UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

ELYSIUM HEALTH INC.,
Petitioner,

v.

TRUSTEES OF DARTMOUTH COLLEGE,
Patent Owner.

Case IPR2017-01795

Patent 8,383,086

DECLARATION OF ZHAOHUI SUNNY ZHOU, PH.D.

Table of Contents

I, Dr. Zhaohui Sunny Zhou, hereby declare as follows:

I. Introduction

1. The facts set forth below are known to me personally, and I have firsthand knowledge of them.

2. I make this declaration in support of the Patent Owner's response to the Petition for *inter partes* review ("IPR") of U.S. Patent No. 8,383,086 ("the '086 patent") (Ex. 1001).

3. I have been retained by Steptoe & Johnson LLP on behalf of the Patent Owner, Trustees of Dartmouth College ("Dartmouth").

4. I am being compensated for my professional consulting services in connection with this matter. My compensation is not dependent in any way on the contents of this Declaration, any further opinions or testimony I may provide, or on the outcome of this matter.

II. Qualifications

5. A summary of my qualifications is provided below and a complete identification of my qualifications is provided in my current curriculum vitae, which is attached as Exhibit A.

6. Since 1989, my research has been at the interface of chemistry and biology. After receiving my B.S. degree in Chemistry from Peking University in

Beijing, China in 1990, I worked as a research scientist on the isolation, analysis and formulation of natural products from traditional Chinese medicines at the Academy of Traditional Chinese Medicine and Materia Medica, Changchun, Jilin, China. In 1997, I received a Ph.D. in Bioorganic Chemistry from The Scripps Research Institute, La Jolla, California. I also served as a Research Fellow in the Department of Biological Chemistry and Biophysics Division at the University of Michigan, Ann Arbor, Michigan from 1997-2000.

7. I have been a professor for over 17 years. From 2000 to 2006, I was an Assistant and Associate Professor in the Department of Chemistry, and a Graduate Faculty in the Program in Pharmacology and Toxicology at Washington State University, Pullman, Washington. Currently I am a tenured professor in the Department of Chemistry and Chemical Biology, a Faculty Fellow in the Barnett Institute for Chemical and Biological Analysis, and affiliated member of the Department of Biology, at Northeastern University in Boston, Massachusetts.

8. Because of the nature of my work, almost all of my work in the past 27 years has involved enzymes and the related chemical biology (e.g., aging). In particular, I have studied many natural products and the related biochemistry, including vitamins (e.g., niacin, vitamin B3; folic acid, vitamin B9; and cobalamin, vitamin B12; and ascorbic acid, vitamin C) and naturally existing metabolites (e.g.,

S-adenosyl-methionine, AdoMet, SAM, which is sold as a nutritional supplement under the name SAM-e).

9. I have published more than 45 peer-reviewed articles in the areas of chemistry, biochemistry, and enzymology. As relevant to this case, I have published in the following peer-reviewed journals: Amino Acids, Analytical Chemistry, Analytical Biochemistry, BMC Microbiology, Biochemistry, Experimental Biology and Medicine, Journal of the American Chemical Society, Journal of Biological Chemistry, Journal of Pharmaceutical Science, Natural Product Communications, and others.

10. I have received grants from a number of different sources, including the Department of Defense (DoD), the National Institutes of Health (NIH), the National Science Foundation (NSF), the American Heart Association (AHA), the Autism Research Institute, and the Food and Drug Administration of China (cFDA). I have also received support from industry sources, including Amgen, Colgate Palmolive, and the Novartis Institutes for Biomedical Research.

11. Currently, I serve as an editor or editorial board member for several scientific journals. I have been a reviewer for more than 155 manuscripts in a broad range of peer-reviewed journals and over 100 proposals for the NIH, the NSF and other funding agencies, including Small Business Innovation Research/Small Business Technology Transfer (SBIR/STTR) grants, in the fields

of biochemistry, biological chemistry, enzymology, natural products and drug development. In addition, I am a co-inventor on a number of patent applications.

12. In addition to my academic research, I have also focused my research on drug discovery and development, closely collaborating with the pharmaceutical industry and regulatory agencies. I have also served as an instructor at the Biopharmaceutical Analysis Training Laboratory at Northeastern University, and have taught various workshops on drug development to academic researchers, scientists working in the biopharmaceutical industry, and officers from regulatory agencies including the U.S. Food and Drug Administration (FDA) and foreign countries (e.g., China and Singapore). I also serve on the Advisory Board of the Chinese-American BioMedical Association (CABA). Moreover, I have served as an expert witness in a number of legal proceedings on pharmaceuticals and nutritional supplements (e.g., SAM-e, a natural metabolite and substrate for multiple enzymes).

III. Materials Considered

13. The analysis provided in this Declaration is based on my education as well as my experience in this field. In addition to relying on my knowledge and experience in the relevant field, I have considered the documents described in this Declaration, including the references cited in the Petition and the supporting declaration of Dr. Baur (Ex. 1002).

IV. Level of Ordinary Skill in the Art

14. I understand that my analysis of the ’086 patent and the interpretation of the claims of that patent must be done from the perspective of a person of ordinary skill in the art (“POSITA”) of the ’086 patent.

15. I understand that the hypothetical person of ordinary skill in the art is considered to have the normal skills and knowledge of a person in a certain technical field. I understand that factors that may be considered in determining the level of ordinary skill in the art include: (1) the education level of the inventor; (2) the types of problems encountered in the art; (3) the prior art solutions to those problems; (4) rapidity with which innovations are made; (5) the sophistication of the technology; and (6) the education level of active workers in the field. I also understand that “the person of ordinary skill” is a hypothetical person who is presumed to be aware of the universe of available prior art.

16. I also understand the level of ordinary skill in the art can be evidenced by the prior art. Accordingly, I have also considered the prior art discussed herein in determining the level of ordinary skill in the art.

17. In my opinion, a POSITA with respect to the ’086 would be someone with a Ph.D. in biochemistry or similar field in the pharmaceutical sciences, with familiarity and experience with pharmacokinetics.

18. I have reviewed Dr. Baur's proposed level of ordinary skill, which does not include any particular experience in the pharmaceutical sciences or pharmacokinetics. However, for purposes of my review, Dr. Baur's proposed level of ordinary skill in the art is not materially different from my proposal above and I possess the qualifications of both proposals. Accordingly, my opinions and conclusions presented herein would not differ if the Board adopted my proposal for a POSITA or that of Dr. Baur's.

V. Patent Law Standards

19. I understand that the Petitioner has the burden to prove a proposition of unpatentability by a preponderance of the evidence. I further understand that Petitioner has only asserted unpatentability on anticipation grounds.

20. I understand that a patent claim is only anticipated if the Petitioner establishes that a single prior art reference discloses every element in the claim, either expressly or inherently. I further understand that the prior art must disclose the patented subject matter with sufficient detail such that its existence in the prior art reference would be understood by a POSITA. I also understand that a prior art reference inherently anticipates a claim only when that reference necessarily includes any limitation that is not expressly disclosed.

21. I also understand when a prior art reference is silent about a particular element, such missing information may be filled in with extrinsic evidence. I

further understand, however, that this extrinsic evidence must make clear that the missing descriptive matter is necessarily present, and that it would be so recognized by a POSITA.

22. I understand that the first step in an anticipation analysis is to construe the claim and that the second step is to compare the properly construed claim to the prior art reference. I understand that in an IPR, claim terms are construed according to their broadest reasonable construction in light of the specification of the patent. I am informed that the broadest reasonable interpretation dictates that claim terms are given their ordinary and customary meaning, as would be understood by a POSITA in the context of the entire disclosure or specification of the patent, unless the inventor, as a lexicographer, has set forth a special meaning for a term. I understand that a patent's "specification" includes all the figures, discussion, and claims within the patent document.

VI. The '086 Patent

23. I have reviewed the '086 patent (Ex. 1001) and understand the patent to be directed to pharmaceutical formulations that can be used to treat conditions that are connected to NAD+ biosynthesis. The '086 patent emphasizes nicotinamide riboside ("NR") and its use as an active agent in the claimed pharmaceutical compositions.

24. The ’086 patent describes methods of treating diseases or conditions with “an effective amount of a nicotinamide riboside composition so that the signs or symptoms of the disease or condition are prevented or reduced.” Ex. 1001, at 4:22-24. The patent further identifies the diseases or conditions that can be prevented or treated with an NR pharmaceutical composition, including those that benefit from increased lipid profiles (Ex. 1001, at 8:57-59), stroke (8:61-62), Alzheimer’s Disease, Parkinson’s Disease and multiple sclerosis (27:32-36), neurotoxicity before, during or after cytotoxic chemotherapy (27:45-47), fungal infections (27:57-59), and aging (28:12).

25. The ’086 patent further provides a definition for the “effective amount of nicotinamide riboside,” which can be adjusted based on clinical evaluation “before and after treatment with the nicotinamide riboside.” Ex. 1001, at 28:36-43.

26. The specification also explains that other NAD+ precursors can be added to the NR compositions of the invention, and that these additional precursors may be necessary for optimizing NAD+ metabolism for certain conditions. Ex. 1001, at 28:44-48. This is consistent with claim 4 of the ’086 patent, which identifies the same additional pharmaceutically acceptable components that may be optionally added to the pharmaceutical composition, namely “tryptophan, nicotinic acid, or nicotinamide.” *Id.* at claim 4.

27. The ’086 patent also explains that the NR compositions of the invention can be used to treat the identified conditions because the NR increases NAD+ levels. Ex. 1001, at 28:3-15. This particular disclosure is further reflected in claim 5, which claims the pharmaceutical composition of claim 1 which “increase[s] NAD+ biosynthesis upon oral administration.” *Id.* at claim 5.

28. Based on these disclosures, and the ’086 patent specification as a whole, NR plays a critical role in the claimed pharmaceutical compositions and is not simply a filler or inactive excipient.

VII. Claim Construction

29. In the context of the ’086 patent, the phrase “pharmaceutical composition comprising nicotinamide riboside” should be construed to mean “a composition containing nicotinamide riboside as the active agent.” This definition is appropriate because the descriptions of the claimed NR compositions in the ’086 patent are consistent with how a person of ordinary skill in the art understands pharmaceutical compositions generally.

30. A POSITA understands that a pharmaceutical composition relates to medicinal drugs. For example, the McGraw-Hill Dictionary of Scientific and Technical Terms defines “pharmaceutical” as “[a] chemical produced industrially (medicinal drug), which is useful in preventive or therapeutic treatment of a physical, mental, or behavioral condition.” Ex. 2004, at 1571. Similarly, The New

Oxford American Dictionary defines "pharmaceutical" as "a compound manufactured for use as a medicinal drug." Ex. 2005, at 1275.

31. A pharmaceutical composition, at its most basic level, contains an active ingredient. This concept is so fundamental to the pharmaceutical sciences that it is repeatedly reflected in the Remington compendium for pharmacy (Ex. 2006), which is identified expressly in the '086 patent specification. Ex. 1001, at 28:56-60. For example, in the chapter discussing Preformulation, Remington reflects the understanding that "choosing the molecular form that will be the active pharmaceutical ingredient (API) is a critical milestone because all subsequent development will be affected by this decision." Ex. 2006, at 700-701. As a further example of this concept, Chapter 45 of Remington discusses Oral Solid Dosage Forms, and acknowledges that the "[l]arge-scale production methods used for their preparation…require the presence of other materials in addition to the active ingredients" (Ex. 2006, at 858), and that "[i]n addition to the active or therapeutic ingredient, tablets contain a number of inert materials" (Ex. 2006, at 860). These statements, and the countless others within Remington, reflect this basic understanding that a pharmaceutical, including the pharmaceutical compositions of the '086 patent, must contain an active ingredient.

32. In medicinal drugs, the active component may be, and often is, mixed with one or more carriers and/or excipients to form the pharmaceutical

composition itself. For example, as identified above, Remington describes this concept in the context of Oral Solid Dosage Forms. Ex. 2006, at 860 ("[i]n addition to the active or therapeutic ingredient, tablets contain a number of inert materials"). I understand that in the context of the '086 patent, the Board construed pharmaceutically acceptable carriers and carriers to mean (Paper 9, at 6-7):

> A liquid or solid filler, diluent, excipient, or solvent encapsulating material, [that] is involved in carrying or transporting the subject compound from one organ, or portion of the body, to another organ, or portion of the body. Each carrier must be acceptable in the sense of being compatible with the other ingredients of the formulation and not injurious to the patient.

33. This definition, and the remainder of the specification's disclosure regarding carriers, is consistent with the role of carriers in medicinal drugs. In particular, I understand "the subject compound" to refer to the active agent of the composition, which in the claims of the '086 patent, is NR. Accordingly, I further understand the "pharmaceutical composition comprising nicotinamide riboside" claimed in the '086 patent to mean "a composition containing nicotinamide riboside as the active agent."

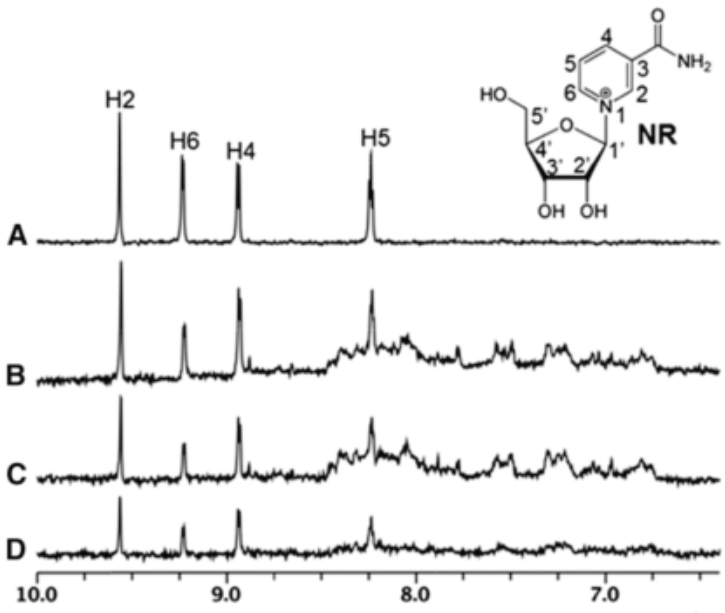
VIII. Petitioner's Asserted Prior Art References Do Not Anticipate the '086 Patent

34. Claim 1 requires a "pharmaceutical composition comprising nicotinamide riboside," and pursuant to the proper construction of that phrase therefore requires "a composition containing nicotinamide riboside as the active agent." Neither Goldberger et al. (Ex. 1005) nor Goldberger and Tanner (Ex. 1006) disclose such a composition. The other references Petitioner cites to support the conclusion that NR is present in milk and buttermilk do not establish that NR is an active agent in either Goldberger et al. or Goldberger and Tanner.[1]

35. Even if one were to assume that the milk and buttermilk may contain NR, Petitioner does not provide any evidence of whether it is present in a state sufficient to act as an active agent. The references cited by Petitioner and Dr. Baur fail to provide any evidence regarding the extent to which NR binds to other molecules in milk in a manner that would impact its bioavailability or activity. Specifically, Trammell I states that NR might be complexed to a protective factor in milk. Ex. 1007 at 5. As a result, to the extent NR is not freely available in milk, NR may not act as an active agent under those conditions. Petitioner does not

[1] Petitioner's second proposed anticipation reference, Goldberger and Tanner, differs from the Goldberger et al. reference only in that it discloses buttermilk instead of milk. For purposes of analyzing whether Goldberger and Tanner anticipates the claims of the '086 patent, there is no material difference between these two references. Accordingly, the analyses and conclusions presented in this Declaration apply to both the milk of Goldberger et al. and the buttermilk of Goldberger and Tanner.

establish otherwise. As demonstrated in the nuclear magnetic resonance (NMR) spectra of Trammell I, reproduced below, NR binds to other molecules within milk and the binding varies in different types and fractions of milk. In the absence of additional data, which both Petitioner and Dr. Baur fail to provide, there is no evidence to establish that any NR in Goldberger et al. or Goldberger and Tanner was available as an active agent.



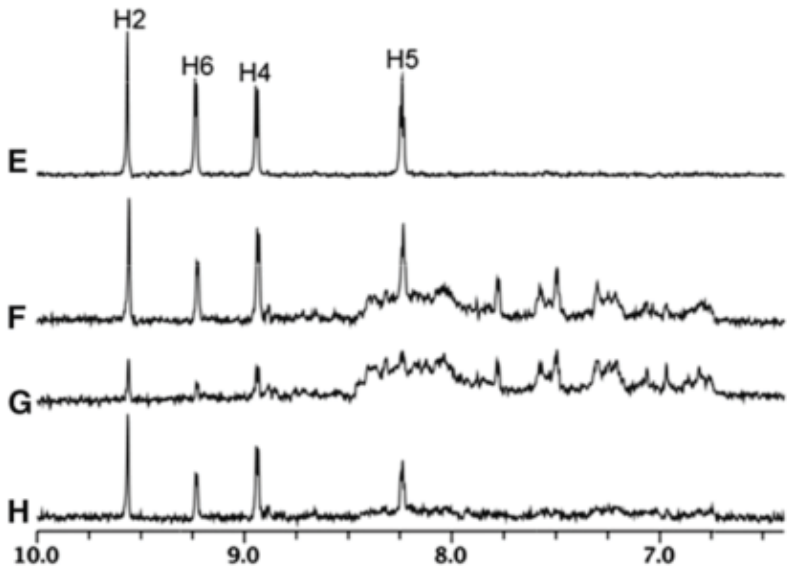


FIG. 2 of Trammell I, Ex. 1007

36. Because NR binds to other molecules in milk, any data regarding its activity as an unbound compound cannot be used to draw conclusions about its hypothetical activity as a bound compound within milk. But, all of the data reported in the other references relied on by Baur reflect NR in its unbound form. For example, in the experiments Trammell II conducted, the NR was chemically synthesized to form "NR Cl" (a chloride salt of NR). Ex. 1008 at 12. In Tummala, the mice were on "NR diet" to restore NAD+ to control levels. Ex. 1017 at 832-33. Similarly, in Gong, the mice were fed only NR that was chemically synthesized. Ex. 1019 at 1582. And in Cantó, the NR was custom synthesized. Ex. 1018 at 845. Accordingly, there is no data regarding NR in bound form in the milk of Goldberget et al. or the buttermilk of Goldberger and Tanner.

37. Petitioner also does not account for the fact that any NR contained in the milk of Goldberger et al. or in the buttermilk of Goldberger and Tanner may have been degraded. NR is not stable in milk because it is readily absorbed and further metabolized by bacteria that naturally exist in milk and/or as common contaminants. Indeed, the reference relied on by the Petitioner states that "Milk from samples testing positive for *Staphylococcus aureus* contained lower concentrations of nicotinamide riboside" and "NR was degraded by *S. aureus*." Ex. 1007 at 1. In addition to *S. aureus*, which is a common contaminant of cow milk, other naturally existing bacteria and fungi may similarly degrade NR in milk. Ex. 1007 at 1; Ex. 2007 (Raats, et al., *Molecular analysis of bacterial communities in raw cow milk and the impact of refrigeration on its structure and dynamics*, Food Microbiology, Vol. 28, pp. 465-71 (2011)); Ex. 2008 (Rasolofo, et al., *Molecular analysis of bacterial population structure and dynamics during cold storage of untreated and treated milk*, Int'l J. Food Microbiology, Vol. 138, pp. 108-18 (2010)); Ex. 2009 (Kurnasov, et al., *Ribosylnicotinamide Kinase Domain of NadR Protein: Identification and Implications in NAD Biosynthesis*, J. Bacteriology, Vol. 184, No. 24, pp. 6906-17 (Dec. 2002)); Ex. 2010 (Johnson, et al., *Characterization of NAD salvage pathways and their role in virulence in Streptococcus pneumoniae*, Microbiology, Vol. 161, pp. 2127-36 (2015)). Petitioner has not established that the milk or buttermilk of the references do not contain this or any other bacteria

that would have degraded NR, if present. Moreover, the milk processing procedures used at the time of Goldberger et al. and Goldberger and Tanner (the 1920s) was more likely to lead to biodegradation of NR by bacteria and other microbes because modern refrigeration and pasteurization commonly used to reduce bacteria and microflora were not widely available. *See* Ex. 2011 (Holsinger, et al., Rev. Sci. Tech. Off Int. Epiz (1997)).

38. I also disagree with Dr. Baur's conclusion that NR "is present at a substantial level in milk" because it is not supported by any evidence. Ex. 1002 ¶ 11. First of all, Dr. Baur relies on Trammell I (Ex. 1007) as evidence for what was contained in the milk of Goldberger et al. and the buttermilk of Goldberger and Tanner, which is a leap that cannot be made. In fact, the amount of NR varies significantly among the sources of milk reported in Trammell I. As stated in Trammell I, "milk from *Staphylococcus aureus*–positive samples contained lower concentrations of NR and nicotinamide, and that milk sold as organic milk contained lower concentrations of NR than conventionally sourced milk." Ex. 1007 at 2. As shown in Table 3 of Trammell I, reproduced below, significant variation in NR concentrations also exists among conventional (1.7 to 5.4 μmol/L) and organic (0.84 to 3.1 μmol/L) cow milk.

TABLE 3 NAD^+ precursor concentrations in commercial cow milk[1]

	Organic					Conventional				
	Brand A	Brand B	Brand C	Brand D	All	Brand A	Brand B	Brand C	Brand D	All
Nicotinamide, μmol/L	2.4	7.1	5.0	7.9	5.6 ± 2.5	5.6	0.67	8.9	5.4	5.2 ± 3.4
NR, μmol/L	3.1	0.84	2.2	1.4	1.9 ± 1.0	2.5	1.7	5.4	2.7	3.1 ± 1.6

[1] Values are expressed as means ± SDs, $n = 4$. NR, nicotinamide riboside.

Table 3 of Trammell

39. None of Petitioner's references establish that milk or buttermilk was formulated with NR "in admixture with a carrier" as required by claim 1. Based on the disclosure of the '086 patent, and the reference to the Remington compendium for pharmacy (Ex. 2006), a pharmaceutical composition should be prepared by purposefully mixing the carrier with the active agent (i.e., NR). Ex. 1001, at 28: 49-60. In fact, there is nothing in any of Petitioner's references that explain how the milk of Goldberger et al. or the buttermilk of Goldberger and Tanner was made.

40. Claim 5 of the '086 patent requires the pharmaceutical composition of claim 1 "which increases NAD+ biosynthesis upon oral administration." Ex. 1001, at claim 5. Petitioner has not presented any evidence that Goldberger et al. or Goldberger and Tanner discloses a pharmaceutical composition that increases NAD+ biosynthesis.

41. None of the references that Petitioner and Dr. Baur rely on regarding the ability of NR to increase NAD+ levels, as required by claim 5, actually establish its ability to do so in milk or buttermilk. As explained above, these other

prior art references fail to provide any evidence regarding the extent to which NR binds to other molecules in a manner that would impact its ability to increase NAD+ levels. *See* ¶¶ 35-36; Ex. 1007. In the absence of additional data, which both Petitioner and Dr. Baur fail to provide, there is no evidence to establish that any NR in Goldberger et al. or Goldberger and Tanner was capable of increasing NAD+ biosynthesis.

42. Because NR binds to other molecules in milk (as described above), any data regarding its activity as an unbound compound is not reflective of its ability to increase NAD+ biosynthesis in its bound form within milk or buttermilk. As described above, all of the data cited by Petitioner and Dr. Baur reflect NR in its unbound form. *See* ¶ 36; Ex. 1008 at 12; Ex. 1017 at 832-33; Ex. 1018 at 845; Ex. 1019 at 1582. There is simply no data available to establish that NR in milk, whether freely available or not, increases NAD+ biosynthesis. Accordingly, there is no evidence regarding NR's ability to increase NAD+ levels as one of many ingredients in the milk fed to dogs in Goldberger et al. or the buttermilk used in Goldberger and Tanner.

43. Not only is there no evidence in Goldberger et al. or Goldberger and Tanner that NAD+ biosynthesis increased, there is no way to determine what, if anything, is responsible for that result based on the evidence reported. One of the reasons for this lack of evidence is that the other NAD+ precursors, including

nicotinamide and tryptophan, which are also found in milk, are principle components of NAD+ biosynthesis. *See* Ex. 2006 (Remington), at 1799, 1808-09. In fact, the roles of nicotinamide and tryptophan in milk for NAD+ biosysthesis were well established and widely recognized (Ex. 1011, at 4), and the evidence suggests that one of those components would be sufficient to lead to any increase in NAD+ biosynthesis that may have occurred in Goldberger et al. or Goldberger and Tanner. Ex. 2006 (Remington), at 1799, 1808-09. Petitioner and Dr. Baur do not account for this.

44. Accordingly, there is no evidence that NR acted as an active agent in the milk of Goldberger et al. or the buttermilk of Goldberger and Tanner to increase NAD+ biosynthesis.

IX. Conclusion

45. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date: 4 June 2018

Dr. Zhaohui Sunny Zhou

EXHIBIT A

Curriculum Vitae

Zhaohui Sunny Zhou

424 Hurtig Hall
Northeastern University
360 Huntington Avenue
Boston, MA 02115-5000

Phone: 617-373-4818
E-mail: z.zhou@northeastern.edu
Web: www.northeastern.edu/sunnyland
www.linkedin.com/in/sunnyzhou

Research Interests

protein chemistry	bioanalytical chemistry	enzymology
protein engineering	protein pharmaceuticals	chemical biology

My laboratory, aka SunnyLand, applies chemistry to biology and medicine. One program is "Hybrid Modality Engineering" of proteins—a process to introduce non-canonical chemical moieties and/or scaffolds into peptides and proteins to confer novel functions otherwise unavailable. The second is to devise chemo-enzymatic methodologies to characterize protein modifications, such as crosslinking, isoaspartic acid formation (asparagine deamidation) and S-adenosyl-methionine (AdoMet or SAM)-dependent methylations. In collaboration with biologists and clinicians alike, we also investigate their biological effects, and moreover, as critical attributes in protein pharmaceuticals. A third program area is the mechanistic studies of and inhibitor design for enzymes with intriguing mechanisms and biomedical significance.

Education

1997-2000	Research Fellow, University of Michigan, Ann Arbor, Michigan. Advisor: Professor Rowena G. Matthews
1991- 1997	Ph.D. in Bioorganic Chemistry. The Scripps Research Institute, California. Advisor: Professor Donald Hilvert (currently at the Federal Institute of Technology (ETH) Zurich, Hönggerberg, Switzerland)
1986 - 1990	B.S. in Organic Chemistry. Peking University, Beijing, China. Advisor: Professor Qing-Zhong Zhou.

Positions and Research Experiences

2007-present	Professor (since 2016) and Associate Professor, Department of Chemistry and Chemical Biology; Faculty Fellow, Barnett Institute of Chemical and Biological Analysis; Affiliated Faculty, Bioengineering and Biology; Northeastern University, Boston, Massachusetts.
2000 – 2006	Associate Professor with tenure (2006) and Assistant Professor, Department of Chemistry; Associate Member, School of Molecular Biosciences; Graduate Faculty, Program in Pharmacology and Toxicology; Faculty, NIH Biotechnology Training Program on Protein Chemistry; Washington State University, Pullman, Washington.

1997 - 2000 Biochemical and biophysical studies of zinc enzymes. Research Fellow in the laboratory of Professor Rowena G. Matthews in the Biophysics Research Division and the Department of Biological Chemistry, University of Michigan, Ann Arbor, Michigan.

1991 - 1997 Catalytic antibodies for pericyclic reactions, cofactor-dependent oxidations and reductions. Doctoral student with Professor Donald Hilvert in the Departments of Chemistry and Molecular Biology, The Skaggs Institute of Chemical Biology, The Scripps Research Institute, La Jolla, California.

1990 - 1991 Natural product isolation, analysis and derivatization. Research Associate with Dr. Qi-Pin Gao in Department of Medicinal Chemistry, Academy of Traditional Chinese Medicine & Materia Medica, Changchun, Jilin, China.

1989 - 1990 Polymer chemistry and phase transfer catalysis. Undergraduate student in the laboratory of Professor Qing-Zhong Zhou in the Department of Chemistry, Peking University, Beijing, China.

Honors and Awards

Barnett Fund for Innovative Research, Barnett Institute, Northeastern University, 2008.
Young Faculty Performance Award, College of Sciences, Washington State Univ, 2005.
Young Investigator Development Award, Academy of Traditional Chinese Medicine and Materia Medica, Changchun, Jilin, China, 1990 (declined due to study in USA).

Professional Activities

Editorial Board, Antibody Therapeutics, by Chinese Antibody Society, 2018-present
Assistant Editor, mAbs, Taylor & Francis, 2017-present
Editorial Board, Molecules, MDPI (Multidisciplinary Digital Publishing Inst), 2016-present

Advisory Board, Chinese-American BioMedical Association (CABA), 2015-present
Advisory Board, Wuhan Institute for Drug and Medical Device Control (FDA), China, 2016-present
Director, regulatory analysis training programs for Chinese FDA scientists, 2013-present
Instructor, Biopharmaceutical Analysis Training Laboratory (BATL), NU, 2016-present

Co-founder and Chief Scientific Officer (CSO), Amethyst Isotopes, 2011 to 2014

Consultant, Nuvelo, San Carlos, California, 2005-2006
Consultant, AbbVie (formerly Abbott), Worcester, Massachusetts, 2009-17
Consultant, Cubist Pharmaceuticals, Lexington, Massachusetts, 2010-11
Consultant, Syros, Cambridge, Massachusetts, 2015-present
Consultant, Takeda, Cambridge, Massachusetts, 2016
Consultant, Genentech/Roche, 2017-present

Expert witness, SAM-e (S-adenosyl-methionine) supplement legal case, 2003-4
Expert witness, monoclonal antibody drug, High Court of Justice, London, UK, 2013-4
Expert witness, protein pharmaceuticals (enzyme replacement therapy), 2016-7
Expert witness, protein chemistry, United States Patent and Trademark Office, 2017

Guest Lecture, Honors Chemistry, Wellesley High School, 19 October 2015
Science Demonstration and Math, Wellesley Middle School, 2012
Science Demonstrations and Science Fair Judge, Washington State Univ Children's Center, Franklin Elementary School, and Montessori School, Pullman, Washington, 2002-6
Chapter review for Organic Chemistry (textbook), 4th and 6th edition, Paula Bruice

Pre-Health Advisory Committee, Northeastern University, 2007-present
Request for Proposal (RFP) Committee, Dept Chemistry & Chemical Biology, 2007-13
Patent Review Committee, Northeastern University, 2009
Graduate Admission Committee, Dept of Chemistry, 2009-13, 2015-6; Chair; 2011-3
College of Science Graduate Curriculum Committee, 2011-3
Council, College of Science, Northeastern University, 2013-6; Chair, 2014-6
Biochemistry Committee, Northeastern University, 2014-5
Tenure and Promotion Committee, College of Sciences, Northeastern, 2016-present
Search Committee, Analytical Chemistry Faculty, 2016-7
Coordinator, Industry PhD Program, College of Science, 2016-present
Review Committee, Goldwater Scholarship, Northeastern, 2017

Professional Societies

American Association for Advancement of Science (AAAS)
American Chemical Society (ACS)
American Society for Mass Spectrometry (ASMS)
Chinese-American Chemistry Professors Association (CACPA), Board Member and Member of the Award Committee, 2007 to present
Advisory Board, Chinese-American BioMedical Association (CABA), 2015 to present
Wellesley Chinese American Network (WeCAN), co-founder, board member, 2016-present

Grant Proposal Review

2003: American Chemical Society (ACS), Petroleum Research Fund (PRF)
2004: National Inst Health (NIH), Panel Reviewer, Bioorganic & Natural Products (BNP);
National Science Foundation (NSF)
2005: American Chemical Society (ACS), Petroleum Research Fund (PRF)
2007: Herman Frasch Foundation (administrated by ACS), Panel Reviewer;
NIH, Panel Reviewer, Drug Discovery and Development SBIR/STTR (BCMB 11),
NSF, Panel Reviewers, Chemistry Research Instrumentation and Facilities:
Multi-User Instrumentation (CRIF:MU) mass spectrometry and chromatography
2008: Michael Smith Foundation for Health Research, British Columbia, Canada;
NIH COBRE Center in Protein Structure and Function at the University of Kansas;
National Science Foundation (NSF), Division of Chemistry
2009: NIH, Panel Reviewer, Drug Discovery and Development SBIR/STTR (BCMB 11)
2010: North Carolina Biotechnology Center.
2011: Research Corporation; NIH, Panel Reviewer, Partnership for Biodefense;
NIH Panel, Chemical Approaches to Target Validation for Drug Resistant Pathogens
2012: NIH, Panel, ZRG1 MDCN-J (50) R: Counter Act U01;
NSF, Chemistry, Mail-in Reviewer
2013: National Science Centre (Narodowe Centrum Nauki), Poland;
Research Corporation
2014: NIH, Neurobiology of Learning and Memory (LAM);
Fellowships: Synthetic and Biological Chemistry F04A-W(20)L
2015: NIH, Synthetic and Biological Chemistry A Study Section [SBCA];
NIH, synapses, Cytoskeleton and Trafficking (SYN)
2016: NSF, Chemistry of Life Processes, Mail-in Reviewer;
Wellcome Trust, Mail-in Reviewer
French National Research Agency (ANR), Mail-in Reviewer
National Science Centre (Narodowe Centrum Nauki – NCN), Poland
2017: NIH, Synthetic and Biological Chemistry A Study Section [SBCA], ZRG1 BCMB-H

Manuscript Review (155)

AAPS PharmSciTech
ACS Chemical Biology
ACS Chemical Neuroscience
ACS Sustainable Chemistry & Engineering
Advanced Synthesis & Catalysis
Analytical Biochemistry
Analytical Chemistry
Applied Microbiology
Archives of Pharmacal Research
Atherosclerosis
Autoimmunity
Biochemistry
Biochimica et Biophysica Acta
Bioconjugate Chemistry
Biomacromolecules
Biomaterials
Bioorganic and Medicinal Chemistry
Bioorganic & Medicinal Chemistry Letters
Canadian Journal of Microbiology
Carbohydrate Research
Chemical Communication
Chemistry-A European Journal
Chemistry & Biology
Computational and Structural Biotechnology Journal
Current Radiopharmaceuticals
Electrophoresis
Epigenetics & Chromatin
European Journal of Medicinal Chemistry
Herald of Medicine 《医药导报》
HVAC&R Research (Am Society of Heating, Refrigerating and Air-Conditioning Engineers)
Investigative Ophthalmology & Visual Science (IOVS)
Journal of the American Chemical Society
Journal of The American Society for Mass Spectrometry
Journal of Applied Microbiology
Journal of Biomolecular Structure & Dynamics
Journal of Chromatography B
Journal of Medicinal Chemistry
Journal of Molecular Microbiology and Biotechnology
Journal of Organic Chemistry
Journal of Sulfur Chemistry
Journal of Visualized Experiments (JoVE)
Langmuir
mAbs
Mass Spectrometry Reviews
MedChemComm
Medicinal Research Reviews
Metallomics
Mini-Reviews in Medicinal Chemistry
Molecular Biology Reports
Molecular BioSystems
Molecular Microbiology
Molecular Pharmaceutics
Nature Communications
Organic and Biomolecular Chemistry
Organic Letters
Peptides
Plant Cell
PLoS ONE
Rapid Communications in Mass Spectrometry
RCS Advances
Scientific Reports (Nature)
Phosphorus, Sulfur, and Silicon and the Related Elements
Trends in Analytical Chemistry
Tuberculosis

Patent Applications and Licensing

Assays for S-Adenosyl-methionine-Dependent Methyltransferases. Zhaohui Sunny Zhou and Kathleen Dorgan, PCT/US2007/060930, Filing Date: January 23, 2006.
The assays have been licensed to and commercialized by G-Biosciences/Geno Technology, St. Louis, Missouri and Cayman Chemical, Ann Arbor, Michigan.
www.gbiosciences.com/SAM-Methyltransferase.aspx
www.caymanchem.com/product/700150

Methods for Detecting L-Isoaspartyl or D-Aspartyl Residue in Polypeptides. Zhaohui Sunny Zhou, Min Liu, Da Ren. PTC/US/2012/036772 (7 May 2012). Provisional filed 6 May 2012.

Compositions, Methods and Kits for the Detection, Identification and Isolation of Methyltransferase Substrates. Zhaohui Sunny Zhou, Wanlu Qu, Tianyi Bai. Application 61/619,113 (WO2013151975 (A1), April 2, 2013. Converted in 2014.

Se-Adenosyl-L-selenohomocysteine selenoxide as a modulator of methyltransferase and other enzyme activities. Zhaohui Sunny Zhou, Richard I. Duclos, Jr., Dillion C. Cleary, Kalli C. Catcott. US Provisional Patent Application No. 62/057,956. Filed Sept 30, 2014. Converted in September 2015. Application Number: 14/871099

Chemo-Enzymatic Derivatization of Peptides. Zhaohui Sunny Zhou, Kevin Moulton, ShanShan Liu. U.S. Application No. 62/325,043. Filed 20 April 2016.

Site-Specific Derivatization of Peptides and Protein. Zhaohui Sunny Zhou, ShanShan Liu. U.S. Application No. 62/379,440. Filed 25 August 2016.

Derivatives of Exenatide via Site-Specific Bioconjugation. Zhaohui Sunny Zhou, ShanShan Liu. U.S. Application No. 62468509. Filed 8 March 2017.

Chemo-Enzymatic Site-Specific Modification of Proteins and Peptides to Form Photo-Cleavable Conjugates. Zhaohui Sunny Zhou, Kevin Moulton, ShanShan Liu. U.S. Application No. 62/508,999. Filed 19 May 2017

Publications

Google Scholar: scholar.google.com/citations?user=DkpPDoYAAAAJ&hl=en

Publications as Principal Investigator

Detection of Alkynes via Click Chemistry with A Brominated Coumarin Azide by Simultaneous Fluorescence and Isotopic Signatures in Mass Spectrometry. Lihua Yang, Chris Chumsae, Jenifer B. Kaplan, Kevin Ryan Moulton, Dongdong Wang, David H. Lee, Zhaohui Sunny Zhou. *Bioconjugate Chemistry*, 2017, 28, 2302-9. PubMed 28825803 doi: 10.1021/acs.bioconjchem.7b00354

Identifying Unknown Enzyme-Substrate Pairs from the Cellular Milieu with Native Mass Spectrometry. Kalli C. Catcott, Jing Yan, Wanlu Qu,Vicki H. Wysocki, Zhaohui Sunny Zhou. *ChemBiochem*, 2017, 18, 613. PubMed 28140508 doi: 10.1002/cbic.201600634

* Cover story for issue 7, Catch me if you can
* Designated as Very Important Paper (VIP)

Comparison of Protein N-Homocysteinylation in Rat Plasma under Elevated Homocysteine Using A Specific Chemical Labeling Method. Tianzhu Zang, Ligi Paul Pottenplackel, Diane E. Handy, Joseph Loscalzo, Shujia Dai, Richard Deth, Zhaohui Sunny Zhou, Jisheng Ma. *Molecules*, 2016, 21, 1195. PubMed 27617989 doi:10.3390/molecules21091195

Capturing Unknown Substrates via in Situ Formation of Tightly Bound Bisubstrate Adducts: S-Adenosyl-vinthionine as a Functional Probe for AdoMet-Dependent Methyltransferases. Wanlu Qu, Kalli C. Catcott, Kun Zhang, Shanshan Liu, Jason J. Guo, Jisheng Ma, Michael Pablo, James Glick, Yuan Xiu, Nathaniel Kenton, Xiaoyu Ma, Richard I. Duclos, Jr, and Zhaohui Sunny Zhou. *Journal of the American Chemical Society,* 2016, 138, 2877-80. PubMed 26901520 doi:10.1021/jacs.5b05950

Mildly Acidic Conditions Eliminate Deamidation Artifact during Proteolysis: Digestion with Endoprotease Glu-C at pH 4.5. Shanshan Liu, Kevin Ryan Moulton, Jared Robert Auclair, Zhaohui Sunny Zhou. *Amino Acids,* 2016, 48, 1059-67. PubMed 26748652 doi:10.1007/s00726-015-2166-z

When Good Intentions Go Awry: Modification of a Recombinant Monoclonal Antibody in Chemically Defined Cell Culture by Xylosone, an Oxidative Product of Ascorbic Acid. Chris Chumsae, Patrick Hossler, Haly Raharimampionona, Yu Zhou, Sean McDermott, Chris Racicot, Czeslaw Radziejewski, Zhaohui Sunny Zhou. *Analytical Chemistry*, 2015, 87, 7529-7534. PubMed 26151084 doi: 10.1021/acs.analchem.5b00801

Synthesis and Characterization of Se-Adenosyl-L-Selenohomocysteine Selenoxide. Richard I. Duclos, Jr., Dillon C. Cleary, Kalli C. Catcott, and Zhaohui Sunny Zhou. *Journal of Sulfur Chemistry*, 2015, 36, 135-44. PubMed 26005494 doi:10.1080/17415993.2014.979173

Discovery of a Chemical Modification by Citric Acid in a Recombinant Monoclonal Antibody. Chris Chumsae, Liqiang Lisa Zhou, Yang Shen, Jessica Wohlgemuth, Emma Fung, Randall Burton, Czeslaw Radziejewski, Zhaohui Sunny Zhou. *Analytical Chemistry*, 2014, 86, 8932–8936. PubMed 24738698 doi: 10.1021/ac502179m

Detection and Quantitation of Succinimide in Intact Protein via Hydrazine Trapping and Chemical Derivatization. Joshua J. Klaene, Wenqin Ni, Joshua F. Alfaro, Zhaohui Sunny Zhou. *Journal of Pharmaceutical Science,* 2014, 103, 3033–3042. PubMed 25043726 doi: 10.1002/jps.24074

Discovery and Characterization of a Novel Photo-Oxidative Histidine-Histidine Crosslink in IgG1 Antibody Utilizing 18O-labeling and Mass Spectrometry. Min Liu, Zhongqi Zhang, Janet Cheetham, Da Ren, Zhaohui Sunny Zhou. *Analytical Chemistry*, 2014, 86, 4940-8. PubMed 24738698 doi: 10.1021/ac500334k

* Highlighted *Staying Current: Formulation of Biopharmaceuticals, 2014, August*

Decreased glutathione and elevated hair mercury levels are associated with nutritional deficiency-based autism in Oman. Nathaniel W. Hodgson, Mostafa I. Waly, Yahya M. Al-Farsi, Marwan M. Al-Sharbati, Omar Al-Farsi, Tianzhu Zang, Zhaohui Sunny Zhou, Richard C. Deth. *Experimental Biology and Medicine,* 2014, 239, 697-706. PubMed 24676906 doi: 10.1177/1535370214527900

Arginine Modifications by Methylglyoxal: Discovery in a Recombinant Monoclonal Antibody and Contribution to Acidic Species. Chris Chumsae, Kathreen Gifford, Wei Lian, Hongcheng Liu, Czeslaw H. Radziejewski, Zhaohui Sunny Zhou. *Analytical Chemistry*, 2013, 85, 11401-9. PubMed 24168114 dx.doi.org/10.1021/ac402384y

Discovery of Undefined Protein Crosslinking Chemistry: a Comprehensive Methodology Utilizing ^{18}O-Labeling and Mass Spectrometry. Min Liu, Zhongqi Zhang, Tianzhu Zang, Chris Spahr, Janet Cheetham, Da Ren, and Zhaohui Sunny Zhou. *Analytical Chemistry*, 2013, 85, 5900-8. PubMed 23634697 dx.doi.org/10.1021/ac400666p

An Integrated Proteomic Analysis of Major Isoaspartyl-Containing Proteins in the Urine of Wild Type and Protein L-Isoaspartate O-Methyltransferase-Deficient Mice. Shujia Dai, Wenqin Ni, Alexander N. Patananan, Steven Gerard Clarke, Barry L. Karger, Zhaohui Sunny Zhou. *Analytical Chemistry*, 2013, 85, 2423–30. PubMed 23327623 dx.doi.org/10.1021/ac303428h

Chapter 287: Peptidyl-Asp Metalloendopeptidase. Handbook of Proteolytic Enzymes, 3rd Ed; 2013, Volume 1, Pages 1281 - 5. Edited by Neil D. Rawlings and Guy Salvesen, Oxford: Academic Press. Shujia Dai, David H. Lee, Nathaniel T. Kenton, Zhaohui Sunny Zhou (invited review, book chapter) dx.doi.org/10.1016/B978-0-12-382219-2.00288-X

Substrate-Induced Control of Product Formation by Protein Arginine Methyltransferase 1 (PRMT1). Shanying Gui, Whitney L. Wooderchak-Donahue, Tianzhu Zang, Dong Chen, Michael P. Daly, Zhaohui Sunny Zhou, Joan M. Hevel. *Biochemistry*, 2013, *52* (1), 199–209. PubMed 23214442 pubs.acs.org/doi/abs/10.1021/bi301283t

Chemical Fingerprinting by RP-RRLC-DAD and Principal Component Analysis of *Ziziphora clinopodioides* from Different Locations. Shuge Tian, Qian Yu, Lude Xin, Zhaohui Sunny Zhou and Halmuart Upur. *Natural Product Communications, 2012, 7 (9), 1181-4.* PubMed 23074902

Protein Isoaspartate Methyltransferase-Mediated 18O-Labeling of Isoaspartic Acid for Mass Spectrometry Analysis. Min Liu, Janet Cheetham, Nina Cauchon, Judy Ostovic, Wenqin Ni, Da Ren, Zhaohui Sunny Zhou. *Analytical Chemistry,* 2012, 84, 1056–1062. PubMed 22132761 pubs.acs.org/doi/abs/10.1021/ac202652z

Zoospore interspecific signaling promotes plant infection by Phytophthora. Ping Kong, Brett M Tyler, Patricia A Richardson, Bobby W. K. Lee, Zhaohui S Zhou and Chuanxue Hong. *BMC Microbiology,* 2010, 10, 313. PubMed 21138563 doi:10.1186/1471-2180-10-31

* Highly accessed article on BioMed Central

Substrates of the *Arabidopsis thaliana* Protein Isoaspartyl Methyltransferase1 identified using phage display and biopanning. Tingsu Chen, Nihar Nayak, Susmita Maitra Majee, Jonathan Lowenson, Kim R. Schafermeyer, Alyssa C. Eliopoulos, Taylor D. Lloyd, Randy Dinkins, Sharyn E. Perry, Nancy R. Forsthoefel, Steven G. Clarke, Daniel M. Vernon, Zhaohui Sunny Zhou, Tomas Rejtar, and Allan Bruce Downie. *J Biol Chem,* 2010, 285, 37281-37292. PubMed 20870712 doi:10.1074/jbc.M110.15700

Analysis of Isoaspartic Acid by Selective Proteolysis with Asp-N and Electron Transfer Dissociation Mass Spectrometry. Wenqin Ni, Shujia Dai, Barry L. Karger and Zhaohui Sunny Zhou. *Anal Chem*, 2010, 82, 7485–7491. PubMed 20712325 pubs.acs.org/doi/abs/10.1021/ac101806e

Structure elucidation of highly polar basic degradants by on-line hydrogen/deuterium exchange hydrophilic interaction chromatography coupled to tandem mass spectrometry. Min Liu, Mike Ronk, Da Ren, Judy Ostovic, Nina Cauchon, Zhaohui Sunny Zhou and Janet Cheetham. *J Chromatogr A,* 2010, 1217, 3598-3611. PubMed 20417519 Publisher Link

Enzyme-Catalyzed Transfer of a Ketone Group from an S-Adenosyl-Methionine Analog: A Tool for the Functional Analysis of Methyltransferases. Bobby W.K. Lee, He G. Sun, Tianzhu Zang, ByungJu Kim, Joshua F. Alfaro, and Zhaohui Sunny Zhou. *J Am Chem Soc*, 2010, 132, 3642-3. PubMed 20196537 pubs.acs.org/doi/abs/10.1021/ja908995p

* Highlighted in *JACS Select* (issue 12; *J Am Chem Soc*, 2011, 133, 13207–13212) collection focused on Chemical Mechanisms in Biochemical Reactions. Professor Peter J. Stang, Editor-in-Chief, commented, "Your Communication was selected because of its high scientific quality and broad appeal." pubs.acs.org/JACSbeta/jvi/issue12.html

* Highlighted in Nachrichten aus der Chemie, 2010, 58 (5), 518; Official journal of the German Chemical Society (Gesellschaft Deutscher Chemiker); Equivalent of Chemical and Engineering News of the American Chemical Society.

Desulfurization of cysteine-containing peptides resulting from sample preparation for protein characterization by mass spectrometry. Zhouxi Wang, Tomas Rejtar, Zhaohui Sunny Zhou and Barry L. Karger. *Rapid Commun Mass Spectrom*, 2010, 24, 267-275. PubMed 20049891 onlinelibrary.wiley.com/doi/10.1002/rcm.4383/abstract

Zoosporic plant pathogensproduce bacterial autoinducer-2 that affects Vibrio harveyi quorum sensing. Ping Kong, Bobby W.K. Lee, Zhaohui Sunny Zhou, and Chuanxue Hong, *FEMS Microbiol Lett* 2010, 303, 55-60. PubMed 20002192 Publisher Link

Chemical Methods for the Detection of Protein N-Homocysteinylation via Selective Reactions with Aldehydes. Tianzhu Zang, Shujia Dai, Dajun Chen, Bobby W. K. Lee, Suli Liu, Barry L. Karger, and Zhaohui Sunny Zhou. *Anal. Chem*. 2009, 81, 9065–9071. PubMed 19874060 Publisher Link

A Naturally Occurring Brominated Furanone Covalently Modifies and Inactivates LuxS. Tianzhu Zang, Bobby W.K. Lee, Lisa M. Cannon, Kathryn A. Ritter, Shujia Dai, Dacheng Ren, Thomas K. Wood, and Zhaohui Sunny Zhou. *Bioorg Med Chem. Lett*. 2009, 21, 6200-6204. PubMed 19775890 Publisher Link

* Highlighted in Nachrichten aus der Chemie, 2015, 63(12), 1163-7. Official journal of the German Chemical Society (Gesellschaft Deutscher Chemiker); Equivalent of Chemical and Engineering News of the American Chemical Society. “Wie Bakterien uns mit Naturstoffen krank machen? (How bacteria make us sick with natural products?)”

Synthetic Strategies Toward Carbocyclic Purine-Pyrimidine Hybrid Nucleosides. Joshua M. Sadler, Sylvester L. Mosley, Kathleen M. Dorgan, Zhaohui Sunny Zhou, and Katherine L. Seley-Radtke. *Bioorg Med Chem*. 2009, 17, 5520-5. PubMed 19592260 Publisher Link

PRMT1 Demonstrates Primary Amino Acid Sequence Selectivity: Discrimination of Substrates and Altered Product Formation. Whitney L. Wooderchak, Tianzhu Zang, Zhaohui Sunny Zhou, Marcela Acuña, Stanley M. Tahara, Joan M. Hevel, *Biochemistry,* 2008, 47, 9456-66. PubMed 18700728 pubs.acs.org/doi/abs/10.1021/bi800984s

Methyltransferases Assays. Whitney L. Wooderchak, Zhaohui Sunny Zhou, Joan M. Hevel, *Curr. Protoc. Toxicol*. 2008, 38:4.26.1-4.26.12. Publisher Link

Chemo-enzymatic Detection of Protein Isoaspartate using Protein Isoaspartate Methyltransferase and Hydrazine Trapping. Joshua F. Alfaro, Laura A. Gillies, He G. Sun, Shujia Dai, Tianzhu Zang, Joshua J. Klaene, Byung Ju Kim, Jonathan D. Lowenson, Steven G. Clarke, Barry L. Karger, and Zhaohui Sunny Zhou, *Anal. Chem*. 2008, 80, 3882-9. PubMed 18419136 pubs.acs.org/doi/abs/10.1021/ac800251q

Colorimetric activity measurement of a recombinant putrescine N-methyltransferase from *Datura stramonium L.* Stefan Biastoff, Michael Teuber, Zhaohui Sunny Zhou, and Birgit Dräger, *Planta Medica* 2006, 72, 1136-41. PubMed 16924584 www.thieme-connect.com/DOI/DOI?10.1055/s-2006-947191

Carbocyclic Pyrimidine Nucleosides as Inhibitors of S-Adenosylhomocysteine Hydrolase. Sylvester L. Mosley, Brian A. Bakke, Joshua M. Sadler, Naresh K. Sunkara, Kathleen M. Dorgan, Zhaohui Sunny Zhou, and Katherine L. Seley-Radtke, *Bioorg. Med. Chem.* 2006, 14, 7967-7971. PubMed 16904326 www.sciencedirect.com/science/article/pii/S0968089606006067

An Enzyme-Coupled Continuous Spectrophotometric Assay For S-Adenosylmethionine-Dependent Methyltransferases. Kathleen M. Dorgan, Whitney L. Wooderchak, DonRaphael P. Wynn, Erin L. Karschner, Joshua F. Alfaro, Yinqiu Cui, Zhaohui Sunny Zhou, and Joan M. Hevel, *Anal. Biochem.* 2006, 350, 249-255. PubMed 16460659 www.sciencedirect.com/science/article/pii/S0003269706000078

Potential Beneficial Metabolic Interactions Between Tamoxifen and Isoflavones via Cytochrome P450-mediated Pathways in Female Rat Liver Microsomes. Jun Chen, Steven C. Halls, Joshua F. Alfaro, Zhaohui Zhou, and Min Hu, *Pharm. Res.* 2004, 21, 2095-2104. PubMed 15587933 link.springer.com/article/10.1023%2FB%3APHAM.0000048202.92930.61

Synthesis of LuxS Inhibitors Targeting Bacterial Cell-Cell Communication. Joshua F. Alfaro, Tiao Zhang, DonRaphael P. Wynn, Erin L. Karschner, and Zhaohui Sunny Zhou, *Org. Lett.* 2004, *6*, 3043-6. PubMed 15330583 pubs.acs.org/doi/abs/10.1021/ol049182i

An Enzyme-Coupled Colorimetric Assay for S-Adenosylmethionine-Dependent Methyltransferases. Cheryl L. Hendricks, Jeannine R. Ross, Eran Pichersky, Joseph P. Noel and Zhaohui Sunny Zhou, *Anal. Biochem.* 2004, *326*, 100-105. PubMed 14769341 www.sciencedirect.com/science/article/pii/S0003269703008236

Rapid Screening for S-Adenosylmethionine-Dependent Methylation Products by Enzyme-Transferred Isotope Patterns Analysis. Wei Wan, Gang Zhao, Khalid Al-Saad, William F. Siems, and Zhaohui Sunny Zhou, *Rapid Comm. Mass Spectrom.* 2004, *18*, 319-324. PubMed 14755618 onlinelibrary.wiley.com/doi/10.1002/rcm.1335/abstract

Chemical Synthesis of S-Ribosyl-L-Homocysteine and Activity Assay as a LuxS Substrate. Gang Zhao, Shahrzad Mansouri, Joshua F. Alfaro, Wei Wan, Bonnie L. Bassler, Kenneth A. Cornell, and Zhaohui Sunny Zhou, *Bioorg. Med. Chem. Lett.* 2003, *13*, 3897-3900. PubMed 14592470 www.sciencedirect.com/science/article/pii/S0960894X03009697

A Stereospecific Colorimetric Assay for (*s,s*)-Adenosylmethionine Quantification Based on Thiopurine Methyltransferase-Catalyzed Thiol Methylation. Lisa M. Cannon, Felice N.

Butler, Wei Wan, and Zhaohui S. Zhou, *Anal. Biochem*. 2002, *308*, 358-363. PubMed 12419350 www.sciencedirect.com/science/article/pii/S0003269702002671

Vinyl Sulfonium as Novel Proteolytic Enzyme Inhibitor. Gang Zhao, and Zhaohui S. Zhou, *Bioorg. Med. Chem. Lett*. 2001, *11*, 2331-2335. PubMed 11527725 www.sciencedirect.com/science/article/pii/S0960894X01004401

Current Developments in Biological Methylations. Zhaohui S. Zhou, Gang Zhao, and Wei Wan, *Front. Biotechnol. Pharm*. 2001, *2*, 256-274. (Invited review)

Publications as postdoc and graduate student

Cobalamin-dependent and Cobalamin-independent Methionine Synthases: Are there Two Solutions to the Same Chemical Problem? Rowena G. Matthews, April E. Smith, **Zhaohui S. Zhou**, Rebecca Taurog, Vahe Bandarian, John C. Evans, and Martha Ludwig. *Helv. Chim. Acta* 2003, 86, 3939-3954. PubMed 8304207 onlinelibrary.wiley.com/doi/10.1002/hlca.200390329/abstract

Probing Ligand and Structural Changes at the Zinc Site Upon Homocysteine Binding in Cobalamin-independent and Cobalamin-dependent Methionine Synthase of Escherichia coli by X-ray Absorption Spectroscopy. Katrina Peariso, **Zhaohui S. Zhou**, April E. Smith, Rowena G. Matthews, and James E. Penner-Hahn. *Biochemistry*, 2001, 40, 987-993. PubMed 11170420 pubs.acs.org/doi/abs/10.1021/bi001711c

L-Selenohomocysteine: One-Step Synthesis from L-Selenomethionine and Kinetic Analysis as Substrate for Methionine Synthases. **Zhaohui S. Zhou**, April E. Smith, and Rowena G. Matthews. *Bioorg. Med. Chem. Lett*. 2000, 10, 2471-2475. PubMed 11078203 www.sciencedirect.com/science/article/pii/S0960894X00004984

Identification of the Zinc Ligands in Cobalamin-Independent Methionine Synthase (MetE) from Escherichia coli. **Zhaohui S. Zhou**, Katrina Peariso, James E. Penner-Hahn, and Rowena G. Matthews. *Biochemistry*, 1999, 38, 15915-15926. PubMed 10625458 pubs.acs.org/doi/abs/10.1021/bi992062b

Antibody-Catalyzed Allylic Sulfoxide-Sulfenate Rearrangement. **Zhaohui S. Zhou**, Alexander Flohr, and Donald Hilvert. *J. Org. Chem*. 1999, 64, 8334-8341. PubMed 11674756 pubs.acs.org/doi/abs/10.1021/jo991299a

Antibody-Catalyzed Selenoxide Elimination. **Zhaohui S. Zhou**, Ning Jiang, and Donald Hilvert. *J. Am. Chem. Soc*. 1997, 119, 3623-3624. pubs.acs.org/doi/abs/10.1021/ja963748j

Doctoral Thesis

Catalytic Antibodies for Pericyclic Reactions and Cofactor-Dependent Oxidations and Reductions. January 6, 1997, The Scripps Research Institute, La Jolla, California.

Invited Lectures

Lanzhou University, 2018
Nankai University, 2018
7th Annual Cell Line Development and Engineering Asia, Shanghai, 15-17 May 2018
American Society for Photobiology Biennial Meeting, Tampa, Florida, 12-15 May 2018
PEGS - the essential protein engineering summit, Boston, April 30 - May 4, 2018
Biotherapeutics Analytical Summit, Baltimore, March 12-16, 2018

Bioprocessing Technology Institute, A*STAR, Singapore, 23 October 2017
Nanyang Technological University (NTU), Singapore, 22 October 2017
Health Sciences Authority (HSA), Singapore, 20 October 2017
APEC Biotherapeutics Center of Excellence (CoE) Training Workshop, 11-15 Sept 2017
College of Pharmacy, WenZhou Medical University, 1 August 2017
Pfizer, Cambridge, Massachusetts, 8 May 2017

Wuhan Institute for Drug and Medical Device Control, Wuhan, China, 14 Dec 2016
Bristol-Myers Squibb (BMS), Davens, MA, 2 Dec 2016
APEC Biotherapeutics Center of Excellence (CoE) Pilot Training, 7 Nov 2016
Boston College, Chemistry, 1 Nov 2016
Horvath Medal Award Symposium, Yale, 26 Oct 2016
Johns Hopkins School of Medicine, Pharmacology, 5 Oct 2016
APEC Biotherapeutics Center of Excellence (CoE) Pilot Training, Sept 13-16, 2016
Workshop on antibody-drug conjugates (ADC), Takeda, Cambridge, MA, 2 June 2016
Workshop on antibody-drug conjugates (ADC), Takeda, Cambridge, MA, 27 April 2016
Genentech, South San Francisco, California, 4 March 2016
Epigenetic Enzymes in Drug Discovery Conference, San Diego, March 1-2, 2016
UC-Irvine, 29 February 2016
Sanibel Conference, Characterization of Protein Therapeutics by Mass Spectrometry
Am Soc Mass Spec, Clearwater, Florida, 21-24 January 2016

11th International Congress of Corneal Cross-Linking (CXL), Boston, 5 December 2015
New Drug Development Summit, sFDA and Biolake, Wuhan, China, 27 November 2015
Wuhan Institute for Drug and Medical Device Control, Wuhan, China, 26 November 2015
Protein Biophysics Structure and Function (PBSF), Northeastern Univ, 6 November 2015
Syros, Cambridge, Massachusetts, 5 November 2015
Yunnan Baiyao, Kunming, China, 5 July 2015
Overseas Chinese Entrepreneurship Development Fair, Wuhan, July 1-3, 2015
Changchun Institute of Applied Chemistry, Chinese Academy of Sciences, 26 June 2015
Epigenomics & Novel Therapeutic Targets Conference, Boston, May 21-22, 2015
Dept of Biological Chemistry, University of Michigan, Ann Arbor, 24 March 2015

MASSEP, Boston, 20 Nov 2014
Hubei Institute for Food and Drug Control (sFDA), Wuhan, China, 13 Nov 2014
Chinese Society of Biotechnology Annual Conference, Wenzhou, China, Nov 8-10, 2014

Beijing University of Chemical Technology, Beijing, 4 Nov 2014
College of Pharmacy, Tianjin University, Tianjin, China, 3 Nov 2014
ETH Hönggerberg, Zürich, Switzerland, June 28, 2014
Krull Family Lecture, Chemistry and Chemical Biology, Northeastern Univ, April 29, 2014
Department of Chemistry, MIT, Cambridge, MA, February 10, 2014

Targeting Histone Methyltransferases, Boston, MA, September 24-25, 2013
Dept of Pharmaceutical Chemistry, University of Kansas, Lawrence, Sept 17, 2013
WuXi AppTec, Shanghai, China, Aug 30, 2013
Key Laboratory of Anal Chem for Biology and Medicine, Wuhan University, Aug 28, 2013
Hubei Institute for Food and Drug Control (sFDA), Wuhan, China, Aug 27, 2013
Amgen, Thousand Oaks, California, July 23, 2013
Dept Chemistry and Biochemistry, UC-Santa Barbara, July 22, 2013
3rd Epigenetics in Drug Discovery Conference, Boston, MA, May 8-10, 2013
Keynote speaker, Northeast Bioengineering Conference, Syracuse, New York, April 6, 2013
Department of Chemistry, Georgia State University, Atlanta, March 8, 2013
Dept Chemistry & Biochemistry, Florida International University, Miami, Feb 8, 2013

Dept Chemistry & Biochemistry, Boise State University, Boise, Idaho, Dec 14, 2012
Trainer, Protein Drug Analysis, CABA Regulatory Training Program, Boston, Sept 27, 2012
Gordon Conference, Enzymes, Coenzyme Metab Path, Waterville Valley, NH, July 15, 2012
Methods in Protein Structure Analysis (MPSA), Ottawa, Canada, June 26-28, 2012.
Northern Essex Community College, Dept of Natural Sciences, Haverhill, MA, April 5, 2012
Novartis, Cambridge, April 3, 2012
Department of Chemistry, Brandeis University, April 2, 2012
Biosimilars and Biobetters, Baltimore, MD, March 19-20, 2012

Department of Chemistry, Shanghai Normal University, 18 December 2011
College of Pharmacy, Tianjin University, Tianjin, China, 15 December 2011
College of Life Sciences, Jilin University, Changchun, China, 8 December 2011
Jilin Agricultural University, Changchun, August 29, 2011
Trainer, Protein-Based Drug Analysis, CABA 2011 Regulatory Training Program, Boston.
Dept of Chemistry and Biochemistry, University of California, Los Angeles, March 4, 2011
Amgen, Thousand Oaks, March 2, 2011
Chungnam National University, Korea, February, 2011
Yonsei Proteome Research Center, Yonsei University, Korea, February, 2011

College of Pharmacy, Nankai University, Tianjin, December 22, 2010
Beijing University of Chemical Technology, Beijing, December 20, 2010
Northern Essex Community College, Dept of Natural Sciences, Haverhill, MA, Oct. 25, 2010
HPLC 2010, Boston, Massachusetts, June 19-24, 2010
Lecturer, Short Course: State of the Art Protein Analysis and Regulatory Science sponsored by the Barnett Institute at Northeastern University, June 7 to 10, 2010
AnaSpec, Fremont, California, March 24, 2010
Am Chem Soc, 239 National Meeting, Biochemical Tech Div, San Francisco, Mar 21, 2010

Selected for webinar presentation, May 28, 2010
Organix Inc, Woburn, Massachusetts, March 11, 2010

College of Pharmacy, Tianjin University, Tianjin, China, Aug. 14, 2009
College of Sciences, Beijing University of Chemical Technology, Aug. 5, 2009
Martin Luther University of Halle-Wittenberg, Germany, June 25, 2009
7th Int Conference on Homocysteine Metabolism, Prague, Czech, June 21-25, 2009
Abbott Bioresearch Center (ABC), Worcester, Massachusetts, April 17, 2009
Pharmaceutical Science, Northeastern University, Boston, Massachusetts, April 2, 2009.
Chemical Biology Program, University of Maryland at Baltimore County, Mach 4, 2009
Biology Department, Northeastern University, Boston, Massachusetts, Jan. 26, 2009.

Millipore Bioscience Division, Danvers, Massachusetts, July 30, 2008.
Northeastern Regional Meeting of Am Chem Soc, Burlington, Vermont, June 29, 2008.
FASEB Conference on Biological Methylation, Carefree, Arizona, June 1 to 6, 2008.
GOT Summit (Getting Optimized Tools for Diagnostics), Boston, , May 19-20, 2008.
American Chemical Society 234th National Meeting, Boston, Aug. 19 to 23, 2007.

Second Sino-US Chemistry Professors Conference, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, July 7-9, 2006.
Session Chair and Speaker, Small Molecule Methylation, FASEB Summer Research Conference on Biological Methylation, Saxtons River, Vermont, June 24-29, 2006.
Medicinal Chem and Natural Products, Univ North Carolina, Chapel Hill, March 29, 2006.
College of Pharmacy, Oregon State University, Corvallis, Oregon, March 13, 2006.
Department of Chemistry, Portland State University, Portland, Oregon, March 10, 2006.
Department of Chemistry, University of Nevada at Reno, Nevada, February 24, 2006.
Barnett Inst and Dept of Chem and Chem Biol, Northeastern Univ, Boston, Feb. 9, 2006.
Department of Medicinal Chemistry, Pharmacy, Univ of Utah, Salt Lake City, Jan 30, 2006.

Key Laboratory for Molecular Enzymology and Engineering of Ministry of Education, Jilin University, Changchun, China, January 4, 2005.
Shanghai Institute of Organic Chemistry, Shanghai, China, December 27, 2004.
College of Chemistry, Peking University, Beijing, China, December 24, 2004.
Department of Biochemistry, Emory University, Oct. 21, 2004.
Department of Chemistry, Boise State University, Boise, Idaho, October 15, 2004.
FASEB Sum Res Conf Biological Methylation, Saxtons River, Vermont, July 14, 2004.
Key Laboratory for Molecular Enzymology and Engineering and College of Life Science, Jilin University, Changchun, China, January 8, 2004.

Pharmaceutical Sciences, Washington State Univ, Pullman, Washington, Dec. 6, 2002.
Department of Chemistry, Washington State University, Pullman, March 28, 2000
Department of Chemistry, West Virginia University, Morgantown, 2000.
Department of Chemistry, Florida International University, Miami, 2000.

Gordon Graduate Res Seminar on Bioinorganic Chem, Ventura, California, 28 Jan 1999.

Research Funding

Federal

Department of Defense (DOD)
National Institutes of Health (NIH)
National Institute of Allergy and Infectious Diseases (NIAID)
National Institute of General Medical Sciences (NIGMS)
National Science Foundation (NSF)

Foundation

American Heart Association
Amgen Medical Education Foundation
Autism Research Institute
Herman Frasch Foundation, administrated by American Chemical Society

Industrial

Amgen
Colgate Palmolive Company
Ischemia Technologies
Novartis Institutes for BioMedical Research (NIBR), Cambridge, Massachusetts
Nuvelo

International

Food and Drug Administration (FDA) of China (training program)

Internal

Northeastern University, Provost Office, Seed Project
Washington State University (WSU), Student Support for Research from
Honors College, College of Sciences, School of Pharmacy, Biotechnology Program

Donation

IBM employee and matching fund
AbbVie employee and matching fund

Teaching at Northeastern University

Nominated by students for Excellence in Teaching Award, Northeastern University
2010, 2011

Chemistry and Design of Protein Pharmaceuticals (CHEM 5625, new course I developed)
Enzymes: Chemistry, Mechanism and Application (CHEM 4700 and CHEM 5700, new course I developed)
Mechanistic and Physical Organic Chemistry (CHEM 5627)
Principles of Chemical Biology (CHEM 5621, advanced undergraduates and graduates)
Advanced Topics in Organic Chemistry (CHM G310, Protein Chemistry, undergraduates and graduates)
Bioorganic Chemistry (CHM G376, advanced undergraduates and graduates)
Organic Chemistry I for Chemistry Majors (CHM U315, undergraduate)
Organic Chemistry Laboratory I for Majors (CHM U316, undergraduate)
Organic Chemistry II for Chemistry Majors (CHM U317, undergraduate)
Organic Chemistry Laboratory II for Majors (CHM U318, undergraduate)
Organic Chemistry II (CHEM 2313, undergraduate)

Instructor, Biopharmaceutical Analysis Training Laboratory (BATL), Northeastern University, 2016-present

Teaching at Washington State University

Organic Reaction and Mechanism (Chem 540, advance undergraduate and graduate)
Enzyme Catalysis and Inhibition (Chem 529, advance undergraduate and graduate)
Protein Chemistry (Chem 543, advance undergraduate and graduate)
Proteins and Enzymes (MBioS 567, graduate course, guest lecturer on catalytic antibody)
Principles of Pharmacology (P/T 506), graduate course, guest lecturer on drug discovery)
Advanced Topics in Organic Chemistry (Chem 544, graduate research)
Seminar in Organic Chemistry (Chem 594, graduate students seminar)
Organic Chemistry I (Chem 340 and Chem 345, undergraduate)
Organic Chemistry Laboratory I (Chem 341 and Chem 345, undergraduate)

File name: Sunny Zhou CV 2018-04-12 16.docx