

PROMOTION RECOMMENDATION  
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL  
DEPARTMENT OF BIOLOGICAL CHEMISTRY

Approved by the Regents

May 17, 2007

James C. A. Bardwell, Ph.D., Associate Professor of Biological Chemistry, without tenure, Department of Biological Chemistry, Medical School, is recommended for promotion to Professor of Biological Chemistry, without tenure, Department of Biological Chemistry, Medical School [also Professor of Molecular, Cellular, and Developmental Biology, with tenure, Department of Molecular, Cellular, and Developmental Biology, College of Literature, Science, and the Arts].

Academic Degrees:

Ph.D.	1987	University of Wisconsin-Madison
B.Sc.	1981	University of Saskatchewan

Professional Record:

2006-Present	Professor of Molecular, Cellular, and Developmental Biology, University of Michigan
2005-Present	Associate Professor of Biological Chemistry, University of Michigan
2001-2006	Associate Professor of Molecular, Cellular, and Developmental Biology, University of Michigan
1996-2001	Assistant Professor of Biology, University of Michigan

Summary of Evaluation:

Teaching: Since joining the faculty in the Department of Biology at the University of Michigan in 1996, Dr. Bardwell has been actively involved in teaching many undergraduate and graduate students. Dr. Bardwell began his teaching career at Michigan by teaching a new course that he created called Protein Structure and Function (Biol 401). This protein structure & function course was developed by Dr. Bardwell when he was an assistant professor, and it exposes students to the rapidly advancing field of bioinformatics. Dr. Bardwell has incorporated computer simulations as well as primary research articles into this course, and he emphasizes critical thinking and experimental design to his students. His efforts have been very well received, and he has earned excellent evaluations from students in this course. Dr. Bardwell also contributed to the revival of Biol 615, a course that is required of all incoming graduate students. Beginning in 1999, Dr. Bardwell became a member of several dissertation committees including the Undergraduate Honor's committee. Dr. Bardwell has devoted much of his time to the teaching of others and has received outstanding evaluations from his students. Since joining the faculty in 1996, Dr. Bardwell has become very involved in teaching and mentoring many students and serving on thesis committees. His addition to our faculty provided increased opportunities for formal teaching to graduate students. In addition to his graduate students and

postdoctoral fellows, each semester he has 3-5 undergraduates involved in research, and many of these students have been so successful that they have earned co-authorships on publications.

Research: The focus of Dr. Bardwell's research is to understand the mechanisms that allow proteins to fold correctly. Proteins are synthesized as linear chains of amino acids, but unless they fold into their proper three-dimensional shapes they have no biological function. The importance of folding proteins correctly has been recently brought to the attention of the general public by the emergence in Britain of a major outbreak of mad cow disease in humans. Misfolding of a single protein causes this fatal brain disease. Diseases that affect millions of humans, such as Alzheimer's disease, may also result from protein misfolding. Dr. Bardwell is able to focus his work on protein folding in bacteria, because there is abundant evidence that all complex organisms use the same basic mechanisms that are employed by bacteria. The major advantages of using bacteria for experimental studies are twofold. First, the complete DNA sequence is available for numerous bacterial species, so all the essential genes can be identified. Second, it is possible to genetically manipulate bacteria rapidly, to test the importance of particular folding proteins (chaperones), and to produce large quantities of material for biochemical and structural studies.

Dr. Bardwell has made two contributions of fundamental scientific importance. First, he has demonstrated that the folding of many proteins requires enzyme-mediated formation of disulfide bonds. He has followed this up by exploring in detail the complex biochemical pathways that allow such bonds to form with the proper specificity. The initial observations that motivated this work were made while he was a postdoctoral fellow, but the bulk of the work elucidating this pathway was done after he became an independent investigator. Second, he has identified a number of other chaperones using bioinformatic and genomic approaches. This second line of research has been carried out entirely at Michigan. He began by using computational tools to identify a large number of genes of unknown function as having the potential to be involved in protein folding. He has gone on to use molecular genetic tools to test the biological roles of the proteins these genes encode. This has been an incredibly productive enterprise, which has already led to the discovery of four proteins with novel functions.

#### Recent and Significant Publications:

Masip L, Pan JL, Haldar S, Penner-Hahn J, Georgiou G, Bardwell JCA and Collet J-F: A *de novo* engineered pathway for the formation of protein disulfide bonds. *Science* 303:1185-1189, 2004.

Regeimbal J, Gleiter S, Trumppower BL, Yu CA, Diwakar M, Ballou DP and Bardwell JCA: Disulfide bond formation involves a quinhydrone-type charge-transfer complex. *Proc Natl Acad Sci USA* 100:13779-13784, 2003.

Bader MW, Hiniker A, Regeimbal J, Goldstone D, Haebel PW, Riemer J, Metcalf P, and Bardwell JCA: Turning a disulfide isomerase into an oxidase: DsbC mutants that imitate DsbA. *EMBO J* 20:1555-1562, 2001.

Bader M, Muse W, Ballou DP, Gassner C and Bardwell JCA: Oxidative protein folding is driven by the electron transport system. *Cell* 98:217-227, 1999.

Jakob U, Muse W, Eser M and Bardwell JCA: Chaperone activity with a redox switch. Cell 96:341-352, 1999.

Service: Dr. Bardwell was one of approximately 30 investigators from across the campus invited to serve on the Life Science Commission. This committee filed a report that stimulated the President to implement revolutionary changes in the way that the Life Sciences are organized at the University. Dr. Bardwell has served on the program committee of the interdepartmental graduate program in Cell and Molecular Biology, and on the executive committee of the Molecular, Cellular and Developmental Biology group within the Department of Biology. He is also a member of various graduate student program committees at the University level, and a member of two grant review panels and two scientific meeting organizing committees at the national level. In addition to his local service, he also serves on the editorial board of the *Journal of Bacteriology*.

External Review:

Reviewer A: "...it's easy to say that he is one of the top investigators in the field, brilliant, imaginative, and incisive....He is one of the best biochemists on the planet, surely deserving of the promotion."

Reviewer B: "He is always rigorous and creative and is definitely a first rank scientist....there is no question that James is ready for promotion to the level of Professor with tenure; he would be a tremendous asset to any department that is lucky enough to employ him."

Reviewer C: "He is a clear leader in his field of research and I am confident that he will continue to be very productive....based on James' outstanding scientific accomplishments, his obvious potential for continued success, and his leadership role in the field of protein folding, I enthusiastically support his promotion."

Reviewer D: "Jim is a maverick who always follows his own intuition, often into new and uncharted territory....The most remarkable thing about Bardwell is the range of his talent."

Reviewer E: "Jim is one of the most innovative, imaginative and successful scientists that I have encountered. Jim thinks broadly and deeply and has established an international reputation as a clear leader in the protein folding..."

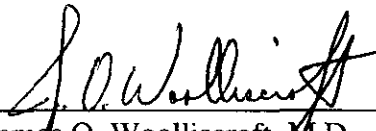
Reviewer F: "He has established himself as a major contributor and important figure in a contemporary area of science of wide interest and impact. He has demonstrated creativity, ingenuity, ability to identify important and approachable scientific issues and a pattern of sustained scientific contributions."

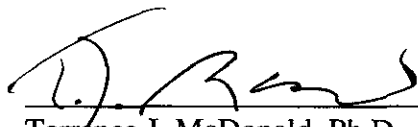
Reviewer G: "Jim's scientific career is simply stunning....What impresses me most is his enormous range of techniques that he uses - from genetics and whole organisms to X-ray structure and molecular details. Jim is a sure bet for the future!"

Reviewer H: "...I believe that Jim is one of the best prokaryotic molecular biologists in his peer group....Perhaps what is most remarkable about Jim's career is that he has made a major contribution at each and every stage."

Summary of Recommendation:

Dr. Bardwell is a highly visible, creative, and productive researcher. His work has fundamentally advanced our understanding of the formation and evolution of protein structure, which has broad implications in basic cell biology and the biomedical sciences. Dr. Bardwell is a dedicated and conscientious teacher, in the classroom and in the laboratory. He has provided helpful service to the Department and the University. I recommend that James Bardwell be promoted to the rank of Professor of Biological Chemistry, without tenure, Medical School.

  
James O. Woolliscroft, M.D.  
Interim Dean, Medical School  
*Lyle C. Roll Professor of Medicine*

  
Terrence J. McDonald, Ph.D.  
Dean, College of Literature, Science,  
and the Arts

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