

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PATHOLOGY

Celina G. Kleer, M.D., associate professor of pathology, with tenure, Department of Pathology, Medical School, is recommended for promotion to professor of pathology, with tenure, Department of Pathology, Medical School.

Academic Degrees:

M.D.	1993	University of Buenos Aires, Argentina
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Professional Record:

2005-present	Associate Professor of Pathology, University of Michigan
1999-2005	Assistant Professor of Pathology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Kleer has been involved in numerous teaching activities. She mentors medical students during their senior elective in pathology. She also mentors pathology residents rotating through the Breast Surgical Pathology Diagnostic Service. She also gives regular lectures and consultation case conferences to the residents. She is head of the Breast Pathology Fellowship Program where she is responsible for scheduling and for the curriculum for the breast pathology fellow, a one-year fellowship. In her laboratory, she has mentored undergraduate students, graduate students, and postdoctoral fellows, continually. She has also been a member of several thesis committees. A number of her research trainees come from institutions in other parts of the world. At the national level, she has been teaching the breast pathology didactic lecture, for the Resident Review Course for the American Society for Clinical Pathology, and her ratings have always been in the top 25% of all the lecturers in that course, many of whom are well-known subspecialists in pathology nationally. She has also lectured at the Advanced Molecular Pathology Conference of the United States and Canadian Academy of Pathology and for the American Society for Investigative Pathology. Dr. Kleer has made a profound commitment to the educational mission of the Department of Pathology, and she has been successful in this regard.

Research: Dr. Kleer has been involved in translational studies in breast cancer. Her laboratory identified that EZH2, a repressor of gene transcription, is able to transform mammary epithelial cells. She found that this marker can predict survival in patients with breast cancer. She recently developed a mouse model of EZH2 overexpression targeted to the mammary gland and found that EZH2 regulates the tumor suppressor BRCA1. Her laboratory has identified a novel tumor suppressor gene from inflammatory breast cancer, CCN6, also called WISP3, and she discovered its mechanism of function. Her work has continuously been funded from external sources. Currently, she holds an R01 for the study of the role of CCN6 in the progression in metastasis of breast cancer, and another R01 for the role of EZH2 in breast cancer progression. She is the author or co-author of 45 publications since her promotion to associate professor, most of which are in high-quality, peer-reviewed journals, both in cancer research and in pathology, including *Cancer*, *Modern Pathology*, *Clinical Cancer Research*, *Human Pathology*, *Oncogene*, *Journal of Surgical Oncology*, and the

American Journal of Surgical Pathology. In addition to her scientific publications, she is also a co-author on multiple clinical studies, working in conjunction with surgeons, oncologists and radiologists involved with clinical breast cancer care and diagnosis. She has been invited to present her work at numerous venues in the United States and abroad, including the Mayo Clinic, the Burroughs Welcome Fund in North Carolina, Georgia Tech University, Breast Cancer Conference in Argentina, the University of Massachusetts, M.D. Anderson Cancer Center, University of Pennsylvania, and Memorial Sloan Kettering Cancer Center.

Recent and Significant Publications:

Huang W, Gonzalez ME, Toy K, Banerjee M and Kleer CG: Blockade of CCN6 (WISP3) activated growth factor-independent survival and resistance to anoikis in human mammary epithelial cells. *Cancer Res* 70:3340-3350, 2010.

Gonzalez ME, Li X, Toy K, DuPrie M, Banerjee M, Ljungman M, Merajver SD and Kleer CG: Downregulation of Enhancer of Zeste-2 decreases growth of estrogen receptor negative invasive breast carcinoma and requires BRCA1. *Oncogene* 28: 843-853, 2009.

Li X, Gonzalez, ME, Toy K, Filzen T, Merajver SD and Kleer CG: Targeted overexpression of EZH2 in the mammary gland disrupts ductal morphogenesis and causes epithelial hyperplasia. *Am J Pathol* 175:1246-1254, 2009.

Hayes MJ, Thomas D, Emmons (Witkiewicz) A, Giordano TJ and Kleer CG: Genetic changes of Wnt pathway genes are common events in metaplastic carcinomas of the breast. *Clinical Cancer Research* 14:4038-4044, 2008.

Huang W, Zhang Y, Varambally S, Chinnaiyan AM, Banerjee M, Merajver SD and Kleer CG: Inhibition of CCN6 (WISP3) down-regulates E-cadherin in the breast epithelium through induction of Snail and ZEB1. *American Journal of Pathology* 172:893-904, 2008.

Service: Dr. Kleer has made significant contributions to the University of Michigan and to the profession of pathology. Locally, she has been a member of the Breast Care Center Task Force, a member of the Steering Committee for the Cancer and Aging Initiative, a member of the Admissions Committee for the Medical School and the Admissions Committee for the Cellular and Molecular Pathology Graduate Program and the East Ann Arbor Planning Committee, to name a few. Nationally, she has been a member of the College of American Pathologists Breast Cancer Panel and a member of the Education Committee of the United States and Canadian Academy of Pathology, the latter being a very prestigious appointment. Since 2007, she has been a member of the editorial board of Human Pathology, and since 2009 she has been a member of the editorial board of the *American Journal of Pathology*. She is currently associate editor of *BMC Cancer*. She has also been an ad hoc reviewer for numerous journals and for NIH grants. She is now a permanent member of the NIH Tumor Progression and Metastasis Study Section. Dr. Kleer is the director of the Breast Pathology Service, a subspecialty diagnostic service that began in 2004. She handles approximately 20% of the cases from the University Hospital and clinics and she is also the primary consultant for difficult breast pathology cases sent to her from pathologists outside the institution. She is regarded as a superb diagnostician. She interacts constantly with the clinical and diagnostic multidisciplinary team involved in breast diseases, especially breast cancer, and she is considered to be a wonderful collaborator.

External Review:

Reviewer A: "The impact of her work has been highlighted by featured articles and journal cover selections, as well as book chapter requests, invitations to speak at conferences and meetings, and national and international invited seminars. Her work is novel and timely, and well-funded...I would easily rank Dr. Kleer in the top 5% of her peers."

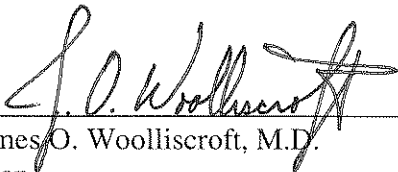
Reviewer B: "Her studies are very important because they may point to the regulation of CCN6 expression as a therapeutic approach for breast cancer...Dr. Kleer's work on CCN6 has been pioneering...her work is consistently well regarded in the CCN community."

Reviewer C: "Dr. Kleer is certainly an important contributor to organizational services in pathology ranging from service on the Education Committee of the USCAP to her services on an NIH study section. She has also been on the Editorial Board of *Human Pathology*...she has shown a dedication to education..."

Reviewer D: "...her colleagues regard her as both an exceptional pathologist and an outstanding translational scientist, who brought some very innovative and original discoveries to the breast cancer clinical and research community...I can safely say that she rises above most that could be compared to her at this stage of her career."

Reviewer E: "Dr. Kleer is a highly accomplished breast cancer translational researcher with an international reputation for her work in WISP3 signaling. Dr. Kleer's exceptional scientific productivity, record of R01 research funding, and the translational significance and innovation of her work makes her in the top 1% of investigators in her field. Dr. Kleer has an exceptional record of mentorship and committee service."

Summary of Recommendation: Dr. Celina Kleer is a highly accomplished translational scientist in breast cancer work who has made seminal discoveries including the role of EZH2 in the growth of estrogen receptor negative breast cancer and intraductal hyperplasia, and the role of CCN6 as important in the development of invasion in breast cancer. She is also an accomplished diagnostician who handles a large part of the breast pathology load in her department. She is an effective educator for medical students, residents, fellows and graduate students, and she has demonstrated service to her pathology community, from local to national organizations. I am pleased to recommend Dr. Celina G. Kleer for promotion to professor of pathology, with tenure, Department of Pathology, Medical School.



James O. Woolliscroft, M.D.
Dean

Lyle C. Roll Professor of Medicine

May 2011