American Chemical Society

National Awards Nomination Packet

Ronald Breslow Award for Achievement in Biomimetic Chemistry:2018
for: Jean Chmielewski

Received: 10/25/2016 *Cycle Year: 1*

"Professor Jean Chmielewski is recognized for her many highly innovative and ground-breaking contributions to the chemistry and biochemistry of biomimetic systems."

NOMINATOR:

Arun Ghosh
Email: akghosh@purdue.eduXXX
Dept of Chemistry
560 Oval Dr
West Lafayette, IN 47907-2084
UNITED STATES

- Have you discussed this award nomination with the nominee? *Yes*

NOMINEE:

Jean Chmielewski
Tel: (765)429-5422
Email: chml@purdue.eduXXX
Purdue Univ
560 Oval Dr
West Lafayette, IN 47907-2084
UNITED STATES

ACS Current Member: Yes
Years of Service: 29
Date of birth: 01/01/1961
Present Position: AW Kramer Distinguished Professor
Industry: Academia

CODE OF CONDUCT:

- To the best of my knowledge, including past and present circumstances, the nominee:
  1. Employs and requires good safety protocols and practices in his/her laboratory and/or work environment;
  2. Upholds the highest ethical standards in his/her laboratory and/or work environment; and
  3. Otherwise engages in conduct that is consistent with both the objects of the American Chemical Society as stated in Article II Section 1 of its Constitution and the Chemical Professional Code of Conduct.

Code of Conduct Answer: *Yes*

SUPPORTER 1

Barbara Imperiali
Tel: (617)253-1838
Fax: (617)452-2419
Email: imper@mit.eduXXX
MIT
77 Mass Ave 68-380
Cambridge, MA 02139-4301
UNITED STATES

PURDUE
UNIVERSITY

October 14, 2016

Office of Awards Program
American Chemical Society
1155 16th St., NW
Washington, DC 20036

Dear Awards Committee:

It is my great pleasure to nominate **Jean Chmielewski**, the AW Kramer Distinguished Professor of Chemistry and Biomedical Engineering, for the Ronald Breslow Award for Achievement in Biomimetic Chemistry. Professor Chmielewski is a truly outstanding scientist who is internationally renowned and respected for her biomimetic discoveries. She has forged a uniquely interdisciplinary research program to address fundamentally important problems at the interface of Chemistry, Biology and Medicine. She is a highly creative scientist with an amazing eye for highly significant problems. I believe that she is truly worthy of recognition with the Ronald Breslow Award, honoring her accomplishments and excellence in Biomimetic Chemistry.

Professor Chmielewski's many highly creative and ground-breaking contributions place her among the top Biomimetic Chemists worldwide and make her an exceptional candidate for the Ronald Breslow Award. Chmielewski's major areas of research have focused on four interrelated areas: (1) Modulating Protein Assembly, (2) Inhibiting Drug Resistance Efflux Transporters, (3) Targeting Intracellular Pathogenic Bacteria, and (4) Bio-Nanotechnology. In each of these areas outstanding and novel discoveries have been made that have dramatic implications for a wide range of disciplines. Some of Chmielewski's highest achievements are highlighted below.

Disrupting Protein-Protein Interactions

Professor Chmielewski has been at the vanguard of researchers developing agents to modulate protein-protein interactions. In the early 1990's, Professor Chmielewski was one of the first to actively explore this important area of research. Her works capitalized on the fact that the enzymes of HIV, for instance, rely on dimer formation for optimum catalytic activity. Professor Chmielewski's groundbreaking publications in the early 1990's, using crosslinked peptide fragments that mimic protein interfaces, were some of the first in this now extensive field of drug discovery. In addition, Professor Chmielewski's research has *lead to potent protein-protein interaction inhibitors of the anti-HIV targets HIV protease and HIV-integrase, transcription factors, pore-forming proteins of pathogenic bacteria, and restriction enzymes.* Her successes have lead many other researchers to this field in both academic and industrial settings. Overall the impressive biomimetic platform technology developed by Chmielewski has been applied to many other disease targets.

1393 H. C. BROWN/R. B. WETHERILL LABORATORIES OF CHEMISTRY
WEST LAFAYETTE, IN 47907-1393

Inhibiting Drug Resistance Efflux Transporters

Over the past decade Professor Chmielewski has initiated a highly successful program targeting a number of multi-drug resistance proteins. Multidrug resistance transporters consist of families of membrane-bound proteins that have recently emerged as major players in limiting the accumulation of therapeutics into specific organs, cells and sub-cellular organelles involved in disease states, such as cancer, HIV, malaria and schizophrenia, to name a few. Professor Chmielewski's research provides a highly innovative and general strategy to both block the efflux function of transporters and deliver the required therapy to the disease site. This project is unique in that a very wide range of disease states may be tackled with a single interdisciplinary platform technology. The innovation comes from the combination of two areas that Chmielewski's group has pioneered: dimeric inhibitors of multidrug resistance transporters and the development of traceless linkers so that the dimeric inhibitors may serve as prodrugs of the therapy as well. The activity of multidrug resistance transporters such as P-glycoprotein and the chloroquine resistance transporter of *P. falciparum* (PfCRT) have been modulated using this strategy. *With P-glycoprotein, a new strategy to limit the formation of HIV reservoirs in the brain has resulted, and with PfCRT, a new paradigm for the development of anti-malaria therapies that directly target resistance mechanisms has emerged.*

Targeting Intracellular Pathogenic Bacteria: Coupling Antibacterial Activity with Macrophage Penetration

Designing shuttles to bring therapeutic agents into cells has been a strong theme in Professor Chmielewski's research over the last decade. With this in mind, she recently developed an ingenious biomimetic approach to the significant challenge of creating effective antibacterial agents against bacterial pathogens that have evolved to inhabit mammalian cells, such as phagocytic macrophages. Within these intracellular safe havens the bacteria reproduce and form a repository, and are able to evade the host immune response as well as a number of antibiotic drugs. Therefore, there is a great need to develop antibiotics with the ability to enter mammalian cells and target intracellular pathogens at their specific sub-cellular site. Professor Chmielewski has developed a novel class of biomimetic peptides, cationic amphiphilic polyproline helices (CAPHs), that enter mammalian cells through both direct transport and endocytosis. Importantly, she has determined that CAPHs also have potent antibacterial activity *in vitro* with a non-lytic mechanism of action. *This dual mode of action, non-lytic antibacterial activity with the ability to localize within mammalian cells, has provided agents with a pronounced ability to target and kill pathogenic intracellular bacteria, including Mycobacterium tuberculosis, Salmonella and Brucella, within human macrophages. These agents also have potent activity against pre-formed biofilms and in vivo activity in infected wound models, and are being pursued as novel, first-in-class preclinical drug candidates for treatment of complicated skin and soft tissue infections.*

Bio-Nanotechnology

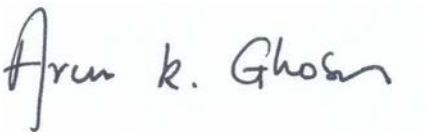
Professor Chmielewski's research in bio-nanotechnology has focused on two major areas: self-replicating peptides and designer biomaterials based on peptide hierarchical

assembly. Chmielewski has described biomimetic peptide-based systems that use the well-known coiled-coil dimerization motif as a way to achieve templated peptide synthesis. Her pioneering discoveries with self-replicating peptides produced the first example of self-replication with peptides that can be controlled by environmental cue, including a highly impressive publication in *Nature* that demonstrated the interplay between four simultaneous self replicating processes. This is an area of great interest due to its relevance to early chemical evolution on earth. *In addition to having the potential to shed light on the molecular origins of life, this work has produced highly efficient peptide replication on demand – a feature that has applications in sensing and signal amplification.*

More recently Professor Chmielewski has described the remarkable hierarchical assembly of modified triple helical collagen and coiled-coil mimetic peptides. For instance, collagen peptides containing strategically placed metal binding sites have led to a fascinating array of higher order structures via a metal ion-templated strategy. For instance, tunable nano- to micro-scale collagen peptide-based structures have been obtained, such as banded fibers, florettes, disks, hollow spheres, cages, meshes and sheets, with unique cell binding capabilities and controlled protein release. *These robust and biocompatible materials have outstanding potential for use in tissue engineering and regenerative medicine, as demonstrated by recent work in the Chmielewski labs on stem cell differentiation and scaffold-mediated cell assembly.* Very recent work used a metal ion-mediated crystal design strategy to successfully engineer coiled-coil peptides to rapidly form hexagonal 3D crystals with a controlled morphology. Equally impressive, unsatisfied ligands within the crystals were harnessed as a powerful means to direct His-tagged cargoes to specific crystal locations for future use in drug delivery and sensor design.

In conclusion, it is clear that Professor Chmielewski is a truly remarkable scholar who has achieved an exceptional international reputation in the area of Biomimetic Chemistry. She fearlessly and successfully tackles some of the most significant problems at the interface of chemistry, biology and medicine today. Chmielewski's selection as the recipient of the Ronald Breslow Award would be well received and is exceptionally well deserved.

Sincerely,



Arun K. Ghosh
Ian Rothwell Distinguished Professor
Department of Chemistry
Purdue University

JEAN CHMIELEWSKI

EDUCATION

COLUMBIA UNIVERSITY, New York, NY
Ph.D. in Chemistry, March 1988
Research Advisor: Professor Ronald Breslow

ST. JOSEPH'S UNIVERSITY, Philadelphia, PA
B.S., in Chemistry, May 1983
Undergraduate Research Advisor: Dr. George Nelson

PREVIOUS EXPERIENCE

UNIVERSITY OF CALIFORNIA, BERKELEY
Postdoctoral Fellow, November 1988 - July 1990
Research Director: Professor Peter Schultz

ROCKEFELLER UNIVERSITY
Postdoctoral Fellow, March 1988 - October 1988
Research Director: Dr. Emil Thomas Kaiser

PRESENT POSITION

PURDUE UNIVERSITY, West Lafayette, IN
Alice Watson Kramer Distinguished Professor of Chemistry, 2005-present
Professor, Weldon School of Biomedical Engineering, 2009-present
Professor, Department of Chemistry, April 2000
Associate Professor, Department of Chemistry, April 1996
Assistant Professor, Department of Chemistry, August 1990

AWARDS AND HONORS

Vincent du Vigneaud Award, American Peptide Society, 2015
Keynote Lecturer, 7th Peptide Engineering Meeting, Pune India, 2015
Keynote Lecturer, American Peptide Society Symposium, 2015
Team Award, College of Science, Purdue, 2015
Keynote Lecturer, American Peptide Society Symposium, 2013
Outstanding Undergraduate Student Mentor Award, College of Science, Purdue, 2013
The Book of Great Teachers Awardee, Purdue, 2013
Arthur E. Kelly Award for Excellence in Teaching, Purdue University, 2012
Outstanding Graduate Student Mentor Award, College of Science, Purdue, 2012
Edward Leete Award in Organic Chemistry, American Chemical Society, 2011
Teaching Academy Member, Purdue, 2011
Bill and Melinda Gates Grand Challenges Explorations Award, 2010
Charles B. Murphy Award, Purdue University, 2010
Fellow, American Association for the Advancement of Science, 2008
The Outstanding Teacher in the College of Science, Purdue, 2008-2009
Woman of Purdue, Purdue University, 2008
Outstanding Teacher in the College of Science, Purdue, 2007-2008
Outstanding Teacher in the College of Science, Purdue, 2006-2007
The Alice Watson Kramer Distinguished Professorship in Chemistry, 2005
Arthur E. Kelly Award for Excellence in Teaching, Purdue University, 2006
W. S. Johnson Symposium Distinguished Lecturer, 2005
Robert A. Welch Conference, Distinguished Lecturer, 2004
Arthur C. Cope Scholar Award, American Chemical Society, 2003
Agnes Fay Morgan Research Award, Iota Sigma Pi, 2001
University Faculty Scholar, Purdue University, 2000-2004

Arthur E. Kelly Award for Excellence in Teaching, Purdue University, 2000
Alfred P. Sloan Fellow, 1996-1998
National Science Foundation, National Young Investigator, 1994-1999
First Awardee, National Institutes of Health, 1992-1997
National Institutes of Health Postdoctoral Fellowship, 1988-1990
The George B. Pegram Distinguished Award, Columbia University, 1987
The Molloy Award for Promise in Research, St. Joseph's University, 1983

PROFESSIONAL AND SCHOLARLY ASSOCIATIONS

American Chemical Society, member
American Peptide Society, member
American Association for the Advancement of Science, member

SELECTED RECENT INVITED TALKS

1. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Department of Chemistry, University of Puerto Rico, Rio Piedras, October 27, 2014.
2. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Department of Chemistry, University of Arizona, Tucson AZ, February 19, 2015.
3. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Department of Chemistry, University of Nebraska, Lincoln, NB, April 17, 2015.
4. **Keynote Lecture**: *Targeting Intracellular Pathogenic Bacteria with Unnatural Proline-rich Peptides: Coupling Antibacterial Activity with Macrophage Penetration*, American Peptide Symposium, Orlando, FL, June 22, 2015.
5. **Invited Lecture**: *Hierarchical Assembly of Collagen Peptide-Based Materials for Use in Regenerative Medicine*, Collagen Gordon Conference, Colby Sawyer College, July 15, 2015.
6. *Transforming Chemistry Curricula for Premedical and Life Science Undergraduate Students: A Competency-based, Biochemically-focused Approach to Teaching Organic Chemistry*, National Meeting of the American Chemical Society, Boston, MA, August 19, 2015.
7. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Department of Chemistry, Rutgers University, Picataway, NJ, November 10, 2015.
8. **Keynote Lecture**: *Targeting Intracellular Pathogenic Bacteria with Cationic Amphiphilic Polyproline Helices*, 7th Peptide Engineering Meeting, IISER, Pune, INDIA, December 5, 2015.
9. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Indiana University Medical School, Indianapolis, IN, January 21, 2016.
10. *Next Generation Therapeutic Targets: Multidrug Resistance and Regenerative Medicine*, Department of Chemistry, University of Colorado, Boulder, CO, April 25, 2016.

SELECTED PUBLICATIONS

1. Yao, S.; Ghosh, I.; Zutshi, R.; Chmielewski, J., "Selective Amplification via Auto- and Cross-Catalysis in a Replicating Peptide System", *Nature*, **1998**, *396*, 447-450.

2. Yao, S.; Ghosh, I.; Zutshi, R.; Chmielewski, J., "A Self-Replicating Peptide under Ionic Control", *Ang. Chem.*, **1998**, *37*, 478-479.

3. Shultz, M. D.; Bowman, M. J.; Ham, Y.-W.; Zhao, X.; Tora, G.; Chmielewski, J., "Small Molecule Dimerization Inhibitors of HIV-1 Protease", *Ang. Chem.*, **2000**, *39*, 2710-2713.

4. Issac, R.; Chmielewski, J., "Approaching Exponential Growth with a Self Replicating Peptide", *J. Am. Chem. Soc*, **2002**, *124*, 6808-6809.

5. Li, X.; Chmielewski, J. "Highly Efficient Peptide Self Replication with a Proline Hinge", *J. Am. Chem. Soc.* **2003**, *125*, 11820-11821.

6. Shultz, M.; Lee, S.; Ham, Y.; Chmielewski, J. J. "Small Molecule Dimerization Inhibitors of Wild Type and Mutant HIV Protease: A Focused Library Approach", *J. Am. Chem. Soc.* **2004**, *126*, 9886-9887.

7. Fillon, Y.; Anderson, J.; Chmielewski, J. "Cell Penetrating Agents Based on a Polyproline Scaffold" *J. Am. Chem. Soc*., **2005**, *127*, 11798-11803.

8. Przybyla, D., Chmielewski, J. "Metal Triggered Radial Self Assembly of Collagen Peptide Fibers" *J. Am. Chem. Soc.* **2008**, *130*, 12610-12611.

9. Lee, S.-G.; Lee, J.; Chmielewski, J. "Investigation of pH-Dependent Collagen Peptide Triple Helix Formation" *Ang. Chem.*, **2008**, *47*, 8429-8432.

10. Pires, M. M.; Chmielewski, J. "Self Assembly of Collagen Peptides into Microflorettes via Metal Coordination" *J. Am. Chem. Soc.* **2009**, *131*, 2706-2712.

11. Pires, M. M.; Przybyla, D.; Chmielewski, J. "A Metal-Collagen Peptide Framework for 3-Dimensional Cell Culture" *Ang. Chem.*, **2009**, *48*, 7813-7817.

12. Przybyla, D.; Chmielewski, J. "Metal-Triggered Self Assembling Collagen Peptide Disks" *J. Am. Chem. Soc.* **2010**, *132*, 7866-7867.

13. Pires, M. M.; Przybyla, D.; Rubert Perez, C.; Chmielewski, J. "Metal-Mediated Tandem Coassembly of Collagen Peptides into Banded Microstructures" *J. Am. Chem. Soc.* **2011**, *133*, 14469-14471.

14. Namanja, H; Emmert, D.; Hrycyna, C.; Chmielewski, J. “Toward Eradicating HIV Reservoirs in the Brain: Inhibiting P-glycoprotein at the Blood-Brain Barrier Prodrug Abacavir Dimers” *J. Am. Chem. Soc.,* **2012**, *134*, 2976-2980.

15. Kuriakose, J.; Hernandez, V.; Nepal, M.; Brezden, A.; Pozzi, V. Seleem, M,; Chmielewski, J. “Targeting Intracellular Pathogenic Bacteria with Unnatural Proline-rich Peptides: Coupling Antibacterial Activity with Macrophage Penetration” *Ang. Chem.* **2013**, *52*, 9644-9667.

16. Przybyla, D.; Rubert Perez, C.; Gleaton, J.; Nandwana, V.; Chmielewski, J. “Hierarchical Assembly of Collagen Peptide Triple Helices into Curved Disks and Metal Ion-promoted Hollow Spheres” *J. Am. Chem. Soc.* **2013**, *135*, 3418-3422.

17. Hernandez-Gordillo, V.; Chmielewski, J. “Mimicking the Extracellular Matrix with Functionalized, Metal-assembled Collagen Peptide Scaffolds” *Biomaterials* **2014**, *35*, 736-7373.

18. Gleaton, J.; Chmielewski, J. “Thermally Controlled Collagen Peptide Cages for Biopolymer Delivery” *ACS Biomater. Sci. Eng.* **2015**, *1*, 1002-1008.

19. Brezden, A.; Mohamed, M. F.; Nepal, M.; Harwood, J. S.; Kuriakose, J.; Seleem, M. N.; Chmielewski, J. “Dual Targeting of Intracellular Pathogenic Bacteria with a Cleavable Conjugate of Kanamycin and an Antibacterial Cel-Penetrating Peptide” *J. Am. Chem. Soc.,* **2016**, *138*, 10945-10949.

20. Nepal, M.; Sheedlo, M. J.; Das, C.; Chmielewski, J. “Accessing Three-Dimensional Crystals with Incorporated Guests through Metal-Directed Coiled-Coil Peptide Assembly” *J. Am. Chem. Soc.,* **2016**, *138*, 11051-11057.

BARBARA IMPERIALI
Class of 1922 Professor

Massachusetts Institute of Technology
77 Massachusetts Avenue, Building 68-380
Cambridge, Massachusetts 02139–4307

Department of Biology
Department of Chemistry

Phone 617–253-1838
Fax 617–253-6241
Email imper@mit.edu
http://web.mit.edu/imperiali

October 18, 2016

Professor Arun Ghosh
Department of Chemistry
Purdue University
560 Oval Drive
West Lafayette, IN 47907

Dear Selection Committee,

This letter is prepared in very strong support of the nomination of Jean Chmielewski, the Alison Watson Kramer Distinguished Professor of Purdue University, for the Ronald Breslow Award for Achievement in Biomimetic Chemistry. I initially met Jean at the first Bioorganic Gordon Conference in 1990, and have interacted extensively with her since that time. Chmielewski has gained international renown as a key contributor to our understanding of the bioorganic and biological chemistry of peptides and she has established a uniquely interdisciplinary program integrating the tools of organic synthesis, structural biology, supramolecular chemistry, molecular biology, and enzymology to address fundamentally important and intriguing problems in biomimetic chemistry. She is an outstanding scientist, a rigorous and conscientious experimentalist and a dedicated mentor. I believe that she would be truly worthy of this recognition.

Chmielewski has made many important and creative contributions that define her in the tops ranks of bioorganic and biomimetic chemists, and make her an excellent candidate for recognition with the Ronal Breslow Award. As her earlier research successes attest, Chmielewski is fearless when approaching new and highly challenging research areas. For instance, she was one of a small group of pioneers who first developed agents to **disrupt protein-protein interactions** in the early 1990's. These studies formed the basis for a viable novel strategy using crosslinked peptides that mimic the interfacial regions of proteins for the inhibition of multimeric proteins, including HIV enzymes and transcription factors. Chmielewski also investigated the potential role of peptides in the molecular origins of life by developing peptides with the ability to self replicate, mimicking natural replication. In a very exciting series of publications, Chmielewski demonstrated efficient **peptide self replication** that could be controlled by environmental factors, including a *Nature* paper that demonstrated the control of 4 simultaneous replicating peptide reactions.

Chmielewski's more recent research has served to further solidify her position in the uppermost echelon of bioorganic and biomimetic chemists. For instance, she has introduced to the scientific community the remarkable properties of triple helical **collagen mimicking peptides that self-assemble into fascinating higher order structures** via a metal-templating strategy. It is very clear from the unusually robust and highly biocompatible

nature of these materials that they will have far-reaching potential in medicine and biotechnology, as they mimic and expand upon the structures available to natural collagen. Indeed, Chmielewski has demonstrated the use of these peptide biomaterials in regenerative medicine and drug delivery. Also, Chmielewski has tackled the challenging task of **inhibiting the P-glycoprotein drug efflux pump** to enhance the efficacy of therapeutic agents – this is indeed a very novel and exciting strategy that has major medical implications, including HIV and cancer. This is an area in which Chmielewski is making major progress that will have a broad impact in many areas of drug discovery. Most recently, Chmielewski has developed a class of **cell penetrating peptides that serve the dual role as antibacterial agents**. This unique combination of activities, has allowed Chmielewski to target highly elusive pathogenic bacteria that dwell within human macrophages. This is a particularly exciting and important area of biomimetic research that is being developed into therapies to treat tuberculosis, cystic fibrosis and chronic wounds.

In all aspects of her research, Chmielewski's approach is characteristically creative and forward thinking, yet unerringly rigorous in her attention to detail. She is energetic and an exceptional role model for young scientists, always leading by example and always able to make her colleagues and collaborators truly enjoy the science that she shares with them. Throughout her career, Chmielewski has always taken the extra time to serve as an active and valued member of the scientific community. For instance, she has most recently served on the Medicinal Chemistry Long Range Planning committee for the ACS, and is an active member of the American Peptide Society currently serving as a Councilor and on the Organizing Committee for the biannual symposia.

Chmielewski's creative and biomimetic approaches to fundamental problems at the interface of organic chemistry and protein biochemistry make her a highly valued member of the chemical community and an outstanding candidate for recognition with the Ronald Breslow Award in Biomimetic Chemistry. I enthusiastically support her nomination.

Sincerely,

Barbara Imperiali, Ph.D.
Class of 1922 Professor of Biology
And Professor of Chemistry