PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF BIOLOGICAL CHEMISTRY

Approved by the Regents
May 20, 2010

Ming Lei, Ph.D., assistant professor of biological chemistry, Department of Biological Chemistry, Medical School, is recommended for promotion to associate professor of biological chemistry, with tenure, Department of Biological Chemistry, Medical School.

Academic Degrees:

Ph.D.	2001	Harvard University
M.Sc.	1996	McGill University

Professional Record:

2004-present	Assistant Professor of Biological Chemistry, University of Michigan

Summary of Evaluation:

Teaching: Dr. Lei has excelled in teaching as well as research. During the past three years, Dr. Lei has taught the Biochemistry 452 course (13-14 lectures), a core course for undergraduate students with a concentration in biochemistry at the University of Michigan. The average class size is 70 students. Since 2006, Dr. Lei has taught in the Biochemistry Critical Analysis 597 course for first- and second-year biological chemistry Ph.D. students. In 2008, he taught the Biophysics 602 course, the *Principles of Macromolecular Crystallography*, to advanced graduate students in the Biophysics Program. Dr. Lei has received well above average teaching evaluations in all of his teaching roles, demonstrating that he is an effective teacher in the Department. Comments by students include: "Dr. Lei's efforts over the years resulted in my growth as a researcher and student, and I was ultimately a co-author of two publications…..professors like Dr. Lei are quite rare." Another student wrote: "Dr. Lei was also a great mentor in that he would always set time aside to press me to reach my standards and to motivate me to set them higher. Dr. Lei's laboratory was also the most productive I have been a part of." In addition to classroom teaching, Dr. Lei does a superb job of mentoring. He presently mentors three graduate students, two post-doctoral fellows, one research scientist, and two research assistants in his laboratory. Six Ph.D. students have performed research rotations in Dr. Lei's laboratory, and he has advised seven undergraduate students. There is always at least one undergraduate student working in his laboratory. Dr. Lei has served on one thesis dissertation committee and three Ph.D. student preliminary examination committees. He also personally tutors individuals from several research groups on the subject of protein X-ray crystallography.

Research: Dr. Lei is recognized as an emerging leader in structural biology. He is employing biochemical and structural methods (primarily X-ray crystallography and electron microscopy) to determine the nature of the interactions among the protein and nucleic acid components of

telomeres. He is currently investigating the detailed molecular mechanisms by which the human telomeric complex performs its two major functions: to protect the ends of chromosomes and to mediate their replication and maintenance. Dr. Lei's laboratory is one of the few laboratories in the world addressing this important area at the atomic level, and he has made great strides in understanding the structures and functions of the most important human telomere proteins. For example, Dr. Lei and his colleagues discovered that human POT1-TPP1 is a telomerase processivity factor, the first demonstration of telomerase processivity activity for any protein complex (*Nature*, 2007). Dr. Lei also discovered how two closely related telomere proteins, TRF1 and TRF2, act as selective telomere recruitment factors. His research revealed that TRF1 and TRF2 recognize different short-peptide motifs and function as docking sites to recruit distinct protein factors to telomeres. This work paves the way for identifying novel TRF1/TRF2 mediated interactions at telomeres (*Science,* 2008). Dr. Lei's studies on telomeres also involve examining the enzyme that lengthens them—telomerase—and a protective multi-protein complex called shelterin comprised of six telomere-associated proteins. His current plans are to define the molecular interactions between the RecQ Family of DNA helicases and the shelterin complex and to determine how these interactions protect and regulate human telomeres. Dr. Lei's research findings have and will continue to impact our understanding of telomere biology, DNA repair, epigenetics, and cancer biology. During the period from 1995 to mid 2009, Dr. Lei has published an impressive 20 peer-reviewed articles in well-refereed scientific journals, including the *Journal of Biological Chemistry*, *Nature*, *Molecular Cell,* and *Biochemistry*. He has published six papers based on work in his laboratory at the University of Michigan. He is the corresponding author on four of these including one in *PNAS*, one in *Science* and one in *Nature*. Dr. Lei's contributions to the structural biology and biochemical signaling research community are being recognized by an increasing number of speaking invitations. In 2009, he was invited to speak at Yale University, the National Institute of Aging (NIH) and the National Cancer Institute (NIH). In 2008, he was asked to speak at numerous meetings including the University of Cincinnati, the University of California Los Angeles, the University of Illinois, Baylor College of Medicine in Texas, and at the American Society of Human Genetics Annual Meeting in Philadelphia. In 2008, he also presented at the Tsinghua University and at the National Institute of Biological Sciences Meeting both in Beijing, China and at Nankai University in Tianjin, China. In 2006 and in 2008, he was invited to speak at the Telomeres and Genome Stability Meeting in Villars-sur-Ollon, Switzerland. Dr. Lei will chair a session of the 2010 EMBO meeting on telomeres and genome stability in France. Dr. Lei received a Paul Sigler Fellowship from the Agouron Institute for the period of 2001-2004, and after arriving at the University of Michigan he received a Kimmel Award from the Sidney Kimmel Foundation for the period of 2006-2008. Dr. Lei was recently awarded a Howard Hughes Medical Institute Early Career Award (2009-2014). This honor will allow him to resolve the structure of all of the protein molecules that bind and maintain the function of telomeres. Additionally, Dr. Lei has an NIH R01 (2008-2012) and an award from the American Cancer Society (2006-2010).

Recent and Significant Publications:

Wang W, Yang Y, Gao Y, Zhu S, Wang F, Old W, Resing K, Ahn N, Lei M*, and Liu X*: Structural and mechanistic insights into Mps1 kinase activation. *Journal of Cellular and Molecular Medicine*, 2009, in print. (*co-corresponding authors). Published Online: Dec 16, 2008. DOI: 10.1111/j.1582-4934.2008.00605.

Chen Y, Yang Y, van Overbeek M, Donigian JR, Baciu P, de Lange T, and Lei M: A shared docking motif in TRF1 and TRF2 used for differential recruitment of telomeric proteins. *Science* 319(5866):1092-1096, 2008.

Sowd G, Lei M, and Opresko PL: Mechanism and substrate specificity of telomeric protein POT1 stimulation of the Werner Syndrome helicase. *Nucleic Acids Research* 36(13): 4242-4256, 2008.

Yu EY, Wang F, Lei M, and Lue NF: Analysis of *Candida albicans* telomerase protein Est3: evidence for an OB-fold structure with a novel protein interaction surface. *Nat Struct Mol Biol* 15(9):985-989, 2008.

Opresko PL, Mason PA, Podell ER, Lei M, Hickson ID, Cech TR, and Bohr VA: POT1 stimulates RecQ helicases WRN and BLM to unwind DNA substrates. *J Biol Chem* 280(37): 32069-32080, 2006.

Service: With respect to departmental service, it should be noted that Dr. Lei was elected by faculty to serve on the Departmental Advisory Committee (2008-2010). He also has served on the Department's Graduate Student Recruitment Committee (2007) and the Computer Technology Committee (2005-2006). In terms of external service, Dr. Lei has been a reviewer for prestigious journals such as the *Journal of Biological Chemistry,* the *Proceedings of the National Academy of Sciences*, and *Molecular and Cellular Biology*. Dr. Lei was an *ad hoc* grant reviewer for the Chinese Science Foundation (2005 and 2009), the START Prize of the Austrian Science Fund (2007), and the Israel Science Foundation (2007).

External Review:

Reviewer A: "…..he gives excellent talks at those conferences, and that he has energetically and apparently very effectively done crystallographic and other structural work on several telomeric proteins…I certainly support his promotion to Associate Professor."

Reviewer B: "…Dr. Lei cracked open the field of telomere protein structural biology during his post-doctoral work by contributing two crystal structures of single-stranded telomeric DNA binding proteins from fission yeast and human…Dr. Lei's impact on the telomere field as a structural biologist is without doubt the largest and the leading presence…Dr. Lei has a deserved reputation for top-quality science, which is always presented clearly both in publication and talks formats."

Reviewer C: "This series of papers have [sic] established Dr. Lei as a seminal player in the area of telomere structural biology and as a world expert on OB-domains. They have provided important new insights into the structure and interactions of the protein components of telomeres."

Reviewer D: "How normal human cells maintain their telomere integrity is the focus of intense and highly competitive biological research. Dr. M. Lei made at least three discoveries of

paramount importance in this field...In my opinion (and I think that this is shared by many colleagues) he is currently the best in the world in the field of telomere structural biology."

Reviewer E: "...Dr. Lei is one of the few people doing structural work in the telomere field, and his contributions are moving the field forward. He is very talented, smart and productive and I anticipate he will make major contributions over the next few years. I am confident that Dr. Lei would be promoted to Associate Professor at my Institution."

Reviewer F: "His list of invited talks at meetings and departmental seminars is remarkable for a junior faculty member and accurately reflects the esteem with which [he] is held by the scientific community...Dr. Ming Lei is an extraordinarily talented scientist and a rising star in telomere biology. He has established a strong track record of accomplishment in securing extramural funding for his research program and his laboratory has made novel and important discoveries that have significantly advanced the field."

Reviewer G: "Ming is simply an outstanding early-career researcher, who has clearly already established him self [sic] as an internationally recognized, well funded, and highly productive investigator...All indications are that he will remain a leader in his chose fields and that he will significantly impact science and medicine throughout his career...His reputation of being creative and highly productive has earned him a great deal of respect and admiration both locally and internationally. It is also clear that he has been able to attract and train high quality researchers. I think that you are fortunate to have him on your faculty and I enthusiastically recommend his promotion."

Summary of Recommendation:

Dr. Lei has made excellent progress as an independent investigator and is a superb academic citizen. He has performed well in the areas of research, teaching, and service. In recognition of his accomplishments, I enthusiastically recommend that Dr. Ming Lei be promoted to associate professor, with tenure, in the Department of Biological Chemistry.

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

May 2010