

Christopher T. Calderone

Curriculum Vita

Department of Biology
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I. EDUCATION

- 2005-2008 **Postdoctoral studies, Harvard Medical School**
Department of Biological Chemistry and Molecular Pharmacology
Advisor: Christopher T. Walsh
- 2000-2005 **Ph.D., Chemistry and Chemical Biology, Harvard University**
Advisor: David R. Liu
Thesis title: Iterated Branching Reaction Pathways Enabled by DNA-Templated Synthesis
- 1999-2000 **M.Phil., Chemistry, Cambridge University (conferred 2001)**
Advisor: Dudley H. Williams, FRS
Thesis title: The Study of Bonding vs. Motion in Non-Covalent Complexes
- 1995-1999 **S.B., Chemistry, The University of Chicago**

II. ACADEMIC EMPLOYMENT

2008-present **Assistant Professor, Department of Biology, Macalester College**

III. PUBLISHED SCHOLARLY WORKS

Peer-reviewed articles

1. Bumpus, S.B.; Magarvey, N. A.; Kelleher, N. L.; Walsh, C. T.; **Calderone, C. T.** "Polyunsaturated Fatty Acid-Like *Trans*-Enoyl Reductases Utilized in Polyketide Biosynthesis." *J. Am. Chem. Soc.*, **2008**, *130*, 11614-11616.
This paper describes a previously unknown enzyme activity in polyketide biosynthesis, and to my knowledge represents the first in vitro characterization of an enzyme involved in the bacterial biosynthesis of polyunsaturated fatty acids. I designed all the experiments and performed a majority of them, as well as wrote the manuscript. The Journal of the American Chemical Society is arguably the premier academic chemistry journal (impact factor 8.091).
2. **Calderone, C. T.**; Magarvey, N. A.; Bumpus, S. B.; Kelleher, N. L.; Walsh, C. T. "A Ketoreductase Domain in the PksJ Protein of the Bacillaene Assembly Line Carries Out Both

α - and β -Ketone Reduction During Chain Growth.” *Proc. Natl. Acad. Sci. USA*, **2008**, *105*, 12809-12814.

This paper describes an unusual enzyme activity in polyketide biosynthesis. I designed all the experiments and performed a majority of them, as well as wrote the manuscript. Proceedings of the National Academy of Science (USA) is one of the top five journals publishing papers across all fields of science (impact factor 9.38).

3. **Calderone, C. T.**; Iwig, D. F.; Dorrestein, P. C.; Kelleher, N. L.; Walsh, C. T. “Incorporation of Non-Methyl Branches by Isoprenoid-Like Logic: Multiple β -Alkylation Events in the Biosynthesis of Myxovirescin A1.” *Chem. Biol.*, **2007**, *14*, 835-846.

This paper extends the work described in #7 below, characterizing a variant of the alkylation pathway I discovered in 2006. I designed all the experiments and performed a majority of them, as well as wrote the manuscript. Chemistry and Biology is a premier journal publishing original research in the field of chemical biology (impact factor 5.603).

4. Aron, Z. D.; Fortin, P. D.; **Calderone, C. T.**; Walsh C. T. “FenF: Servicing the Mycosubtilin Synthetase Assembly Line *in Trans*.” *ChemBioChem*, **2007**, *8*, 613-616.

This paper describes an unusual class of acyltransferase enzymes utilized in polyketide biosynthesis. I provided purified protein for the study.

5. Dorrestein, P. C.; Bumpus, S. B.; **Calderone, C. T.**; Garneau-Tsodikova, S.; Aron, Z. D.; Straight, P. D.; Kolter, R.; Walsh, C. T.; Kelleher, N. L. “Facile Detection of Acyl and Peptidyl Intermediates on Thiotemplate Carrier Domains via Phosphopantetheinyl Elimination Reactions During Tandem Mass Spectrometry.” *Biochemistry*, **2006**, *45*, 12756-12766.

This paper describes a mass spectrometric technique to detect thioester intermediates in polyketide and non-ribosomal peptide biosynthetic pathways. I provided purified protein for the study.

6. **Calderone, C. T.**; Kowtoniuk, W. E.; Kelleher, N. L.; Walsh, C. T.; Dorrestein, P. C. “Convergence of Isoprene and Polyketide Biosynthetic Machinery: Isoprenyl-*S*-Carrier Proteins in the *pksX* Pathway of *Bacillus subtilis*.” *Proc. Natl. Acad. Sci. USA*, **2006**, *103*, 8977-8982.

This paper describes the first identification and characterization of a widely distributed methylation pathway in secondary metabolism, and has been cited more than 40 times as of March 2010. I designed all the experiments and performed a majority of them, as well as wrote the manuscript.

7. **Calderone, C. T.**; Liu, D.R. “Small-Molecule Diversification from Iterated Branching Reaction Pathways Enabled by DNA-Templated Synthesis.” *Angew. Chem. Int. Ed. Engl.*, **2005**, *44*, 7383-7386.

This paper represents the culmination of my doctoral work and describes the application of DNA-templated synthetic techniques to the synthesis of highly diverse chemical libraries. I designed and performed all the experiments and wrote the manuscript.

8. Gartner, Z. J.; Grubina, R.; **Calderone, C. T.**; Liu, D. R. "Two Enabling Architectures for DNA-Templated Organic Synthesis." *Angew. Chem. Intl. Ed. Engl.*, **2003**, *42*, 1370-1375

This paper describes an extension of DNA-templated synthesis. I participated in experimental design and performed some of the experiments, and edited the manuscript. Angewandte Chemie International Edition English has the highest impact factor of any journal dedicated to the field of chemistry (impact factor 10.879). The editors of Chemical and Engineering News (a news magazine published by the American Chemical Society) featured this paper as a Science and Technology Concentrate (2003, 81, 24).

9. **Calderone, C. T.**; Puckett, J. W.; Gartner, Z. J.; Liu, D.R. "Directing Otherwise Incompatible Reactions in a Single Solution by Using DNA-Templated Organic Synthesis." *Angew. Chem. Intl. Ed. Engl.*, **2002**, *41*, 4104-4108.

This paper describes an extension of DNA-templated synthesis that was a key development in its application toward the synthesis of highly diverse chemical libraries. I designed all the experiments and performed a majority of them, as well as wrote the manuscript. The editors of Science featured this article as an Editor's Choice (2002, 298, 1517).

10. Williams, D. H.; **Calderone, C. T.**; O'Brien, D. P.; Zerella, R. "Changes in Motion vs. Bonding in Positively vs. Negatively Cooperative Interactions." *Chem. Comm.*, **2002**, 1256-1257.

This paper proposes a theoretical model for the relationship of entropy/enthalpy compensation with negative cooperativity. I provided data and wrote much of the manuscript while at Cambridge University. Chemical Communications is a journal published by the Royal Society of Chemistry that predominantly publishes short communications of initial results (impact factor 5.14).

11. **Calderone, C. T.**; Williams, D. H. "An Enthalpic Component in Cooperativity: The Relationship Between Enthalpy, Entropy, and Noncovalent Structure in Weak Associations." *J. Am. Chem. Soc.*, **2001**, *123*, 6262-6267.

This paper proposes and verifies a now widely accepted model for the role of enthalpy in cooperative interactions. I performed all the experiments, and participated in their design, as well as wrote the manuscript. As of March 2010, this paper has been cited over 60 times.

12. Bishop, D. K.; Ear, U.; Bhattacharyya, A.; **Calderone, C.**; Beckett, M.; Weichselbaum, R. R.; Shinohara, A. "Xrcc1 Is Required for Assembly of Rad51 Complexes *in Vivo*." *J. Biol. Chem.*, **1998**, *273*, 21482-21488.

This paper describes the characterization of several proteins involved in recombination events in yeast. I provided microscopy images for the paper.

Invited Review Articles

1. **Calderone, C. T.** “Isoprenoid-Like Alkylations in Polyketide Biosynthesis.” *Nat. Prod. Rep.*, **2008**, 25, 845-853.

This paper reviews the state of knowledge of the distribution and biochemistry of the alkylation pathway described in peer-reviewed article #6 above.

2. **Calderone, C. T.;** Liu, D. R. “Nucleic-Acid-Templated Synthesis as a Model System for Ancient Translation.” *Curr. Opin. Chem. Biol.*, **2004**, 8, 645-653.

This paper examines the parallels between DNA-templated synthesis techniques I developed during my doctoral studies and possible prebiotic informational polymers, and the consequences for the evolution of life. I wrote the bulk of the manuscript.

Other

1. Interview with Minnesota Public Radio (January 22, 2010)

*I was interviewed by Minnesota Public Radio about my studies on *Aspergillus nidulans* and their relation to human health. The interview was in response to the awarding (with Rebecca Hoye [Chemistry, Macalester College]) of a Research Corporation Multi-Investigator Cottrell College Science Award (see below).*

IV. SCHOLARLY WORK IN PROGRESS (*MACALESTER UNDERGRADUATES)

Biochemical Studies on the Biosynthesis of TAFC

1. Fitzsimmons, C.M.*; Colehour, A.*; **Calderone, C.T.** “Biochemical characterization of the ornithine hydroxylase SidA required for siderophore biosynthesis in *Aspergillus*.”

*This work will describe the characterization of the N-hydroxylase responsible for provision of N-hydroxyornithine during the biosynthesis of hydroxamate-type siderophores in *Aspergillus nidulans*. In collaboration with Christina Fitzsimmons ('11) and Alese Colehour ('09), we have successfully cloned and overexpressed the enzyme SidA and kinetically characterized it. We submitted a manuscript in late 2010 describing this work, which is currently being edited for resubmission.*

Biochemical Studies on Acylation in Fungal Siderophore Biosynthesis

2. Snavely, M.E.*; **Calderone, C.T.** “Characterization of the Acetylation of N-Hydroxyornithine in Ferricrocin”

*The siderophore ferricrocin produced by *A. nidulans* contains three N-acetyl-N-hydroxyornithine residues. In collaboration with Michael Snavely ('12), we have initiated work over summer 2010 to clone and heterologously overexpress the acetyl transferase enzyme predicted to be involved in formation of this residue from N-hydroxyornithine.*

Biochemical Studies on Adenylation in Fungal Siderophore Biosynthesis

3. Heimisdottir, D.*; Allen, J.A.*; Berto, T.J.*; Dalgalan, D.*; Erickson, H.E.*; Han, X.*; Lee, S.Y.*; **Calderone, C.T.** “Deconvoluting the Logic of Fungal Non-Ribosomal Peptide Biosynthesis.”

Preliminary studies of the biosynthetic logic of fungal non-ribosomal peptide synthesis were undertaken in the context of the course BIOL474 Research in Biochemistry. Unlike bacterial non-ribosomal peptide synthetases, which act in a linear, assembly line-like manner, the logic fungal non-ribosomal peptide biosynthesis is not well-understood. As a first step in a long-term (> 3 years) research program aimed at characterizing the sequence of reactions occurring in non-ribosomal peptide biosynthesis in fungus, students in the Fall 2009 offering of the Research in Biochemistry course undertook the cloning of several adenylation domains from fungal non-ribosomal peptide synthetases. This work continued over summer 2010 with Dagny Heimisdottir ('12).

Engineering of Ketoacid-Adenylating Domains from Non-Ribosomal Peptide Synthetases

4. **Calderone, C.T.** “Rational Engineering of Ketoacid-Activating Adenylation Domains.”

This work builds on observations I made during my post-doctoral work in the Walsh lab. In the work described in peer-reviewed article #2 above, I characterized an adenylation domain that activates an α -ketoacid instead of the usual α -amino acid. I hypothesize that relative to canonical adenylation domains, a single mutation shifts the substrate preference from amino acids to ketoacids. To test this hypothesis, I designed a semester-long laboratory module in BIOL/CHEM352 Biochemistry II in which students in the course clone, express, and purify a ketoacid-activating adenylation domain and identify its substrate; perform guided bioinformatic analysis to identify the key mutation; and finally generate and characterize the mutant. Future work on this project requires access to radiolabeled materials and assays, which will be achieved over my planned sabbatical Fall 2011.

Structural Characterization of the trans-enoyl reductase PksE

5. Festin, G.M.; Mellgren, E.F.*; Ames, B.D.; Magarvey, N.A.; Walsh, C.T.; **Calderone, C.T.**; Tsai, S.C. “Structural Characterization of a Polyunsaturated Fatty Acid-Like Enoyl Reductase Utilized in Polyketide Biosynthesis.”

This work is a joint effort with the Tsai lab at the University of California-Irvine. In collaboration with Emil Mellgren ('10) we provided purified PksE (first characterized in peer reviewed article #1 during my post-doctoral studies) for X-ray crystallographic studies in the Tsai lab.

V. PRESENTATIONS

Lectures

1. “Biosynthetic Hydroxylation of Non-Ribosomal Peptides.” Lecture delivered to Department of Biology, Hamline University, Saint Paul, MN, November 19, 2010.
2. “Chimeric Natural Product Biosynthesis: Deviations from Assembly-Line Enzymology.” Lecture delivered to Department of Biology, Carleton College, Northfield, MN, January 18, 2010.
3. “An Isoprenoid-Like Alkylation in Polyketide Biosynthesis.” Lecture delivered at Polyketide/Non-Ribosomal Peptide Symposium, Brown University, Providence, RI, August 4-7, 2007.
4. “A New Source of Diversity Enabled by DNA-Templated Synthesis.” Lecture delivered at Bristol-Myers Squibb Chemistry Award Symposium, Wallingford, CT, May 14, 2004.

Published Abstracts Arising from National Meetings

1. Gartner, Z.J.; Kanan, M.W.; **Calderone, C.T.**; Grubina, R.; Tse, B.; Li, X.; Doyon, J.; Snyder, T.; Puckett, J.W.; Liu, D.R. (2004) “DNA-Templated Organic Synthesis: Mimicking Nature’s Effective Molarity-Based Approach to Controlling Chemical Reactivity.” *Protein Science*, 13:283.
2. Liu, D.R.; Gartner, Z.J.; Kanan, M.W.; **Calderone, C.T.** (2003) “DNA-Templated Synthesis as a Basis for the Evolution of Synthetic Molecules.” *Abstracts of Papers of the American Chemical Society*, 225:612-ORGN.
3. Liu, D.R.; Gartner, Z.J.; Kanan, M.W.; **Calderone, C.T.** (2002) “DNA-Templated Synthesis as a Basis for Molecular Evolution.” *Abstracts of Papers of the American Chemical Society*, 224:050-PHYS.

Presentations at National Meetings

1. **Calderone, C.T.**; Puckett, J.W.; Liu, D.R. “Small-Molecule Diversity Accessed Through Iterated Branching Reaction Pathways and DNA-Templated Synthesis.” 2005 American Chemical Society National Organic Symposium, Salt Lake City, UT, June 12-16, 2005.

*Presentations at Regional Meetings (*Macalester undergraduates)*

1. Fitzsimmons, C.M.*; **Calderone, C.T.** “Expression and Characterization of a Flavin Hydroxylase Involved in Siderophore Biosynthesis in *Aspergillus nidulans*.” 2010 Winchell Undergraduate Symposium, Minnesota Academy of Science, University of St. Thomas, St. Paul, MN, April 23-24, 2010.

This presentation by Macalester student Christina Fitzsimmons ('11) on the ornithine N-hydroxylase SidA from A. nidulans was awarded Best in Session.

2. Colehour, A.*; Fitzsimmons, C.M.*; **Calderone, C.T.** “Expression of Proteins Involved in Siderophore Biosynthesis in *Aspergillus nidulans*.” 2009 Winchell Undergraduate Symposium, Minnesota Academy of Science, University of St. Thomas, St. Paul, MN, April 16-17, 2009.
3. Mellgren, E.F.*; **Calderone, C.T.** “Cloning and Expression of Truncated Polyketide Synthase Enzymes for Structural Analysis.” 2009 Winchell Undergraduate Symposium, Minnesota Academy of Science, University of St. Thomas, St. Paul, MN, April 16-17, 2009.

VI. PATENTS AND PATENT APPLICATIONS

1. Liu, D.R.; Gartner, Z.J.; **Calderone, C.T.** “Evolving New Molecular Function.” USSN 10/643,752; US Patent number 7,491,494 (issued February 17, 2009)
2. **Calderone, C.T.**; Liu, D.R. “Iterated Branching Reaction Pathways Via Nucleic Acid-Mediated Chemistry.” U.S. Patent Application 2008/0318807
3. Liu, D.R.; Rozenman, M.M.; **Calderone, C.T.** “Nucleic Acid-Templated Chemistry in Organic Solvents.” U.S. Patent Application 2006/023487
4. Liu, D.R.; Gartner, Z.J.; Doyon, J.B.; **Calderone, C.T.**; Kanan, M.W.; Li, X.; Snyder, T.M.; Rosenbaum, D.M. “Evolving New Molecular Function.” U.S. Patent Application 2005/0170376.

VII. AWARDS, RECOGNITION, AND GRANTS

Awards

2007-2008	National Institutes of Health NRSA Post-Doctoral Fellowship
2003-2004	American Chemical Society Division of Organic Chemistry Graduate Research Fellowship
2002	Derek Bok Award for Excellence in Teaching, Harvard University
2000-2003	Department of Defense (NDSEG) Research Fellowship
2000-2003	National Science Foundation Graduate Research Fellowship (declined)
1999-2000	Churchill Scholarship
1999	S.B. with General and Departmental Honors, The University of Chicago
1999	Student Marshal, The University of Chicago
1999	Norman Nachtrieb Award (Outstanding Chemistry Student), The University of Chicago
1998	Elected Phi Beta Kappa
1997-1999	Goldwater Scholarship
1995-1999	Dean’s List, The University of Chicago

External Funding

- 2010 National Science Foundation Major Research Instrumentation grant, “Acquisition of a 400 MHz NMR Spectrometer to Facilitate Research and the Integration of NMR Techniques Across the Curriculum” (PI Paul J. Fischer [Chemistry]) Contributed text to unfunded proposal; co-PI on resubmission.
- 2010 National Science Foundation, “Improving the Quantity and Quality of Plant Metabolomics Information” (PI Adrian Hegeman [University of Minnesota], co-PI Jerry Cohen [University of Minnesota]) Contributed text; participating in grant administration as “Key Collaborator” \$950,738
- 2010-2011 Research Corporation Multi-Investigator Cottrell College Science Award, “Combining Organic Synthesis and Biochemistry to Study Siderophore Biosynthesis in Fungi.” \$75,000 (Rebecca Hoye [Chemistry], co-PI).
- 2008-2012 Dreyfus Foundation Faculty Start-up Award, “Biochemical Investigations of Non-Ribosomal Peptides: Provision and Incorporation of Non-Proteinogenic Monomers.” \$30,000

Competitive Internal Funding (Macalester College)

- 2010 Student-Faculty Summer Research Fellowship, “Characterization of Ornithine Hydroxylation During TAFC Biosynthesis by *A. nidulans*” (with Christina M. Fitzsimmons ’11). \$3,850
- 2009 Student-Faculty Summer Research Fellowship, “Studies on TAFC Biosynthetic Enzymes” (with Emil F. Mellgren ’10). \$5,350
- 2009 Student-Faculty Summer Research Fellowship, “Studies on the Prenylation of Tyrosine During Sirodesmin Biosynthesis” (with Christina M. Fitzsimmons ’11). \$3,500
- 2008 Presidential Initiative for Curricular Renewal, Macalester College, “Incorporating Original Research into the Biochemistry Teaching Laboratory.” \$2,000, 2008.

VIII. TEACHING

Courses Taught at Macalester

- BIOL255 Cell Biology and Genetics Lab (Spring 2009 team taught with Michael Anderson; Spring 2010)
- BIOL260 Genetics (lecture, Fall 2009, Fall 2010)
- BIOL265 Cell Biology and Genetics II (lecture, Fall 2008 team taught with Devavani Chatterjea and Paul Overvoorde)
- BIOL/CHEM351 Biochemistry I Lab (Fall 2008)
- BIOL/CHEM352 Biochemistry II (lecture and lab, Spring 2009 and Spring 2010)
- BIOL/CHEM359 Chemical Biology (lecture, Fall 2010)
- BIOL474 Research in Biochemistry (lecture and lab, Fall 2009)

Courses Taught Elsewhere

Chemistry E-2 Organic Chemistry Lab (teaching assistant, Harvard Extension School)
Chemistry and Chemical Biology 170 Chemical Biology (lecture teaching assistant, Harvard University)
Chemistry and Chemical Biology 27 The Organic Chemistry of Life (lecture teaching assistant, Harvard University)
Part II Chemistry Lab (teaching assistant, Cambridge University)
Part IB Chemistry Lab (teaching assistant, Cambridge University)
Introductory Organic Chemistry (lab and lecture teaching assistant, The University of Chicago)

Honors Project Research Advisor

Emil Mellgren ('10) "Transposon-Mediated Gene Integration in Human T Cells for the Use in Adoptive Cell Transfer Therapy"

Honors Project Review Committee

Jamal Malik (Chemistry, '09) "Towards a Total Synthesis of Azaspirorene"
Leonor Ano ('10) "Immune Semaphorin and Receptor Expression in the C57BL/6 Murine Thymus and Bone Marrow at Different Stages of Development"
Kelsey Speer ('10) "Development of Asymmetric Bivalent Peptides that Target the X-Linked Inhibitor of Apoptosis Protein"

Summer/Academic Year Research Advisor

2008-09 Christina Fitzsimmons ('11), Emil Mellgren ('10), Alese Colehour ('09)
2009-10 Christina Fitzsimmons ('11), Michael Snavely ('12), Dagny Heimisdottir ('12)
2010-11 Christina Fitzsimmons ('11)

IX. SERVICE

Professional Service

1. Panelist, National Science Foundation Graduate Research Fellowship Program, 2010
2. Panelist, National Defense Science and Engineering Grant, 2010
3. Chairman, Biochemistry Section, Midstates Consortium for Math and Science Undergraduate Research Symposium, 2008
4. Ad hoc reviewer, *Bioorganic and Medicinal Chemistry Letters*; Ad hoc reviewer, *Nature Chemical Biology*; Ad hoc reviewer, National Science Foundation

Macalester College Service

1. Presented talk “Teaching Without a Net: The Textbookless Classroom” in the Talking About Teaching series at the Serie Center for Scholarship and Teaching, February 2, 2010
2. Served as scribe for Mid-Course Interview Program administered by Serie Center for Scholarship and Teaching, 2009, 2010
3. Faculty Advisor, Mayo Innovation Scholars Program, 2009-present
4. Radiation Safety Officer, Department of Biology, 2009-present
5. Founder’s Day Planning Committee, 2010

Membership in Professional Societies and Community Service

1. American Chemical Society, 2004-present
2. American Society for Biochemistry and Molecular Biology, 2008-present
3. Moderator, Minnesota Academy of Science High School Science Bowl, 2009-present
4. Member, Board of Directors, Minnesota Academy of Science, 2010-present