

PROMOTION RECOMMENDATION  
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL  
DEPARTMENT OF INTERNAL MEDICINE

Margaret R. Gyetko, 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.	1981	Michigan State University
B.A.	1975	University of Michigan

Professional Record:

1997-Present	Associate Professor of Internal Medicine, University of Michigan
1991-1997	Assistant Professor of Internal Medicine, University of Michigan
1988-1991	Instructor of Internal Medicine, University of Michigan

Summary of Evaluation:

Teaching: Dr. Gyetko has been a dedicated teacher of housestaff and students throughout her medical career. Her appointment as Chief Resident at the University of Michigan is evidence of her long-standing involvement in medical education. Dr. Gyetko has been an inpatient attending physician for two to three months per year, spending approximately 225 hours per year in the formal instruction of third- and fourth-year medical students assigned to Internal Medicine. Dr. Gyetko provides formal instruction in differential diagnosis, pathogenesis of disease and treatment of disease in the context of bedside rounds, case presentation, and formal lectures. In addition, she serves as an attending physician in the bronchoscopy suite at the VA Ann Arbor Healthcare System. Dr. Gyetko is an articulate teacher of third- and fourth-year medical students and Internal Medicine housestaff. Dr. Gyetko has served as the Assistant Chief of Medicine at the Ann Arbor VA since 1996. This role is largely a teaching and mentoring role; Dr. Gyetko has participated extensively in morning report, intern conferences, and noon conferences. She provides guidance and mentoring in more informal settings. Dr. Gyetko has mentored several senior medical residents in senior research projects within her laboratory. This role as Assistant Chief of Medicine is particularly important in regards to the mentoring of women students and trainees. Her presence as a senior faculty woman who actively pursues research and is in a position of leadership provides an invaluable role model for women students and trainees who desire a career in academic medicine. Finally, Dr. Gyetko participates as a faculty member in the graduate program for immunology. Dr. Gyetko has distinguished herself in educational roles involving the entire gamut of students at the University of Michigan.

Research: Dr. Gyetko has investigated pulmonary immune and inflammatory responses throughout her career. The primary focus of her research has been the role of the urokinase (uPA)/urokinase receptor (uPAR) system in the regulation of these host responses. Dr. Gyetko

has made major contributions to our understanding of cellular recruitment, cellular proliferation and differentiation, and the initiation of effector mechanisms in inflammatory cells. Dr. Gyetko's work has unambiguously demonstrated crucial individual roles for urokinase and for its cellular receptor. Furthermore, her work has challenged two prevailing paradigms. First, she demonstrated that the biological effects of uPA are not limited to its known ability to mediate pericellular proteolysis, but extend to cellular signaling and cell activation events. Second, she demonstrated that the effect of the urokinase receptor is not always ligand dependent. Dr. Gyetko has made three seminal observations which led to a paradigm shift in our understanding of the uPA/uPAR system. She was the first to report a requirement for uPAR during cellular recruitment *in vivo* in response to a clinically relevant pathogen. Dr. Gyetko extended these findings by being the first to demonstrate that uPAR mediated signals were required for lymphocyte recruitment to antigen inflamed lungs. Second, Dr. Gyetko demonstrated that uPA was importantly involved in T cell activation and differentiation into cytokine producing effector cells. Third, Dr. Gyetko demonstrated that both urokinase and urokinase receptor are required for full expression of neutrophil antimicrobial activation.

Dr. Gyetko has funded her research throughout her appointment at the University of Michigan. She was funded by a NIH RO1 from 2000-2004. She has been funded by a Merit Review Grant throughout her career at the University of Michigan and is presently the recipient of a Merit Review Grant (The Role of Urokinase in Lung T Lymphocyte Responses, 2006-2010). Dr. Gyetko is a valued co-investigator; she is a co-investigator on a NIH RO1. Dr. Gyetko served as a chairperson of the NIH NHLBI ARDS network review committee in 2000 and served on an NIH NHLBI program project grant review committee in 1999. She served as a Merit Review ad hoc reviewer from 1994-2000.

#### Recent and Significant Publications:

Gyetko MR, Sud S, Chensue SW: Urokinase-deficient mice fail to generate a type 2 immune response following schistosomal antigen challenge. *Infection & Immunity* 72(1):461-467, 2004.

Gyetko MR, Aizenberg D, Mayo-Bond L: Urokinase-deficient and urokinase receptor-deficient mice have impaired neutrophil antimicrobial activation *in vitro*. *Journal of Leukocyte Biology* 76(3):648-656, 2004.

Gyetko MR, Sud S, Chen GH, Fuller JA, Chensue SW, Toews GB: Urokinase-type plasminogen activator is required for the generation of a type 1 immune response to pulmonary *Cryptococcus neoformans* infection. *Journal of Immunology* 168(2):801-809, 2002.

Gyetko MR, Sud S, Sonstein J, Polak T, Sud A, Curtis JL: Antigen-driven lymphocyte recruitment to the lung is diminished in the absence of urokinase-type plasminogen activator (uPA) receptor, but is independent of uPA. *Journal of Immunology* 167(10):5539-5542, 2001.

Gyetko MR, Sud S, Kendall T, Fuller JA, Newstead MW, Standiford TJ: Urokinase receptor-deficient mice have impaired neutrophil recruitment in response to pulmonary *Pseudomonas aeruginosa* infection. *Journal of Immunology* 165(3):1513-1519, 2000.

Service: Dr. Gyetko has provided substantial service to the University of Michigan. She has been the Associate Chair for Faculty Affairs for the Department of Internal Medicine from 2000 to the present. Dr. Gyetko has developed a comprehensive system for annual evaluation and feedback on academic progress and performance. Academic performance is formally evaluated annually for instructional track faculty (Assistant and Associate Professor) by the Department Advisory Committee for Promotion and Tenure. This committee provides senior peer evaluation and feedback to faculty members during these critical years of career development. This program is of major importance since it results in improved faculty understanding of the promotion and tenure process at the University of Michigan. Dr. Gyetko served as the chair of the Task Force to Evaluate the Instructional Track. This work led to service for the past two years at the University level on the Committee to Consider a More Flexible Tenure Probationary Period. Dr. Gyetko also served on the University Gender in Science and Engineering Committee to address potential policy changes to make the University of Michigan more inclusive of women.

Professional Work: Dr. Gyetko is an accomplished clinician. She serves as an attending physician in the pulmonary clinic at the Ann Arbor Veteran's Affairs Hospital for one afternoon each week. Additionally, she serves as an attending physician on the inpatient services for the Division of Pulmonary and Critical Care Medicine for one month each year and as an attending physician in the bronchoscopy suite. She is skilled in the care of patients with acute and chronic lung injury and in the care of patients who are critically ill.

External Review:

Reviewer A: "...Dr. Gyetko is known by her peers as someone who consistently does high quality research in a sincere effort to understand the basis of human disease processes with the goal of profoundly influencing patient therapy. She is clearly someone who takes all of her responsibilities seriously and is an outstanding citizen in the academic medical enterprise. Hence, she is seen as being one of those few individuals that can still be a 'triple threat', and someone who contributes to the greater good both by her leadership activities, and mentoring of younger faculty and students."

Reviewer B: "...she is well respected nationally as a balanced, critical thinker with excellent leadership skills....Unquestionably, Dr. Gyetko has developed a national reputation based upon her scientific contributions and knowledge....Her continuing scientific contributions and her multi-faceted local and national roles make her an extremely valuable faculty member."

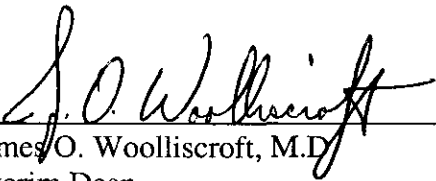
Reviewer C: "I would describe Dr. Gyetko's scholarly and professional niche as outstanding....Her observations may readily translate into the management of patients afflicted with pulmonary immune disorders or interstitial lung disease. Accordingly, Dr. Gyetko's contributions are highly significant."

Reviewer D: "Nationally and internationally, Dr. Gyetko is recognized as the consummate team player....She is outstanding in clinical, investigative and administrative work. I have personally observed her leadership skills. It is noteworthy that she enhances any program with her participation."

Reviewer E: "...I would say that Dr. Gyetko qualifies for promotion to professor based on her leadership abilities and responsibilities, her national reputation based on involvement on NIH and society study sections and her presentations at national meetings, her continuously funded research program and the quality of her peer-reviewed publications. She also makes substantial contributions to teaching and service related activities."

Summary of Recommendation:

Dr. Gyetko is a distinguished physician scientist whose work is held in the highest regard. We are, therefore, delighted to recommend Dr. Gyetko for promotion to Professor of Internal Medicine in the Medical School.



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

May 2007