

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

Anthony W. Oipari, Jr., M.D., Ph.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.	1994	University of Michigan
Ph.D.	1994	University of Michigan
B.S.	1986	Wayne State University

Professional Record:

2000-Present	Assistant Professor of Obstetrics and Gynecology, University of Michigan
1998-2000	Lecturer, Department of Obstetrics and Gynecology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Oipari has established an excellent reputation as a teacher at the University of Michigan. He has developed instructional and curricular material for trainees in the Medical School, residency and fellowship programs. Since 1998, Dr. Oipari has lectured regularly in the third-year curriculum in areas that include general gynecology, diagnosis and management of human papilloma virus infections, lower genital tract dysplasia, and cervical cancer screening and treatment. In addition, Dr. Oipari is an evaluator for the third-year student theses presentations, a requirement of the clerkship rotation in obstetrics and gynecology. For the residency program, Dr. Oipari lectures in additional areas of expertise including gynecologic complications of graft versus host disease, and the management and treatment of genital tract neoplasia. In the clinic and operating room, Dr. Oipari provides direct instruction to medical students and residents in surgical procedures that include colposcopy, gynecologic surgery, and management of diseases of the lower genital tract. Dr. Oipari's teaching evaluations are consistently excellent. Since 2001, he has regularly been invited to present at the Primary Health Care of Women and Clinical Update in Obstetrics and Gynecology annual postgraduate courses. Finally, in the research laboratory, Dr. Oipari serves as research mentor and advisor for many students at the undergraduate, graduate, postdoctoral and junior faculty levels. Importantly, a number of Dr. Oipari's trainees have been successful in securing prestigious fellowships and postdoctoral research training positions. In his position as Associate Chair for Research, he has taken on substantial responsibility for the academic development of junior faculty within the Department of Obstetrics and Gynecology.

Research: Dr. Opipari's research focuses on understanding how cell death and bioenergetic mechanisms can be selectively targeted by small molecules to treat cancers and autoimmune diseases. His contributions in these areas have been numerous and of significant importance. First, Dr. Opipari has worked to elucidate tractable mechanisms of cell death in several human malignancies. His group has identified important roles for the transcription factor NF- κ B and the caspase death proteins in chemotherapy-induced killing of neuroblastoma. He has been a major contributor to other work in this disease that uncovered a molecular mechanism to explain how histone deacetylase inhibitors kill tumor cells. In addition to neuroblastoma, Dr. Opipari's laboratory has contributed to understanding mechanisms of chemotherapy induced cell death in models of ovarian cancer and melanoma. Perhaps most significant, however, is his work that has resulted in the discovery of a novel family of compounds and their molecular target that are now in late-stage pre-clinical development for treating psoriasis, lupus, graft versus host disease, and early stage development for B cell cancers. This work is a result of his highly productive collaboration with Dr. Gary Glick (Chemistry, LS&A). Dr. Opipari's current work includes mechanistic studies of Bz-423 action against malignant cells, determining pharmacologic properties of this family of compounds that might allow them to work against cancer, and work to investigate the possible link between cellular bioenergetic pathways targeted by these molecules and the pathogenesis of autoimmune and cancer cells. Dr. Opipari's research is funded by the National Institutes of Health. He is principal investigator of an RO1 to study and develop therapeutic benzodiazepines against cancer; he is or has been a co-investigator on three additional RO1 grants in related areas of study. Dr. Opipari's research will proceed to advance the understanding and therapeutic applications of the family of cytotoxic benzodiazepines, represented by Bz-423. Additionally, the work that identified the mitochondrial molecular target of these molecules has opened up additional research opportunities, pointing to a link between bioenergetic pathways and autoimmune and neoplastic diseases. These areas are the focus of a second RO1 proposal that he has submitted to the NIH, which is currently being reviewed. Finally, Dr. Opipari is co-inventor of a suite of technologies, owned by the University, some of which have been licensed for commercial purposes and are currently returning royalties to the University and others that are the subject of ongoing patent examinations. The capacity that his laboratory has developed to interface with chemistry faculty and students, with expertise in organic synthesis, is expected to result in new discovery efforts to identify small molecule leads that target specific cellular and molecular processes relevant to other diseases of particular interest to his laboratory, including neuroblastoma and gynecologic cancers.

Recent and Significant Publications:

Subramanian C, Opipari AW Jr, Bian X, Castle VP, Kwok RPS: Ku-70 Acetylation mediates neuroblastoma cell death induced by histone deacetylase inhibitors. *Proc Natl Acad Sci USA* 102:4842-4847, 2005.

Johnson KM, Chen X, Boitano A, Swenson L, Opipari AW Jr, Glick GD: Identification and validation of the mitochondrial F1F0-ATPase as the molecular target of the immunomodulatory benzodiazepine Bz-423. *Chem Biol* 12:485-496, 2005.

Boitano A, Ellman JA, Glick GD, Opipari AW Jr: The proapoptotic benzodiazepine Bz-423 affects the growth and survival of malignant B cells. *Cancer Res* 63:6870-6876, 2003.

Blatt NB, Bednarski JJ, Warner RE, Leonetti F, Johnson KM, Boitano A, Yung R, Richardson BC, Johnson KJ, Ellman JA, Opipari AW Jr, Glick GD: Benzodiazepine-induced superoxide signals B cell apoptosis: mechanistic insight and potential therapeutic utility. *J Clin Invest* 110:1123-1132, 2002.

Bian X, McAllister-Lucas LM, Shao F, Schumacher KR, Feng Z, Porter AG, Castle VP, Opipari AW Jr: NF- κ B activation mediates doxorubicin-induced cell death in N-Type neuroblastoma cells. *J Biol Chem* 276:48921-48929, 2001.

Service: Dr. Opipari provides outpatient clinical service in the Comprehensive Cancer Center where he sees patients two days each week. Additionally, he is an attending physician for patients he admits to the gynecology service and to the Labor and Delivery Unit. His area of special expertise and interest is colposcopy and the management of lower genital tract disease, a nice fit to his research interests in early neoplasia. Dr. Opipari serves as Associate Chair for Research for the Department of Obstetrics and Gynecology overseeing all matters that pertain to the Department's research programs. He is a key leader and role model for the future departmental research initiatives. He has exhaustively reviewed the Department's research portfolio to analyze risk, create a strategy for growth and identify ways to make specific projects cross disciplines and become translational to meet the objectives articulated by the NIH Roadmap. By careful analysis of data on grant submissions, funding success, and direct faculty interviews, he identified obstacles that significantly delay grant submissions by junior tenure-track faculty. To solve this, he has aggressively implemented a creative team-based approach to support grant submissions and faculty members when they are submitting grants. This model recognizes that the Department has a considerable stake in the success of each investigator and every research proposal. The model he developed ensures that the Department takes an *active* role in ensuring timely submissions and improving the quality of all submissions. In summary, he has become a key leader of the research mission of this Department. Finally, consistent with the scope of his training and clinical practice, he serves as Laser Safety Officer for Obstetrics and Gynecology. In the Medical School, Dr. Opipari is a member of the Career Advisory Committee for the Medical Scientist Training Program. Dr. Opipari is also a member of the Advisory Committee on Cervical Cancer Screening for the Department of Community Health for the State of Michigan.

External Review:

Reviewer A: "I have been most impressed with the careful science carried out by Anthony and his group, often in the context of very difficult experimental systems. His work is visible and appreciated on the National and International scene and I believe he has significant momentum in his scientific program, with the best yet to come."

Reviewer B: "It is very unusual for an obstetrician gynecologist to be publishing in these venues, and that should be noted....This record of extramural support places Dr. Opipari in the upper tier of academic obstetrician gynecologists....He has clearly accomplished many things that are rarely done by physician faculty members in departments of obstetrics and gynecology."

His credentials including number and quality of publications and extramural grant support are strong and portend a very promising future.”

Reviewer C: Dr. Opirari has made significant contributions to the signaling pathways that promote malignant cell death....In this era of big science, collaborations of the type built by Drs. Glick and Opirari are often necessary for significant advances. They have formed a nicely complementary team, bringing different strengths to the collaboration, and both deserve academic credit for carrying this novel work forward....it is apparent to me that Dr. Opirari has developed his own scientific niche.”

Reviewer D: “The grant support is impressive, with several NIH and an Alliance for Lupus Research grant. The work on pro-apoptotic benzodiazepines is novel...There is an impressive list of students and fellows that have been mentored.”

Reviewer E: “He is an accomplished basic researcher with a clear track record in mentoring both clinically-oriented as well as bench-oriented young scientists. In my experience, he is also very open to engaging in new collaborations.”

Reviewer F: “He has had an excellent publication record as an author in excellent journals such as PNAS and JBC...Moreover, Dr. Opirari has shown excellent research collaboration, as evidenced by his presence as Co-I on two NIH grants and one foundation grant. Importantly, the quality of his research has now been vetted by his own RO1 grant.”

Summary of Recommendation:

Dr. Opirari has developed a successful independent research program as a clinician scientist while maintaining a strong clinical and teaching presence in the Department. He can be expected to continue his personal scholarly success and, as Associate Chair for Research, to have an important influence on the academic success of the Department of Obstetrics and Gynecology and assure its sustained contributions to the research portfolio of the University of Michigan Health System. I am pleased to recommend Dr. Anthony Opirari for promotion to Associate Professor of Obstetrics and Gynecology, with tenure.



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

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