BIOGRAPHICAL SKETCH

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NAME: Koo, Christopher Wellington

eRA COMMONS USER NAME (credential, e.g., agency login): CWKOO1

POSITION TITLE: Doctoral Student

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of California, Los Angeles	B.S.	06/2013	Biochemistry
Northwestern University	PhD	-	Molecular Biosciences

A. Personal Statement

An important part of biology is understanding how organisms interact with their environment using biochemistry. The variety of environmental niches on this planet have led to an abundance of biochemical challenges and opportunities for extracting energy from the environment. Through natural selection and evolution, organisms have developed elegant solutions to these problems in the form of enzymes. Enzymes hold many keys to improving our relationship with our environment and living sustainably. It is crucial to study enzymes to uncover efficient, natural solutions to issues such as climate change and clean energy. I am interested in applying novel techniques to characterize otherwise intractable classes of enzymes to uncover new chemistry. As an undergraduate student, I studied enzymes related to *Mycobacterium tuberculosis* infection using recombinant protein expression and x-ray crystallography. As a graduate student, I am using cryo-electron microscopy (cryoEM) and a synthetic biology-based technique, cell-free protein synthesis, to characterize a membrane-bound metalloenzyme called particulate methane monooxygenase (pMMO). pMMO catalyzes the selective conversion of methane to methanol and has implications for renewable energy and biofuels. In the Rosenzweig lab, I use nanodisc technology in combination with cryoEM to study a catalytically active form pMMO in a lipid bilayer. CryoEM is ideal for studying membrane proteins because the lipid bilayer can be maintained and the enzyme can be characterized in a native state. My initial studies have shown that the metal-binding ligands in pMMO are slightly shifted from those in the crystal structure and have shown a highly conserved loop region that is absent in the crystal structure. This study will provide insight into biological methane oxidation by studying a catalytically active form of pMMO. I am also interested in developing new technology for studying membrane proteins. In this project, I use *E. coli*-based cell-free protein synthesis to synthesize pMMO in vitro. This platform mimics the cellular environment in a test tube and can be a method for synthesizing otherwise intractable membrane enzymes. Throughout my time at Northwestern University, I have taken advantage of many mentoring opportunities, guiding the research of undergraduate researchers and other graduate students. I served two quarters as a teaching assistant and have volunteered with middle school students for quarter-long science fair projects. I presented my work via an oral presentation at the Northwestern University Molecular Biosciences department retreat and poster presentations at the Penn State Bioinorganic Symposium and Microbial Basis of C1 Metabolism GRC conference.

Selected Publications:

Ro, S.Y.; Schachner, L.F.; **Koo, C.W**.; Purohit, R.; Remis, J.P.; Kenney, G.E.; Liauw, B.W.; Thomas, P.M.; Patrie, S.M.; Kelleher, N.L.; Rosenzweig, A.C. “Native Top-Down Mass Spectrometry Provides Insights into the Copper Centers of Membrane-Bound Methane Monooxygenase” *Nat. Commun.,* **2019***,* 10: 2675*.* PMC6572826

B. Positions and Honors

Positions of Employment

2013-2015 Staff Research Associate UCLA DOE Protein Expression Technology Center
2015-present Doctoral Student, Dept. of Molecular Biosciences, Northwestern University

Academic and Professional Honors

2018 1st place poster, Biophysics Symposium at Northwestern University
2018 IBiS travel award, GRC: Molecular Basis of Microbial One Carbon Metabolism
2017 IBiS travel award, Bioinorganic workshop at Penn State University
2016-2017 NIH Molecular Biophysics Training Fellowship

C. Contributions to Science

My doctoral research focuses on understanding the biology of methane-consuming bacteria called methanotrophs. These bacteria are essential players in the global carbon cycle, acting as a sink for methane. In contrast to costly and inefficient industrial processes, methanotrophs convert methane to methanol at ambient temperature and pressure. My work is focused on characterizing the primary enzyme they use for this chemistry, particulate methane monooxygenase (pMMO). I use novel techniques to express and characterize pMMO using cell-free protein synthesis and cryo-election microscopy. Understanding this enzyme has implications for generating biofuels and combating climate change by reducing global levels of methane.

Contribution 1: Using nanodisc-embedded pMMO for structure and functional studies using cryo-EM

The Rosenzweig group has developed methods for purifying pMMO directly from methanotrophs. Under high-copper conditions, pMMO is effectively overexpressed in methanotrophs, representing an estimated 25% of the total proteome. At this level of protein expression, purifying pMMO from the native organism is a viable strategy for obtaining large quantities for biochemical studies. During purification, detergents are typically used to solubilize pMMO. A general issue with membrane protein biochemistry is that detergents often exert strain on the enzyme or otherwise cause a loss of function. My work has focused on exploring methods of maintaining the phospholipid bilayer environment surrounding pMMO after isolation from the organism in order to maintain the enzyme's native function. I have shown that nanodiscs can be used to obtain functional pMMO in native-like lipid bilayer. With this platform established, I have contributed to using nanodisc-embedded pMMO for native top-down mass spectrometry to link enzymatic activity to copper loading at the PmoC site. I am currently focusing on using cryo-EM to characterize the structure and function of pMMO in an active form.

Publications:

Ro, S.Y.; Schachner, L.F.; **Koo, C.W**.; Purohit, R.; Remis, J.P.; Kenney, G.E.; Liauw, B.W.; Thomas, P.M.; Patrie, S.M.; Kelleher, N.L.; Rosenzweig, A.C. "Native Top-Down Mass Spectrometry Provides Insights into the Copper Centers of Membrane-Bound Methane Monooxygenase" *Nat. Commun.,* **2019***,* 10: 2675*.* PMC6572826

Contribution 2: Heterologous expression of pMMO using cell-free protein synthesis. (unpublished)

Protein expression in a heterologous host such as *E. coli* is advantageous for a variety of reasons. Typically, the protein yield from *E. coli* is high enough to perform biochemical analysis and protein characterization. The ability to control the DNA that is input into the bacteria enables amino acid mutagenesis to identify and characterize amino acids that are critical for structure and/or function. Membrane proteins, however, are notoriously difficult to overexpress in *E. coli* because they tend to disrupt the delicate membrane environment of the cell, leading to cell death or repression of the exogenous gene. Cell-free protein synthesis (CFPS) is a method of synthesizing protein in vitro by decoupling protein expression from cell vitality. By this method, cell lysate containing transcription and translation machinery is isolated from the cell and protein synthesis is triggered when DNA and other energy cofactors are added to this lysate. I am developing CFPS to be a viable platform for multi-subunit membrane-bound metalloenzymes using nanodiscs as a membrane mimetic. Using CFPS, I am working on synthesizing the subunits of pMMO and assembling them into a functional enzyme complex.

D. Additional Information: Research Support and/or Scholastic Performance

Research Support:

2017-2018 Molecular Biophysics Training Program (NIH NIGMS 5T32 GM008382)

Scholastic Performance:

2015	Quantitative Biology	A
2015	Eukaryotic Molecular Biology	B
2016	Bioinformatics	A-
2016	Human Proteome	A-
2016	Molecular Biophysics	A
2016	Advances in Biotechnology	A

NAME: Amy C. Rosenzweig

eRA COMMONS USER NAME (credential, e.g., agency login): rosenzweig

POSITION TITLE: Weinberg Family Distinguished Professor of Life Sciences, Professor of Molecular Biosciences and of Chemistry

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Amherst College, Amherst, MA	B. A.	05/1988	Chemistry
Masschusetts Institute of Technology, Cambridge, MA	Ph. D.	02/1994	Inorganic Chemistry
Harvard Medical School and Dana Farber Cancer Institute, Boston, MA	Postdoc	02/1997	Structural Biology

A. Personal Statement

I have conducted research in the field of metallobiochemistry for >30 years. As an undergraduate student, I worked on the copper-containing enzyme nitrous oxide reductase. As a graduate student and postdoctoral fellow, I determined the first crystal structure of the soluble diiron methane monooxygenase (sMMO). As an independent investigator at Northwestern for the past 22 years, I have pursued a range of forefront problems in bioinorganic chemistry and structural biology. My NIH R01-funded research programs in the areas of metal homeostasis and particulate methane monooxygenase (pMMO), which were in years 18 and 12, respectively, were replaced in 2016 with a MIRA R35 award. We have published numerous reviews and perspectives in the field. Beyond the laboratory's core work, I have collaborated extensively with other investigators to structurally characterize important metalloenzymes. I have mentored a total of 20 predoctoral fellows (5 current) and 19 postdoctoral fellows (3 current). Of these trainees, 23 are female and 3 are underepresented minorities. Former trainees have gone on to successful academic positions at top research universities (Stanford University, Lehigh University, University of Kansas, Georgia Institute of Technology, Penn State University, University of Maryland-Baltimore County), top liberal arts colleges (Pomona College, Swarthmore College), and teaching universities. All who have reached the appropriate stage have been promoted with tenure thus far. Notably, 10 of 13 former trainees currently in faculty positions are women. A number of other trainees have pursued careers in industry or are currently conducting postdoctoral work. I have also mentored 52 undergraduate researchers (33 female, 19 male, 3 underrepresented minorities). I have served extensively as a reviewer for NIH, including 4 years of service on the MSFA study section (2006-2010), ad hoc review for MSFA (February 2015), ad hoc review for Metallobiochemistry (February 2004, October 2004, February 2006), ad hoc review for MBBP (October 2013), a special emphasis panel (May 2012), a program project special emphasis panel (November 2011), ad hoc review for the Roadmap Initiative for Membrane Proteins (June 2005), and ad hoc review for Nutritional Biochemistry (October 2003). I will be serving on a MIRA review panel in November 2019 as well. I am currently a member of the *Science* Board of Reviewing Editors and serve on the Editorial Boards of *Proc. Natl. Acad. Sci. USA*, *Biochemistry*, and *Acc. Chem. Res*. Additional activities are listed below.

a. Kenney, G. E.; Rosenzweig, A. C. Chalkophores. *Annu. Rev. Biochem.* **2018**, *87*, 645-676, PMC6013396.
b. Lawton, T. L.; Rosenzweig, A. C.; Methane-oxidizing enzymes: an upstream problem in biological gas-to-liquids conversion. *J. Am. Chem. Soc.* **2016**, *138*, 9327-9340, PMC5242187.
c. Sirajuddin, S.; Rosenzweig, A. C. Enzymatic oxidation of methane. *Biochemistry* **2015**, *54*, 2283-2294, PMC5257249.
d. Boal, A. K.; Rosenzweig, A. C. Structural biology of copper trafficking. *Chem. Rev.* **2009**, *109*, 4760-4779, PMC 2768115.

B. Positions and Honors

Positions

1994-1997 NIH postdoctoral fellow, Dept. of Biological Chemistry and Molecular Pharmacology, Harvard Medical School and Dana Farber Cancer Institute
1997-2002 Assistant Professor, Depts. of Biochemistry, Molecular Biology, and Cell Biology and of Chemistry, Northwestern University
2002-2005 Associate Professor, Depts. of Biochemistry, Molecular Biology, and Cell Biology and of Chemistry, Northwestern University
2004-2006 Irving M. Klotz Research Professor, Northwestern University
2005-present Professor, Depts. of Molecular Biosciences and of Chemistry, Northwestern University
2012-present Weinberg Family Distinguished Professor Life Sciences, Northwestern University

Awards

1988 White Prize for excellence in Chemistry
1988 Howard Waters Doughty Prize for best thesis in Chemistry
1999 David and Lucile Packard Fellow
2001 Camille and Henry Dreyfus Teacher-Scholar Award
2003 MacArthur Fellow
2005 Honorary Degree, Doctor of Science, Amherst College
2006 ACS Nobel Laureate Signature Award for Graduate Education in Chemistry
2007 Elected Fellow, American Association for the Advancement of Science
2014 Elected Fellow, American Academy of Arts and Sciences
2014 Royal Society of Chemistry Joseph Chatt Award
2014 Ivano Bertini Award
2014 Fletcher Undergraduate Research Faculty Award
2017 Elected Member, National Academy of Sciences

Professional Activities

Elected member, Advanced Photon Source Users Organization Steering Committee (APSUO), 2000-2003
Co-organizer, Biological Crystallography Workshop, 2001 APS Users Meeting
Local chair, Midwest Enzyme Chemistry Conference, 2002
Co-organizer, Bader Award Symposium, 227th National Meeting of the American Chemical Society, Anaheim, CA, March 28-April 1, 2004
Scientific Organizing Committee for the 4th International Meeting on Copper Homeostasis and its Disorders: Molecular and Cellular Aspects, Ischia, Italy, October 22-28, 2004
Editorial Advisory Board of the *Journal of Biological Inorganic Chemistry*, 2004-2006
Elected Councilor, Division of Biological Chemistry, American Chemical Society, 2005-2008
Co-Editor, Bioinorganic Chemistry section of *Current Opinion in Chemical Biology*, April 2006 issue
Member, MFSA Study Section, Center for Scientific Review, National Institutes of Health, 2006-2010
Scientific Organizing Committee for the 6th International Copper Meeting, Alghero, Sardinia, October 11-15, 2008
Elected Chair, Bioinorganic Subdivision, American Chemical Society, 2009
Editorial Advisory Board of the *Journal of Biological Inorganic Chemistry*, 2009-2011
Editorial Advisory Board of *Inorganic Chemistry*, 2009-2012
Co-organizer, Dioxygen Activation Chemistry and Catalytic Oxidation Reactions Symposium, Pacifichem 2010, December 15-20, 2010
Editorial Advisory Board of the *Journal of Inorganic Biochemistry*, 2010-2014
Member, Proposal Review Panel, Stanford Synchrotron Radiation Light Source, 2010-2015
Co-editor, *Methods in Enzymology* volumes 494 and 495, *Methods in Methane Metabolism*, 2011
Scientific Organizing Committee for the 8th International Copper Meeting, Alghero, Sardinia, September 30-October 5, 2012
Vice Chair, Metals in Biology Gordon Conference, 2012
Chair, Metals in Biology Gordon Conference, 2013
Member, NSF CLP Review Panel, March 2013
Elected Councilor, Society for Biological Inorganic Chemistry, 2013-2017
Scientific Advisory Board of the Cluster of Excellence “Unifying Concepts in Catalysis, UniCAT,” Berlin, Germany, 2013-2017
Member, Stanford Synchrotron Radiation Light Source Structural Molecular Biology Advisory

Committee (SMBAC), 2014-present
Co-organizer, Dioxygen Activation Chemistry of Metalloenzymes and Models Symposium, Pacifichem 2015, December 15-20, 2015
Co-editor, Catalysis and Regulation section of *Current Opinion in Structural Biology*, December 2015 issue
Board of reviewing editors, *Science*, 2015-present
Elected Member, ASBMB Nominating Committee, 2015-2018
Editorial Advisory Board of *Biochemistry*, 2017-present
Editorial Advisory Board of *Accounts of Chemical Research*, 2018-present
Member, DOE Enzyme Structure and Function Review Panel, March 2018
Co-organizer, Metals in Biological Chemistry: C-H Bond Activation by Metalloenzymes and Models Symposium, Pacifichem 2020, December 15-20, 2020
Editorial Board, *Proceedings of the National Academy of Sciences USA*, 2019-present
Co-chair, 12th International Copper Meeting (Copper 2020 Sorrento), September 20-25, 2020

C. Contributions to science

Full list of publications:
https://www.ncbi.nlm.nih.gov/sites/myncbi/amy.rosenzweig.1/bibliography/40508873/public/?sort=date&direction=descending

1. Determined the first crystal structures of both types of methane monooxygenase (MMO).
Methane monooxygenases (MMOs) are enzymes that catalyze the oxidation of methane to methanol in methanotrophic bacteria. As potential targets for bioremediation applications, new gas-to-liquid methane bioconversion processes, and technologies to mitigate the deleterious effects of global warming, MMOs have attracted intense attention. Understanding MMO function on the molecular level is critical to such applications. Moreover, methane is the most inert hydrocarbon, and determining how an enzyme can break its 105 kcal C-H bond is of fundamental importance. As a graduate student, I determined the crystal structure of the 251 kDa soluble MMO (sMMO) hydroxylase, which contains a catalytic diiron center. This structure was the largest protein structure solved at the time, and set the stage for a detailed understanding of the sMMO mechanism. Then, in groundbreaking work conducted in my independent laboratory at Northwestern, we determined the first and only structures of the particulate MMO (pMMO). As a multisubunit integral membrane enzyme isolated from a native source, pMMO presented a formidable challenge to the field. Our structures provided the starting point for addressing questions about the pMMO active site, mechanism, and overall function.

a. Rosenzweig, A. C.; Frederick, C. A.; Lippard, S. J.; Nordlund, P. Crystal structure of a bacterial non-haem iron hydroxylase that catalyses the biological oxidation of methane. *Nature* **1993**, *366*, 537-543.
b. Lieberman, R. L.; Rosenzweig, A. C. Crystal structure of a membrane-bound metalloenzyme that catalyses the biological oxidation of methane. *Nature* **2005**, *434*, 177-182.
c. Smith, S. M.; Rawat, S.; Telser, J.; Hoffman, B. M.; Stemmler, T. L.; Rosenzweig, A. C. Crystal structure and characterization of particulate methane monooxygenase from *Methylocystis s*pecies strain M. *Biochemistry* **2011**, *50*, 10231-10240, PMC3364217.
d. Sirajuddin, S.; Barupala, D.; Helling, S.; Marcus, K.; Stemmler, T. L.; Rosenzweig, A. C. Effects of zinc on particulate methane monooxygenase activity and structure. *J. Biol. Chem.* **2014**, *289*, 21782-21794, PMC4118136.

2. Provided key insights into particulate methane monooxygenase (pMMO) catalysis.
Debate over the nature of the pMMO catalytic site started in the early 1990s and intensified as different models involving various numbers of copper and iron ions were considered in the context of our crystal structures, which revealed several distinct metal binding sites. We definitively showed that pMMO activity requires copper ions. We recently demonstrated through advanced paramagnetic spectroscopic techniques that pMMO contains two mononuclear copper centers, one in the PmoB subunit and one in the PmoC subunit. We further localized these two sites via native top down mass spectrometry (nTDMS), and established a correlation between enzymatic activity and occupancy of the PmoC site. In addition, we demonstrated that the membrane environment is crucial for pMMO function. Our ongoing work addressing the nature and location of the copper active site will frame the design and understanding of all future mechanistic studies of pMMO. Finally, we identified and characterized a novel copper binding protein, PmoD, which forms an unusual Cu_A-like site and is critical for methanotroph growth under pMMO-utilizing conditions.

a. Ro, S. Y.; Ross, M. O.; Deng, Y. W.; Batelu, S.; Lawton, T. J.; Hurley, J. D.; Stemmler, T. L.; Hoffman, B. M.; Rosenzweig, A. C. From micelles to bicelles: effect of the membrane on particulate methane monooxygenase activity. *J. Biol. Chem.* **2018**, *293*, 10457-10465, PMC6036204.
b. Ross, M. O.; MacMillan, F.; Wang, J.; Nisthal, A.; Lawton, T. J.; Olafson, B. D.; Mayo, S. L.; Rosenzweig, A. C.; Hoffman, B. M. Particulate methane monooxygenase contains only monocopper centers. *Science* **2019**, *364*, 566-570, PMC6664434.
c. Ro, S. Y.; Schachner, L. F.; Koo, C. W.; Purohit, R.; Remis, J. P.; Kenney, G. E.; Liauw, B. W.; Thomas, P. M.; Patrie, S. M.; Kelleher, N. L.; Rosenzweig, A. C. Native top-down mass spectrometry provides insights into the copper centers of membrane-bound methane monooxygenase. *Nat. Commun.* **2019**, *10*, 2675, PMC6572826.
d. Fisher, O. S.; Kenney, G. E.; Ross, M. O.; Ro, S. Y.; Lemma, B. E.; Batelu, S.; Thomas, P. M.; Sosnowski, V. C.; DeHart, C. J.; Kelleher, N. L.; Stemmler, T. L.; Hoffman, B. M.; Rosenzweig, A. C. Characterization of a long overlooked copper protein from methane- and ammonia-oxidizing bacteria. *Nat. Commun.* **2018**, *9*, 4276, PMC6189053.

3. Characterized a novel copper uptake system in methanotrophic bacteria, establishing new paradigms in metal handling and natural products biosynthesis.

Methanobactins (Mbns), small peptidic natural products produced by methanotrophs, are secreted under copper-limited conditions and are believed to acquire copper from the environment followed by re-internalization of the copper-loaded form. We obtained the first direct evidence for Mbn internalization and demonstrated that Mbn uptake is an active transport process mediated by a specific receptor. In a seminal bioinformatics study, we identified operons that contain genes encoding precursor peptides that are converted to Mbn by post-translational modifications as well as genes encoding putative biosynthetic enzymes and transporters. We then demonstrated that these operons are indeed copper-regulated, and characterized the Mbn transport machinery both in vivo and in vitro. Notably, the operons are also found in non-methanotrophs, suggesting that the known Mbn structures represent just a fraction of what is available in nature and that these pathways are more widespread than anticipated. In recent work, we identified and characterized a novel redox-active iron-containing metalloenzyme complex that performs the key steps in Mbn biosynthesis.

a. Kenney, G. E.; Rosenzweig, A. C. Methanobactins: maintaining copper homeostasis in methanotrophs and beyond. *J. Biol. Chem.* **2018**, *293*, 4606-4615, PMC5880147.
b. Kenney, G. E.; Rosenzweig, A. C. Genome mining for methanobactins. *BMC Biol.* **2013**, *11*, 17, PMC362179.
c. Dassama, L. M. K.; Kenney; G. E.; Ro, S. Y.; Zielazinski, E. L.; Rosenzweig, A. C. Methanobactin transport machinery. *Proc. Natl. Acad. Sci. USA* **2016**, *113*, 13027-13032, PMC5135309.
d. Kenney, G. E.; Dassama, L. M. K.; Pandelia, M.-E.; Gizzi, A. S.; Martinie, R. J.; Gao, P.; DeHart, C. J.; Schachner, L. F.; Skinner, O. S.; Ro, S. Y., Zhu, X.; Sadek, M.; Thomas, P. M.; Almo, S. C.; Bollinger, J. M., Jr.; Krebs, C.; Kelleher, N. L.; Rosenzweig, A. C. The biosynthesis of methanobactin. *Science* **2018**, *359*, 1411-1416, PMC5944852.

4. Determined the first three dimensional structures of metallochaperone proteins and elucidated their molecular mechanisms for target recognition and metal ion transfer.

Acquisition and management of metal ions is a critical part of metabolism for all forms of life. A host of proteins, including metallochaperones and membrane transporters, ensure that the correct ions are provided to essential enzymes and proteins, but do not accumulate to deleterious levels. In humans, aberrant handling of copper, zinc, iron, and manganese is linked to numerous diseases. My laboratory determined the first crystal structures of yeast and human chaperones involved in multiple copper delivery pathways. We also determined the first structure of a metallochaperone-target protein complex. These structures, together with biochemical studies, provided a molecular-level understanding of how intracellular metal ions are transferred between protein partners. In recent work, we have focused on the membrane transporters targeted by some of these metallochaperones, the P_{1B}-type ATPases. Despite their universal importance, very little is known about P_{1B}-ATPase biochemistry, structure, and metal binding properties. Our work has provided key new insights into P_{1B}-ATPase domain structure and how specific metal ions are recognized by these transporters.

a. Wernimont, A. K.; Huffman, D. L.; Lamb, A. L.; O'Halloran, T. V.; Rosenzweig, A. C. Structural basis for copper transfer by the metallochaperone for the Menkes/Wilson disease proteins. *Nat. Struct. Biol.* **2000**, *7*, 766-771.
b. Lamb, A. L.; Torres, A. S.; O'Halloran, T. V.; Rosenzweig, A. C. Heterodimeric structure of superoxide dismutase in complex with its metallochaperone. *Nat. Struct. Biol.* **2001**, *8*, 751-755.

c. Smith, A. T.; Barupala, D.; Stemmler, T. L.; Rosenzweig, A. C. Discovery and characterization of a novel metal binding domain involved in cadmium, cobalt, and zinc transport. *Nat. Chem. Biol.* **2015**, 11, 678-684, PMC4543396.
d. Purohit, R.; Ross, M. O.; Batelu, S.; Kusowski, A.; Stemmler, T. L.; Hoffman, B. M.; Rosenzweig, A. C. A Cu^{+}-specific CopB transporter: revisiting P_{1B}-type ATPase classification. *Proc. Natl. Acad. Sci. USA* **2018**, *115*, 2108, PMC5834730.

5. Determined structures of numerous other metalloproteins and metalloenzymes.
Through collaborative work, we have made major contributions to understanding a range of bioinorganic systems. Our structures have provided key insight into the mechanisms of biologically important radical enzymes, including the RNA methylating enzyme RlmN, iron- and manganese-containing ribonucleotide reductase (RNR) β2 proteins, and the antibiotic-biosynthesizing enzymes β-lactam synthetase, CarA, and CarC. We determined the first high resolution protein-protein complex structure of a RNR system as well as the first structure of a heterodimeric RNR β2 complex.

a. Boal, A. K.; Grove, T. L.; McLaughlin, M. I.; Yennawar, N. H.; Booker, S. J.; Rosenzweig, A. C. Structural basis for methyl transfer by a radical SAM enzyme. *Science* **2011**, *332*, 1089-1092, PMC3506250.
b. Chang, W. C.; Guo, Y. S.; Wang, C.; Butch, S. E.; Rosenzweig, A. C.; Boal, A. K.; Krebs, C.; Bollinger, J. M., Jr. Mechanism of the C5 stereoinversion reaction in the biosynthesis of carbapenem antibiotics. *Science* **2014**, *343*, 1140-1144, PMC4160820.
c. Boal, A. K.; Cotruvo, J. A.; Stubbe, J.; Rosenzweig, A. C. Structural basis for activation of class Ib ribonucleotide reductase. *Science* **2010**, *329*, 1526-1530, PMC3020666.
d. Voegtli, W. C.; Ge, J.; Perlstein, D. L.; Stubbe, J.; Rosenzweig, A. C. Structure of the yeast ribonucleotide reductase Y2Y4 heterodimer. *Proc. Natl. Acad. Sci. USA* **2001**, *98*, 10073-10078.

D. Research Support

Ongoing

NIH R35 GM118035, Amy C. Rosenzweig, P. I. 4/1/16-3/31/21
Metalloenzymes and metal homeostasis
This project focuses on metalloenzymes and metal transporters.

DE-SC0016284, Amy C. Rosenzweig, P. I. 9/1/19-8/31/22
Missing links in biological methane and ammonia oxidation
The goal of this project is to biochemically and functionally characterize recently identified proteins that may play a role in biological methane oxidation.

Intrexon Corporation, Amy C. Rosenzweig, P. I. 11/21/17-11/20/19
Microbial methane ultilization
The goal of this project is to understand the biology of methanotrophic bacteria.

Completed during the last three years

DE-SC0016284, Amy C. Rosenzweig, P. I. 9/1/16-8/31/19
Missing links in biological methane and ammonia oxidation
The goal of this project is to biochemically and functionally characterize recently identified proteins that may play a role in biological methane oxidation.

NSF-STTR 1534743, Barry Olafson (Protabit LLC), P. I., Amy C. Rosenzweig, Subcontract 9/15/15-8/31/17 (in NCE until 8/31/18)
Engineering a recombinant methane monooxygenase to convert methane to methanol for the production of fuels and chemicals
The goal of this project was to computationally design a recombinant methane oxidizing enzyme.

NIH R01 GM070473, Amy C. Rosenzweig, P. I. 6/1/13 – 5/31/16 (in NCE until 5/31/17)
Particulate methane monooxygenase
The goal of this project was to structurally and biochemically characterize membrane-bound methane monooxygenase.

NIH R01 GM58518, Amy C. Rosenzweig, P. I. 4/1/12 – 3/31/16 (in NCE until 3/1/17)

Structure and specificity in metal ion homeostasis

The goal of this project was to understand the molecular mechanisms of metal transport across membranes in molecular detail.