

PROMOTION RECOMMENDATION  
 UNIVERSITY OF MICHIGAN MEDICAL SCHOOL  
 DEPARTMENT OF INTERNAL MEDICINE  
 DEPARTMENT OF HUMAN GENETICS  
 UNIVERSITY OF MICHIGAN SCHOOL OF PUBLIC HEALTH  
 DEPARTMENT OF EPIDEMIOLOGY

Stephen B. Gruber, M.D., Ph.D., Associate Professor of Internal Medicine, with tenure, Department of Internal Medicine, and Associate Professor of Human Genetics, without tenure, Department of Human Genetic, Medical School, and Associate Professor of Epidemiology, without tenure, Department of Epidemiology, School of Public Health, is recommended for promotion to Professor of Internal Medicine, with tenure, Department of Internal Medicine, and Professor of Human Genetics, without tenure, Department of Human Genetics, Medical School, and Professor of Epidemiology, without tenure, Department of Epidemiology, School of Public Health.

Academic Degrees:

M.D.	1992	University of Pennsylvania
Ph.D.	1988	Yale University
M.A.	1986	Yale University
B.A.	1984	University of Pennsylvania

Professional Record:

2004-Present	Associate Professor of Internal Medicine, Human Genetics, and Epidemiology, University of Michigan
2002-2004	Assistant Professor of Human Genetics, University of Michigan
1997-2004	Assistant Professor of Internal Medicine and Epidemiology, University of Michigan

Summary of Evaluation:

Teaching: Teaching has been and remains an important aspect of Dr. Gruber's academic life. He consistently invests substantial time and energy to: 1) formal teaching in the Medical School and the School of Public Health, 2) clinical teaching to residents, fellows, and allied health professionals, and 3) individual mentoring of graduate students. An assessment of the "Quality of Teaching Provided" by each faculty has consistently rated Dr. Gruber at 9.0 or higher. This has placed him among the top three faculty that interact with our fellows each year over the past several years. His didactic teaching in classroom effectiveness rates him "outstanding" in all categories evaluated (i.e., organization, quality, instructional materials used, practical value, and improvement of understanding).

Within the Medical School, Dr. Gruber served on the Curriculum Committee and helped design the Patients and Populations sequence for first-year medical students. He also was Co-Director of the Medical Decision Making component of this sequence. Dr. Gruber devotes

approximately 25 hours per year to the Patients and Populations sequence, providing all the lectures introducing biostatistics and epidemiology as well as didactic teaching for the genetics component. He also leads small workgroups in the Medical Decision Making sequence for upper-class medical students. In the School of Public Health, Dr. Gruber has taught Epidemiology classes each year (except 1997, when he was on sabbatical).

Dr. Gruber has served on the American Society of Clinical Oncology (ASCO) Education Committee for two separate terms and served on the editorial board and as author of the ASCO Cancer Genetics Curriculum. As the Director of the Cancer Genetics Clinic, he is also responsible for curriculum development and implementation for rotating medical students, house-officers, fellows, and genetic counseling students. With joint appointments in Epidemiology and Human Genetics, he has also had the opportunity to chair dissertation committees for 17 Ph.D. students as well as supervising the master's thesis for 28 graduate students.

Research: Since Dr. Gruber's second year on the faculty at the University of Michigan, he has had continuous NIH R01 funding and has organized and led one of the world's largest case-control studies of colorectal cancer together with an international group of collaborators. His research has led to several important insights including the seminal demonstration that long-term use of statins is associated with a reduced risk of colorectal cancer. This major study was subsequently published in the *New England Journal of Medicine* in 2005. In further advances related to colorectal cancer, Dr. Gruber established new roles for CDX2 and chromosomal variations in determining patient risk (*Cancer Research*, 2005; *Cancer Biology Therapy*, 2007).

Dr. Gruber also serves as the Michigan principal investigator for the NCI funded Genes, Environment and Melanoma study and has recruited more than 535 melanoma patients for this international collaboration. Most recently, his group delineated crucial signaling pathways that are affected by activating mutations in BRAF (*Melanoma Research*, 2006). Finally, in a recent, but equally important new line of studies, a new breast cancer susceptibility gene has been discovered by his group (*Nature Genetics*, 2007).

In recognition of his international stature in the field, Dr. Gruber was named the H. Marvin Pollard Professor of Internal Medicine (2006) and appointed as the Director of the new Clinical Cancer Genetics Program at the University (2006).

#### Recent and Significant Publications:

Gruber SB, Moreno V, Rozek LS, Rennert HS, Lejbkowitz F, Bonner JD, Greenson JK, Giordano TJ, Fearon ER, Rennert G: Genetic Variation in 8q24 Associated with Risk of Colorectal Cancer. *Cancer Biol Ther* 2007; 6(7):e1-e5. (epublication ahead of print), July 6, 2007.

Pujana, MA, Han JDJ, Starita LM, Stevens KN, Tewari M, Ahn JS, Rennert G, Moreno V, Kirchhoff T, Gold B, Assmann V, ElShamy WM, Rual JF, Levine D, Rozek LS, Gelman RS, Gunsalus KC, Greenberg RA, Sobhian B, Bertin N, Venkatesan K, Ayivi-Guedehoussou N, Solé X, Hernández P, Lázaro C, Nathanson KL, Weber BL, Cusick ME, Hill DE, Offit K, Livingston DM, Gruber SB [co-senior/corresponding author], Parvin JD, Vidal M: Network modeling links breast cancer susceptibility and centrosome dysfunction. (in press) *Nature Genetics* 2007.

Poynter JN, Elder JT, Fullen DR, Nair RP, Soengas MS, Johnson TM, Redman B, Thomas NE, Gruber SB: BRAF and NRAS mutations in melanoma and melanocytic nevi. *Melanoma Res* 16:267-73, 2006.

Poynter JN, Gruber SB [corresponding author], Higgins PDR, Almog R, Bonner JD, Rennert HS, Low M, Greenson JK, Rennert G: Statins and the risk of colorectal cancer. *N Engl J Med* 352:2184-92, 2005.

Rozek LS, Lipkin SM, Fearon ER, Hanash S, Giordano TJ, Kuick R, Misek DE, Taylor JMG, Greenson JK, Rennert G, Gruber SB: *CDX2* polymorphisms, RNA expression, and risk of colorectal cancer. *Cancer Research* 65:5488-92, 2005.

Service: Currently, Dr. Gruber is a full-member of the Epidemiology of Cancer Study Section at the National Cancer Institute. He devotes considerable time to the peer review process, and has served on multiple national and international ad-hoc study sections. Dr. Gruber has served on the editorial boards of *Clinical Cancer Research* and *Cancer Epidemiology Biomarkers and Prevention*. He has actively served the American Society of Clinical Oncology in several capacities, including membership on the Tumor Biology and Human Genetics Subcommittee, the Cancer Education Committee, and the Genetic Testing Statement Working group. He is also chair of the Colorectal Family Registry Advisory Panel for the National Cancer Institute. Internationally, has served on faculty panels in Israel, Spain, and Uruguay and has lectured in Australia. In 2004-2005, Dr. Gruber was appointed Visiting Scientist at the Catalan Institute of Oncology in Barcelona, Spain, where he completed a highly productive sabbatical.

Professional Work: Dr. Gruber is the Director of the Cancer Genetics Clinic at the University of Michigan, which is one of the busiest and most respected cancer genetics clinics in the United States. His formal training in cancer genetics as an oncology fellow at Johns Hopkins, followed by a second residency in Medical Genetics at the University of Michigan, allows him to provide expert clinical care from an informed oncologic and genetics perspective. He has a busy consultative practice, seeing 236 new consults and 53 self-referred new patients last year (out of 445 total patients). More than 47% of new patient referrals live outside the local tri-county area, and almost 9% are from outside the State. He has been invited to give clinical grand rounds locally, nationally and internationally, and he serves on the National Cancer Institute's expert clinical panel for Colorectal Cancer Genetics. Dr. Gruber was also a founding member of the National Comprehensive Cancer Network's panel for Colorectal Cancer Screening.

External Review:

Reviewer A: "Dr. Gruber has contributed substantially to what we know about the genetic and environmental etiology of several cancers...These are important contributions, and are likely to stand the test of time....Dr. Gruber has what I would regard as a substantial presence on a number of committees and organizations relevant to his expertise..."

Reviewer B: "Dr. Gruber has made many solid observations utilizing his knowledge of molecular genetics to understand risk of solid tumor development in patients....In addition to his

own work, he has been a successful mentor for many doctoral trainees and graduate students... Dr. Gruber has established both a national and international reputation for excellence."

Reviewer C: "In my opinion, Steve is a first-rate physician scientist. I would place him in the top ten percent of physician scientists doing research in cancer worldwide."

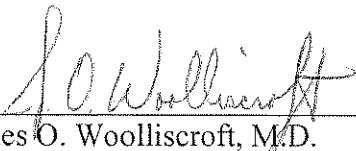
Reviewer D: "In sum, he is an extraordinary cancer genetics investigator, certainly one of the very best (perhaps THE best) among his peers. And if you think it is easy to find investigators with this amazing set of skills, just try to hire another one like him!...Michigan is exceedingly fortunate to have Dr. Gruber on its faculty. I cannot envision anyone more qualified for promotion to the rank of professor."

Reviewer E: "He is highly respected by his peers and viewed as a leader by more senior scientists, including myself...He is clearly a widely sought after collaborator. His best known work has implicated statins in colorectal cancer risk and these observations have received intense interest."

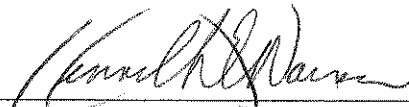
Reviewer F: "Dr. Gruber's educational pathway has situated him uniquely to contribute to studies of the hereditary cancers with one foot firmly planted in the clinical realm and the other in that of molecular genetics."

Summary of Recommendation:

Dr. Stephen Gruber is a highly valued physician-scientist in the fields of cancer genetics, epidemiology and biostatistics. He embodies the finest principles of academic medicine and is a highly gifted and productive investigator who has achieved international recognition for his contributions to the field of cancer genetics. We are delighted to enthusiastically recommend Dr. Stephen B. Gruber for promotion to Professor in the Departments of Internal Medicine (with tenure), Epidemiology, and Human Genetics (without tenure) at the University of Michigan.



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



Kenneth E. Warner, Ph.D.  
Dean, School of Public Health

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