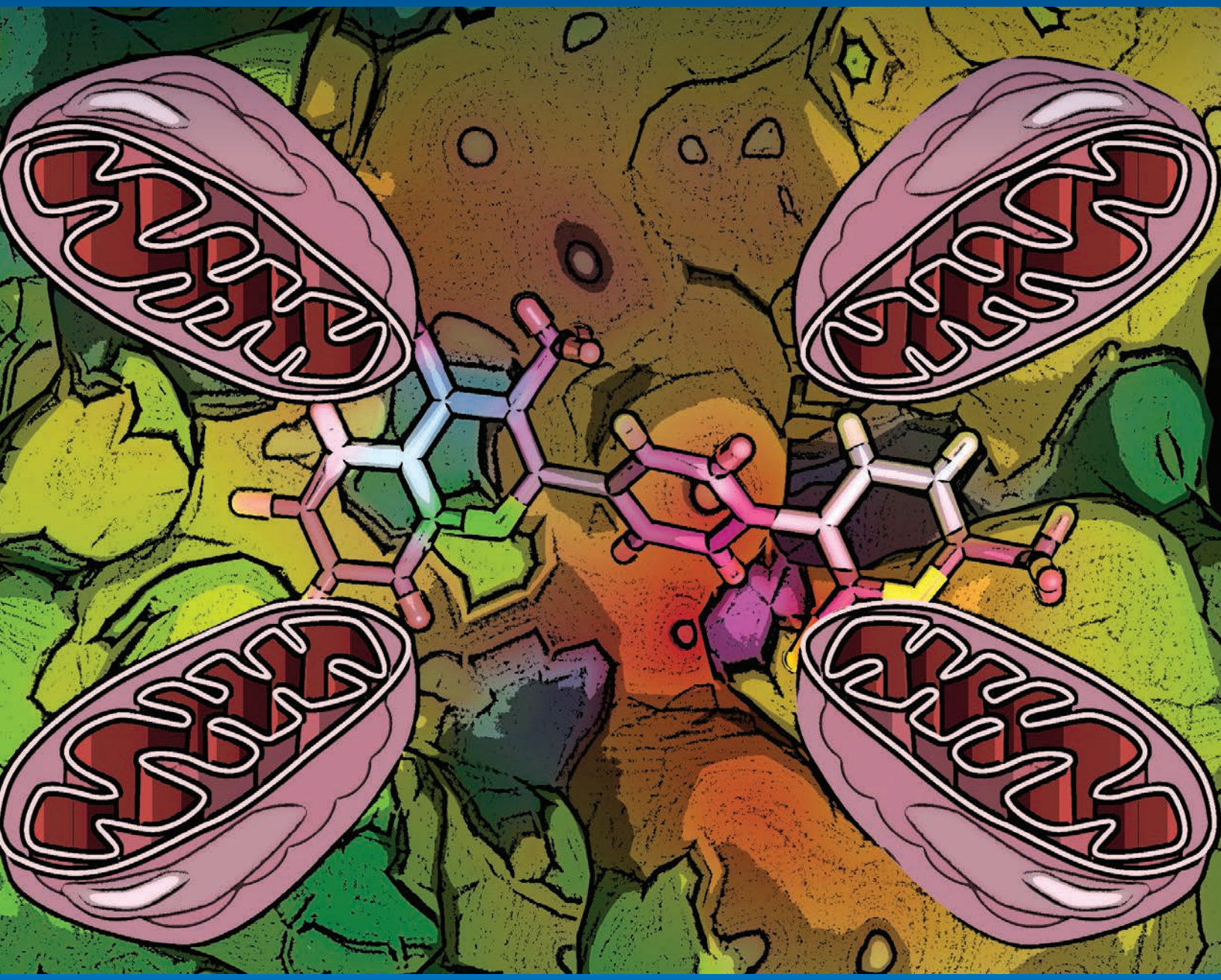
BIOLOGICAL CHEMISTRY
News & Review
2018



MICHIGAN MEDICINE
UNIVERSITY OF MICHIGAN

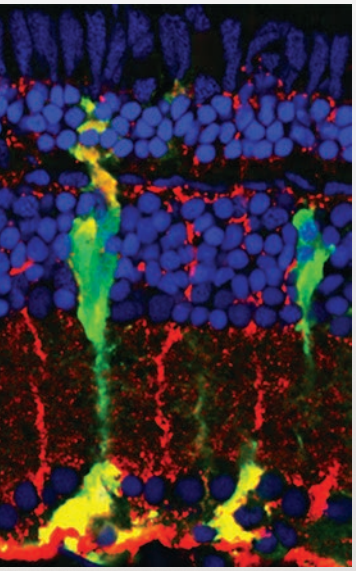
BIOLOGICAL CHEMISTRY

Letter from the Interim Chair Dan Goldman, Ph.D.

Dear Friends of Biological Chemistry

A little over three years ago, I assumed the role of interim chair for the Department of Biological Chemistry. I was honored to be asked to do this and I have found the experience to be very rewarding. Most satisfying to me was taking a deep dive into all the great science taking place in our department, helping faculty and students as they pursued their research and educational activities, and just getting to know everyone at a much deeper level than before. I have learned a chair needs to be selfless and I have tried my best to put the department needs above my own. I am especially proud of the six faculty that were recruited over these past 3 years and our greatly improved NIH ranking. The support I received from the faculty over the past 3 years has been remarkable and I am very grateful for this. Finally, I would like to introduce Dr. Phyllis Hanson, our new chair as of November 1. Phyllis comes to us from Washington University School of Medicine and her research focuses on AAA+ ATPases and their substrates. These proteins play critical roles in vesicle formation, endolysosomal trafficking, and membrane repair. Please join me in welcoming Dr. Hanson to the University of Michigan. We are in good hands!

I am very happy to share this past year's department news with you. Keeping with tradition, we held our annual Biological Chemistry Department Retreat at the Kellogg Biological Station. Thanks to faculty members Kaushik Ragunathan and Yan Zhang, and graduate student Christine Ziegler for organizing such a wonderful event. As usual, our graduate student and postdoc research presentations were the highlight of the retreat. For the first time, we included a town hall-type of event to discuss challenges and opportunities the department is facing. This year's retreat activities, along with student and faculty interviews were captured on videotape thanks to Mike Uhler. Please visit our web page to see the edited film.



The Goldman lab studies mechanisms underlying retina regeneration in zebrafish. We aim to understand this regenerative process in fish so we can apply it to mammals. Shown is a cross section of an injured retina in a transgenic fish that expresses GFP in reprogrammed proliferating Muller glia-derived stem cells. These reprogrammed Muller glial cells are responsible for regenerating retinal neurons in the injured and diseased retina. Blue is DAPI stained nuclei and red is glutamine synthetase stained quiescent Muller glia.

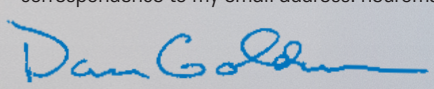
Our faculty continue to push the boundaries of research and contribute to our scientific enterprise and educational mission. Please visit the Faculty Awards and Faculty Highlights sections of the newsletter for the latest updates. Of special note, Steve Ragsdale will receive this year's University of Michigan Distinguished Faculty Achievement Award; Ruma Banerjee will receive the 2019 ASBMB Merck Award; and Ryan Baldridge received a Breakthrough Scientists Award from the Damon Runyan Cancer Research Foundation. New to the faculty this year is Dr. Allison Lamanna who was hired as a lecturer III. Dr. Lamanna comes to us from Boston University, but is also a Michigan alum – she did her postdoctoral training in the lab of Rowena Matthews. Allison will contribute to teaching and will serve on variety of departmental committees. We are thrilled to have her among our ranks.

As in the past, our named lectureship series brings in the best scientists from around the world to talk on their work. The complete list of these lectureships is detailed in the newsletter. Please take a look and help us fulfill those that remain underfunded. Our alumni play a key role in the success of our department. We are proud of your accomplishments and they serve as inspiration to our students. Some of you have participated in career development activities organized by the department and we hope to continue to tap into your expertise in future years. Alumni also help us support our students and faculty in their research and educational efforts. We are very grateful for your support and hope to continue to engage you in our academic mission.

I am saddened to inform you that Minor "Jud" Coon recently passed away. Jud was a stellar scientist, respected by all that met him. Jud was chair of the department from 1970-1990. Jud was a mentor to many of us who joined the department during his chairmanship (including me). He also trained many scientists that have gone on to be leaders in their own fields. Jud favored discovery and was blind to gender. He was ahead of his time and will be sorely missed.

If you haven't done so yet, please visit our web page at https://medicine.umich.edu/dept/biological-chemistry where you can find more news and details about the department.

As in the past, I would like to conclude with a reminder that we are interested in hearing from you. Our department members and the friends of the department would love to keep abreast of what you are up to. Please send correspondence to my email address: neuroman@umich.edu – I will be sure to forward to Dr. Hanson.



Letter From Chair Phyllis Hanson M.D., Ph.D.

By the time you read this, the leaves will have fallen, Ann Arbor will have its first snow, and I will have moved at the beginning of November from Washington University in St. Louis to the University of Michigan.

I am honored and thrilled to join this illustrious Department, building on the deep tradition and strengths that so many of you helped develop as the Department heads into an exciting future. These are challenging times, but the potential and need for progress in fundamental science has never been greater. Advances in biochemistry are central to these priorities. Strategic investments across the University, along with recent positive directions in congressional support for the NIH, are promising signs for the immediate future, and research in the Department can and should take advantage of these opportunities. My goals are to leverage new recruitment to complement existing strengths and the most promising new directions. Together with outstanding teaching and service, we can position the Department to lead both locally and nationally.

I look forward to spending the winter getting to know our faculty, trainees, and staff. Interests in the Department now span a wide range of problems in biology, unified by a goal of understanding underlying mechanisms in chemical and quantitative terms. I am particularly excited about working with and supporting the outstanding cadre of assistant professors new to Michigan over the last few years, each of whom brings emerging areas and cutting-edge technology to our community. My own research interests lie in understanding how proteins interact to regulate the structure and organization of cell membranes both inside and outside the cell, and I am excited to join the active membrane trafficking community at the U of M.

We are actively recruiting and hope that you will send the best and brightest trainees and faculty candidates our way. I am happy to hear from you and look forward to meeting anyone coming through Ann Arbor.

Happy New Year!

Phyllis J. Hanson

In this Issue

On the Cover

Submitted by Jeanne Stuckey, Research Associate Professor, Life Sciences Institute and The Department of Biological Chemistry

Credit: U-M Life Sciences Institute | Stephanie King, Multimedia Designer

A representation of the design and synthesis of novel class of brequinar-like inhibitors with increased bioavailability and potency against the mitochondrial membrane protein dihydroorotate dehydrogenase, which catalyzes the oxidation of dihydroorotate to orotate. Inhibition of this committed step in the de novo pyrimidine biosynthesis pathway has been exploited to develop therapies for many diseases including bacterial and viral infections, parasitic diseases (i.e., malaria), autoimmune disorders, and cancer.

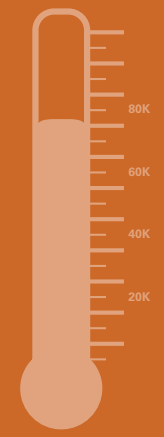
Reference Article: Madak JT, Cuthbertson CR, Miyata Y, Tamura S, Petrunak EM, Stuckey JA, Han Y, He M, Sun D, Showalter HD, Neamati N. Design, Synthesis, and Biological Evaluation of 4-Quinoline Carboxylic Acids as Inhibitors of Dihydroorotate Dehydrogenase. J Med Chem. 2018 Jun 28;61(12):5162-5186.

THE ENDOWED LECTURESHIPS: 2018-2019

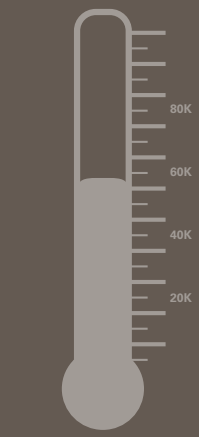
Irwin J. Goldstein Lectureship in Glycobiology

Suzanne Walker, Ph.D.
Professor of Microbiology
and Immunology
Harvard Medical School

May 7th, 2019



GOLDSTEIN LECTURESHIP
GOAL – $100,000



LUDWIG LECTURESHIP
GOAL – $100,000

Martha Ludwig Lectureship in Structural Biology

Leemor Joshua-Tor, Ph.D.
W.M. Keck Professor of
Structural Biology
Cold Spring Harbor Laboratory
Investigator, Howard Hughes
Medical Institute

April 2nd, 2019

George William Jourdian Lectureship in Biological Chemistry

Jue Chen, Ph.D..
Professor in the Laboratory of
Membrane Biology and Biophysics
The Rockefeller University
Investigator, Howard Hughes
Medical Institute

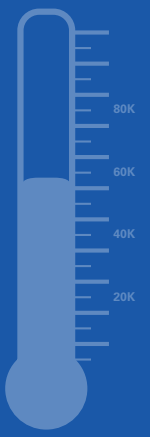
April 9th, 2019

JOURDIAN LECTURESHIP
GOAL – $100,000

G. Robert Greenberg Lectureship in Biological Chemistry

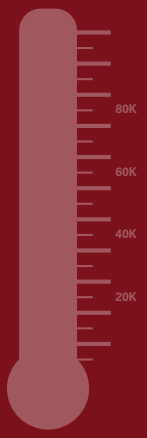
Gary Patti, Ph.D.
Associate Professor,
Department of Chemistry
Washington University in St. Louis

March 12, 2019



GREENBERG LECTURESHIP
GOAL – $100,000

William E.M. Lands Lectureship on the Biochemical Basis for the Physiology of Essential Nutrients



LANDS LECTURESHIP
GOAL – $100,000

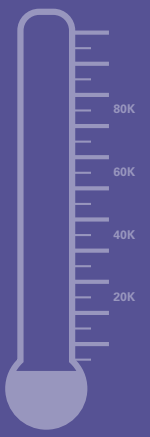
Steven Kliewer, Ph.D.
Professor of Molecular Biology
UT Southwestern Medical School

October 2nd, 2018

Rowena Matthews Lectureship in Biological Chemistry

Krishna Niyogi, Ph.D.
Professor of Plant
and Microbial
Biology University of
California, Berkeley

September 18th, 2018



MATTHEWS LECTURESHIP
GOAL – $100,000

Pimchai Chaiyen, Ph.D.
Professor of Biochemistry
Mahidol University,
Thailand

April 30th, 2019

The Distinguished Graduate Lectureship

PLEASE SEE PAGE 12 OF THE NEWSLETTER FOR INFORMATION ON LECTURESHIP FUNDING

New Faculty Highlights

Allison Lamana, Ph.D.
Allison received her Ph.D. in Biochemistry from the University of Wisconsin-Madison, working with Laura L. Kiessling to study the effects of receptor oligomerization in bacterial and neutrophil chemotaxis. She began her post-doctoral training in the Life Sciences Institute at the University of Michigan with Rowena Matthews investigating the conformational changes of methionine synthase. She completed her post-doctoral training in the Chemistry Department with Katrin Karbstein, mapping RNA conformational changes in eukaryotic ribosome assembly. In the Chemistry Department, Allison was able to combine her research experience with teaching opportunities in the undergraduate curriculum, developing curriculum for and teaching a biochemical techniques laboratory course for majors.

Allison then spent seven years as a lecturer and then senior lecturer in the Chemistry Department at Boston University. There, she taught chemistry and biochemistry to molecular science majors, students in the seven-year medical program, and students in the health sciences. She worked on a project to bring undergraduates into the classroom as peer-instructors as well as to utilize problem-based group work. She mentored undergraduates and graduate students in teaching in addition to supervising postdoctoral faculty fellows.

In the Chemistry Department, Allison was able to combine her research experience with teaching opportunities in the undergraduate curriculum, developing curriculum for and teaching a biochemical techniques laboratory course for Biochemistry majors.

Faculty Awards and Achievements

Jeanne Stuckey
Voted Chairman of the LS CAT Management Board

Ruma Banerjee
2019 ASBMB Merck Award

Audrey Seasholtz
Academy of Educators

Kaushik Ragunathan
EBS Innovation Initiative Award

Steve Ragsdale
Distinguished Faculty Achievement Award (Rackham)

Bruce Palfey
Academy of Educators

Neil Marsh
Appointed to the Journal of Biological Chemistry Editorial Board

AAAS Fellow

Anne Vojtek
Associate Director, PIBS

Janet Smith
Associate Director, Life Science Institute, UM

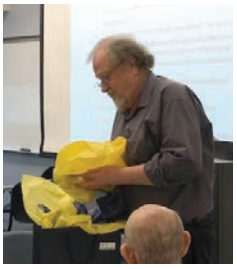
David Turner
EBS Teaching Award

Jim Morrissey
Joint Editor-in-Chief of the Journal of Thrombosis and Haemostasis

Ryan Baldridge
Breakthrough Scientists Award Damon Runyon Cancer Research

Retirements

Jerry Menon, Ph.D. Dr. Menon, Professor of Biological Chemistry, began a phased retirement this year with his full retirement becoming effective on July 1, 2019. During his retirement, Dr. Menon plans to spend more time with family and friends, and is especially excited to watch his grandchildren grow up. He would like to read all the books he never had time to read during his years working, travel, take yoga classes and attempt to figure out how to relax! He will continue to keep up with advances being made in his field of study.



Erik Zuiderweg, Ph.D. Dr. Zuiderweg, Professor of Biological Chemistry, retired on May 31, 2018. In his retirement, Dr. Zuiderweg will live in the Netherlands and assist a local University with NMR (Nuclear Magnetic Resonance) technology, and potentially create his own business to develop further uses for NMR.

Bob Lyons, Ph.D. Dr. Lyons retired on September 15th, 2018 as Assistant Professor of Biological Chemistry and the Director of the DNA Sequencing Core. He is an avid saxophonist and flutist, particularly involved in jazz music. In retirement, he plans to get more involved in the music scene around Ann Arbor.

Symposium to celebrate Dr. Jerry Menon's UM career held April 20, 2018

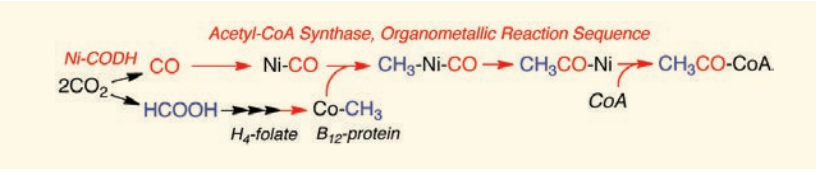
A career celebration symposium was held on April 20, 2018 for Dr. Jerry Menon as he made preparations to retire. The Biological Chemistry Department along with the Obstetrics and Gynecology Department celebrated his stellar 48-year academic career with a day of seminars at the Rackham Graduate School given by his former trainees and colleagues. Dr. Menon's former students and colleagues presented their research and also highlighted the impact that Jerry has had on their career paths. The event included a career development workshop for graduate students and postdoctoral fellows with advice from Jerry and his past trainees. The symposium ended with a keynote lecture by Dr. Jerry Strauss, Executive Vice President for Medical Affairs of the VCU Health System. A dinner with more informal comments from his colleagues and trainees was held at The Graduate and the Menon Family announced an intended gift fund in Jerry Menon's name for the Biological Chemistry Department. About 250 UM faculty and students participated along with many colleagues from around the world.

Faculty Highlights

Stephen Ragsdale, Ph.D.

I'm studying how metal ions and metallocofactors are involved in regulating and catalyzing some important biological processes. Questions my laboratory is addressing include:

- What are the enzymatic mechanisms and intermediates of the key enzymes in anaerobic carbon dioxide fixation?
- What is the enzymatic mechanism of the key and rate-limiting enzyme involved in microbial methane synthesis (methyl-CoM Reductase)? What is the mechanism of anaerobic methane oxidation – the use of methane as a carbon & energy source?
- How can we use the mechanistic information on the pathways of methane and CO_2 metabolism (above) to benefit the environment and efficiently generate fuels and chemicals?
- What is the mechanism used by microbes to make the pervasive and extremely toxic ground-water contaminant, methyl-mercury?
- How do heme, CO and redox processes impact Rev-Erb and other heme-regulated proteins in regulating the mammalian circadian clock and other metabolic processes?
- How is heme degradation by the human heme oxygenase (HO) regulated in cells? How is HO integrated into the labile heme pool?
- How can we better connect to and celebrate the passion and creativity in science? How can we better unlock our creative potential?



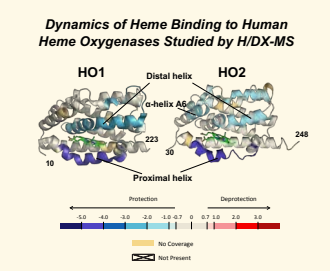
Here I'll focus on the subject I've been studying for the longest time. It is a process that apparently emerged with the origin of life; in fact, it – the reductive acetyl-CoA or Wood-Ljungdahl pathway – is rumored to have been the first metabolic pathway. Conceptually, it is a simple process that converts two molecules of an abundant one-carbon compound (carbon dioxide) into the two-carbon compound, acetyl-CoA, which participates in many metabolic and energy-producing reactions. We are collaborating with an innovative biotech company that is using this process to convert waste gases (mostly CO_2, CO and H_2) from power plants, steel mills and other industries into fuels and chemicals.

Just over thirty years ago, Harland Wood and I proposed a novel biochemical mechanism for how this pathway works (see Figure). We proposed that it occurs through a series of organometallic (metal-carbon) bonds. The Co-CH_3 (blue) is also made from CO_2 and transferred to the Ni by a protein similar to methionine synthase, studied in our department by Rowena Matthews, Martha Ludwig and Ruma Banerjee.

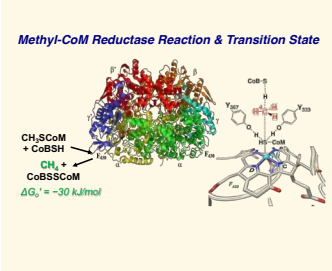
A lot of complex biochemistry was revealed over the last 30 years … crystal structures of all the proteins in the pathway, many involving a collaboration with Cathy Drennan, a former grad student of Rowena and Martha … lots of kinetic and spectroscopic studies involving many students, postdocs and collaborators. The catalysts responsible for all that "simple" biochemistry, shown in red in the figure turned out to be some of the most complex metal clusters found in nature.

The proposed "simple" reaction sequence became entrenched in the literature, described in hundreds of papers and serving as the basis of various industrial and academic research labs, only recently was the central tenet confirmed – *that a nickel ion in acetyl-CoA synthase is indeed the metal ion in the metal-carbon bonds involved in this pathway*. Just in the last couple of years have the key Ni-based intermediates been trapped and characterized. Many mechanistic mysteries remain and we keep moving forward to figure out how bonds are made, how electrons are transferred, how proteins interact … questions similar to those being pursued in many other labs.

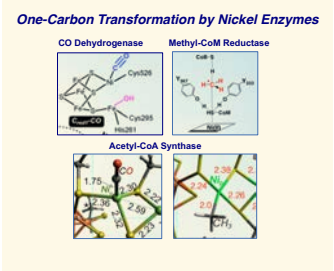
Feeling firmly rooted on Giants' shoulders, we survey just beyond the horizon. When shoulders shake, we follow Nature's scarce signs into foreign lands, sampling joy, sorrow, failure & success. We keep climbing, sinking, casting picks & nets, incessantly gathering, creating, destroying with ears grounded & eyes soaring ever hoping to perceive the truth. Revised 2018 from Standing on Shoulders, SWR, 2015



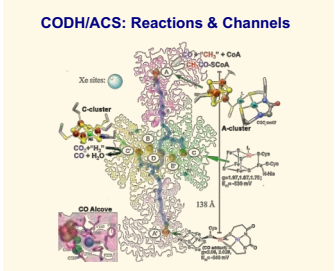
Dynamics of heme oxygenase binding heme.



Transition state for methane synthesis by Methyl CoM Reductase.

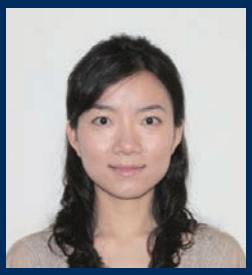


Catalytic Intermediates at the active sites of key enzymes in the global carbon cycle.



Structure of the key carbon fixing enzyme, CO dehydrogenase/acetyl-CoA synthase.

Faculty Highlights



Yan Zhang, Ph.D.

Dr. Yan Zhang received her B.S. in Biological Sciences from Peking University, China. She then earned her Ph.D. from the University of Wisconsin Madison, where she studied post-transcriptional gene regulation of cell fate determinants in vertebrate embryos with Dr. Michael Sheets. Fascinated by a RNA-guided bacterial defense system called CRISPR-Cas, she pursued postdoctoral training with Dr. Erik Sontheimer at Northwestern University and the University of Massachusetts Medical School.

Dr. Yan Zhang joined the Department of Biological Chemistry at the University of Michigan in 2017. Her research group uses complementary biochemical, genetic, genomic, microbiological, and tissue culture approaches to study the biology, mechanism and application of diverse CRISPR systems. Current members of the Zhang lab include a graduate student (Max Gramelspacher), a postdoctoral fellow (Dr. Xufei Zhou), a staff scientist (Dr. Zhonggang Hou), and three undergraduate students (Jaewon Heo, Ryan Krueger, and Noah McGuire). She enjoys jogging, cooking and traveling in her spare time.

RESEARCH FOCUS:

CRISPR-Cas is a RNA-guided, adaptive immune system widespread in bacteria and archaea that help fend off invaders such as bacteriophages and plasmids. Microbes can store snippets of the invaders' DNA as "immune memories" at their CRISPR loci; and these memories will guide sequence-based defense against future invasions. Cas9 proteins are the "effector" DNA endonucleases for Type II CRISPR systems. Nowadays, CRISPR-Cas9 also provides powerful tools for programmable genome engineering in higher eukaryotes. The main research goal of our laboratory is to understand the fundamental biology and molecular mechanism of the prokaryotic CRISPR-Cas systems. We also aim to adopt novel features of diverse CRISPRs for innovative technological applications. My lab uses the human pathogen *Neisseria meningitidis* (Nme) as our primary model organism, and *Flavobacterium columnare*, *E. coli*, and human embryonic stem cells as additional platforms. We currently focus on the following projects:

(1) CRISPR adaptation: The most fascinating feature of CRISPR-Cas is their ability to generate immunological memory by acquiring new CRISPR sequences from invaders' DNA, in a poorly understood process known as "adaptation". We use genetic, genomic and biochemical approaches to decipher how bacteria (e.g. *N. meningitidis*) employ Cas9, together with the CRISPR DNA integrase Cas1-Cas2, to form new CRISPR memory.

(2) CRISPR-Cas3 based genome engineering: Unlike Cas9 that acts as a DNA scissor, Type I CRISPR relies on a helicase-nuclease fusion enzyme Cas3 to progressively shred a large DNA target. It was unclear whether Type I CRISPR, which is the most prevalent type of CRISPR in the nature, can act on eukaryotic chromosomes. We recently obtained the first proof-of-concept that in human embryonic stem cells, the T. *fusca* Type I-E CRISPR-Cas3 can induce a spectrum of long range chromosomal deletions (from 0.5 to 50 Kb) upstream from a single CRISPR target site (Dolan* and Hou* *et al.*, under revision). We will further characterize diverse Type I CRISPRs in human cells, and develop CRISPR-Cas3 based tools for high throughput genetic screens to interrogate the human non-coding genome.

(3) RNA targeting by CRISPR-Cas9: The conventional wisdom is that Cas9 is a family of DNA-cutting enzymes that cannot cleave RNA. Recently, we found an unexpected feature for NmeCas9: an intrinsic RNase activity that recognizes and cleaves ssRNA target in a RNA-guided, programmable fashion (Rousseau* and Hou* *et al.*, 2018, *Molecular Cell*). This discovery hints at alternative biological functions for NmeCas9 in regulating endogenous bacterial mRNAs; and also set the stage for exploiting NmeCas9 for applications in eukaryotic transcriptome engineering. We are currently pursuing both of these possibilities.

(4) CRISPR-Cas regulation: It remains enigmatic how the expressions of CRISPR-Cas genes are regulated in their native microbe hosts. Our current focus is to understand the physiological cues that *N. meningitidis* receive that can activate or suppress expression of CRISPR RNA, Cas9, and the Cas1-Cas2 integrase, respectively. This is an especially intriguing question given that *Neisseria* naturally takes up foreign DNA frequently for genetic diversity, but in the meantime also possesses CRISPR-Cas9 that serves as a barrier for DNA uptake. We hope to define if, how and why are certain CRISPR activities (i.e. guide RNA production, DNA targeting, and memory formation) turned on/off in *Neisseria*.

2018 Annual Graduate Student Awards

THE HALVOR N. AND MARY M. CHRISTENSEN AWARD for Demonstrated Excellence in Academic Scholarship and Research Contributions

Awardee: **Beth A. Rousseau**

Mentor: David Turner, Ph.D.

THE ADAM A. AND MARY J. CHRISTMAN AWARD for Demonstrated Excellence in Academic Scholarship and Research Contributions

Awardee: **Christine A. Ziegler**

Mentor: Peter Freddolino, Ph.D.

THE ANTHONY AND LILLIAN LU AWARD is presented to a student on the basis of academic background, achievement in the graduate program, and potential as a scientist.

Awardee: **Trever Bostelaar**

Mentor: Ruma Banerjee, Ph.D.

THE LEE MURPHY MEMORIAL PRIZE is awarded annually to a student in the Biological Chemistry Ph.D. program who embodies the highest ideals of scientific integrity and who has published a paper or a series of papers judged most significant by the Awards Committee.

Awardee: **Jennifer A. Bohn**

Mentor: Janet Smith, Ph.D.

THE DZIEWIATKOWSKI AWARD is presented to the student who has submitted the Most Outstanding Ph.D. Dissertation in the past year.

Awardee: **Nicole Motl, Ph.D.**

Mentor: Ruma Banerjee, Ph.D.

Ph.D. Degrees Granted

Samuel T. Slocum, Ph.D.

November 3, 2017

"Biochemical Studies of Polyketide Beta-Branching and Polyketide Synthase Module Architecture"

Mentors: Janet Smith, Ph.D., and David Sherman, Ph.D.

Eric Tse, Ph.D.

November 30, 2017

"Quality Control Mechanisms of Molecular Chaperones in the Folding and Degradation of Client Proteins"

Mentors: Daniel Southworth, Ph.D. and Philip Andrews, Ph.D.

Robert J. Fick, Ph.D.

December 7, 2017

"Characterization of Methyltransferase Carbon-Oxygen Hydrogen Bonding and Sulfur-Oxygen Chalcogen Bonding with the Sulfonium of S-adenosyl-L-methionine"

Mentor: Raymond Trievel, Ph.D.

Grace Mahony Kroner, Ph.D.

April 13, 2018

"Regulation of E. Coli Genome Architecture and Transcription in Response to Changing Nutrient Levels"

Mentor: Peter Freddolino, Ph.D.

Gregory J. Dodge, Ph.D.

June 6, 2018

"Structural and Biochemical Studies of Polyketide Synthase and Fatty Acid Synthase Dehyratase"

Mentor: Janet Smith, Ph.D.

Meredith A. Skiba, Ph.D.

August 30, 2018

"Structural and Biochemical Investigation of Methylation and Elucidation of t-Butyl Formation in Polyketide Biosynthesis"

Mentor: Janet Smith, Ph.D.

Wallace K.B. Chan, Ph.D.

September 12, 2018

"Development and Application of Virtual Screening Methods for G Protein-Coupled Receptors"

Mentor: Yang Zhang, Ph.D.

M.S. Degrees Granted

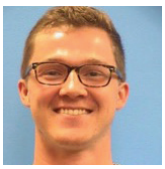
JonCarlos Anderson, M.S.
August 17, 2018
"Sulfide's Effect on Colorectal Cancer"
Mentor: Ruma Banerjee, Ph.D.

Ali Farhat, M.S.
August 17, 2018
"Developing a Tool for Analyzing Protein Interactions with DNA"
Mentor: Peter Freddolino, Ph.D.

Alexander Fischbach, M.S.
August 17, 2018
"(E/Z)-BCI hydrochloride Enhances the Effects of FGF2 and BDNF Gene Regulation in Post-Mitotic Glutamatergic Neurons"
Mentor: Michael Uhler, Ph.D.

Aditi Gupta, M.S.
August 17, 2018
"Missense Patient Mutations in Human Adenosyltransferase and Their Causation of Methylmalonic Aciduria"
Mentor: Ruma Banerjee, Ph.D.

Brian Hardaway, M.S.
August 17, 2018
"Binding of the Ternary Complex of Elongation Factor Tu, GTP and Aminoacylated tRNA to the Amino Acid Sensing T-Box Riboswitch"
Mentor: Nils Walter, Ph.D.



Jordan Hochstetler, M.S.
April 26, 2018
Course Track

Charles Knox, M.S.
August 17, 2018
Course Track

Robin Pearce, M.S.
August 17, 2018
"EvoDesign: Designing Protein-Protein Binding Interactions Using Evolutionary Interface Profiles and Application to Protein Structure Recognition"
Mentor: Yang Zhang, Ph.D.

New Ph.D. Students

Ajay Larkin received his Bachelor of Science from Miami University, Oxford, OH in 2016.
Mentor: Kaushik Ragunathan, Ph.D.

Brian Peterson received his Bachelor of Science from South Dakota State University, Brookings, SD in 2017.
Mentor: Ryan Baldridge, Ph.D.

Tyler McCullough received his Bachelor of Science from Washington Jefferson College, Washington, PA in 2017.
Mentor: Janet Smith, Ph.D.

New M.S. Students

Kristena Abdelmalak received her Bachelor of Science from Oakland University, Rochester, MI in 2018.
Course Track

Mohamad Bazzi received his Bachelor of Science from the University of Michigan, Ann Arbor, MI in 2018.
Course Track

Christine Chang received her Bachelor of Science from the University of Michigan, Ann Arbor, MI in 2017.
Course Track

Max Gramelspacher received his Bachelor of Science from the University of Colorado at Boulder, Boulder, CO in 2013.
Research Track Mentor: Yang Zhang, Ph.D.

Parker Groom received his Bachelor of Science from the University of Michigan, Ann Arbor, MI in 2018.
Course Track

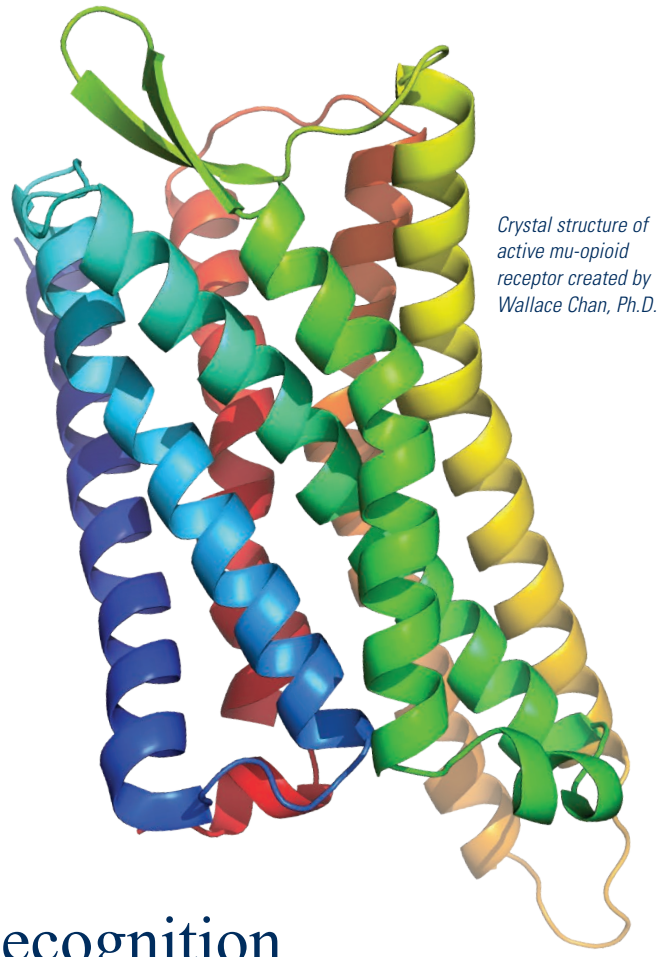
continued on next page

New M.S. Students *continued*

Rebecca Jacobs received her Bachelor of Science from New York University, New York, NY in 2016.
Course Track

Kelsa (Krickett) Kazyak received her Bachelor of Science from Boston College, Chestnut Hill, MA in 2018.
Course Track

Michael Schmidt received his Bachelor of Science from Sierra Nevada College, Incline Village, NV in 2016.
Research Track Mentor: Peter Freddolino Ph.D.



Crystal structure of active mu-opioid receptor created by Wallace Chan, Ph.D.

Student Achievements & Recognition

Congratulations to **Beth Rousseau**, a recipient of a prestigious Graduate Research Fellowship from the National Science Foundation. Beth's proposal was titled the "**RNA-guided RNA targeting by NmeCas9**". Beth is now a third-year student in the laboratory of Dr. David Turner.

Congratulations to **Ajay Larkin**, a second-year student in Kaushik Ragunathan's lab. Ajay was appointed to the Genetics Training Program for 2018-2019.

Congratulations to **Brian Peterson**, a second-year student in Ryan Baldridge's lab. Brian was appointed to the Genetics Training Program for 2018-2019.

Congratulations to **Christine Ziegler**, a third-year student in Dr. Peter Freddolino's lab. Christine was reappointed for a 2nd year to the Genetics Training Program for the 2018-2019 academic year.

Elizabeth Abshire ppresented her CBI Graduate Student Sabbatical Research Seminar on "Metabolic phenotyping of the mitochondrial functions of Nocturnin" on January 4, 2018. Elizabeth's sabbatical was sponsored in part by the **Prasanta Datta Memorial Scholarship Travel Fund**.

Justin McNally, a Ph.D. student in Dr. Pat O'Brien's lab, was awarded the ACS Chemical Biology Sponsored "Best Poster" Award at the 37th Annual Midwest Enzyme Chemistry Conference, October 14, 2017 at Loyola University in Chicago. His poster described studies of the mechanistic differences between human DNA ligases.

Elizabeth Abshire has received a 2017-2018 Endowment for the Development of Graduate Education (EDGE) Award from the Endowment for the Basic Sciences (EBS) in the Medical School. Elizabeth is a member of the Trievel and Goldstrohm laboratories and is studying Nocturnin, a ribonuclease that has been implicated in the regulation of lipid metabolism, skeletal development, adipogenesis, and obesity in mammals.

Supporting BioChem

The Department of Biological Chemistry relies upon the philanthropic generosity of donors to fund many aspects of its operations. Gift funds are essential to supporting activities beyond our basic operations. From endowed professorships and lectureships, to graduate student fellowships, seminar speakers, and gifts in direct support of research, donations help make the department an intellectually exciting and vibrant community. As a benefactor of the Department of Biological Chemistry, you can direct your gift in several ways:

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- Rowena Matthews Lectureship

Scholarship

- Prasanta Datta Memorial Research Travel Endowment

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OR CONTACT:
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Visiting lectureships are endowed funds established to honor a retiring faculty member. The lectureship provides us with resources to bring prominent faculty from other institutions to share their knowledge with the Michigan Medicine and University community. The lectureship helps to support travel and a modest honorarium for the speaker, and a reception after the lecture. Each lectureship needs to be endowed with at least $100,000 or more to provide sufficient annual funds to support the lecture. We hope you will consider donating to one or more of these lectureships. For more information contact Christen Barua, Associate Director of Development, Endowment for the Basic Sciences. Her email address is **cebarua@umich.edu**

PLEASE NOTE:
For 2018 charitable deductions and credits, the IRS has ruled that **credit card gifts** are deductible only in the year the bank processes the transaction. To be processed for tax year 2018 credit card gifts by mail must reach the University by December 16th, OR you may call (888) 518-7888 (toll free) or (734) 647-6179 (local), M-F 9AM-4PM EST, between December 16th and 30, 2018 to donate over the phone. Your **gift by check** must be postmarked by December 31, 2018.

Donate anytime online by visiting https://leadersandbest.umich.edu/find/#!/mimed/mimed/biochem

Thank you!

Biochem Retreat

The department held another very successful annual retreat on August 24 and 25 at the W.K. Kellogg Biological Station, a beautiful site overlooking Gull Lake located not far from Kalamazoo. The retreat started on Friday morning with a series of six talks from graduate students and postdocs, plus one talk from a new faculty member. As usual, the quality of the talks and the discussion was excellent. A new initiative this year by the graduate students in the Career Development Committee (with guidance from Mike Uhler) was to invite attendees to participate in brief video interviews, with a view to editing these clips into videos to be used for recruiting new graduate students and enhancing the departmental web site. These video clips were recorded immediately after lunch, followed by another new initiative this year – a "Town Hall" chaired by Dan Goldman at which the participants reviewed and discussed the many departmental activities and programs currently underway. The early afternoon was given over to recreational activities at this idyllic site, which is a great way for colleagues to get to know each other better. The afternoon and evening scientific sessions included five more talks by graduate students and postdocs, followed by a campfire party and the ever-popular barbecue. The poster session occupied most of Saturday morning, which featured lots of discussions of the students' and postdocs' latest research findings. The final session featured yet another new initiative this year – awards for the best talks (as determined by voting by the participants). Yuqi Wang from Jim Morrissey's lab won the best graduate student talk for her presentation entitled, "Polyphosphate as a potent modulator of the contact pathway of blood clotting," while Hanseong Kim from Uhn-Soo Cho's lab won the best postdoc talk for his presentation entitled, "MMOD-induced structural changes of hydroxylase in soluble methane monooxygenase."

In Memory Jud Coon

Tribute to Minor "Jud" Coon

BY DAVID BALLOU AND PAUL HOLLENBERG

Minor Jesser (Jud) Coon, the retired Victor C. Vaughan Distinguished Professor of Biological Chemistry at the University of Michigan Medical School, died on September 5, 2018 at the Glacier Hills Senior Living Facility. He was born on July 29, 1921 in Englewood, Colorado. He married Mary Louise Newburn in 1948, and they were married for 52 years until her death in 2000. His son, Lawrence Richard Coon unfortunately died a few weeks later. He has a surviving daughter, Susan Louise Coon (Conrad Weiser), and a daughter-in-law, Linda Wilkins Coon, who was a very wonderful companion and gave him attentive loving care, especially in his retirement years. He is also survived by four grandchildren and their spouses, and by four great-grandchildren.

Jud had a stellar career at the University of Michigan where he served from 1955 until he retired in 2002. He earned his Bachelor of Arts degree in Chemistry at the University of Colorado and his Ph.D. in Chemistry at the University of Illinois under the mentorship of the well-known biochemist, William C. Rose. While an undergraduate he carried out research in steroid biochemistry at the University of Chicago under the direction of Professor Reuben Gustavson. His graduate work at Illinois dealt with determining which are the essential amino acids for humans, and this research continued during his first academic position in the Department of Physiological Chemistry at the University of Pennsylvania. At the University of Michigan, he rose to be Professor of Biological Chemistry and was appointed Chair from 1970 until 1990, during which time he helped bring the Department to national recognition in several biochemical areas. During his career he spent two sabbaticals with Nobel Laureates, Severo Ochoa (New York University, 1952) and Vladimer Prelog (Eidgenössische Techniche Hochschule, Zürich, 1961-62).

Jud served as secretary of the American Society for Biochemistry and Molecular Biology from 1981-1984, and was president from 1991-1992. He also was on the international advisory committees for two major meetings in the field of Cytochrome P450. Among his many awards, Jud was elected to the National Academy of Sciences in 1983 as well as to the American Academy of Arts and Sciences in 1984, and to the Institute of Medicine in 1987. He received the State of Michigan Scientist of the Year Award in 1988. Jud was especially humbled by his award in 1991 by the Karolinska Institute in Stockholm of the honorary Degree of Doctor of Medicine and by the International Conference on Cytochrome P450 in France in 2001 that was held in honor of his 80th birthday. He was the Henry Russel Lecturer at the University of Michigan in 1991, which is the highest recognition of a scientist at the University of Michigan. He received the American Chemical Society Award in Enzyme Chemistry (Paul Lewis Award) in 1959, the distinguished Faculty Achievement Award from the University of Michigan in 1976, the William C. Rose Award in Biochemistry in 1978, and the Bernard B. Brodie Award in Drug Metabolism from the American Society for Pharmacology and Experimental Therapeutics in 1980. He was editor-in-chief of Biochemical Preparations. He was on the editorial boards of numerous journals and symposia books including Biochemistry, Molecular Pharmacology, Microsomes, Drug Oxidations and Chemical Carcinogenesis, and the Journal of Biological Chemistry.

His scientific career was extensive but he was best known for his outstanding work in the field of cytochrome P450 systems in which he worked for more than three decades. P450s are crucial to drug metabolism, drug synthesis, hormone biosynthesis, and a myriad of other systems. Jud Coon's seminal contributions in mammalian P450 systems have been remarkable and have provided the basis for studies by countless scientists worldwide. In the course of studying the oxidation of fatty acids he and his postdoctoral fellow, Anthony Lu, succeeded in 1968-69 in separating the mammalian P450 system into its components, Cytochrome P450, NADPH cytochrome P450 Reductase, and phospholipid, and then in reconstituting its catalytic activity. This huge breakthrough in membrane biochemistry and in P450 studies paved the way for P450 science that is even still under active investigation. His work extended to finding multiple forms of mammalian P450s and to studying mechanisms, genetic regulation of P450 levels, and development of heterologous expression systems for P450s in bacteria. As a chemist, he was always interested in mechanism; thus, his studies led to a much better understanding of NADPH Cytochrome P450 reductase, and his work on the mechanisms of oxygenation of substrates by cytochrome P450, especially with collaborations with John Groves (Chemistry Department) in 1978, led to the basis of our current view of P450 oxygenation reactions.

Jud Coon's influence in science goes well beyond his own investigations. He trained a great many scientists, many who have become leaders both in P450 studies, drug metabolism, and in other fields. He was very supportive of women in science and a leader in true equality. He did not see gender as a factor in science and he embraced all types of discovery. He and his wife established the Minor J. and Mary Louise Coon Award to be presented annually to the student at the University of Michigan in Biological Chemistry who best exhibits excellence in research, teaching, and service. This is a charity for which he hoped would grow in perpetuity.

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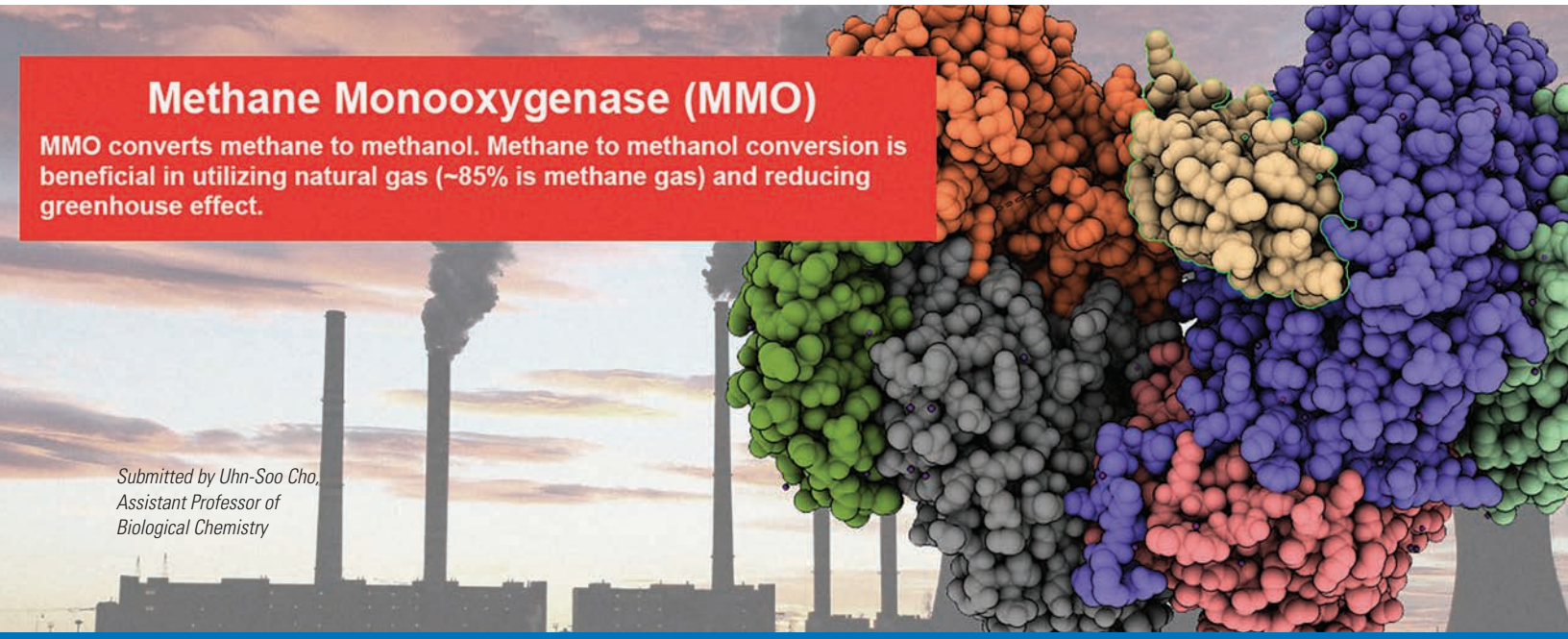

Submitted by Uhn-Soo Cho, Assistant Professor of Biological Chemistry