Approved by the Regents
May 16, 2019

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PATHOLOGY

Andrew G. Muntean, Ph.D., assistant professor of pathology, Department of Pathology, Medical School, is recommended for promotion to associate professor of pathology, with tenure, Department of Pathology, Medical School.

Academic Degrees:

Ph.D.	2006	University of Chicago
B.S.	1999	Indiana University

Professional Record:

2012–present	Assistant Professor of Pathology, University of Michigan

Summary of Evaluation:

Teaching: Dr. Muntean has extensive experience as an educator, through laboratory instruction. He serves on nine dissertation committees and has mentored numerous graduate students and postdoctoral fellows. Dr. Muntean has lectured in three graduate level courses and has served on nine dissertation committees. He has devoted considerable time and effort on committees involving education, including as the chair for the Molecular and Cellular Pathology Graduate Student Admission Committee, and as a member of two preliminary examination committees, and as organizer of the Hematopoiesis Research Group meeting. Dr. Muntean's mentees hold him in high regard and have written strong letters of reference in support of his promotion.

Research: Dr. Muntean's research has focused on the understanding of the role of epigenetic proteins in the mechanisms regulating normal hematopoiesis and acute myeloid leukemia, cooperative mechanisms in the generation of leukemia stem cells, and characterization and therapeutic targeting of epigenetic and transcription complexes in leukemia. He has made important, seminal contributions to these areas of research. He is the principal investigator of an NIH R01 grant, and an American Cancer Society grant. Dr. Muntean is a co-investigator of two NIH R01 grants. He has published 27 peer-reviewed reviewed articles, and has received two prestigious awards, the Hollis Brownstein Research Award from the Leukemia Research Foundation, and a Research Scholar Award from the American Cancer Society. Dr. Muntean has been invited to present his research regionally and nationally at universities and scientific society meetings.

Recent and Significant Publications:

Muntean AG, Chen W, Jones M, Granowicz EM, Maillard I, Hess JL: MLL fusion protein-driven AML is selectively inhibited by targeted disruption of the MLL-PAFc interaction. *Blood* 122(11: 1914-1922, 2013.

Chen L, Chen W, Mysliwski M, Serio J, Ropa J, Abulwerdi FA, Chan RJ, Patel JP, Tallman MS, Paietta E, Melnick A, Levine RL, Abdel-Wahab O, Nikolovska-Coleska Z, Munean AG: Mutated Ptpn

1 1 alters leukemic stem cell frequency and reduces the sensitivity of acute myeloid leukemia cells to Mel 1 inhibition. *Leukemia* 29(6): 1290-1300, 2015.

Chen L, Sun Y, Wang J, Jiang H, Muntean AG: Differential regulation of the c-Myc/Lin28 axis discriminates subclasses of rearranged MLL leukemia. *Oncotarget* 7(18): 25208-25223, 2016.

Serio J, Ropa J, Chen W, Mysliwski M, Saha N, Chen L, Wang J, Miao H, Cierpicki T, Grembecka J, Muntean AG: The PAF complex regulation of Prmt5 facilitates the progression and maintenance of MLL fusion leukemia. *Oncogene* 37(4):450-460, 2018.

Ropa J, Saha N, Chen Z, Serio J, Chen W, Mellacheruvu D, Zhao L, Basrur V, Nesvizhskii AI and Muntean AG: PAF1 complex interactions with SETDB1mediate promoter H3K9 methylation and transcriptional repression of Hoxa9 and Meisl in Acute Myeloid Leukemia. *Oncotarget* 9(31): 22138-22151, 2018.

Service: Dr. Munean has served on several international study sections internationally including for Bloodwise, and the American Society of Hematology as an abstract reviewer and as session chair. He has also served as the session chair of the Midwest Blood Club. He is a member of the University of Michigan Department of Cell and Developmental Biology IDEA Award committee and the Discovery Fund. Dr. Muntean is a reviewer for 19 journals, including the *Journal of Clinical Investigation*, and *PLoS One*.

External Reviewers:

Reviewer A: "His earlier work (2016 Oncotarget) focusing on the differences between biological/transcriptional differences between different MLL fusion oncoproteins also reflects the groups' strengths using quantitative molecular approaches and well defined model systems to discover important principles underlying transformation by this paradigmatic class of leukemia oncogenes. These strong publications from his lab have established him as an important independent force in the leukemia field and have cemented his lab's reputation as producing very meticulous studies that will stand the test of time."

Reviewer B: "He made a strong impact with his 2013 Blood paper showing a critical role for PAFc recruitment in leukemogenesis by MLL fusion proteins. This seminal finding made an impact in the field by counterintuitively revealing a component of the transcriptional elongation machinery to be an Achilles heel in leukemia cells. He has followed up on that work with a series of rigorous and innovative mechanistic papers that dissect the mechanisms for this unanticipated cancer vulnerability."

Reviewer C: "Andy's work has provided important contributions to our understanding of the molecular controls on transcription, especially how these principles change during leukemic transformation. His work is unique because it blends expertise in protein chemistry (which not many people are capable of anymore), with cutting edge molecular analysis. As such, Andy has carved a niche in the myeloid biology work and has generated important insights on the PAF complex and MLL1-fusion oncoprotein leukemia...which are supported by independent funding..."

Reviewer D: "Dr. Muntean has carved out an exciting scientific niche for his laboratory studies at Michigan, in the area of Mixed lineage leukemia's [sic] (MLL_). In particular, his work on studyin the mechanisms of MLL induced transformation, its pharmacologic inhibition by its binding partner

menin as well as his work related to the cooperation between MLL and oncogenic mutations of PTPN11 are outstanding…I consider him a leader in our field in this area."

Reviewer E: "Andy is a critical link for the further development of the understanding of the MLL fusion proteins in leukemia and ways to target this form of leukemia. Dr. Muntean's important contributions include demonstration of the importance of the PAF transcriptional elongation complex in driving aberrant gene expression in AML associated with MLL fusion proteins and discovering ways to interfere with this complex such as the use of MLLMenin inhibitors, disruption of the MLL-PAF interaction, and the interplay of the MLL fusion with signaling mutations such as those of the Ptpn11 gene and the interplay with arginine methyl transfuse PRMT5."

Reviewer F: " His studies reveal a new paradigm for the regulation of pro-leukemic gene programs and challenges the view that inhibition of H3K9 methyltransferases and/or PRMT5 will universally benefit AML patients. This original works greatly impacted the field and I am expecting more exciting breakthrough from Dr. Muntean's work…In summary, I consider Dr. Muntean is a rising star in the field of myeloid malignancies and is a well-recognized investigator in the field."

Summary of Recommendation:

Dr. Muntean has made significant contributions to the study of leukemias, including epigenetics, leading to seminal publications revealing differential functions of epigenetic regulatory proteins in leukemic and normal hematopoietic cells and the efficacy of targeting some of these proteins in acute myeloid leukemia. His work is well-funded, and he is a rising star and leader in his field. I am pleased to recommend Andrew G. Muntean, Ph.D. for promotion to associate professor of pathology, with tenure, Department of Pathology, Medical School.

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

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