PROMOTION RECOMMENDATION THE UNIVERSITY OF MICHIGAN MEDICAL SCHOOL DEPARTMENT OF INTERNAL MEDICINE DEPARTMENT OF HUMAN GENETICS DEPARTMENT OF COMPUTATIONAL MEDICINE AND BIOINFORMATICS

<u>Cristen J. Willer, Ph.D.</u>, associate professor of internal medicine, with tenure, Department of Internal Medicine, associate professor of human genetics, without tenure, Department of Human Genetics, and associate professor of computational medicine and bioinformatics, without tenure, Department of Computational Medicine and Bioinformatics, Medical School, is recommended for promotion to professor of internal medicine, with tenure, Department of Internal Medicine, professor of human genetics, without tenure, Department of Internal Medicine, professor of human genetics, without tenure, Department of Human Genetics, and professor of computational medicine, with tenure, Department of Medicine, and Bioinformatics, Medical School, is recommended for computational medicine and bioinformatics, without tenure, Department of Internal Medicine, professor of human genetics, without tenure, Department of Human Genetics, and professor of computational medicine and Bioinformatics, Medical School.

Academic Degrees:

Ph.D.	2003	University of Oxford
B.Sc.	1998	McMaster University

Professional Record:

2016-present	Associate Professor of computational medicine and bioinformatics, without
	tenure, University of Michigan
2016-present	Associate Professor of human genetics, without tenure, University of
	Michigan
2016-present	Associate Professor of internal medicine, with tenure, University of
-	Michigan
2011-2016	Assistant Professor of computational medicine, University of Michigan
2011-2016	Assistant Professor of human genetics, University of Michigan
2011-2016	Assistant Professor of internal medicine, University of Michigan

Summary of Evaluation:

<u>Teaching</u>: Dr. Willer is extremely active in all aspects of teaching and mentoring. She provides several didactic lectures each year in the Human Genetics HG542 course, Molecular Basis of Human Genetic Disease, and also participates in HG822, a graduate student seminar course. She lectures extensively institutionally and extramurally on topics such as lipid genetics, the genetics of cardiovascular disease, and genome-wide discovery. Dr. Willer is a dedicated mentor, training graduate students, and post-doctoral fellows in the laboratory setting. In addition to her own formal trainees, she welcomes medical students and graduate students into her laboratory for rotations, mentors genetic counseling masters' students on their research projects, and serves on numerous dissertation advisory committees. She is committed to improving access to research training and career development for underrepresented groups, and has been particularly successful in recruiting minority post-baccalaureate students interested in clinical research training to serve as study team staff for the Cardiovascular Center Biobank.

<u>Research</u>: Dr. Willer's research focuses on large-scale genetic studies of complex diseases, such as cardiovascular disease. She has made substantial contributions not only through her findings of genetic loci and the functional consequences of variants involved in human disease, but also through the development of new methods, software, and bioinformatics algorithms for conducting such large scale studies. Her work is highly collaborative, and through her involvement in several consortia, she has contributed to numerous publications in addition to her own senior author work. Dr. Willer has published 146 peer-reviewed articles, with many in top-tier journals such as *Nature Genetics* and *Nature Communications*. She has an outstanding track record of extramural funding and is currently the principal investigator on a seven year R35 grant from the NIH National Heart, Lung and Blood Institute. Dr. Willer's international recognition as a leader in her field is evidenced by her numerous invited presentations, and peer-review service on NIH study sections as well as for many journals. In 2018, Dr. Willer was named as the Frank N. Wilson Professor of Cardiovascular Medicine at the University of Michigan.

Recent and Significant Publications:

Surakka I, Fritsche LG, Zhou W, Lu H, Brumpton B, Nielsen JB, Gabrielsen ME, Skogholt AH, Wolford B, Graham SE, Chen YE, Lee S, Kang HM, Langhammer A, Forsmo S, Asvold BO, Backman J, Baras A, Regeneron Genetics Center, Abecasis GR, Hveem K, Willer CJ: Loss-of-function mutation in the MEPE gene decreases bone mineral density and increases fracture risk. In Press at *Nature Communications*, 2020.

Zhou W, Nielsen JB, Fritsche LG, Dey R, Elvestad MB, Wolford BN, LeFaive J, VandeHaar P, Gifford A, Bastarache LA, Wei W-Q, Denny JC, Lin M, Hveem K, Kang HM, Abecasis GR, Willer CJ, Lee S: Efficiently controlling for case-control imbalance and sample relatedness in large-scale genetic association studies. *Nat Genet* 50(9):1335-1341, 2018.

Nielsen JB, Fritsche L, Zhou W, Skov MW, Graham SE, Herron TJ, Schmidt EM, Surakka I, Mathis MR, Crawford R, Elvestad MB, Skogholt AH, Holmen OL, Lin M, Wolford BN, Dey R, Dalen H, Holst AG, Boehnke M, Kheterpal S, Lee S, Kang HM, Kitzman J, Shavit J, Jalife J, Brummett CM, Abecasis GR, Hveem K, Willer CJ: Biobank-driven genomic discovery yields new insight into atrial fibrillation biology. *Nat Genet* 50(9):1234-1239, 208.

Lu X, Peloso GM, Liu DJ, Wu Y, Zhang H, Li J, Tang CS, Dorajoo R, [many additional authors], Kathiresan S, Mohlke KL, Wu T, Sham PC, Gu D, Willer C: Exome chip meta-analysis identifies novel loci and East Asian-specific coding variants contributing to lipid levels and coronary artery disease. *Nat Genet* 49(12):1722-1730, 2017.

Yang B, Zhou W, Jiao J, Nielsen JB, Mathis MR, Heydarpour M, Lettre G, Folkersen L, Prakash S, Schurmann C, Fritsche L, Farnum GA, Lin M, Othman M, Hornsby W, Driscoll A, Levasseur A, Thomas M, Farhat L, Dubé MP, Isselbacher EM, Franco-Cereceda A, Guo DC, Bottinger EP, Deeb GM, Booher A, Kheterpal S, Chen YE, Kang HM, Kitzman J, Cordell HJ, Keavney BD, Goodship JA, Ganesh SK, Abecasis G, Eagle KA, Boyle AP, Loos RJF, Eriksson P, Tardif JC, Brummett CM, Milewicz DM, Body SC, Willer CJ: Protein-altering and regulatory genetic variants near GATA4 implicated in bicuspid aortic valve. *Nat Commun* 8:15481, 2017.

<u>Service</u>: Institutionally, Dr. Willer provides significant leadership as the co-director for the Precision Health Cohort Development for the University of Michigan Precision Health Initiative, and as the director of the Cardiovascular Health Improvement Project Biobank. She has served on several internal committees and grant review panels, and is involved locally in community service. Nationally, Dr. Willer serves on multiple committees for the Genetic Investigation of Anthropometric Traits (GIANT) international consortium, on the Organizing Committee for the International Common Diseases Alliance, and as a participant in the National Human Genome Research Institute Genomics 2020 Strategic Planning Finale Meeting.

External Reviewers:

<u>Reviewer A:</u> "Cristen quickly established herself as a leading human and statistical geneticist primarily in the field of cardiovascular disease, and also beyond that subspecialty. Indeed, Cristen is revered as one of the leading experts in her specialty, both nationally and internationally. She is highly regarded not just for her success in study design and novel approaches in genomics data analysis, but in large part due to the fact that she contributes her expertise and time selflessly as a co-investigator on multiple colleague's grants, through her leadership in organizations such as the American Society for Human Genetics."

<u>Reviewer B:</u> "Dr. Willer has achieved an international reputation for her contributions to cardiovascular genetics...Dr. Willer has continued to make impactful contributions throughout her career, moving from genome-wide association studies to functional analysis, to provide an improved understanding of the genetic etiology of cardiovascular disease and associated risk factors. What is most impressive is the number of high impact papers that she has led as first author early in her career, and as senior author in more recent years, most of them published in the highest impact journals...Her record of obtaining research funding is outstanding, culminating in her recent prestigious R35 award...Dr. Willer's research and research program, by all criteria, are outstanding and of the highest quality."

<u>Reviewer C:</u> "Since becoming an independent faculty member, Dr. Willer has authored almost 90 additional papers dealing with the genetics of cardiovascular disease, lipid levels, metabolic traits, statistical methods, and heart failure...One particularly notable paper...describes the genetics of atrial fibrillation, identifying a number of risk loci as well as regulatory pathways affecting cardiac development...Overall, I would rate Dr. Willer as among the leaders in the area of complex trait genetics and statistical genetics. At her level, I believe she is among the top few researchers in this area. I have no doubt that Dr. Willer would, at this stage, be considered for promotion to Full Professor with tenure at my institution. I am happy to support her promotion to Full Professor."

<u>Reviewer D:</u> "Dr. Willer continues to show that investigation of genetic variation in humans identified through sequencing can identify variants that define functional genes. This approach is of course the cornerstone of precision medicine and the NIH *All of Us* program...Dr. Willer has made important progress in a difficult area of study. She clearly is a leader in human genetics and the emerging area of precision medicine, which is reflected in the fact that she has given numerous invited talks (national and international), moderated sessions at national meetings, and is a willing participant in media presentations...Dr. Willer's committee, organizational, and volunteer contributions are outstanding. She is clearly a highly regarded community citizen...In summary,

I believe that Dr. Willer has achieved all of the requirements for promotion to tenured Full Professor. She is an outstanding scientist and mentor."

<u>Reviewer E:</u> "...[Dr. Willer] is one of the most brilliant and creative scientists working in the field of cardiovascular genetics...She is the recipient of a MIRA award from the NHLBI, one of the most highly competitive and prestigious awards of the NIH. Her overall h-index is 71 and her work has been in the top 1% of her field as judged by Thomson-Reuters; these metrics are particularly impressive when considering she achieved them before becoming a full Professor...Dr. Willer is an internationally recognized and highly respected leader in genetics and genomics who has [sic] whose work has had a profound impact in cardiovascular genomics. Based on her research, service and teaching, Dr. Willer would easily qualify for promotion to Professor with tenure at my own institution. This in sum, I strongly urge her promotion to Professor with tenure."

Summary of Recommendation:

Dr. Willer is an internationally recognized expert in the area of human genetics and cardiovascular disease. She is also deeply committed to the training of the next generation of scientists, and is active in service at both the institutional and national levels. I am pleased to recommend Cristen J. Willer, Ph.D. for promotion to professor of internal medicine, with tenure, Department of Internal Medicine, professor of human genetics, without tenure, Department of Human Genetics, and professor of computational medicine and bioinformatics, without tenure, Department of Computational Medicine and Bioinformatics, Medical School.

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

May 2021