Approved by the Regents
May 21, 2020

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF INTERNAL MEDICINE

Gregory A. Clines, 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:

M.D.	1999	University of Texas Southwestern Medical Center
Ph.D.	1999	University of Texas Southwestern Medical Center
B.S.	1990	University of Texas, Arlington

Professional Record:

2013-present	Assistant Professor of Internal Medicine, University of Michigan
2009-2013	Assistant Professor, University of Alabama, Birmingham
2005-2009	Assistant Professor, University of Virginia, Charlottesville

Summary of Evaluation:

Teaching: Dr. Clines' teaching included mentoring five undergraduate students, one graduate student, one resident and two fellows. He has served on three dissertation committees. He lectures to medical students in the endocrinology and has taught fellows on the inpatient endocrine consult service. For over 20 years, he has taught a fall course at Cold Spring Harbor Laboratory. In 2017, Dr. Clines was awarded the Teacher of the Year award by the endocrinology fellows. He has presented continuing medical education lectures at the Internal Medicine Board Review course on evaluation and management of hypercalcemia.

Research: Dr. Clines is an exceptional scientist whose research interests include mechanisms of bone metastasis, osteoblasts as mediators of androgen action in skeleton, regulation of spine metastasis by dura, skeletal biology and development, osteoblast biology and cystic fibrosis bone disease. He has secured continuous funding through the Department of Defense, National Institutes of Health and the Veterans Affairs. Dr. Clines was granted a patent on Compositions and Methods Comprising Endothelin A Receptor Antagonists and Androgen Therapies in May 2019. He has published more than 30 peer-reviewed articles in top tier journals including *Science, Cell and Nature Genetics.* Dr. Clines has co-authored two books, *Diagnosis and Management of Osteoporosis.* He has been invited to present his research on 18 occasions regionally, nationally and internationally.

Recent and Significant Publications:

Moon HH, Clines KL, Cooks MA, Cialek CA, Esvelt MA, Clines GA: Castration determines the efficacy of ETAR blockade in a mouse model of prostate cancer bone metastasis. *Endocrinology* 160: 1786-1796, 2019.

Choksi P, Jepsen KJ, Clines GA: The challenges of diagnosing osteoporosis and the limitations of currently available tools. *Clinical Diabetes and Endocrinology* 4: 12 (1-13), 2018.

Clines KL, Clines GA: DKK1 and Kremen expression predicts the osteoblastic response to bone metastasis. *Translational Oncology* 11: 873-882, 2018.

Szerlip N, Calinescu A, Van Poznak CH, Taichman RS, Clines GA: Dural cells release factors which promote cancer cell malignancy and induce immunosuppressive markers in bone marrow myeloid cells. *Neurosurgery* 83: 1306-1316, 2018.

Stalvey MS, Clines KL, Havasi V, McKibbin CR, Dunn LK, Chung WJ, Clines GA: Osteoblast CFTR inactivation reduces differentiation and osteoprotegerin expression in a mouse model of cystic fibrosis-related bone disease. *PLOS One* 8: e80098, 2013.

Service: Dr. Clines is an active member of the American Society for Bone and Mineral Research and Endocrine Society. He is a writing member for the Clinical Practice Guidelines on Hypercalcemia for the Endocrine Society. Dr. Clines chairs the Ann Arbor Veterans Affairs Medical Center Institutional Animal Care and Use Committee and is a member of the MEND Research Conference Committee and Michigan Diabetes Research Center, Enrichment Core Advisory Committee. He has contributed to his field with service as an ad hoc reviewer for 11 journals including *PLoS One*, and the *Journal of Clinical Endocrinology and Metabolism*. He also serves nationally as an ad hoc reviewer for a NIH study group on Understanding Skeletal Effect of Type 1 Diabetes, and internationally as a peer reviewer for the Department of Defense Pre-Musculoskeletal Disorders. Dr. Clines has served as an editorial board member for *The Journal of Clinical Endocrinology & Metabolism*, *The Journal of Bone and Mineral Research* and *Clinical Diabetes and Endocrinology*. In 2019, he became associate editor of *Clinical Diabetes and Endocrinology*.

External Reviewers:
Reviewer A: "Dr. Clines has had a long-standing and productive research program that focuses on bone physiology and the pathophysiology of bone metastases. His work is funded on a NIH R21 award, a Department of Defense grant, and a VA Merit Award. He has also lectured widely on his research interests."

Reviewer B: "I was immediately impressed by his thinking, preparation, and compassion for his patient…I am happy and impressed he was able to successfully renew his VA Merit grant focused on the mechanisms of endothelin and androgen signaling cooperation in prostate cancer bone metastasis… I think Greg's work is vitally important and clearly needed. I find it entirely feasible that his intriguing data may encourage future clinical trials in men with metastatic prostate cancer and move the field forward."

Reviewer C: "He recently renewed his VA Merit Award on endothelin-1 and androgen signaling in prostate cancer bone metastasis. He is also co-investigator on two NIH grants and has recently submitted a foundation grant and an R01. He has filed one patent while at The University of Michigan. His publication record reflects his areas of interest and he has published 5 last author papers in 2018 and is on track to have a very productive 2019."

Reviewer D: "Dr. Clines…has a solid record of peer-reviewed publications and has maintained continuous grant funding from the VA, DoD and the NIH. He is a physician scientist who has performed satisfactory service and teaching and is an acknowledged expert non osteoblastic metastasis and disorders of mineral metabolism associated with cancer and cystic fibrosis."

Reviewer E: "Dr. Clines represents a model clinical scientist who has had an impact in clinical science, both in terms of osteoporosis and metastatic bone disease, as well as in bench research. In respect to the latter, as noted, Greg has continued his work on endothelin-1 and its role in metastatic bone disease. But his exciting work centers on two areas, 1- the role of the dura in secreting factors that enhance metastatic disease to bone; and 2- the impact of androgen secretion from osteoblasts on endothelin-1 and metastatic prostate disease to bone…Targeting osteoblast synthesis of androgens may provide new approaches to prostate cancer and metastates."

Reviewer F: "…I believe that Dr Clines ranks among the best of the physician scientists combining research and clinical care in Endocrinology. He has performed and published nuanced and novel work of high impact in the prostate cancer field, and is poised to contribute substantially to clinical care paradigms in the future. These types of individuals are rare – and they are critical to our academic institutions as mentors, participants in the scientific enterprise and are key to the advance of medicine."

Summary of Recommendations:
Dr. Clines has a presence on the national and international scene as a well-regarded clinical scientist in osteoporosis medicine. He has made vast contributions in the field of bone biology. I am pleased, therefore, to recommend Gregory A. Clines, M.D., Ph.D. for promotioin to associate professor of internal medicine, Department of Internal Medicine, Medical School.

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

May 2020