

PROMOTION RECOMMENDATION  
THE UNIVERSITY OF MICHIGAN  
MEDICAL SCHOOL  
DEPARTMENT OF HUMAN GENETICS  
DEPARTMENT OF UROLOGY  
DEPARTMENT OF OBSTETRICS AND GYNECOLOGY

Jacob L. Mueller, Ph.D., assistant professor of human genetics, Department of Human Genetics, assistant professor of obstetrics and gynecology, Department of Obstetrics and Gynecology, and assistant professor of urology, Department of Urology, Medical School, is recommended for promotion to associate professor of human genetics, with tenure, Department of Human Genetics, associate professor of obstetrics and gynecology, without tenure, Department of Obstetrics and Gynecology, and associate professor of urology, without tenure, Department of Urology, Medical School.

Academic Degrees:

Ph.D.	2005	Cornell University
B.A.	1998	Gettysburg College

Professional Record:

2015-present	Assistant Professor of Urology, University of Michigan
2015-present	Assistant Professor of Obstetrics and Gynecology, University of Michigan
2014-present	Assistant Professor of Human Genetics, University of Michigan

Summary of Evaluation:

Teaching: Dr. Mueller is an effective teacher and mentor both in the classroom and in the laboratory. He has trained seven undergraduate students, 15 graduate students, one fellow, and one faculty member. Each trainee in his group conducts an independent research project and they consistently deliver outstanding presentations at student seminars. He has already completed the training of one Ph.D. student who was funded by the National Science Foundation and published two first-author papers. For the past six years, Dr. Mueller has lead six lectures and two discussion sections in a course on molecular genetics (HG541) and has taught at least one lecture per year in six additional courses. In recognition for his success as an educator, Dr. Mueller was awarded the 2019 Endowment for the Basic Sciences Teaching Award.

Research: Dr. Mueller is well on his way to establishing himself as a world leader on the evolution and function of structurally complex genomic regions important for reproductive function. He has been successful as an assistant professor at the University of Michigan and his major research accomplishments include: (1) developing novel *in vivo* and *in vitro* methodologies to study large complex regions of the genome; (2) improving our understanding of the role of large palindromic sequences on the sex chromosomes; and (3) gaining novel functional and evolutionary insights into why genes on the X and Y chromosomes are massively co-amplified. As a result, he has published a total of 18 manuscripts, including five senior-author manuscripts in top journals as an assistant professor. Dr. Mueller has secured a significant amount of funding, including being a

principal investigator on both an NIH R01, and a prestigious CAREER award from the National Science Foundation.

Recent and Significant Publications:

Swanepoel CM, Gerlinger ER, Mueller JL: Large X-linked palindromes undergo recurrent arm-to-arm gene conversion across *Mus* lineages. *Molecular Biology and Evolution* 37: 1979-1985, 2020.

Arlt MF, Brogley MA, Stark-Dykema ER, Hu YC, Mueller JL: Genomic structure, evolutionary origins and reproductive functions of a large amplified intrinsically disordered protein-coding gene on the X chromosome (*Laidx*) in mice. *G3* 10: 1997-2005, 2020.

Kruger AN, Brogley MA, Huizinga JL, Kidd JM, de Rooij DG, Hu YC, Mueller JL: A neofunctionalized X-linked ampliconic gene family is essential for male fertility and equal sex ratio in mice. *Current Biology* 29: 3699-3706, 2019.

Kruger AN\*, Ellison Q, Brogley MA, Gerlinger ER, Mueller JL: Mice with large inversions or deletions of X-palindrome arms are fertile and express their associated genes during post-meiosis. *Scientific Reports* 8: 8985, 2018.

Bennett-Baker P and Mueller JL: CRISPR-mediated isolation of megabase-sized DNA segments. *Nucleic Acids Research* 45: e165, 2017.

Service: Dr. Mueller is an outstanding citizen who routinely performs service for our department, for the university, and for the broader scientific community. He has served on multiple departmental committees including those for computational support, infrastructure, and seminars and events. He has also served on admissions committees for genetic counseling and Ph.D. programs. Dr. Mueller is a member of the Human Genetics Ph.D. Program Committee and is directing an introductory seminar series for first-year Ph.D. students. He has also served on a total of 11 thesis committees in addition to those for students in his laboratory. Dr. Mueller has been invited to give six external seminars as an assistant professor, including at Cornell University and the University of Pennsylvania. He has reviewed manuscripts for 18 *journals, including Cell, Genome Research, and PLoS Genetics*. He has also performed ad hoc grant review service for multiple internal and external study sections.

External Reviewers:

Reviewer A: “Dr. Mueller has made important contributions to his field in his first years as an independent scientist. His advances have resulted in a steady stream of publications, invitations to leading meetings in the field, an NIH R01, and an impressive NSF Career Award. He has recruited a very productive team to his lab, and he is contributing in many ways to the department and to the teaching mission, where he won an award last year. His area of research, the evolution, molecular function and structure of the sex chromosomes, is a novel area where few people have comparable expertise. It is the sort of research where major and unanticipated discoveries are made, and I expect that it will have a rich and interesting future. In all respects, it is my opinion that Dr. Mueller has met all the criteria for promotion to Associate Professor. I am confident that he would be promoted at [my institution].”

Reviewer B: "...it is safe to say that Dr. Mueller is one of the most exciting [junior] scientists within the field of sex chromosome biology currently, and his trajectory is exceptionally strong. If he were at [my institution], he would easily have crossed the bar for promotion with indefinite tenure and would, I suspect, achieve such a status at most of the top tier institutions in this country. I wholeheartedly recommend his immediate promotion and tenure, and I look forward to seeing an impressive career for this exceptional scientist."

Reviewer C: "I believe that Dr. Mueller has firmly established his scientific mark, and will continue to make high impact contributions in the future...Dr. Mueller will, in my opinion, continue to be an incredible asset and tribute to your program by virtue of his sustained scholarly excellence. He is recognized as a productive scientist by the community of scholars in areas of chromosome dynamics and evolution. His work is influencing our thinking and research directions and is wholly worthy of recognition by promotion in your department. I envy you the excitement and energy he is bringing to your programs!"

Reviewer D: "I am not aware of any other lab addressing the functions of complex ampliconic and palindromic regions of mammalian sex chromosome as Jake is doing. He has developed genome editing methods to manipulate these structures and demonstrated genetic conflict in one case, an exciting finding in its own right that also opens intriguing possibilities for future studies. With his recent publication record, his distinctive research program, and his demonstrated ability to compete successfully for extramural funding, Jake is on a strong trajectory which I expect he will maintain as his investment in developing methods and mouse models continues to bear fruit. Based on these factors, I would welcome him as a colleague at my institution, where I am confident that he would be promoted with tenure."

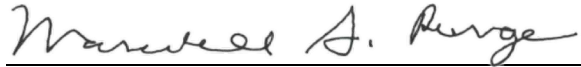
Reviewer E: "Dr. Mueller has a long standing interest in sex chromosome evolution, and he has made several important contributions to this area...In subsequent work he has also taken advantage of CRISPR to target specific repetitive regions on the X. For example, his 2018 Scientific Reports paper engineered deletions of palindrome arms to show that the palindrome structure was not required for the evasion of post-meiotic gene silencing. This paper was important for helping us to understand the functional consequences of the palindrome structures on the X ..."

Reviewer F: "Jake's body of work is empirically and technically groundbreaking, and the quality is top-notch. First, his efforts to sequence and experimentally manipulate palindromic gene blocks are, very simply, heroic. He has chosen a difficult, time-consuming problem, and he's made no compromises, cut no corners. Second, the quality of his work is further evidenced by the venues in which he publishes—predominantly in high-impact journals (*Nature Genetics*, *Cell*, *Current Biology*, *MBE*)— and by his funding success. Third, perhaps the best evidence of quality and impact is that Jake's discoveries have motivated investigations in allied fields and systems...Jake would handily meet the requirements for promotion with tenure at [my institution], and I would enthusiastically endorse his case."

#### Summary of Recommendations:

Dr. Mueller has made major contributions to the Departments of Human Genetics, Urology and Obstetrics and Gynecology through his teaching, service and research. His research investigates the evolution and function of structurally complex genomic regions important for reproductive

function, which is an important niche. I am pleased to recommend the promotion of Jacob L Mueller, Ph.D. to associate professor of human genetics, with tenure, Department of Human Genetics, associate professor of obstetrics and gynecology, without tenure, Department of Obstetrics and Gynecology, and associate professor of urology, without tenure, Department of Urology, Medical School.

A handwritten signature in cursive script that reads "Marschall S. Runge". The signature is written in black ink and is positioned above a horizontal line.

Marschall S. Runge, M.D., Ph.D.  
Executive Vice President of Medical Affairs  
Dean, Medical School

May 2021