PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PATHOLOGY

Approved by the Regents May 21, 2015

David B. Lombard, M.D., Ph.D., assistant professor of pathology, Department of Pathology, Medical School, is recommended for promotion to associate professor of pathology, with tenure, Department of Pathology, Medical School [also being promotion to research associate professor, Institute of Gerontology].

Academic Degrees:

M.D.	2001	Harvard Medical School
Ph.D.	2000	Massachusetts Institute of Technology
B.A.	1992	Harvard College

Professional Record:

2008-present	Assistant Professor of Pathology, University of Michigan
2008-present	Research Assistant Professor, Institute of Gerontology, University of Michigan
2004-2008	Instructor, Department of Pathology, Harvard Medical School

Summary of Evaluation:

Teaching: Since his appointment as an assistant professor in 2008, Dr. Lombard has had a significant teaching role. He has taught graduate students in Pathology 581 where he has been the course director for the past two years, responsible for recruiting instructors, organizing and grading examinations, and giving two to five lectures per year. He is also responsible for presenting one module of one hour lecture and three hours of discussion in Pathology 582. In the laboratory, he has instructed five Ph.D. students, five postdoctoral fellows, medical students in summer research, and also a pathology resident as well as undergraduate students. He has also been involved in teaching pathology residents during diagnostic work in the Molecular Diagnostics Laboratory. For these efforts he has received excellent reviews from the residents. He has also been on numerous student dissertation committees and student seminar series. Thus, it is apparent that Dr. Lombard not only has a significant commitment to education, and he is also regarded as a superb teacher.

Research: Dr. Lombard's research has centered on molecular mechanisms of aging and longevity. His laboratory has focused on the sirtuin family of proteins most of which are deacetylases. His laboratory discovered SIRT5 plays a key role in modulating aspects of mitochondrial energetics. His laboratory discovered that the SIRT5 genetic locus is amplified in 30% of ovarian carcinomas and that knockdown of SIRT5 is important in reversing two metabolic hallmarks of tumor cells. He has also studied SIRT6 and discovered that this is important in suppressing mitochondrial respiration as well as suppressing Myc transcriptional output. He found that various cell types lacking SIRT6 including human intestinal epithelial

cells, have an increased disposition to develop aneuploidy, a feature of many human tumors. His work has been constantly funded. Currently he is the principal investigator of an R01 and an R21 from the NIH as well as a grant from the University of Michigan Cancer Research Committee. He is also a co-principal investigator on three other grants. His work has been recognized by his receiving an Ellison Medical Foundation New Scholar Award in Aging, an American Federation for Aging Research Award and a Pardee Foundation Award. He has also been invited to present his work at 17 venues through June 2014 at places such as a Keystone Meeting, the National Cancer Institute, the Pennington Institute, and the Ellison Foundation at Cold Spring Harbor. Furthermore, he has four additional invitations to present in 2015. His work has been published in high impact journals including *Nature*, *Cell Metabolism*, *PNAS*, *Nature Medicine* and the *Journal of Biological Chemistry*.

Recent and Significant Publications:

Yang B, Zwaans BM, Eckersdorff M, Lombard DB: The sirtuin SIRT6 deacetylates H3 K56Ac in vivo to promote genomic stability. *Cell Cycle* 8:2662-2663, 2009.

Chiang WC, Tishkoff D, Yang B, Wilson-Grady J, Yu X, Mazer T, Eckersdorff M, Gygi SP, Lombard DB, Hsu AL: C. elegans SIRT6/7 Homolog SIR-2.4 Promotes DAF-16 relocalization and function during stress. *PLoS Genet* 8:e1002948, 2012.

Sebastian C, Zwaans BM, Silberman DM, Gymrek M, Goren A, Zhong L, Ram O, Truelove J, Guimaraes AR, Toiber D, Cosentino C, Greenson JK, MacDonald AI, McGlynn L, Maxwell F, Edwards J, Giacosa S, Guccione E, Weissleder R, Bernstein BE, Regev A, Shiels PG, Lombard DB, Mostoslavsky R: The histone deacetylase SIRT6 is a tumor suppressor that controls cancer metabolism. *Cell* 151:1185-1199, 2012.

Park J, Chen Y, Tishkoff DX, Peng C, Tan M, Dai L, Xie Z, Zhang Y, Zwaans BM, Skinner ME, Lombard DB, Zhao Y: SIRT5-Mediated Lysine desuccinylation impacts diverse metabolic pathways. *Mol Cell* 50:919-930, 2013.

Giblin W, Skinner ME, Lombard DB: Sirtuins: guardians of mammalian healthspan TIG 30: 271-286, 2014.

Service: Dr. Lombard has made numerous contributions to his profession. He has been a member of the editorial board of the *Journal of Clinical and Experimental Pathology*, a review editor for *Frontiers in Genetics of Aging*, the associate editor for *CardioRenal Medicine* and a member of the editorial board of *Cell Aging* as well as on the peer review board of *Molecular and Cellular Oncology*. He has also been an ad hoc reviewer for numerous other journals. In addition, he has been on two NIH special emphasis panels and on the study section of Cellular Mechanisms of Aging and Development. He has been a grant reviewer for several national and international organizations including the Wellcome Trust in the UK, the Israeli Science Foundation, the European Research Council and additional organizations in the Netherlands and Canada. At the University of Michigan, he is currently a member and chair of the Pathology 581 Steering Committee, a member of the Medical Student Research Committee, a member of the Biology of Aging T32 Steering Committee. Thus, he has demonstrated an important commitment to his profession and to his

institution. In addition, Dr. Lombard has regular rotations as a clinical pathologist in the Molecular Diagnostics Laboratory where he is involved in signing out complex molecular and genetic diagnostic cases. He has been involved in this activity since January 2010. He is regarded as having superb interpretive skills in this complex and highly relevant laboratory.

External Reviewers:

Reviewer A: "His most important and original work on SIRT6 as a PI stems from his determination in 2009 that it deacetylates acH3K56. While this work was published in Cell Cycle, which is not a high-impact journal, this paper has been highly cited…and led the way to exciting collaborative work showing that SIRT6 functions as a tumor suppressor. That paper, published in Cell, has garnered a similar number of citations since 2012, and was highlighted in numerous scientific highlights publications at the time….Dr. Lombard is an excellent scientist who has established himself at the center of the sirtuin/aging field."

Reviewer B: "…I believe that David has established a vigorous program at the juncture between metabolism, cancer and aging, and that he is recognized as an accomplished scientist in this field. I am looking forward to hearing about David's future and to great breakthrough discoveries from David in the near future."

Reviewer C: "Dr. Lombard's scholarship has had a large impact on the field if sirtuin biology, both in terms of research discoveries and in promoting rigorous thought….He has been a leader in the field at guiding thinking about sirtuin biology in the context of aging…He has already achieved international recognition for outstanding research on sirtuin biology, and I fully anticipate that the upward trajectory of his career will continue. His scientific contributions have been, and continue to be, important, influential, and accurate."

Reviewer D: "David is remarkable for his creative, enthusiastic, and thorough approaches to experimental science, and he has a talent for uncovering important new findings. Clearly, Dr. Lombard is a leader in his field, and he is likely to continue to make seminal research contributions."

Reviewer E: "He has made major contributions in the field of aging biology; his work on the regulation and function of sirtuins have had a major impact on our understanding of the molecular mechanisms that control cellular responses to dietary restriction and other manipulations that extent [sic] lifespan and improve age-related diseases."

Reviewer F: "...he has been invited to present his work at all the major meetings of his field, including Keystone Symposia and the regular Molecular Genetics of Aging Meetings at Cold Spring Harbor….I have to state that I have the highest regard for David as a scientist. I think his research is outstanding, and has had a major impact on the field."

Reviewer G: "That David's work has received much attention is evidenced by his many invitations to speak nationally and internationally and his authorship of multiple reviews/commentaries on his work and that of others."

Summary of Recommendation:

Dr. Lombard is an internationally renowned scientist who has made numerous contributions to the study of aging, with emphasis on evaluation of the genetics and biology of the sirtuin family of proteins. I am pleased to recommend David B. Lombard, M.D., Ph.D. for promotion to associate professor of pathology with tenure, Department of Pathology, Medical School.

James O. Woolliscroft

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

May 2015