

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 AND PRESENTATIONS

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Pending Publications

28. Bakshi, U, Gupta, VK, Lee, AR, Davis, JM, Chandrasekaran, S, Jin, Yong-Su, **Freeman, MF**, Sung, Jaeyun (2021) TaxiBGC: a Taxonomy-guided Approach for the Identification of Experimentally Verified Microbial Biosynthetic Gene Clusters in Shotgun Metagenomic Data. *bioRxiv* DOI: 10.1101/2021.07.30.454505.

27. Miller, FS*, Crone, KK*, Jensen, MR, Shaw, S, Elias, MH§, **Freeman, MF§ (2021)** Conformational rearrangements enable iterative backbone *N*-methylation in RiPP biosynthesis. *Nat. Comm.* 12(1): 5355. DOI: 10.1038/s41467-021-25575-7.

26. Matabaro, E, Song, H, Chepkirui, C, Kaspar, H, Witte, L, Naismith, JH, **Freeman, MF**, Künzler, M (2021) Enzyme-mediated backbone *N*-methylation in ribosomally encoded peptides, *Methods Enzymol.* DOI: 10.1016/bs.mie.2021.04.014.

25. Jensen, MR, **Freeman, MF† (2020)** Structure and biosynthesis of proteusin RiPP natural products, *Comprehensive Natural Products III*, Elsevier Publishing, Amsterdam, NL. Chapter 6(2): 88-118. DOI: 10.1016/B978-0-12-409547-2.14727-4.

24. Rust, M, Helfrich, EJM, **Freeman, MF***, Nanudorn, P*, Field, C, Rückert, C, Kündig, T, Page, MJ, Webb, VL, Kalinowski, J, Sunagawa, S, Piel, J (2020) A multi-producer microbiome generates chemical diversity in the marine sponge *Mycale hentscheli*, *Proc. Natl. Acad. Sci. U.S.A.* 117(17): 9508-9518. DOI: 10.1073/pnas.1919245117.

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.* 11(10): 931-939. 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§, Künzler, 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(32): 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, Kälin, N, Helf, MJ, Piel, J, **Freeman, MF§**, Künzler, 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.* **2017** 56: 13570-13572.]

15. Morinaka, BI, Verest, M, **Freeman, MF**, Gugger, M, Piel, J (**2017**) An orthogonal D₂O-based induction system provides insights into D-amino acid pattern formation by radical S-adenosylmethionine peptide epimerases, *Angew. Chem. Int. Ed.* 56(3): 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(4): 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, Crüsemann, 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, H-G, Matsunaga, S, Piel, J (**2012**) Metagenome mining reveals polytheonamides as posttranslationally modified ribosomal peptides, *Science* 338(6105): 387-390. DOI: 10.1126/science.1226121.

[Concentrates: *Chem. Eng. News* **2012** 90(38): 26.]

[In Brief: *Nat. Rev. Microbiol.* **2012** 10(12): 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(8): 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.* Springer-Verlag Berlin Heidelberg: 1-53. 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 Invited speaker, SIMB Annual Meeting, Austin, TX, August 11, 2021.

Freeman, MF Invited speaker, Marine Natural Products Gordon Research Conference, Ventura, CA, February 25, 2020.

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

Freeman, MF, Novel Methods for creating alpha-*N*-methylated polypeptides, U.S. Application No. 62/979,947, filed February 21, **2020**.

Aebi, M, Künzler, M, Piel, J, **Freeman, MF**, van der Velden, N, Kälin, N, Novel multiply backbone *N*-methyl transferases and uses thereof, US20190112583A1, April 18, **2019**.

Künzler, M, van der Velden, N, **Freeman, MF**, Piel, J, Aebi, M, Kälin, 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, WO2013034579A1, March 14, **2013**.

Townsend, CA, Bodner, MJ, Phelan, RM, **Freeman, MF**, Method for late introduction of the (8*R*)-hydroxyl group in carbapenem β -lactam antibiotic synthesis, EP2513112A2, October 12, **2012**.

Townsend, CA, Bodner, MJ, Phelan, RM, **Freeman, MF**, Method for late introduction of the (8*R*)-hydroxyl group in carbapenem β -lactam antibiotic synthesis, WO2011072287A3, November 10, **2011**.

MENTORING

Current members

Post-docs (1): Takahiro Jomori (5/2021-)

Visiting Scholars (0):

PhD students (3): Kathryn K. Crone (3/2019-)

Aileen R. Lee (4/2018-)

Aman S. Imani (4/2018-)

Master's students (0):

Technicians (1): Nisha Vishwanathan (2/2021-)
Undergraduates (1): Austin Cihak (1/2020-)
High Schoolers (0):

Past members

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

Ph.D. students (1): Fredarla S. Miller (1/2016-6/2020) *Manufacturing Scientist, Beckmann Coulter, Inc., Chaska, MN*

Master's students (1): Marissa R. Quijano (7/2016-9/2018)

Visiting Scholars (5): Floris de Waal (2/2020-8/2020) *Master's student at Wageningen University, the Netherlands*

Sumire Kurosawa, (9/2019-10/2019) *Ph.D. student at University of Tokyo, Japan*

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 (7): Sayuj Suresh (9/2019-8/2021)

Sarah Schmidt-Dannert (9/2019-1/2020)

Chandler N. Hellenbrand (1/2018-12/2019; LSSURP and UROP scholar)

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. Chi-Fang Lee (C/O 2021)
Julie Beenken (C/O 2020)
Matthew Pawlak (C/O 2020)
Michael Wold (C/O 2020)
Kitty Sompiyachoke (C/O 2020)
Morgan Esler (C/O 2018)
Peng Lei (C/O 2018)
Kathryn K. 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 R. Quijano (C/O 2015)

Thesis committees

2021- Kitty Sompiyachoke (BMBB, chair)
Lukas Sonderegger (Microbiology, ETH Zurich, Switzerland)

2020-	Luis Alberto Peña Ortiz (Biological Sci., Friedrich-Schiller University, Jena, Germany) Nathan Hoekstra (MicE) Lambros Tassoulas (BMBB) Seonyun Moon (BMBB, chair)
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

2021, Spring	BioC4331: Biochemistry 1: Structure, Catalysis, and Metabolism (51 students); mean 5.29
2021, Spring	NIH Biotechnology Training Grant workshop series, guest lecturer
2020, Spring	BioC4331: Biochemistry 1: Structure, Catalysis, and Metabolism (74 students); mean 5.58
2019, Spring	BioC4331: Biochemistry 1: Structure, Catalysis, and Metabolism (70 students); mean 4.67
2017, Fall	BioC3960 Research Topics in Biochemistry, guest lecturer
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 <i>Harnessing the Bacterial Biodiversity of Marine Invertebrates</i>

SERVICE

2021	Department of Energy Grant Review Panelist
2020	Primary reader for CBS honors thesis: Yugene Guo
2020	CBS Undergraduate Skills Task Force volunteer
2020	LCME Medical School accreditation site visit participant
2019-present	Co-organizer of the BioTechnology Institute seminar series
2019-2020	CBS Postdoc Symposium – Young Faculty meet & greet
2019	Primary reader for CBS honors thesis: Victoria Rogness
2019	Summa reader for CBS honors thesis: Hosam Alkhatib
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 (14)
 2016-2020 Mentor for Minnetonka Research – Minnetonka High School
 2016-present Manuscript reviewer: *Nat. Chem. Biol.* (4), *Nat. Comm.* (1), *J. Am. Chem. Soc.* (2), *Angew. Chem. Int. Ed.* (1), *Proc. Natl. Acad. Sci. U.S.A.* (1), *Chem. Sci.* (1), *Metab. Eng.* (1), *Nucleic Acids Res.* (1), *Plant Sci.* (1), *ACS Chem. Biol.* (3), *Biochemistry* (2), *Chem. Eur. J.* (1), *J. Ind. Microbiol. Biotechnol.* (1), *Biomolecules* (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 American Society of Pharmacognosy (ASP)
 2017-2020 Royal Society of Chemistry (RSC)
 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)

DIVERSITY, EQUITY AND INCLUSION ACTIVITIES

2021 Preparing Emerging Scientists workshop: Train-the-trainer conference on professional skills, ethics, and inclusion
 2020 Freeman lab book club – organized recurring discussions on “Educated in Whiteness: Good Intentions and Diversity in Schools” by Angelina E. Castagno, “Blood Sugar: Racial Pharmacology and Food Justice in Black America” by Anthony Ryan Hatch, and the controversial (and now retracted) manuscript “The association between early career informal mentorship in academic collaborations and junior author performance” in *Nat. Comm.* DOI: 10.1038/s41467-020-19723-8.
 2018-2019 HHMI Faculty Fellows for Inclusive Excellence Program
 2018 Ableism & Disability Justice seminar, Office of Equity and Diversity certificate course, November 27, 2018.

INTERNATIONAL OUTREACH

2019 University of Tokyo & UMN student exchange
Hosted Sumire Kurosawa (2-mo. program) from the lab of Dr. Makoto Nishiyama
 2018 Poznan University of Life Sciences & BTI student exchange
Hosted Jakub Michalski (2-mo. program)
 2017 Nara Institute of Science and Technology (NAIST) & BTI exchange program
Fredarla S. Miller was an exchange student in Dr. Hiroshi Takagi’s laboratory (2-wk. program)

REFERENCES

Professor Dr. Jörn Piel
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