Approved by the Regents
May 18, 2017

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF INTERNAL MEDICINE

Mark Chiang, M.D., Ph.D., assistant professor of internal medicine, Department of Internal Medicine, Medical School, is recommended for promotion to associate professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

Academic Degrees:

Ph.D.	2001	University of Pennsylvania
M.D.	2001	University of Pennsylvania
B.S.	1993	Yale University

Professional Record:

2010-present	Assistant Professor of Internal Medicine, University of Michigan
2006-2009	Instructor, Department of Medicine, University of Pennsylvania

Summary of Evaluation:

Teaching: Dr. Chiang's teaching activities span research instruction in his laboratory and participating in graduate student dissertation committee meetings, seminars, and recruitment, to clinical teaching for fellows, residents, interns and medical students as well as classroom instruction. He believes that mentoring and providing training to students in his laboratory is his main and most important teaching contribution. Since 2010, he has mentored 23 trainees at all levels from undergraduate freshman to post-doctoral fellows. His trainees have gone on to graduate or professional schools, given presentations at national conferences, and won prestigious awards. Dr. Chiang also values his clinical teaching activities and since 2012, has trained several internal medicine residents and two clinical hematology/oncology fellows in his outpatient hematology clinic. Additionally, he teaches an annual didactic lecture on hematological malignancies in the CB554 course (Cancer Pathogenesis and Treatment) which has received very favorable student evaluations and comments.

Research: Dr. Chiang became interested in how transcription factors, the essential proteins that regulate gene expression, could have pleotropic effects while he was a post-doctoral fellow. When he started his independent lab at the University of Michigan in 2010, he pursued this line of investigation, specifically researching why a transcription factor may cause cancer in one tissue but suppress cancer in another. This research led to an article published in *Blood* in 2013, describing how a transcription factor could drive the self-renewal of leukemia stem cells, but did the opposite in normal blood stem cells, resulting in bone marrow failure. This finding highlighted how total inhibition of a transcription factor kills cancer cells, but also damages normal cells, often resulting in unacceptable toxicities in patients. To tackle this challenge, Dr. Chiang focused on the "crosstalk" between transcription factors that controls growth and cell-type specific gene expression programs. His lab published examples in *PLoS One* and the *Journal of Hematology and Transfusion* before discovering a direct protein-protein interaction that instructed a transcription factor to cause cancer. Breaking this interaction caused leukemic cells to regress without major toxicities. This work was reported in *Cancer Research* and *Immunity*, showing that is was possible to selectively disable the cancer-causing functions of a transcription factor. This work has been favorably reviewed and Dr. Chiang is the recipient of an R01

to continue further investigation as well as funding from the American Cancer Society, the Pediatric Cancer Foundation and the Alex Lemonade Stand Foundation Innovation Award. Since his appointment at the University of Michigan, he has published 13 peer-reviewed publications, seven as first or senior author, with the most recent being a first-authored paper accepted for publication in *Blood*. Dr. Chiang's national and budding international reputation is evidenced by his extramural presentations in San Francisco, CA, Saxtons River, VT, Lewiston, ME and Athens, Greece.

Recent and Significant Publications:

Rakowski LA, Lehotzky EA, Chiang MY: Transient Responses to NOTCH and TLX1/HOX11 Inhibition in T-cell Acute Lymphoblastic Leukemia/Lymphoma. *PLoS ONE* 6:e16761, 2011.

Rakowski LA, Garagiola DG, Li CM, Decker M, Caruso S, Jones M, Kuick R, Cierpicki T, Maillard I, and Chiang MY: Convergence of the ZMIZ1 and NOTCH1 pathways at C-MYC in acute T lymphoblastic leukemias. *Cancer Res* 73:930-941, 2013.

Chiang MY*, Shestova O, Xu L, Aster JC, Pear WS: Divergent effects of supraphysiological Notch signals on leukemia stem cells and hematopoietic stem cells. *Blood* 121:905-917, 2013. *Co-corresponding author.

Pinnell N, Yan R, Cho H, Keeley T, Murai M, Liu Y, Serna Alarcon A, Qin, J., Wang, Q., Kuick R, Elenitoba-Johnson KSJ, Maillard I, Samuelson LC, Cierpicki T, Chiang MY: The PIAS-like coactivator Zmiz1 is a direct and selective cofactor of Notch1 in T-cell development and leukemia. *Immunity* 43:870-883, 2015.

Chiang MY*, Wang Q, Gormley AC, Stein, SJ, Xu L, Shestova O, Aster JC, Pear WS: High selective pressure for Notch1 mutations that induce Myc in T cell acute lymphoblastic leukemia. *Blood* in press, 2016. *Co-corresponding author.

Service: On the national level, Dr. Chiang is a member of the American Society of Hematology Scientific Committee for Blood Disorders in Childhood as well as a standing member of the Tumor Biology and Genomics Study Section for the American Cancer Society. Dr. Chiang serves on the editorial board of the *Journal of Hematology and Transfusion* in addition to serving as an ad hoc reviewer for *PLoS One, Nature Genetics*, *Blood*, and the *Journal of Pathology*, among others. Since his appointment as an assistant professor in 2010, Dr. Chiang has served as an attending for the hematological malignancies service at the University of Michigan Hospital as well as for the hematology consult service at the Ann Arbor VA Hospital. His outpatient clinic serves to diagnose, manage, and refer hematology patients to the appropriate subspecialist.

External Reviewers:

Reviewer A: "Prof. Chiang's produced several landmark papers in the Notch field. His latest discovery of Zmiz1 as a key component of the Notch coactivator complex was a highlight at the international Notch conferences in Athens and Maine."

Reviewer B: "From this vantage point, it is easy to see Dr. Chiang as a standout physician-scientist and an emerging leader in Hematology/Oncology circles... His early work laid a foundation for a deeper understanding of the context-dependent influence of Notch signaling in hematopoietic fate decisions and how misadventures in Notch signaling could contribute to the malignant phenotype... Mark is generous with his ideas and insightful in his perspective... I have no doubt that Mark would sail through the promotion and tenure process at my university."

Reviewer C: "Work on the Zmiz1 transcriptional coregulatory represents the most significant contribution from Dr. Chiang's group to date. This research has been reported in two senior author manuscripts in Cancer Research (2013) and Immunity (2015) and represents a comprehensive body of work. It may be early to assess the long term impact of these studies, but their quality demonstrates significant experimental proficiency and scientific maturity."

Reviewer D: "Dr. Chiang, a physician scientist, has established an independent research program, attained international recognition, and secured funding for his laboratory... The fact that nearly every Notch meeting features Mark as a speaker testifies best to his reception by his peers."

Reviewer E: "Mark is an outstanding...investigator who at this stage of his career had made significant scientific contributions to the area of Notch signaling and its role in leukemogenesis, and has procured substantial external funding to support his research program... Moreover, after hearing his talk this summer at the Notch Signaling GRC, it is clear that there are plenty of additional questions that need to be addressed in this area of biology and I expect Mark will make many more impactful findings."

Summary of Recommendation:

Dr. Chiang is on his way to becoming an internationally recognized expert in the field of notch signaling. His track record of extramural funding, thoughtful teaching, and compassionate clinical care has put him on a trajectory for success in academic medicine and it is for these reasons that I highly recommend Mark Y. Chiang, M.D., Ph.D. for promotion to associate professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

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

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