

PROMOTION RECOMMENDATION  
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL  
DEPARTMENT OF INTERNAL MEDICINE

Lawrence B. Holzman, M.D., Associate Professor of Internal Medicine, with tenure, Department of Internal Medicine, Medical School, is recommended for promotion to Professor of Internal Medicine, with tenure, Department of Internal Medicine, Medical School.

Academic Degrees:

M.D.	1984	UMDNJ - New Jersey Medical School
B.A.	1980	University of Pennsylvania

Professional Record:

1998-Present	Associate Professor of Internal Medicine, University of Michigan
1994-1998	Assistant Professor of Internal Medicine, University of Michigan
1991-1994	Instructor, Department of Internal Medicine, University of Michigan
1989-1990	Lecturer, Department of Internal Medicine, University of Michigan

Summary of Evaluation:

Teaching: Dr. Holzman is an exceptional teacher and outstanding role model. He teaches renal fellows, internal medicine residents, and surgical residents on the transplant service and in the outpatient clinics. He teaches in the Medical School Renal Sequence for second-year medical students. He presents at grand rounds, nephrology clinical conferences, joint transplant conferences, and journal club meetings and regularly participates in the morning report for medical residents. Since 1998, he has mentored six fellows who now hold academic appointments in the U.S. and Germany. Dr. Holzman currently serves as a research mentor to multiple post-doctoral fellows and one nephrology fellow and he is the principal investigator for the Institutional Training Grant in Nephrology Research.

Research: Dr. Holzman's research is principally focused on two key areas: (1) He has become one of the preeminent researchers in the country in the areas of stress activated protein kinase signaling and the cell biology of the podocyte—the critical cell in the renal glomerulus that establishes the glomerular filtration barrier. Early during his independent career, he discovered a critical upstream protein in the stress activated protein kinase family, called DLK or MLK (Dual Leucine zipper Kinase or Mixed Lineage Kinase). His laboratory quickly became one of the leading laboratories in the field and his research led to important biochemical signaling discoveries, some of which have been paradigmatic for work in other areas. One example of this is the description of how DLK-dependent JNK activation is governed by interactions of scaffold protein JIP which was published in *European Molecular Biology Organization (EMBO) Journal* in 2001. (2) His other major area of research has been in the area of podocyte biology where he is clearly one of the leading investigators in the world. Dr. Holzman's contributions have been

manifold but he has probably had the most impact by developing a podocyte specific CRE recombinase mouse in 2003 that has allowed many investigators to develop podocyte specific gene targeted mice. His work on podocyte signaling and especially his recent discoveries on the role of the protocadherin FAT1 and its role in lamellipodial dynamics and planar cell polarity have been seminal. These FAT1 findings, which were published last Fall, also in *EMBO Journal*, helped establish and define the important role of this protein in many cell systems including podocytes. To further underscore his preeminence in the field of podocyte biology and glomerular diseases, he was called upon to organize a NIH Workshop on Glomerular Disease in January of 2005.

#### Recent and Significant Publications:

Moeller MJ, Soofi A, Watzel C, Kriz W, and Holzman LB: Protocadherin FAT1 binds Ena/VASP and is necessary for lamellipodial dynamics, cell polarization, and cell migration. *EMBO J* 23(19):3769-3779, 2004. Epub 2004 Sep 02.

Rakesh V, Wharram B, Kovari I, Riggs L, Nihalani D, Wiggins R, Killen P, Holzman LB: Fyn binds to and phosphorylates the slit diaphragm component Nephhrin. *J Biol Chem* 278(23):20716-20723, 2003. Epub 2003 Mar 31.

Nihalani D, Wong H, Holzman LB: Recruitment of JNK to JIP1 and JNK-dependent JIP1 phosphorylation regulates JNK module dynamics and activation. *J Biol Chem* 278(31):28694-28702, 2003. Epub 2003 May 19.

Moeller MJ, Sanden SK, Soofi A, Wiggins RC, Holzman LB: Two gene fragments that direct podocyte-specific expression in transgenic mice. *J Am Soc Nephrol* 13(6):1561-1567, 2002.

Nihalani D, Meyer D, Pajni S, Holzman LB: Mixed lineage kinase-dependent JNK activation is governed by interactions of scaffold protein JIP with MAPK module components. *EMBO J* 20(13):3447-3458, 2001.

Service: Since 2003, Dr. Holzman has led the Nephrology Training Program at the University of Michigan. He has recently successfully engineered the continued funding of the institutional NIH training grant in nephrology, and has led the program to institute many needed educational reforms. Dr. Holzman has also served on multiple committees for the American Society of Nephrology, was a member of the editorial board of the top nephrology journal from 2001-2004 and has participated in several NIH study sections. He is now a regular member of the Pathobiology of Kidney Disease Study Section at the NIH. His efforts have extended into the community as well. He was a co-founder and now the chair of the scientific advisory board of the NephCure Foundation, a charitable organization committed to curing glomerular diseases.

#### External Review:

Reviewer A: "Dr. Holzman is one of the most talented investigators currently active in the field of kidney research....Dr. Holzman has been a consistently productive investigator, publishing in high impact journals."

Reviewer B: "...Dr. Holzman is an accomplished and successful investigator and a leader in his field. He has achieved national and international recognition as an independent investigator and is a highly respected member of the international scientific community. This recognition derives directly from his original scientific publications that have appeared in leading scientific journals, and has been recognized by continuous extramural funding..."

Reviewer C: "Dr. Lawrence Holzman has shown his strength as an independent investigator in a very important area of kidney research. I am convinced that he will continue to make significant contributions to the field..."

Reviewer D: "Dr. Holzman is clearly one of the leaders in research on the glomerular podocyte and glomerular diseases, and he has made a number of original contributions to the field."

Reviewer E: "The podocyte field is a fast growing area that is extremely competitive. Larry is one of the most visible investigators in the area...Larry Holzman fulfills all the criteria of the triple threat. I believe him to be an excellent scientist, teacher and clinician."

Reviewer F: "Larry is a world leader in the field of kidney research...He is the classic triple threat, being a distinguished teacher, clinician and researcher, who also has remarkable administrative, leadership and mentoring abilities. I have been told by several medical residents and fellows that he is also an outstanding teacher, and he is an excellent ambassador for nephrology internationally, as judged by the number of successful postdocs he has trained in his laboratory."

Reviewer G: "Dr. Holzman has become one of the nation's experts in podocyte biology."

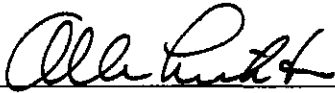
Reviewer H: "...Larry Holzman is an insightful, productive and independent physician-scientist. He is asking important research questions, both about basic signal transduction mechanisms and about pathways regulating glomerular filtration barrier function. This work may lead to the development of novel therapies for a group of diseases associated with great human and economic costs."

Reviewer I: "I regard Doctor Holzman as one of the preeminent investigators in the areas of podocyte biology and signal transduction in general, and as the foremost authority, on a national and international level, in signal transduction as it pertains to the podocyte. Doctor Holzman has made seminal and highly important insights in our current understanding of the podocyte that, in aggregate, speak directly to the physiology of this cell in the healthy kidney, and to the pathobiology of the podocyte in the initiation and evolution of kidney disease."

#### Summary of Recommendation:

In summary, Dr. Holzman is a leader in the investigation of podocyte biology and protein kinase signaling and has been called upon by the renal research community to lead and organize conferences and workshops in this growing research arena. In addition, he continues to play

critical roles in the educational programs of the division and department, primarily by leading the renal nephrology fellowship training program and through his individual teaching efforts. He serves the greater scientific community and the community of patients and their families in many ways. He is a bright and gifted scientist and a wonderful and supportive colleague who will almost certainly make many more important contributions to the fields of podocyte biology and signaling through his individual program and through his collegial and collaborative efforts. I enthusiastically support his promotion to Professor of Internal Medicine in the Medical School.



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Allen S. Lichter, M.D., Dean  
*Newman Family Professor  
of Radiation Oncology*

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