Approved by the Regents
May 20, 2010

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF MICROBIOLOGY AND IMMUNOLOGY

Mary X.D. O'Riordan, Ph.D., assistant professor of microbiology and immunology, Department of Microbiology and Immunology, Medical School, is recommended for promotion to associate professor of microbiology and immunology, with tenure, Department of Microbiology and Immunology, Medical School.

Academic Degrees:

1999	Ph.D.	University of California, San Francisco
1994	M.A.	Princeton University, Princeton
1990	B.S.	University of Washington, Seattle

Professional Record:

2003-present	Assistant Professor of Microbiology and Immunology, University of Michigan

Summary of Evaluation:

Teaching: Dr. O'Riordan has made many contributions to the Department's teaching mission as an assistant professor at the University of Michigan. She has taught in courses covering microbial pathogenesis, cellular biotechnology and microbial physiology, along with proposal writing. She served as director or co-director for three graduate courses, M/I 504 (Cellular Biotechnology; two years), M/I 609 (Bacterial Pathogenesis; two years) and M/I 619 (Bacterial Physiology; one year). Two of these, 609 and 619, are literature-based courses, each requiring approximately 20 hours of preparation and contact time. M/I 504 (cross-listed as Anat 504 and Biochem 504) is the centerpiece course of the important interdisciplinary Cellular Biotechnology Training Program. It includes participation from faculty in many departments and schools, as well as guest lectures from senior scientists and executives in the biotechnology and pharmaceutical industry. The course is labor intensive and Dr. O'Riordan devotes about 35 hours of contact, organization and preparation time to it. The vast majority of students evaluated agreed or strongly agreed that Dr. O'Riordan is an excellent instructor, that she has a thorough knowledge of the subject, and that students learned a great deal from the course. As a research advisor, Dr. O'Riordan already has an excellent track record of training, and her students and fellows have published their work in the form of multiple papers in top journals. In assessing her own record of activity in this area, she considers her role as mentor for these trainees to be "the most important of my academic responsibilities" and indicates that she is "committed to promoting both their scientific education and their professional careers." In addition to those of her own students, Dr. O'Riordan has served on 21 graduate thesis committees for students in a range of departments and programs across the campus, an extraordinary index of her popularity as a scientific advisor.

Research: As a postdoctoral investigator with Daniel Portnoy at UC-Berkeley, Dr. O'Riordan made two important discoveries that have become the basis of her laboratory efforts at Michigan, where she has continued to make important discoveries. First, she discovered that the intracellular bacterial pathogen, *Listeria monocytogenes*, stimulated characteristic innate immune signaling pathways upon entry of the bacterium into the host cytosol, demonstrating that host cells could recognize bacteria in different subcellular compartments. Second, she showed that within the host cytosol, *Listeria* requires specific metabolic regulators to exploit this niche for the essential co-factor, lipoate. Similar regulators have since shown to be required for virulence of other pathogens, thereby establishing the broad relevance of her findings. She has done groundbreaking work as an assistant professor. Using *Listeria* as a model intracellular pathogen, she and her group identified the X-linked inhibitor of apoptosis (XIAP) as a regulator of cytosol-specific innate immune signaling activated in response to bacterial infection. Their work to date demonstrates that XIAP-deficient T-cells are defective for producing interferon-gamma upon stimulation, and also show increased proliferation in response to infection, compared to wildtype cells. She has made other important observations regarding the impact of bacterial infection at the cellular level. She demonstrated that regulation of ion and water homeostasis is a key step in defining the host cell compartment in which pathogens reside. She identified two classes of host protein important for this homeostasis, members of the aquaporin family and the cystic fibrosis transmembrane regulator (CFTR). Finally, continuing her original work studying mechanisms regulating bacterial metabolism within the host cell, she demonstrated that lipoate-dependence is due to a requirement branched chain fatty acids (BCFA), a constituent of the *Listeria* outer membrane. Her work is published in excellent journals including *Science*, *Proceedings of the National Academy of Sciences, PLoS Pathogens* and others, and she has been invited to present seminars and chair sessions at major international meetings. Dr. O'Riordan has also garnered significant resources to support her research, including NIH grants and fellowships from private foundations. In 2007, she earned the ICAAC Young Investigator Award for the promise she has shown as an independent investigator.

Recent and Significant Publications:

Keeney K, Colosi L, Weber W, O'Riordan M: Generation of branched chain fatty acids through lipoate dependent metabolism facilitates intracellular growth of *Listeria monocytogenes*. *J Bacteriol* 191:2187-2196, 2009.

Delbridge Bauler L, Duckett C, O'Riordan M: XIAP regulates cytosolic-specific innate immunity to *Listeria* infection. *PLoS Pathogens* 4:e1000142, 2008.

Radtke A, and O'Riordan M: Homeostatic maintenance of pathogen-containing vacuoles requires TBK1-dependent regulation of *aquaporin-1*. *Cell Microbiol* 10: 2197, 2008.

Keeney K, Stuckey J, O'Riordan M: LplA1-dependent utilization of host lipoyl-peptides enables *Listeria* cytosolic growth and virulence. *Mol Microbiol* 66:758, 2007.

Radtke A, Delbridge L, Balachandran S, Barber G, O'Riordan M: TBK1 protects vacuolar integrity during intracellular bacterial infection. *PLoS Pathogens* 3:e29, 2007.

Service: Dr. O'Riordan is a model colleague. She has served on numerous department committees including Graduate Studies, Appointments & Promotions, and multiple faculty search committees. She organized a special symposium that was well-attended at Michigan on dendritic cell biology, and established the organization for a now-annual department retreat. She established and directs the bi-monthly Bacterial Pathogenesis Journal Club. At the institutional level, she served on the Rackham Predoctoral Fellowship Selection Committee and currently serves on the Research Scientific Program Committee for the NCRC Expansion. Additionally, she has participated in panel discussions on scientific careers organized by the University of Michigan Career Center. At the national level, she is an expert reviewer for numerous important journals (including *Journal of Experimental Medicine, PNAS, Nature Reviews Microbiology* and *Cell Host & Microbe*), serves on the editorial board of *Infection & Immunity* and has participated in multiple NIH study sections. She has been an active member of the American Society for Microbiology (ASM), planning and chairing scientific symposia at the Society's general meeting. Currently she serves as chair-elect of the ASM Division E (Immunology) and will Chair that Division in 2010.

External Review:

Reviewer A: "Dr. O'Riordan is one of the rising stars in the field of microbial pathogenesis...Dr. O'Riordan is an outstanding scientist who has performed exceptionally well during her tenure as Assistant Professor, which earned her great respect from her peers in the field of bacterial pathogenesis. With her remarkable track record, she would clearly be promoted to the rank of Associate Professor with tenure at my Medical School."

Reviewer B: "Her students are publishing papers in high profile journals, they openly celebrated her mentorship when I interacted with them at meetings, and they are securing post-doctoral positions in prestigious laboratories...She is a scientific colleague I hold in high regard, and a woman I predict will emerge as one of the best scientists in the field of microbial immunology."

Reviewer C: "I believe she is considered to be an up-and-coming leader in the field of Listeria pathogenesis, and her focus has provided a niche for her research."

Reviewer D: "It is very rare to review the work of a scientist and say with confidence that everything the person does is interesting--but in her case I feel confident in saying this...I think your Department can feel secure that you have found a strong faculty member with the potential for producing significant results in the years to come."

Reviewer E: "In short she is one of the most outstanding people [of her cohort] in microbial pathogenesis that I have seen at this stage of their career...She is in a rapid growth phase in terms of her research and leadership potential."

Reviewer F: "The papers are marked by originality, rigor and diversity of questions related to her central thematic interest in an enduring and important topic, host-pathogen relationships."

Reviewer G: "...her work in the field is held in very high regard because of the extreme care, rigor and creativity that Mary applies to her research...Her research program is well-funded,

produces quality papers in excellent journals, and addresses problems that are actively pursued by many different labs. She is clearly working right at the cutting edge of the field."

Summary of Recommendation:

Dr. O'Riordan is an outstanding junior investigator and educator in the fields of microbial biology and pathogenesis. Her work is consistently creative and has led to unexpected and exciting new findings in two distinct areas of investigation. Based on requests for her to speak and chair sessions at important international meetings, her election to serve as chair of a major division of her professional society, her solid and consistent record of generating external resources to support her research, and her dedication to training the next generation of scientists both in the laboratory and the classroom, I enthusiastically support her for promotion to associate professor, with tenure, in the Department of Microbiology and Immunology.

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

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