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

<u>Jacob O. Kitzman, Ph.D.</u>, assistant professor of human genetics, Department of Human Genetics, and assistant professor of computational medicine and bioinformatics, Department of Computational Medicine and Bioinformatics, Medical School, is recommended for promotion to associate professor of human genetics, with tenure, Department of Human Genetics, and associate professor of computational medicine and bioinformatics, without tenure, Department of Computational Medicine and Bioinformatics, Medical School.

Academic Record:

Ph.D.	2014	University of Washington
M.S.E.	2006	Massachusetts Institute of Technology
B.S.	2004	Massachusetts Institute of Technology

Professional Record:

2014 – Present	Assistant Professor of Human Genetics, University of Michigan
2014 – Present	Assistant Professor of Computational Medicine and Bioinformatics, University of Michigan

Summary of Evaluation:

Teaching: Dr. Kitzman has proven to be an outstanding teacher and mentor in the classroom and the laboratory. He has directly trained five undergraduates, one graduate student, four post-doctoral fellows, and two clinical assistant professors. Each of these individuals performed, or is performing, at a very high level and directs an independent research project. Underscoring the effectiveness of Dr. Kitzman's mentorship, one post-doctoral fellow who recently completed his training in the Kitzman's lab has presented his research at several international meetings on genetics, published a first-author manuscript on deep mutational scanning in the *American Journal of Human Genetics*, and won the coveted Cotterman Award from the American Society of Human Genetics for publishing one of the top two trainee-written manuscripts in the society's journal. Dr. Kitzman co-developed two courses on computational biology, currently co-directs a course on computational genomics, has made significant contributions to the student paper presentation course, and gives a single lecture in three additional courses at the Medical School.

Research: Dr. Kitzman is well on his way to becoming a world leader in developing and employing cutting-edge approaches to study the functional consequences of genetic variation. He has been quite successful as an assistant professor and his major accomplishments include: (1) improving the clinical interpretability of rare *MSH2* variation through a saturation-scale functional screen of protein-coding variants; (2) establishing a platform for large-scale screens of splice disruption and applying this to identify splice-disrupting variants at *POU1F1*; and (3) making significant advances in technique development for a range of genomic applications (e.g., programmed mutagenesis; genome-wide CRISPR knockout and over-expression screens; and cost-efficient,

library-free targeted sequencing). As a result, he has published a total of 25 manuscripts in top-tier journals as an assistant professor; he also co-wrote a highly cited commentary (with other leaders in this field) on the impact of genetic variation. Dr. Kitzman has secured a significant amount of external funding for his research; he serves as the sole principal investigator of an R01 grant from NIGMS/NIH and as a co-investigator with effort on several awards from the NIH and Department of Defense.

Recent and Significant Publications:
Gergics, P, Smith, C, Bando, H, Jorge, AAL, Rockstroh-Lippold, D, Vishnopolska, SA, Castinetti, F, Maksutova, M, Carvalho, LRS, Hoppmann, J, Mayer, JM, Albarel, F, Braslavsky, D, Keselman, A, Bergada, I, Martí, MA, Saveanu, A, Barlier, A, Jamra, RA, Guo, MH, Dauber, A, Nakaguma, M, Mendonca, BB, Jayakody, SN, Ozel, AB, Fang, Q, Ma, Q, Li, JZ, Brue, T, Millán, MIP, Arnhold, IV JP, Pfaeffle, R, Kitzman, JO, Camper, SA: High-throughput splicing assays identify missense and silent splice-disruptive POU1F1 variants underlying pituitary hormone deficiency. Accepted, *American Journal of Human Genetics*, 2021.

Jia, X, Burugula, BB, Chen. V, Lemons, RM, Jayakody, S, Maksutova, M, Kitzman, JO: Massively parallel functional testing of *MSH2* missense variants conferring Lynch syndrome risk. *American Journal of Human Genetics*; 108(1):163-175, 2021.

Lenk, GM, Park, YN, Lemons, R, Flynn, E, Plank, M, Frei, CM, Davis, MJ, Gregorka, B, Swanson, JA, Meisler, MH, Kitzman, JO: CRISPR knockout screen implicates three genes in lysosome function. *Scientific Reports*; 9(1):9609, 2019.

Pérez Millán, MI, Vishnopolska, SA, Daly, AZ, Bustamante, JP, Seilicovich, A, Bergadá, I, Braslavsky, D, Keselman, AC, Lemons, RM, Mortensen, AH, Marti, MA, Camper, SA, Kitzman, JO: Next generation sequencing panel based on single molecule molecular inversion probes for detecting genetic variants in children with hypopituitarism. *Molecular Genetics & Genomic Medicine*; 6(4):514-25, 2018.

Kitzman, JO, Starita, LM, Lo, RS, Fields, S, Shendure, J: Massively parallel single-amino-acid mutagenesis. *Nature Methods* 12(3):203-6, 2015.

Service: Dr. Kitzman has provided significant, high-quality service to his departments, the university, and to the broader scientific community. He has twice directed the Human Genetics retreat and served on the Infrastructure Committee, Seminar and Events Committee, Ph.D. Admissions Committee, and Preliminary Exam Committee; he has also served on the Medical School's Basic Science IT Committee. Dr. Kitzman has served on 19 Ph.D. thesis committees. He has also reviewed abstracts for the annual meeting of the American Society of Human Genetics and performed ad hoc review service for several top genetics journals including *Nature Genetics* and the *American Journal of Human Genetics*. He has delivered seven invited seminars in both academic and industry settings, and has provided several opportunities for his trainees to present the laboratory's work—in place of himself—at national and international meetings.

External Reviewers:

Reviewer A: "…The quality, quantity, and scholarly impact are strong. The stated focus of his research is to develop technologies to assess how genetic variation affects gene function, to improve understanding of the functional basis of genetic variation. He describes a focus on inherited cancer susceptibility, but also collaborates widely to apply these techniques more broadly in other disease areas. The impact of that work, including several publications that are primarily from his own research group is solid…His AJHG paper (Jia et al) is outstanding and is clearly associated with the declared focus of his research program…His accomplishments are solid and I believe that he is a strong contender for promotion to Associate Professor with tenure."

Reviewer B: "The quality, quantity, focus and scholarly impact of Dr. Kitzman's work is outstanding. He uses cutting edge, genome-wide analyses and applies them to important biological problems. He is the driving intellectual force behind the work. He is one of a rare, special group of scientists who not only understand the biological questions and molecular biological approaches, but also can develop bioinformatic algorithms to analyze the data. He is a patient and articulate teacher, and guides students, postdocs and staff in understanding the big picture as well as the details of how to execute the work. He is an inventive and transformative researcher."

Reviewer C: "Dr Kitzman's work focuses on the problem of 'Variants of Uncertain Significance' or VUS…To address this problem, Dr. Kitzman develops high-throughput approaches to functionally assay VUS. This is vitally important to the field and will remain an area of intense interest and focus for many years. As such, Dr. Kitzman is well position [sic] to make an impact…Dr. Kitzman's 2020 manuscript in the American Journal of Human Genetics best represents the potential impact of his research program…It is clear from this manuscript that the Kitzman Lab has technical capabilities that few other labs have…Based on his current grant funding, publication record, and the importance of the area in which he is working, Dr. Kitzman would very likely be granted tenure at my own institution."

Reviewer D: "As an Assistant Professor on tenure track, Jacob has developed a successful research program with many accomplishments on record. He has strong external funding from about a dozen sources, developed collaborations with multiple colleagues within and outside U of M, and delivered talks at prestigious institutes and seminar series. It is also remarkable that Jacob has published 53 peer reviewed publications in prestigious journals such as Nature, Nature Methods, and the American Journal of Human Genetics, and about 20 manuscripts were published after 2015 as a tenure-track faculty at Michigan…Jacob's contribution to teaching is also remarkable. I find that his efforts towards developing a course for teaching programming skills to students as highly impactful and truly commendable…This level of teaching and service would definitely meet or exceed the bar for tenure at my institution…Without any reservations and with the highest enthusiasm, I strongly recommend providing Jacob Kitzman with tenure and promoting him to Associate Professor."

Reviewer E: "Dr. Kitzman has made research contributions to our understanding how DNA variation impacts protein function, developing and applying new technologies to create large libraries of protein variants and deploying them to measure their impacts on protein activities in cellular assays. His collaboration with a clinical genetics company provides excellent evidence of the profound value and opportunity of this approach in real clinical testing regimes. Consistent with his strong publication record, Dr. Kitzman has developed an emerging national and

international scientific reputation, evidenced by several invited seminars and conference presentations outside of his home institution…Dr. Kitzman has made excellent teaching and service contribution in establishing and teaching short and long-format courses on bioinformatic analysis approaches…In my opinion, Dr. Kitzman is a consummate modern scientist, able to collaborate with others to elevate their research programs while also maintaining a unique line of research within his own lab."

Reviewer F: "This is only one of the four co-corresponding papers he has co-authored as a faculty member, and the others are clearly of value, but honestly I expect that Dr. Kitzman's MSH2 paper (Jia et al., AJHG 2021) would be enough for me to recommend tenure at my own institution, given the combination of technical prowess and translational impact it represents…It is clear that he is a sought-after collaborator, given the number of shared grants and papers. He has been invited to speak at a number of well-respected conferences, including some international, and both in academic and industrial (clinical diagnostic) settings…The number of trainees listed at different stages suggest that he is an active mentor. He is also impressively multidisciplinary, serving as a mentor both on experimental and computational projects. I have no hesitation in recommending Dr. Kitzman favorably for appointment to Associate Professor with Tenure."

Reviewer G: "From the extent to which I know of [Dr. Kitzman] and his work, and on review of the submitted materials, I can speak without reservation as to his eligibility for the role of Associate Professor…His research outputs have been plentiful, high-impact and of direct clinical utility…He has a strong track-record of securing very sizeable awards as co-PI and co-I, and more recently has been successful in leading application as a PI large ($2.1m) NIH grant. He also has a number of other substantial applications currently in process…He has a number of markers at national level of recognition of research excellence, not least the Lindau Young Researcher award and finalist position for the ASHG award…In summary, this is an early-mid career researcher with an impressive track record who has made a substantial contribution institutionally, nationally and internationally genomics research in regard of research, training and contribution to the broader academy."

Summary of Recommendations:
Dr. Kitzman is an outstanding faculty member and colleague. He has made significant contributions to the Medical School's missions in research and education, and has performed extensive service to his departments and nationally. I am pleased to recommend the promotion of Jacob O. Kitzman, Ph.D. to associate professor of human genetics, with tenure, Department of Human Genetics, and associate professor of computational medicine and bioinformatics, without tenure, Department of Computational Medicine and Bioinformatics, Medical School.

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

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