

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF BIOLOGICAL CHEMISTRY

Ursula H. Jakob, 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, College of Literature, Science, and the Arts].

Academic Degrees:

Ph.D.	1995	University of Regensburg, Regensburg, Germany
M.S.	1991	University of Regensburg, Regensburg, Germany

Professional Record:

2011-present	Professor of Molecular, Cellular, and Developmental Biology, University of Michigan
2010-present	Associate Professor of Biological Chemistry, University of Michigan
2007-2011	Associate Professor of Molecular, Cellular, and Developmental Biology, University of Michigan
2001-2007	Assistant Professor of Molecular, Cellular, and Developmental Biology, University of Michigan
1999-2001	Assistant Research Scientist, Department of Biology, University of Michigan

Summary of Evaluation:

Teaching: Since becoming an associate professor, Dr. Jakob has twice taught the large enrollment majors course BC310/MCDB 310 – Introductory Biochemistry (W08 and F09). This critical course is central to many different biology concentrations. Dr. Jakob has taught this course for many years, and has consistently received high marks from students. The positive student reactions to Dr. Jakob in the classroom are especially impressive given the large size (often 300 or more) and the rigorous grading consistently employed in the course (mean grades of 2.46 and 2.65). Dr. Jakob also taught the advanced undergraduate course MCDB 432 – Bacterial Physiology 428 (F07). This is a much different course that provides advanced undergraduates with a sophisticated examination of current research and primary literature into important aspects of bacterial physiology. Dr. Jakob has also contributed to graduate education by teaching MCDB 615, a required course for all first-year MCDB Ph.D. students. Dr. Jakob has designed this class to train our graduate students in paper writing, grant preparation and effective scientific presentations. These are critical skills that are essential for our students to advance through qualifying exams and beyond as they progress as scientists. In the fall of 2011,

Dr. Jakob taught BC552 (literature-based class for MSTP students), an advanced course focused on the critical analysis of seminal publications in the field of biochemistry. Dr. Jakob will continue to teach this course in upcoming years.

In addition to formal classroom teaching, Dr. Jakob has a demonstrated strong commitment to research training. She has provided research opportunities for undergraduates in her own lab, as well as co-sponsoring a large number of undergraduates carrying out research outside of MCDB and Biological Chemistry. She has also trained many graduate students in her lab, including many students enrolled in German universities, and she has served on the thesis committees of over a dozen students. Her students praise her passion and enthusiasm and her concern for their career.

Research: Proteins are made as long polymers of amino acids, and these linear chains must be accurately folded to achieve the proper structure that determines their functional activity. Any malfunction that prevents them from achieving their mature, properly folded structure can disrupt their activity and may therefore be detrimental to the cell. Several human diseases are known that are caused by improper folding of proteins, and thus this area of investigation, besides being a fascinating field of basic biology, has important practical implications. Dr. Jakob has a well-funded research program focused on the proteins involved in protein folding known as 'heat-shock proteins (HSPs),' in particular the bacterial protein known as HSP33. In a series of papers in high-impact journals, including a *Nature Structural and Molecular Biology* paper in 2007 and culminating in a 2008 *Cell* paper, she and her research team have reported fundamental discoveries about the mechanism of action of this protein. This work has caused a paradigm shift in our understanding of how HSPs can operate, and Dr. Jakob has unquestionably established herself as one of the top investigators in this area. The crux of her most important discovery is that bacterial HSP33 is regulated by oxidation. The new regulatory mechanism she has uncovered is quite elaborate and sophisticated, and Dr. Jakob's thorough and mechanistic elucidation of the biochemistry of this reaction was a *tour de force*. The *Cell* paper has received particular notice because it employed bleach, a common household ingredient, and it showed how it affected HSP33, thus bringing together a basic science question with a very practical application. Expert reviewers uniformly comment on the high quality and visibility of her papers in this area.

In a second line of research, beginning in 2004 Dr. Jakob's group published a new method for visualizing reduction-oxidation (redox) changes in proteins. They expanded on this by developing the OxICAt technique, published in *PNAS* in 2008, which is a method to analyze *en masse* changes in the redox state of proteins. Since protein oxidation plays a role in aging, there is considerable interest in identifying proteins susceptible to oxidation and in studying the consequences of such oxidation. This new direction of research has a very strong potential for major advances in our understanding of environmental modifications that impact protein function.

Recent and Significant Publications:

Brandes N, Reichmann D, Tienson H, Leichert LI, Jakob U: Using quantitative redox proteomics to dissect the yeast redoxome. *J Biol Chem* 286:48193-41903, 2011.

Kumsta C, Thamsen M, Jakob U: Effects of oxidative stress on behavior, physiology, and the redox thiol proteome of *Caenorhabditis elegans*. *Antioxidant and Redox Signaling*, 14:1023-1037, 2011.

Thamsen M, Kumsta C, Li F, Jakob U: Is overoxidation of peroxiredoxin physiologically significant? *Antioxidant and Redox Signaling* 14:725-730, 2011.

Xu Y, Schmitt S, Tang L, Jakob U, Fitzgerald MC: Thermodynamic analysis of a molecular chaperone binding to unfolded protein substrates. *Biochemistry* 49:1346-1353, 2010.

Cremers CM, Reichmann D, Hausmann J, Ilbert M, Jakob U: Unfolding of metastable linker region is at the core of Hsp33's activation as a redox-regulated chaperone. *J Biol Chem* 285:11243-11251, 2010.

Service: With respect to departmental service, Dr. Jakob is currently serving on the Biological Chemistry Awards Committee. She has served on several committees in MCDB, including the Step Committee in 2007, the Executive Committee in 2008, and two different Pre-TRP Committees in 2010. Dr. Jakob is currently a member of the Biomedical Research Council and is the associate director for the Cellular Molecular Biology Program. She has been an ad hoc reviewer for the Office of the Vice President for Research Grants and University of Michigan Medical School Grants. Outside of the University, she has been the co-organizer for national scientific meetings both in 2003 and 2005, and a member of an international organizing committee in 2007. Currently, Dr. Jakob is the co-chair of the Gordon Research Conference on Stress Proteins in Growth, Development, and Disease. She will hold this title until 2014.

External Reviewers:

Reviewer A: "...Dr. Jakob is an outstanding scientist who has developed an extremely strong independent research program during her years at the University of Michigan....Her work is a nice blend of biochemistry and biology, a combination that is all too rare."

Reviewer B: "She has become a leader and innovator, moving to the very top rank of scientists. Specifically, she has set a paradigm for a whole new class of stress proteins....Ursula Jakob is a spectacular scientist..."

Reviewer C: "She is one of the top people in understanding how the redox state of the proteome is regulated....She compares favorable [sic] to other full professors in the general area of stress biology."

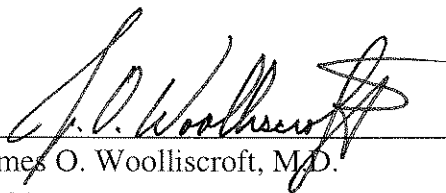
Reviewer D: "In that short time [since 2006] she has published a number of high-profile papers that have shaped the field....Only a handful of people worldwide rank with Ursula in terms of the understanding she has brought to oxidative stress."

Reviewer E: “The work on Hsp33 is simply phenomenal....Ursula is clearly the leader in the field that she initiated and she is well respected internationally for her achievements....Ursula is on the top of her age group. She is exceptionally innovative, fearless, and thorough.”

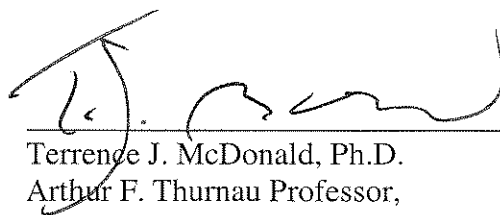
Reviewer F: “I believe that Ursula merits this promotion. Were she at [my institution], I think her accomplishments would merit promotion here as well.”

Summary of Recommendation:

Professor Jakob has established herself as a leader in the important field of redox regulation and protein folding through her insightful and novel research built on both theoretical analysis and technological developments. She has consistently produced high profile publications and she is sought after as a speaker for scientific conferences and university seminars. She is a passionate and dedicated teacher, who inspires and challenges her students both in the classroom and in the research laboratory. Her service contributions are extensive and include leadership roles at the departmental and university levels and in the broader academic community. Accordingly, I am pleased to recommend Ursula H. Jakob, Ph.D. for promotion to professor of biological chemistry, without tenure, Department of Biological Chemistry, Medical School.



James O. Woolliscroft, M.D.
Dean
Lyle C. Roll Professor of Medicine



Terrence J. McDonald, Ph.D.
Arthur F. Thurnau Professor,
Professor of History and Dean
College of Literature, Science, and the Arts

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