

PROMOTION RECOMMENDATION  
THE UNIVERSITY OF MICHIGAN  
MEDICAL SCHOOL  
DEPARTMENT OF HUMAN GENETICS

Shigeki Iwase, Ph.D., assistant professor of human genetics, Department of Human Genetics, Medical School, is recommended for promotion to associate professor of human genetics, with tenure, Department of Human Genetics, Medical School.

Academic Degrees:

Ph.D.	2006	University of Tsukuba, Tsukuba, Japan
B.S.	2001	University of Tsukuba, Tsukuba, Japan

Professional Record:

2012 – present	Assistant Professor of Human Genetics, University of Michigan
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Summary of Evaluation

Teaching: Dr. Iwase is a creative designer of novel didactic lectures and curricula, an inspirational leader of educational research seminar courses, and a caring supporter in the development of junior scientists. He originated and developed Human Genetics 480/580, Neurobiology of Developmental Disorders for Ph.D., M.S. and advanced undergraduate students in 2014. This course examines the genetic and epigenetic principles underlying the development and maintenance of the mammalian nervous system. The focus on human disorders that lead to structural brain abnormalities, intellectual disability, and autism is extremely timely and attracts many students from a variety of disciplines and majors. Dr. Iwase is heavily invested in providing the genetic and epigenetic components of the Neuroscience 623 course, Neuroscience Boot Camp. He teaches two lectures/discussions in Human Genetics 803, Advanced Topics, and HG541 Molecular Genetics. He invests a great deal of time and effort to nurture and guide the students in his research group through his mentoring which includes the thesis projects of ten undergraduate and four graduate students as well as mentoring four post-doctoral trainees. Dr. Iwase has served on 18 Ph.D. thesis committees students and has mentored five additional doctoral rotation students. His Ph.D. graduate students have been extraordinarily productive, and have obtained NIH individual fellowships (F31), NIH training grant fellowships (T32), and NSF Fellowship awards. He is an active member of Neuroscience Training Program, the Michigan Predoctoral Training Program in Genetics, Genome Science Training Program, and the Career Training Program in Reproductive Sciences. Dr. Iwase is a committee member involved with the recruitment and admissions process for the department and for the Program in Biomedical Sciences.

Research: Dr. Iwase's research work is impactful. He studies chromatin regulatory mechanisms engaged in the development and function of the brain. Chromatin deregulation has emerged as a major cause of neurodevelopmental disorders such as intellectual disabilities, autism spectrum disorders, and schizophrenia. His work lays the foundation for understanding the molecular basis of cognitive deficits and, eventually, their treatment. This science provides a merging of chromatin biology and advanced neuroscience. Dr. Iwase's work demonstrates that post-translational modifications of histones are recognized as a "language" controlling critical events in the nucleus. Intriguingly, many mutations associated with human neurodevelopmental disease are now known to be histone modification

regulators. Accurate interpretation of the histone modification network, therefore, is widely regarded as essential for understanding proper brain development and function. Dr. Iwase has organized internal and external symposia to promote the new research fields of chromatin biology and neuroscience. These include the Epigenetic Etiology of Intellectual Disability symposium at the 2017 Society for Neuroscience Annual Meeting with an attendance of 30,000 people, and the University of Michigan Chromatin in Development and Disease Symposium. In 2018, Dr. Iwase was recognized as a national leader in his field by the American Society of Human Genetics by being selected to organize the Chromatin Dysregulation in Neurodevelopmental Disorders symposium at the October 2018 Annual Meeting of American Society of Human Genetics. He has a strong and consistent history of grant funding to support his research which includes his role as the principal investigator of an NIH R01 grant, an NIH R21 grant, and a grant from the PRISM Pharmaceutical Company. Dr. Iwase is a superb collaborator and is currently the co-investigator on two NIH R01 grants, one March of Dimes grant, one Kellogg Eye Center P.R. Lichter Research Discovery Fund, and two fellowships for his graduate students.

#### Recent and Significant Publications:

AVallianatos CN, Farrehi C, Friez MJ, Burmeister M, Keegan CE, and Iwase S: Altered gene-regulatory function of KDM5C by a novel mutation associated with autism and intellectual disability. *Front Mol Neurosci.* 11:104, 2018.

Porter RS, Murata-Nakamura Y, Nagasu H, Kim HG, Iwase S: Transcriptome analysis revealed impaired cAMP responsiveness in PHF21A-deficient human cells. *Neuroscience*, 370:170-180, 2018.

Iwase S, Bérubé NG, Zhou Z, Kasri NN, Battaglioli E, Scandaglia M, Barco A: Epigenetic etiology of intellectual disability. *J. Neuroscience*, 37(45):10773-10782, 2017.

Iwase S, Brookes E, Agarwal S, Badeaux AI, Ito H, Vallianatos CN, Tomassy GS, Kasza T, Lin G, Thompson A, Gu L, Kwan KY, Chen C, Sartor MA, Egan B, Xu J, Shi Y: A mouse model of X-linked intellectual disability associated with impaired removal of histone methylation. *Cell Reports* 14(5): 1000-1009, 2016.

Agarwal S, Macfarlan TS, Sartor MA, Iwase S: Sequencing of first-strand cDNA library reveals full-length Transcriptomes. *Nature Comm.* 6: 6002, 2015.

Service: Institutionally, Dr. Iwase has been the chair of the Communication Committee for the past two years. In that capacity, he is the leader for all external communication implementation with a committee of six faculty members and one staff support. Together with Dr. Kenneth Kwan, Dr. Iwase has also implemented a daily Twitter feed from the department. Dr. Iwase also serves on the Master's Degree curriculum and training committee for the department, and has organized the departmental preliminary examinations and the annual retreat. Nationally, he has served as a reviewer for ten scientific journals and as an ad hoc grant reviewer for Massachusetts General Hospital, the Wellcome Trust, the United Kingdom Medical Research Council, and institutionally, the Michigan Institute for Clinical and Health Research post-doctoral career development awards. He was guest editor for *Molecular and Cellular Neuroscience* in 2018. Dr. Iwase is a member of the American Society of Human Genetics and the American Neuroscience Society. He has organized internal and external symposia to promote the new research fields of chromatin biology and neuroscience.

## External Reviewers:

Reviewer A: "...he made not one but several seminal contributions to the field...the very first paper linking genetic mutations in a histone demethylase gene to neurodevelopmental disease and at least to the best of my knowledge, that paper was the first paper in the epigenetics field to provide conclusive proof for a histone demethylase gene being encoded in the eukaryote genome. The paper was both from a technical and scientific perspective a truly seminal contribution to the field...Given his outstanding performance in the field of epigenomics and neuroscience, and his strong track record in this field, I give him my highest-highest recommendation for promotion Associate Professor with Tenure. Every institution should feel lucky to have him on their tenured faculty roster."

Reviewer B: "I consider both his Nature Comm. and Cell Reports papers to be outstanding and worthy of promotion to Assoc. Professor...I would rate him as internationally competitive and certainly on par with other Assoc. Professors working the same field. In addition to his high quality publications, he has been awarded a competitive R01 in 2015 and is PI and co-PI on a number of other grants. ... Outstanding, he has reviewed a number of international and national grants, served as guest editor for a special issue of MCN and reviewed manuscripts for top international journals in the field...I have no doubt that he would meet the requirements for promotion at [my institution]."

Reviewer C: "I find Dr. Iwase to be an extremely thoughtful, creative and passionate scientist. The picture that emerges from his packet is one of a highly successful [junior] investigator who has built a strong research program in all respects, including funding and publications...he has served on numerous other types of committees...this indicates an enormous and selfless commitment to the local academic community, and makes his accomplishments in his lab and his success in obtaining funding even more impressive...I suspect that he is well on his way of being a highly sought after investigator, especially in the hot field of neuroepigenetics..."

Reviewer D: "Shigeki is a very talented scientist who has made important contributions to the field of neuroepigenetics...Since Dr. Iwase started his independent laboratory at the University of Michigan Medical School in 2012, Shigeki has been operating a very productive laboratory. He published a new innovative method for strand-specific RNA-seq...as well as the first animal model of intellectual disability associated with impaired removal of histone methylation, i.e. Smcx knockout mouse... Dr. Iwase already has trained several graduate students and postdoctoral investigators, and their positions following training in his laboratory speaks highly to his ability to train the next generation of scientists."

Reviewer E: "Shigeki is an [sic] smart experimentalist, but in addition he is exceptional in his scholarship and ability to synthesize and integrate information from a variety of sources...the quality of his primary publications he is one of the emerging leaders in the field of X-chromosome neuroepigenetics...[His] accomplishments are measures of national reputation and at this stage in his career he is well recognized. He has organized and spoken in sessions at the Society for Neuroscience and the Society for Human Genetics, both international venues... I think that his national and international reputations are solid and in light of his intense publication activity over the past 3 years is recognition [he] is on an uphill trajectory...Shigeki would more than qualify for tenure at [my institution]."

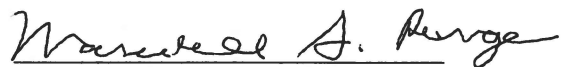
Reviewer F: "In short, I believe Dr. Iwase is an exceptional talent as a scientist, who has pursued an innovative and successful research program over the past six years. I consider him to be one of the most promising [junior] scientists in the field of epigenetics...Based on the creativity of his research

program and fundamental insights he has obtained about epigenetics in the brain, I would place Dr. Iwase in the top 5% of early career scientists I have encountered. ... it is also clear that Dr. Iwase is superb colleague, teacher, and mentor to those who have the pleasure to work with him in your department.”

Reviewer G: “...I find Dr. Iwase to be a rigorous and insightful scientist who has built a strong foundation for his work and looks to be on a steep upward trajectory. I think he is highly qualified for tenure...I saw Dr. Iwase present his data from these studies [Cell Reports in 2017] at the Society for Neuroscience meeting in 2017, and was impressed by the rigor and the volume of the data as well as the potential for this work to continue to advance understanding of the chromatin regulation of brain development moving forward...In my opinion, the quality and innovation of Dr. Iwase’s publications compare favorably against his peers who do molecular genetics to study chromatin regulation in brain development.”

Summary of Recommendation:

Dr. Iwase is a nationally and internationally recognized scholar and scientist studying human developmental disorders and epigenetic developmental control. Since joining the University of Michigan, he has built a strong and sustainable research program and has obtained consistent and significant funding to support his work. He is a generous, supportive, and insightful teacher and mentor. He serves willingly and effectively within the department, the institution, and nationally. Dr. Iwase is strongly positioned for a multi-decade research career in a complex and topical biomedical field. I am pleased to recommend Shigeki Iwase, Ph.D. for promotion to associate professor of human genetics, with tenure, Department of Human Genetics, Medical School.



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

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