

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN MEDICAL SCHOOL
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

J. Rebecca Liu, M.D., Assistant Professor of Obstetrics and Gynecology, Department of Obstetrics and Gynecology, Medical School, is recommended for promotion to Associate Professor of Obstetrics and Gynecology, with tenure, Department of Obstetrics and Gynecology, Medical School.

Academic Degrees:

M.D.	1991	Vanderbilt University
A.B.	1987	Princeton University

Professional Record:

2001-present	Assistant Professor of Obstetrics and Gynecology, University of Michigan
1999-2001	Lecturer, Department of Obstetrics and Gynecology, University of Michigan
1996-1999	Fellow, Gynecologic Oncology, Department of Obstetrics and Gynecology, University of Michigan
1995-1996	Clinical Instructor, Department of Obstetrics and Gynecology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Liu is actively involved in the educational activities of the Division of Gynecologic Oncology and the Department and she has established an excellent reputation as a teacher at the University of Michigan. She provides didactic and practical instruction on cancer biology, clinical oncology and surgical techniques for medical students, house officers and fellows from several training programs. Dr. Liu's teaching evaluations are consistently excellent. She has served as research advisor, career mentor and role-model for more than 25 trainees, including undergraduate students, residents, and gynecologic oncology fellows. Most of the trainees who have worked in her laboratory have presented their work at national meetings and co-authored papers. Impressively, six of these individuals received awards for their work from the American College of Obstetricians and Gynecologists or the American Association of Cancer Research. A number of Dr. Liu's mentees have gone on to pursue graduate degrees in cancer biology and medicine, and several have followed her lead to pursue a career in obstetrics/gynecology and/or gynecologic oncology. Her reputation as an exceptional mentor for undergraduate students has resulted in invitations to speak regularly in the "Professional Autobiography" lecture series through the Health Sciences Scholars Program at the University of Michigan. Her role as a mentor has been recognized on the international level as well; and she has conducted several workshops for gynecologic oncology fellows and junior faculty at the International Society of Gynecologic Cancer meeting regarding topics such as "Finding the

Right Mentor,” and “Pre-Clinical Research: Establishing a Foundation.” Dr. Liu lectures regularly in the Ob/Gyn Core Curriculum for both the University of Michigan, and St. Joseph Mercy Hospital residency programs in areas that include tumor biology, and the diagnosis and management of gynecologic malignancies.

Research: Dr. Liu’s research has focused on finding molecular mechanisms that can be targeted with drugs to kill ovarian cancer cells, particularly ovarian cancer that is resistant to conventional chemotherapy (sadly, this develops in most patients with this type of tumor). Her research training with Gabriel Nuñez, M.D., provided a foundation for her to study apoptosis and allowed her to independently propose the hypothesis that ovarian chemoresistance results from abnormal (deficient) apoptosome function. Her work in this area demonstrated that chemoresistance is related to apoptosome dysfunction and further traced the problem to quantitative and functional deficiencies in a protein called Apaf-1, which normally multimerizes to form the apoptosome. These important findings provided the basis for her current K08-funded research to study Apaf-1 in this disease and have now led to a unique collaboration with Roland Kwok, Ph.D to study histone acetylases and deacetylases as therapeutic leads in ovarian cancer because of their ability to specifically increase Apaf-1 expression and function in chemoresistant ovarian cancer. Dr. Liu has explored the potential of certain natural products, including resveratrol, and genestein, to circumvent defective apoptosome function and kill ovarian cancer cells by non-apoptotic means. This work, part of an ongoing collaboration with Anthony Pipari, MD, PhD, was based on her hypothesis that the metabolic requirements of ovarian cancer cells exemplified by high rates of glucose utilization (e.g. the basis for clinical detection of this disease by PET scanning), would make this type of tumor cell susceptible to agents that disrupt metabolism. In pursuing this idea, Dr. Liu demonstrated the potential of these agents to kill ovarian cancer cells and showed that this approach to target metabolism causes a unique non-apoptotic form of cell death (autophagy) which indeed circumvents defective apoptosome function. Dr. Liu’s work is featured in the Ovarian Cancer Research Program portion of the 2007 Congressionally Directed Medical Research Programs (CDMRP) annual report. Dr. Liu has had continuous funding since joining the Gynecologic Oncology Division in 1999. Completed awards include awards from the American Association of Obstetricians and Gynecologists Foundation, the University of Michigan Comprehensive Cancer Center, the Eli Lilly Centre for Women’s Health (2000-2002), the Ovarian Cancer Research Fund (2001-2004), the Gynecologic Cancer Foundation (2003-2005), and the National Center for Complementary and Alternative Medicine at the NIH (2003-2007). She is currently the principal investigator on a K08 award from the National Cancer Institute (2004-2009) and an Idea Development award from the Department of Defense (2006-2009). Dr. Liu’s future research in these areas is particularly promising as she is expected to continue to develop her work with Apaf-1, her collaborative programs with Drs. Kwok and Pipari related to new therapeutic targets and to advance her basic work into translational studies.

Recent and Significant Publications:

Wahl H, Tan L, Griffith KA, Choi M, and Liu JR: Curcumin enhances APO2/TRAIL induced apoptosis in chemoresistant ovarian cancer cells. *Gynecologic Oncology* 105(1):104-112, 2007.

Williams JA, Lucas PC, Griffith K, Choi M, Fogoros S, Hu YY, and Liu JR: Expression of Bcl-x_L in ovarian carcinoma is associated with chemoresistance and recurrent disease. *Gynecologic Oncology* 96(2):287-295, 2005.

Opipari AO, Tan L, Boitano A, Aurora A, and Liu JR: Resveratrol induced autophagocytosis in ovarian cancer cells. *Cancer Research* 64:696-703, 2004.

Liu JR, Opipari AW, Tan L, Jiang Y, Zhang Y, Tang H, and Nuñez G: Dysfunctional apoptosome activation in ovarian cancer: implications for chemoresistance. *Cancer Research* 62:924-931, 2002.

Kueck, A, Opipari, A, Tan, L, Choi, M, Huang, J, Wahl, H, and Liu, JR: Inhibition of glucose metabolism: novel therapeutic target for ovarian cancer. In press, *Gynecologic Oncology*.

Service: Dr. Liu serves as a reviewer for numerous journals including *Clinical Cancer Research*, *Cancer*, *Cancer Research*, *Gynecologic Oncology and Obstetrics & Gynecology*. She is an active member of numerous societies including the Society of Gynecologic Oncologists, American Association for Cancer Research, and the International Gynecologic Cancer Society. Dr. Liu was an invited speaker for the First International Symposium "Ovarian Cancer: State of the Art and Future Developments" in Crete, Greece, and has conducted workshops for fellows and junior faculty for the International Society of Gynecologic Cancer. She has participated on the scientific review committees for the Department of Defense Ovarian Cancer Research Program as well as the Gynecologic Cancer Foundation Awards Committee since 2005. Dr. Liu's clinical effort is critical to the Department and the Division of Gynecological Oncology and the Comprehensive Cancer Center. She provides medical and surgical care for patients with gynecologic malignancies. She is very active clinically and treats patients with all types of gynecological malignancies. To provide the most appropriate care to her patients and the best possible training for residents and fellows, she has become fully credentialed for robot-assisted (DaVinci) cancer staging procedures. Dr. Liu maintains a full surgical schedule. Finally, she is held in high regard by her patients, their families and her professional colleagues at the University of Michigan's Comprehensive Cancer Center.

External Review:

Reviewer A: "Her research niche has been in the area of apoptosis in ovarian cancer. In this regard, the first name that comes to mind in our subspecialty when thinking of the words 'ovarian cancer' and 'apoptosis' is Rebecca Liu. This name recognition is attributable to her continuous contributions over the past decade."

Reviewer B: "Dr. Liu's scholarly and professional accomplishments would place her in the top 5% of her peers."

Reviewer C: "Dr. Liu is certainly one of the rising stars in Gynecologic Oncology. Her commitment to the tripartite mission of patient care, research, and teaching is well known

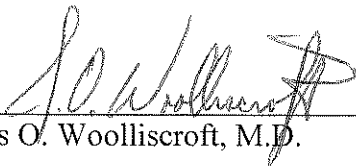
throughout the Gynecologic Oncology community and she is well respected in all three of these areas and, in fact, excels in all of these areas.”

Reviewer D: “She is well-recognized nationally as an expert in the investigation into the molecular biology of ovarian carcinoma, specifically as it relates to chemoresistance, and complimentary and alternative medicine approaches in the treatment of ovarian cancer patients...she remains on the cutting edge of clinical care in this field, presently leading the way in the utilization of the da vinci robot for surgical procedures. She has earned an outstanding reputation in the care of patients with gynecologic malignancies, and is a nationally recognized expert.”

Reviewer E: “Rebecca is one of the new breed of oncologists who have accompanied clinical excellence with scholarly achievements.....Rebecca is an excellent example of a growing number of extremely talented oncologists [of her cohort] who are extending the field beyond mere surgical care to an in depth understanding of cancer mechanisms. Dr. Liu is in the forefront of this group...”

Summary of Recommendation:

Dr. Liu has proven herself to be an extremely capable surgeon, teacher and researcher. It is anticipated that she will continue her outstanding academic and scholarly pursuits and further enhance her valuable contributions to the Department of Obstetrics and Gynecology and the University of Michigan Health System. I am pleased, therefore, to recommend Dr. Liu for promotion to Associate Professor, with tenure, in the Department of Obstetrics and Gynecology.



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

May 2008