

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

Benjamin H. Singer, M.D., Ph.D., assistant professor of internal medicine, Department of Internal Medicine, Medical School, is recommended for appointment to associate professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

Academic Degrees:

M.D.	2010	University of Michigan
Ph.D.	2010	University of Michigan
B.S.	2002	University of Michigan

Professional Record:

2017-Present	Assistant Professor of Internal Medicine, University of Michigan
2016-2017	Clinical Lecturer of Internal Medicine, University of Michigan

Summary of Evaluation:

Teaching: Dr. Singer has been actively involved in teaching and mentoring throughout his training and career, in both the clinical and research settings. He has trained undergraduate students, a post-doctoral fellow, a medical student, clinical fellows, and an advanced post-graduate fellow. He has been an active participant in medical student education in a variety of venues, regularly facilitating small group instruction for the preclinical pulmonary medicine and pulmonary physiology courses, as well the dyspnea and shock sessions for the Transitions to the Clinic course. In the clinical setting, Dr. Singer has been actively involved in the supervision and teaching of internal medicine residents as an attending physician. As a designated clinic preceptor for the Division of Pulmonary and Critical Care's fellowship program, Dr. Singer provides clinic supervision teaching for a half-day clinic, twice per month. In addition, he instructs and supervises fellows in the interpretation of pulmonary function tests. Dr. Singer has mentored two clinical fellows in Pulmonary and Critical Care Medicine who had relatively little experience in the laboratory before their fellowship. Under his mentorship, they have continued to find success in laboratory-based science, one of them successfully competing for an NIH K08 award. Given that a small proportion of graduates from pulmonary and critical care fellowships continue in research, with an even smaller proportion pursuing basic and translational research careers, Dr. Singer considers intensive mentorship of these fellows as an important contribution to the field and the University of Michigan. He is a committee member for seven dissertation committees.

Research: As a critical care physician-scientist, Dr. Singer studies the mechanisms of persistent organ dysfunction in survivors of critical illness. Since 2017, the focus of his research has been on understanding mechanisms of brain injury and dysfunction in sepsis survivors that persist beyond the initial period of acute illness. He has used naturalistic models of infection and sepsis to identify pathways that lead to chronic neuroinflammation and reprogramming of microglial phenotype. These initial studies of neuroinflammation have evolved to consider how co-existing neuropathology increases vulnerability to brain dysfunction in sepsis survivors. Dr. Singer is

making tremendous scientific strides in this space, which he hopes will result in more accurate prediction for which patients are vulnerable to chronic brain dysfunction, as well as the discovery of treatable mechanisms of brain injury, in order to prevent or reverse the functional decline often experienced by survivors of critical illness. His groundbreaking research findings have been recognized by the *American Thoracic Society*, the *Central Society for Clinical and Translational Research*, and the *American Society for Clinical Investigation*. His future research plans include the expansion of his research program to include more granular investigations of behavior and neurophysiology in sepsis survivor animals. Within the next year, Dr. Singer plans to develop several collaborative projects that are currently at the pilot stage, including studies of the neurophysiology of Cytokine Release Syndrome in CAR-T therapy and studies of the role of sepsis in promoting the development of steatohepatitis. Dr. Singer is well funded, currently serving as the principal investigator of an R01 award and co-principal investigator on an R61 and institutional grant. He currently serves as a co-investigator on another four grants. He has authored 33 peer-reviewed publications in leading industry journals including *Blood*, and *Endocrinology*. In recognition of his scholarly excellence, Dr. Singer was the recipient of the 2019 Young Physician-Scientist Award given by the American Society for Clinical Investigation.

#### Recent and Significant Publications:

- Su SH, Song Y, Newstead MW, Cai T, Wu M, Stephens A, Singer BH\*, Kurabayashi K\* (\*co-senior authors), "Ultrasensitive Multiparameter Phenotyping of Rare Cells Using an Integrated Digital-Molecular- Counting Microfluidic Well Plate," *Small* 17(31): e2101743, 2021. PM34170616/PMC8349899
- Bustamante AC, Opron K, Ehlenbach WJ, Larson EB, Crane PK, Keene CD, Standiford TJ, Singer BH, "Transcriptomic Profiles of Sepsis in the Human Brain," *Am J Respir Crit Care Med* 201(7): 861-863, 2020. PM31940219/PMC7124721
- Denstaedt SJ, Spencer-Segal JL, Newstead M, Laborc K, Zeng X, Standiford TJ, Singer BH, "Persistent Neuroinflammation and Brain Specific Immune Priming in A Novel Survival Model of Murine Pneumosepsis," *Shock* 54(1): 78-86, 2019. PM31415473/PMC7015772
- Denstaedt SJ, Spencer-Segal JL, Newstead MW, Laborc K, Zhao AP, Hjelmaas A, Zeng X, Akil H, Standiford TJ, Singer BH, "S100A8/A9 Drives Neuroinflammatory Priming and Protects against Anxiety like Behavior after Sepsis," *J Immunol* 200(9): 3188-3200, 2018. PM29563178/PMC5915914
- Singer BH, Dickson RP, Denstaedt SJ, Newstead MW, Kim K, Falkowski NR, Erb-Downward JR, Schmidt TM, Huffnagle GB, Standiford TJ, "Bacterial Dissemination to the Brain in Sepsis," *Am J Respir Crit Care Med* 197(6): 747-756, 2018. PM29232157/PMC5855074

Service: Dr. Singer is a superb critical care physician who provides care to chronically ill patients, most with advanced lung disease, neuromuscular disease, and chronic critical illness who require mechanical assistance with ventilation while living at home. He provides sub-specialty care to this population as part of the outpatient Assisted Ventilation Clinic. He also treats these patients as an inpatient attending on the medical moderate inpatient care service. In addition to his excellence in clinical care, he continues to excel in citizenship and service within Michigan Medicine and beyond. Institutionally, as the medical director of the Medicine Pulmonary service, where he supervises a group of 21 Advanced Practice Providers who provide care in both the moderate care services and intensive care units. Dr. Singer is also a co-lead of the Pulmonary and Critical Care Division's task force, a group responsible for envisioning the future state of moderate

and critical care provided by the Division of Pulmonary and Critical Care Medicine. Nationally, Dr. Singer is an active member of numerous organizations, including the American Association of Immunologists and the American Thoracic Society (ATS), among others. Currently, he serves as the program coordinator for the ATS Early Career Professional Working Group. He also has performed ad hoc peer reviews for more than ten industry-leading journals, including *Critical Care Medicine*, *Annals of the American Thoracic Society*, and the *American Journal of Respiratory and Critical Care Medicine*. He has served ad hoc on six NIH study sections.

External Reviewers:

Reviewer A: “As a translational ARDS researcher, I am well aware of Dr. Singer’s work in the field and view him as a rising star in the critical care community...His scientific productivity is impressive, and the quality and originality of his work are top notch. He is a leader in the field of defining biologic mechanisms of neurocognitive dysfunction during sepsis and beyond and publishes work of the highest quality in the leading journals in the field.”

Reviewer B: “In my view, Dr. Singer is one of the leading scientists in the nation and in the world on the topic of biological mechanisms of brain dysfunction in sepsis and related critical illness...His speaking invitations, selection for NIH study sections, and invitations as a peer reviewer testify to his national reputation in this field, and his impressive grant funding portfolio (which includes an R01 on this topic) provides further support for his scientific excellence.”

Reviewer C: “With respect to Prof. Singer’s standing in relation to others in his peer group who are working in the same field, the field of fundamental research in sepsis-associated neuroinflammation and brain dysfunction has been seriously underpopulated and this marks out his work as highly novel...His inclusion on several other studies in clinical biomarker development, again in the context of sepsis and COVID19 illustrates that he is a collaborative clinical researcher and is highly responsive to emerging phenomena and populations in the ICU setting.”

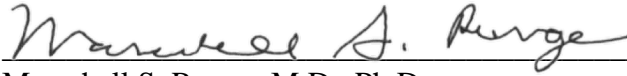
Reviewer D: “In term[s] of Dr. Singer’s standing in relation to others in their peer group – he is in a very small category of clinician-scientists critical care intensivists that run a basic science laboratory. Very few physicians, especially those working in the intensive care unit, can sustain a successful research laboratory – especially one with the translational breadth of research Benjamin’s lab...In terms of teamwork and team leadership, I can see Dr. Singer is building a strong network of collaborators.”

Reviewer E: “Dr. Singer’s particular interest is in using naturalistic models of infection and sepsis to look at pathways leading to chronic inflammation and reprogramming of microglial phenotypes are particularly well timed...I am particularly encouraged by his entry into this arena of sepsis survivorship because we must all recognize this as a burgeoning area of health concern in our country and world...Dr. Singer’s work will surely bring light to this area of study and hopefully help us find answers for the millions of people suffering in these ways.”

Summary of Recommendation:

Dr. Singer is a remarkable and enthusiastic physician-scientist who has made outstanding contributions in the areas of clinical care, education, research, and service. He is a leader in the

field of sepsis-associated neuroinflammation and brain dysfunction. I recommend Benjamin H. Singer, M.D., Ph.D. for promotion to associate professor of internal medicine, with tenure, Department of Internal Medicine, Medical School.

A handwritten signature in cursive script that reads "Marschall S. Runge". The signature is written in black ink and is positioned above a horizontal line.

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

May 2023