

PROMOTION RECOMMENDATION  
THE UNIVERSITY OF MICHIGAN  
MEDICAL SCHOOL  
DEPARTMENT OF PATHOLOGY

Jolanta E. Grembecka, Ph.D., associate professor of pathology, with tenure, Department of Pathology, is recommended for promotion to professor of pathology, with tenure, Department of Pathology, Medical School.

Academic Degrees:

Ph.D.	2000	Wrocław University of Technology, Poland
M.S.	1995	University of Opole, Poland

Professional Record:

2016 - present	Associate Professor of Pathology, with tenure, University of Michigan
2009 - 2016	Assistant Professor of Pathology, University of Michigan
2006 - 2009	Research Assistant Professor, University of Virginia
2000 - 2002	Adjunct Faculty, Wrocław University of Technology, Poland
1995 - 1996	Research Assistant, University of Opole, Poland

Summary of Evaluation:

Teaching: Dr. Grembecka has extensive teaching didactically and through mentoring. She teaches ChemBio 502 and MedChem 533. In addition, she has mentored one Medical Science Training Program (MTSP) student and co-mentored five graduate students, one from the Molecular and Cellular Pathology and four from the Chemical Biology doctoral programs. Over the past 11 years, Dr. Grembecka has trained 18 post-doctoral fellows, and has served on 18 preliminary Ph.D. examination and dissertation committees. She has provided continuous and extensive teaching effort throughout her career at the University of Michigan. Her evaluations indicate that she is considered a very effective teacher and educator. She has served on several recruitment committees for Chemical Biology and Medicinal Chemistry, Molecular and Cellular Pathology and the Program in Biomedical Sciences (PIBS).

Research: Dr. Grembecka's research focuses on the development of small molecule inhibitors of proteins involved in acute leukemia. Her laboratory has targeted the development of small molecule inhibitors of the menin-MLL1 interaction as a new targeted therapy for acute leukemia, resulting in the development of very potent menin-MLL1 inhibitors. These represent the first reported small molecule inhibitors of this protein-protein interaction. The most current generation of these inhibitors demonstrates complete and long-lasting remission in acute leukemia models, including patient-derived xenograft (PDX) models. The successful development of the menin-MLL1 inhibitors has led to a partnership with a biotech company, Kura Oncology, which resulted in co-development of the KO-539 menin-MLL1 inhibitor that is currently in phase I/IIa clinical trials in acute myeloid leukemia patients and shows promising effects. The findings derived from her research have and will continue to have a significant impact on the field of cancer and inhibitors of critical pathways. Dr. Grembecka has had robust external grant funding from the National Institutes of Health, the Department of Defense, and the Leukemia and Lymphoma Society, for well over a decade, and she has been invited to present her work extensively at national and international conferences and universities. She has published 60 research articles, with 25 of them focused on menin-MLL1 inhibitors, and she has been granted nine patents with more in progress.

#### Recent and Significant Publications:

Rogawski DS, Deng J, Li H, Miao H, Borkin D, Purohit T, Song J, Chase J, Li S, Ndoj J, Klossowski S, Kim E, Mao F, Zhou B, Ropa J, Krotoska MZ, Jin Z, Ernst P, Feng X, Huang G, Nishioka K, Kelly S., He M, Wen B, Sun D, Muntean A, Dou Y, Maillard I, Cierpicki T, Grembecka J: Discovery of first-in-class inhibitors of ASH1L histone methyltransferase with anti-leukemic activity *Nat Commun* 12: 2792, 2021. PMC8121805

Miao H, Kim E, Chen D, Purohit T, Kempinska K, Ropa J, Klossowski S, Trotman WE, Danet-Desnoyers GA, Cierpicki T, Grembecka J: Combinatorial treatment with menin and FLT3 inhibitors induces complete remission in AML with activating FLT3 mutations. *Blood* 136(25): 2958-2963, 2020. PM33024997/PMC7751359.

Huang H, Howard CA, Zari S, Cho HJ, Shukla S, Li H, Ndoj J, González-Alonso P, Nikolaidis C, Abbott J, Rogawski DS, Potopnyk MA, Kempinska K, Miao H, Purohit T, Henderson A, Mapp A, Sulis ML, Ferrando A, Grembecka J: Covalent inhibition of NSD1 histone methyltransferase. *Nat Chem Biol* 16(12): 1403-1410, 2020. PM32868895/PMC7669657

Klossowski S, Miao H, Kempinska K, Wu T, Purohit T, Kim E, Linhares BM, Chen D, Jih G, Perkey E, Huang H, He M, Wen B, Wang Y, Yu K, Lee SC, Danet-Desnoyers G, Trotman W, Kandarpa M, Cotton A, Abdel-Wahab O, Lei H, Dou Y, Guzman M, Peterson L, Gruber T, Choi S, Sun D, Ren P, Li LS, Liu Y, Burrows F, Maillard I, Cierpicki T, Grembecka J: Menin inhibitor MI-3454 induces remission in MLL1-rearranged and NPM1-mutated models of leukemia. *J Clin Invest* 130: 981-997, 2020. PM31855575

Borkin D, Klossowski S, Pollock J, Miao H, Linhares B, Kempinska K, Jin Z, Purohit T, Wen B, He M, Sun D, Cierpicki T, Grembecka J The complexity of blocking bivalent proteinprotein interactions: development of a highly potent inhibitor of the menin-Mixed Lineage Leukemia (MLL) interaction. *J Med Chem* 61: 4832-4850, 2018. PM29738674

Service: Dr. Grembecka has provided and continues to provide extensive service to the department, the university, national and international societies and organizations. She serves on multiple institutional committees, including as a grant reviewer for the Kay Kendall Leukemia Fund and Leuka: Leading Leukemia Research in the United Kingdom, and the United States - Israel Bi-national Science Foundation, and Killam Program in Canada. Dr. Grembecka is a member of two NIH study sections and is a grant reviewer for the Leukemia and Lymphoma Society. She is an ad hoc reviewer for numerous journals and institutionally is a permanent member of the Biomedical Research Council.

#### External Reviewers:

Reviewer A: “The results of Dr. Grembecka’s efforts have had a high impact and exceed expectations for a full professor at my own institution. Since earning tenure, she has co-authored an impressive twenty-nine manuscripts, many in top journals such as Nature Communications, Cell Chemical Biology, Nature Chemical Biology, Journal of Clinical Investigation, Blood, and the ACS Journal of Medicinal Chemistry. She is a highly sought-after speaker, and has given thirty-two invited lectures at national and international venues in the past five years. Her grantsmanship is also outstanding; she serves as PI or co-PI on six current grants and co-investigator on another six. Dr. Grembecka’s funded projects cover at least seven different drug targets.”

Reviewer B: “Dr. Grembecka deserves the promotion, because she is exceptionally well qualified, productive and very well funded. Furthermore, her translational research is significant and

impactful....She is among the top chemical biologists in the hematologic malignancies field, and my impression is that any institution would be glad to have her as a professor on their faculty.”

Reviewer C: “Dr. Grembecka is an internationally recognized leader in the field of epigenetic drug discovery. In particular, she is the unequivocal leader and pioneer in discovering and developing small-molecule inhibitors of menin/MLL...In addition, Dr. Grembecka recently discovered the first ASH1L selective inhibitors (published in Nature Communications in 2021) and the first NSD1 covalent inhibitors (published in Nature Chemical Biology in 2020). Both ASH1L and NSD1 are extremely challenging epigenetic drug targets...In summary, Dr. Grembecka is an internationally recognized leader and pioneer in the epigenetic drug discovery field. Her research accomplishments are truly exceptional.”

Reviewer D: “I rank Dr. Jolanta Grembecka among the top class of medicinal chemists for her high-standard, rigorous and broadly-recognized scientific accomplishment, profound taste and significant contribution in the field of leukemia and epigenetic research as an interdisciplinary scientist, courage and ability to ace the most challenging drug targets in highly creative manners and with translational impact, and collegiality to collaborate with biologists and physician scientists...Jolanta’s team reported the first-in-class inhibitor BT5 with distinct covalent mode of interaction and of high quality (Nat Chem Biol 2020). This work is pioneering in several aspects: identification of a noncanonical allosteric binding pocket in NSD1, development of the small-molecule binders to perturb NSD1’s methyltransferase activity, and lead optimization with a covalent warhead for selective and effective target engagement...Jolanta not only continues the legacy as a top medicinal chemist by presenting BT5 against such a challenging target NSD1 but also demonstrated her leadership to lead multi-disciplinary efforts along the path of drug development. The latter is rarely seen among most of medicinal chemists but is clearly a visionary merit allowing Jolanta to stand out among her peers...Jolanta’s accomplishment would be promoted to a tenured professor if she were a faculty member in our institute.”

Reviewer E: “Dr. Grembecka has made major contributions to the hematologic malignancy field by studying the biochemical interaction between MLL and Menin...Dr. Grembecka is considered an internationally recognized leader in rational drug design to target fusion proteins deregulated in hematopoietic malignancies.”

Summary of Recommendation:

Dr. Grembecka is an internationally renowned researcher with many years of expertise designing potential therapeutic targets for use in cancer treatment. Her outstanding career not only illustrates top tier scholarship and research, but also outstanding mentorship, teaching and service. I am pleased to recommend Jolanta E. Grembecka, Ph.D. for promotion to 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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