) Investigations into PoyH, a promiscuous protease from polytheonamide biosynthesis, *J. Ind. Microbiol. Biotechnol.* 46(3-4): 551-563. DOI: 10.1007/s10295-018-02129-3.
[Special issue: "Natural product discovery and development in the genomic era 2019".]

20. Song, H, van der Velden, NS, Shiran, SL, Bleiziffer, P, Zach, C, Sieber, R, Imani, AS, Krausbeck, F, Aebi, M, **Freeman, MF**, Riniker, S§, Kuenzler, M§, Naismith, JH§ (**2018**) A molecular mechanism for the enzymatic methylation of nitrogen atoms within peptide bonds, *Sci. Adv.* 4(8): eaat2720. DOI: 10.1126/sciadv.aat2720.

19. Miller, FS, **Freeman, MF†** (**2018**) Impact of synthetic biology on secondary metabolite biosynthesis, *Modern biocatalysis: Advances towards synthetic biological systems*. RSC Publishing Cambridge, UK. Chapter 11: 287-320. DOI: 10.1039/9781788010450.

18. **Freeman, MF†** (**2018**) Cobalamin-dependent C-methyltransferases from marine microbes: accessibility via rhizobia expression, *Methods Enzymol.* 604:259-286. DOI: 10.1016/bs.mie.2018.02.013.

17. Imani, AS, **Freeman, MF†** (**2018**) RiPPing apart the rules for peptide natural products, *Syst. Synth. Biotechnol.* 3(2): 81-82. DOI: 10.1016/j.synbio.2018.03.002.

16. van der Velden, NS, Kaelin, N, Helf, MJ, Piel, J, **Freeman, MF§**, Kuenzler, M§ (**2017**) Autocatalytic backbone N-methylation in a family of ribosomal peptide natural products, *Nat. Chem. Biol.* 13(8): 833-835. DOI: 10.1038/nchembio.2393.
[News and Views: *Nat. Chem. Biol*. **2017** 13: 821-822.]
[Highlight: *Angew. Chem. Int. Ed. Engl.* **2017** 56: 2-5.]

15. Morinaka, BI, Verest, M, **Freeman, MF**, Gugger, M, Piel, J (**2017**) An orthogonal $D_2O$-based induction system provides insights into D-amino acid pattern formation by radical *S*-adenosylmethionine peptide epimerases, *Angew. Chem. Int. Ed. Engl.* 56: 762-766. DOI: 10.1002/anie.201609469.

14. **Freeman, MF§**, Helf, MJ, Bhushan, A, Morinaka, BI, Piel, J§ (**2017**) Seven enzymes create extraordinary molecular complexity in an uncultivated bacterium, *Nat. Chem*. 9: 387-395. DOI: 10.1038/nchem.2666.
[Research Highlight: *Nat. Chem. Biol.* **2017** 13: 129.]
[Leading Edge: *Cell* **2017** 169: 373.]

13. **Freeman, MF**, Vagstad, AL, Piel, J (**2016**) Polytheonamide biosynthesis showcasing the metabolic potential of sponge-associated uncultivated 'Entotheonella', *Curr. Opin. Chem. Biol.* 31: 8-14. DOI: 10.1016/j.cbpa.2015.11.002.

12. Buller, AR, **Freeman, MF**, Schildbach, JF, Townsend, CA (**2014**) Exploring the role of conformational heterogeneity in *cis*-autoproteolytic activation of ThnT, *Biochemistry* 53(26): 4273-4281. DOI: 10.1021/bi500385d.

11. Morinaka, BI, Vagstad, AL, Helf, MJ, Gugger, M, Kegler, C, **Freeman, MF**, Bode, HB, Piel, J (**2014**) Radical *S*-adenosyl methionine epimerases: regioselective introduction of diverse D-amino acid patterns into peptide natural products, *Angew. Chem. Int. Ed.* 53(32): 8503-8507. DOI: 10.1002/anie.201400478.

10. Cai, X, Teta, R, Kohlhass, C, Cruesemann, M, Ueoka, R, Mangoni, A, **Freeman, MF**[§], Piel, J[§] (**2013**) Manipulation of regulatory genes reveals complexity and fidelity in hormaomycin biosynthesis, *Chem. Biol.* 20(6): 839-846. DOI: 10.1016/j.chembiol.2013.04.018.

9. **Freeman, MF***, Gurgui, C*, Helf, MJ, Uria, AR, Oldham, NJ, Sahl, HG, Matsunaga, S, Piel, J (**2012**) Metagenome mining reveals polytheonamides as posttranslationally modified ribosomal peptides, *Science* 338: 387-390. DOI: 10.1126/science.1226121.
[Concentrates: *Chem. Eng. News* **2012** 90(3): 26.]
[In Brief: *Nat. Rev. Microbiol.* **2012** 10:802.]

8. Buller, AR, Labonte, JW, **Freeman, MF**, Wright, NT, Schildbach, JF, Townsend, CA (**2012**) Autoproteolytic activation of ThnT results in structural reorganization necessary for substrate binding and catalysis, *J. Mol. Biol.* 422(4): 508-518. DOI: 10.1016/j.jmb.2012.06.012.

7. Labonte, JW, Kudo, F, **Freeman, MF**, Raber, ML, Townsend, CA (**2012**) Engineering the synthetic potential of β-lactam synthetase and the importance of catalytic group dynamics, *MedChemComm.* 3: 960-966. DOI: 10.1039/C2MD00305H.

6. Buller, AR, **Freeman, MF**, Wright, NT, Schildbach, JF, Townsend, CA (**2011**) Insights into cis-autoproteolysis reveal a reactive state formed through conformation rearrangement, *Proc. Natl. Acad. Sci. U.S.A.* 109(7): 2308-2313. DOI: 10.1073/pnas.1113633109.

5. Bodner, MJ, Li, R, Phelan, RM, **Freeman, MF**, Moshos, KA, Lloyd, E, Townsend, CA (**2011**) Definition of the common and divergent steps in carbapenem β-lactam antibiotic biosynthesis, *ChemBioChem.* 12(14): 2159-2165. DOI: 10.1002/cbic.201100366.

4. Gulder, TAM, **Freeman, MF**, Piel, J (**2011**) The catalytic diversity of multimodular polyketide synthases: natural product biosynthesis beyond textbook assembly rules, *Top. Curr. Chem.* (pp. 1-53) Springer-Verlag Berlin Heidelberg. DOI: 10.1007/128_2010_113.

3. Bodner, MJ, Phelan, R, **Freeman, MF**, Li, R, Townsend, CA (**2010**) Non-heme iron oxygenases generate natural structural diversity in carbapenem antibiotics, *J. Am. Chem. Soc.* 132(1): 12-13. DOI: 10.1021/ja907320n.

2. Raber, ML, **Freeman, MF**, Townsend, CA (**2009**) Dissection of the stepwise mechanism to β-lactam formation and elucidation of a rate-determining conformational change in β-lactam synthetase, *J. Biol. Chem.* 284(1): 207-217. DOI: 10.1074/jbc.M805390200.

1. **Freeman, MF**, Moshos, KA, Bodner, MJ, Li, R, Townsend, CA (**2008**) Four enzymes define the role of coenzyme A in thienamycin biosynthesis, *Proc. Natl. Acad. Sci. U.S.A.* 105(32): 11128-11133. DOI: 10.1073/pnas.0804500105.
[Research Highlight: *ACS Chem. Biol.* **2008** 3(9): 522.]

*Oral Presentations*

**Freeman, MF** Convener, SIMB Annual Meeting, Washington DC, July 24, **2019**.

**Freeman, MF** Invited speaker, SIMB Annual Meeting, Chicago, IL, August 16, **2018**.

**Freeman, MF** Invited speaker, ASBMB / Experimental Biology 2018, San Diego, CA, April 23, **2018**.

**Freeman, MF** MinnCrest training seminar "How to start a lab?", University of Minnesota, April 18, **2018**.

**Freeman, MF** Invited speaker, MycoNet seminar, University of Minnesota, MN April 11, **2018**.

**Freeman, MF** BTI lunch training seminar, University of Minnesota, MN, March 26, **2018**.

**Freeman, MF** Invited speaker, ACS National Conference, New Orleans, LA, March 22, **2018**.

**Freeman, MF** Invited speaker, Developmental Biology Center Seminar, University of Minnesota, December 7, **2017**.

**Freeman, MF** Invited speaker, Bug Club, University of Minnesota, October 13, **2017**.

**Freeman, MF** BMBB annual retreat, Itasca State Park, University of Minnesota, October 1, **2017**.

**Freeman, MF** Joint Symposium on Microbial Biotechnology, University of Minnesota, August 8, **2017**.

**Freeman, MF** Invited speaker, Biofilm club, University of Minnesota, April 4, **2017**.

**Freeman, MF** Directing Biosynthesis V, Norwich England, March 22, **2017**. (*Lightning talk*)

**Freeman, MF** Co-organizer, 2017 Microbial Factories Symposium, University of Minnesota, February 6, **2017**.

**Freeman, MF** Invited speaker, Microbial Communication Colloquium, Friedrich Schiller University, Jena, Germany, November 30, **2016**.

**Freeman, MF** Invited speaker, Mini-symposium: Structural aspects of synthetic biology systems, University of Minnesota, St. Paul, Minnesota, USA, August 3, **2016**.

**Freeman, MF** Invited Speaker, Biofilm Club Symposium, University of Minnesota, St. Paul, Minnesota, USA, May 20, **2016**.

**Freeman, MF** Invited Speaker, Science on the Spot, University of Minnesota, St. Paul, Minnesota, USA, April 14, **2016**.

**Freeman, MF** Invited Speaker, Host: Prof. Dr. Yaniv Brandvain. PBS Colloquium, University of Minnesota, St. Paul, Minnesota, USA, April 5, **2016**.

**Freeman, MF** Invited Speaker, Host: Prof. Dr. Michael H. Walter. University of Northern Iowa, Cedar Falls, Iowa, February 29, USA, **2016**.

**Freeman, MF** BMBB annual retreat, Itasca State Park, University of Minnesota, September 25, **2015**.

## PATENTS

Aebi, M, Kuenzler, M, Piel, J, **Freeman, MF**, van der Velden, N, Kaelin, N, Novel multiply backbone N-methyl transferases and uses thereof, US20190112583A1, April, 4, **2019**.

Kuenzler, M, van der Velden, N, **Freeman, MF**, Piel, J, Aebi, M, Kaelin, N, Novel multiply backbone N-methyl transferases and uses thereof, WO2017EP58327, October 12, **2017**.

Piel, J, Gurgui, C, **Freeman, MF**, Uria, AR, Helf, MJ, Biosynthetic gene cluster for the production of peptide/protein analogues, WO2013034579 A1, March 14, **2013**.

Townsend, CA, Bodner, MJ, Phelan, RM, **Freeman, MF**, Method for late introduction of the (8R)-hydroxyl group in carbapenem beta-lactam antibioitc synthesis, EP2513112 A2, October 24, **2012**.

## MENTORING

*Current members*

Post-docs (0):

Visiting Scholars (0):

PhD students (4): Kathryn K. Crone (3/2019- )
Aileen R. Lee (4/2018- )
Aman S. Imani (4/2018- )
Fredarla S. Miller (1/2016- )

Undergraduates (3): Chandler N. Hellenbrand (1/2018- ; LSSURP 6/2018-8/2018, UROP 6/2019-8/2019)
Sayuj Suresh (9/2019- )
Sarah Schmidt-Dannert (9/2019- )

*Past members*

Post-docs (2): Matthew Jensen (10/2017-8/2018) *Assistant Professor at Concordia University, St. Paul*
Keshav Nepal (2/2016-6/2017) *Postdoc at University of Washington in St. Louis*

Master's students (1): Marissa R. Quijano (7/2016-8/2018)

Visiting Scholars (3): Chloé Lopez (5/2019-8/2019) *Biotechnology Master's student at the University of Lille, France*
Anna von Linden Glöckle (1/2019-3/2019) *Ph.D. student at Technische Universität München, Germany*
Jakub Michalski (7/2018-8/2018) *Ph.D. student at Poznań University, Poland*

Technicians (1): Amani S. Imani (6/2016-8/2017)

Undergraduates (4): Alexander Hutchens (1/2018-6/2019)
Ryan Baer (2/2017-12/2017)
Jacob Anderson (9/2016-5/2017; UROP scholar)
Kinsey Philips (6/2016-5/2017)

High Schoolers (5): Sayuj Suresh (12/2018-2/2019)
Saahil Chadha (6/2018)
Elena Romanshkova (6/2018)
Lucy Chen (01/2018-05/2018; PSEO)
Luke Bunday (9/2016-9/2017)

*Rotation students*

BMBB Ph.D. Morgan Esler (C/O 2018)
Peng Lei (C/O 2018)

| | |
|---|---|
| | Kathryn Crone (C/O 2018) |
| | Aileen R. Lee (C/O 2017) |
| | Aman S. Imani (C/O 2017) |
| | Nathaniel Gaut (C/O 2016) |
| | Fredarla S. Miller (C/O 2015) |
| MicE Master's | Nisha Vishwanathan (C/O 2017) |
| | Marissa Quijano (C/O 2015) |

*Thesis committees*

| | |
|---|---|
| 2019- | Judee Sharon (BMBB) |
| | Wakana Sato (BMBB) |
| | Amani S. Imani (BMBB) |
| | Aileen R. Lee (BMBB) |
| | Colin Pierce (BMBB) |
| 2018- | Colette Rogers (BMBB) |
| | Serina Robinson (MiCAB) |
| | Nathaniel Gaut (BMBB) |
| 2017- | Fredarla S. Miller (BMBB) |
| | Komal Joshi (BMBB, *chair*) |
| | Lev Ostrer (BMBB) |
| 2016- | Suzie Hzu (BMBB) |

## TEACHING

| | |
|---|---|
| 2019, Spring | BioC4331: Biochemistry 1: Structure, Catalysis, and Metabolism (70 students) |
| 2017, Fall | BioC3960 Research Topics in Biochemistry, Guest lecturer, University of Minnesota |
| 2017, Summer | Co-director of MCSB graduate research course, Itasca Biological Station, University of Minnesota. |
| 2017, Spring | BioC5309 Biocatalysis and Biodegradation, Guest lecturer, University of Minnesota |

## AWARDS AND HONORS

| | |
|---|---|
| 2016-2017 | Residence Workplace Agreement, The Institute of Microbiology, Eidgenössische Technische Hochschule (ETH) Zurich, Zurich, Switzerland |
| 2015 | ETH Institute of Microbiology Performance Award |
| 2011-2014 | Human Frontier Science Program (HFSP) Long-Term Fellowship recipient<br>*Harnessing the Bacterial Biodiversity of Marine Invertebrates* |

## SERVICE

| | |
|---|---|
| 2018-2019 | HHMI Faculty Fellows for Inclusive Excellence Program |
| 2018 | LSSURP mock graduate student interviewee |
| 2018 | Session leader in round-table discussion for MinnCRest event: 'How to start your new lab?' |
| 2016-present | Ph.D. thesis committee member (12) |
| 2016-present | Mentor for Minnetonka Research – Minnetonka High School |
| 2016-present | Manuscript reviewer: *Nat. Chem. Biol. (3)*, *Nat. Comm. (1)*, *J. Am. Chem. Soc. (2), Angew. Chem. Int. Ed. (1)*, *Proc. Natl. Acad. Sci. U.S.A. (1), Metab. Eng. (1), Nucleic Acids Res. (1)*, *Plant Sci. (1)*, *ACS Chem. Biol. (2)*, *Biochemistry (2), Chem. Eur. J. (1)* |
| 2016-present | BMBB graduate student recruitment committee |

| | |
|---|---|
| 2016-present | Microbial Engineering graduate student recruitment committee |
| 2016-2017 | Co-organizer: Biocatalysis Initiative – Microbial Factories Symposium |
| 2016 | Outside reviewer for NSF Career Award |
| 2015 | AAAS Webinar: Careers for US Scientists in Europe and China |

## MEMBERSHIPS

| | |
|---|---|
| 2018-present | Society for Industrial Microbiology and Biotechnology (SIMB) |
| 2018-present | University of Minnesota Biotechnology Training Grant mentor |
| 2018-present | American Chemical Society (ACS) |
| 2017-present | American Society for Biochemistry and Molecular Biology (ASBMB) |
| 2017-present | Royal Society of Chemistry (RSC) |
| 2017-present | American Society of Pharmacognosy (ASP) |
| 2016-present | Microbial and Plant Genomics Institute faculty member, University of Minnesota |
| 2016-present | Microbial Engineering graduate program faculty member, University of Minnesota |
| 2016-present | Minnesota Craniofacial Research Training Program (MinnCRest) mentor, University of Minnesota |
| 2015-2016 | American Association for the Advancement of Science (AAAS) |

## REFERENCES

Professor Dr. Jörn Piel
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Institute of Microbiology
Vladimir-Prelog-Weg 1-5/10
8093 Zürich, Switzerland
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Department of Biochemistry, Molecular Biology, and Biophysics
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Professor Dr. Michael Sadowsky
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BioTechnology Institute
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