Approved by the Regents
May 19, 2022

PROMOTION RECOMMENDATION
THE UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PEDIATRICS

Antonia Popova, M.D., assistant professor of pediatrics, Department of Pediatrics, Medical School, is recommended for promotion to associate professor of pediatrics, with tenure, Department of Pediatrics, Medical School.

Academic Degrees:

M.D.	1996	Medical University of Varna, Bulgaria

Professional Record:

2012 - present	Assistant Professor of Pediatrics, University of Michigan
2010 - 2012	Clinical Lecturer of Pediatrics, University of Michigan
2000 - 2004	Software Engineer, Siemens Medical Solutions, Issaquah, WA
1999 - 2000	Library Runner, Information Express, Palo Alto
1997 - 1998	Physician Observer, Barzilai Medical Center, Israel

Summary of Evaluation:

Teaching: Dr. Popova has instructed pre- and post-doctoral learners throughout her career in clinical and research settings. Clinically, she teaches and supervises medical students during their inpatient pediatrics clerkship, house officers on their endocrinology/pulmonary rotation, and pediatric pulmonology fellows on the inpatient service, during bronchoscopies, and in outpatient clinics. In the research setting, she has served as a research mentor for graduate students, house officers and fellows. She has participated on research advisory committees for multiple house officers and fellows and on graduate student preliminary exam committees and graduate student seminars in the Graduate Program of Immunology. Dr. Popova also serves as a member of the Immunology Preliminary Exam Committee and has mentored undergraduate students from the University of Michigan interested in neonatal lung inflammation research. Evidence of her effectiveness as a research mentor is demonstrated by having one of her undergraduate student mentees receive an Undergraduate Student Research Award at the Department of Pediatrics Research Symposium (2018). In recognition or her excellence in education, she received the Pediatric Medical Student Education Award in 2015. One of her most significant teaching contributions has been in developing lectures to prepare fellows and faculty for board certification in Pediatric Pulmonology.

Research: Dr. Popova has a nationally recognized research program on the mechanisms of chronic pulmonary complications related to premature birth including Bronchopulmonary Dysplasia (BPD) and asthma. Among her many unique contributions to the field has been the concept that airway inflammation in BPD is caused by Damage-associated Molecular Pattern (DAMP)-induced activation of $CD103^{+}$ $Clec9a^{+}$ dendritic cells. Dr. Popova's program is supported as principal investigator by her NHLBI R01 grant entitled "Early life hyperoxic exposure, lung innate immune responses, bronchopulmonary dysplasia and asthma." Her research studies span both pre-clinical and clinical research. She has active research studies

examining clinical samples from premature infants with respiratory distress syndrome (who may go on to develop BPD) and she has collaborations through which she shares tracheal aspirate samples and lung mesenchymal cells from BPD infants with other investigators for research. In recognition of her contributions to this field, Dr. Popova was appointed the physician lead for the C.S. Mott Children's Hospital Bronchopulmonary Dysplasia Collaborative Team. In this role, she contributes to national research efforts on BPD with other clinical researchers from around the nation. Evidence of her national reputation is demonstrated by her peer service and the invited talks she has given at peer institutions, including the University of Rochester, The Ohio State University, University of Washington, and University of California-San Diego. Dr. Popova has published 24 original research articles and 34 abstracts.

Recent and Significant Publications:

Cui TX, Fulton CT, Brady AE, Zhang YJ, Goldsmith AM, Popova AP: Lung CD103+dendritic cells and Clec9a signaling are required for neonatal hyperoxia-induced inflammatory responses to rhinovirus infection. *Am J Physiol Lung Cell Mol Physiol* 320(2): L193-L204, 2021.

Cui TX, Brady AE, Fulton CT, Zhang YJ, Rosenbloom LM, Goldsmith AM, Moore BB, Popova AP: CCR2 Mediates Chronic LPS-Induced Pulmonary Inflammation and Hypoalveolarization in a Murine Model of Bronchopulmonary Dysplasia. *Front Immunol* 11: 579628, 2020.

Fulton CT, Cui TX, Goldsmith AM, Bermick J, Popova AP: Gene Expression Signatures Point to a Male Sex-Specific Lung Mesenchymal Cell PDGF Receptor Signaling Defect in Infants Developing Bronchopulmonary Dysplasia *Sci Rep* 8(1): 17070, 2018.

Cui TX, Maheshwer B, Hong JY, Goldsmith AM, Bentley JK, Popova AP: Hyperoxic exposure of immature mice increases the inflammatory response to subsequent rhinovirus infection: association with danger signals *J Immunol.* 196(11): 4692-705, 2016.

Popova AP, Bentley JK, Cui TX, Richardson MN, Linn MJ, Lei J, Chen Q, Goldsmith AM, Pryhuber GS, Hershenson MB: Reduced platelet-derived growth factor receptor expression is a primary feature of human bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol* 307(3): L231-L239, 2014.

Service: Dr. Popova's clinical expertise is in the care of infants with BPD and other pediatric lung diseases including asthma, childhood interstitial lung disease, pediatric post-COVID syndrome, cystic fibrosis, and others. She serves as an attending pediatric pulmonologist on our inpatient service and in the outpatient general pulmonary clinic. Additionally, she has a weekly clinic devoted to the care of BPD patients. Dr. Popova has important and significant service in her field including service as a member of the editorial board of the *American Journal of Physiology: Lung Cell and Molecular Physiology*. She is also a member of the Early Career Professional Working Group Pediatrics Assembly (2019-present) and prior to that was a member on the Assembly on Allergy, Immunology and Inflammation (2016-2017) of the American Thoracic Society. She also serves on the Steering Committee of the Neonatal and Developing Lung Interest Group of the American Thoracic Society (2019-present). In 2021, Dr. Popova was appointed as an ad-hoc application reviewer for the NIH/NHLBI Extramural Loan Repayment for Pediatric Research and Reviewer for the NIH/NIAID Asthma and Allergic Diseases

Cooperative Research Centers. She has reviewed manuscripts for many journals including *Scientific Reports* and the *American Journal of Respiratory and Critical Care Medicine*. Dr. Popova serves on the Steering Committee for Neonatal and Developing Lung Interest Group for the American Thoracic Society (2019-present).

External Reviewers:
Reviewer A: "Dr. Popova published very important research describing how tracheal MSCs are elevated in severe BPD and thus might not always be beneficial. This prompted further research into the mechanisms of how MSCs differentiate into myofibroblasts, cells that may lead to worsening lung disease in preterm neonates. Dr. Popova continues to study important pathways involved in the pathogenesis of severe BPD and her work remains influential in the field."

Reviewer B: "She is a bright, motivated, productive physician-scientist who has over the past 8 years has [sic] established a national reputation in pediatric pulmonology focused on her investigations of the pathogenesis of bronchopulmonary dysplasia (BPD) in premature infants…Over the past 8 years Dr. Popova has built an innovative basic and translational research laboratory focused primarily on investigating the pathogenesis of BPD and prematurity-related chronic respiratory disease, as well as the effects of early life exposures associated with preterm birth (e.g. hyperoxia or infection) through release of damage associated molecular patterns (DAMPs) on priming immature innate immune responses…She has demonstrated a sustained and accelerating record of professional achievements in teaching, service, and research."

Reviewer C: "As evident [sic] from her publications, Antonia has been involved in research for many years with the goal of uncovering novel innate pathways causing long-term lung disease in preterm newborns and identifying new targets for therapeutic intervention. Funded with grants from the National Institutes of Health, her research work has its focus on DAMP receptor mediated activation of CD103+ DCs. She also studies TLR3 receptors which are of great significance. She uses both hyperoxia and LPS mediated models to study BPD and hence contributes significantly to the field of neonatal lung injury. Given her accomplishments, I see a promising future for Dr. Popova as a physician scientist in the research world. I strongly believe that she is indeed an asset to the scientific community."

Reviewer D: "Dr. Popova is recognized nationally for her work on the impact of early life exposures and lung responses and pathogenesis of bronchopulmonary dysplasia. Her seminal work on the effects of neonatal viral infection and allergic asthma provides the basis by which many of us in the field design our experimental models. The significance of her research and stature in the field are demonstrated by the invitations to present her work in department seminars and major invited speeches…Her work on the innate sensing pathways activated during viral infection or under hypoxic conditions in neonates is of high impact with direct relevance to the development of bronchopulmonary dysplasia and allergic asthma in children."

Reviewer E: "Dr. Popova has published in high quality journals that are widely read by the leading investigators in this field. My impression is that most of her mansucripts [sic] originate directly from her laboratory and therefore the number seems excellent for a [of her cohort] physician-scientist. Most manuscripts focus on common themes in lung development, injury,

and the mechanisms of pediatric lung disease…Among her publications, the 2016 J Immunol paper was particularly provocative. The role of endogenous DAMP mediators signaling through Clec9 could prove to be an exciting mechanism, both in terms of basic biology and potential therapeutic strategies…Dr. Popova's peer group is much smaller today than it might have been 15-20 years ago. Nonetheless, she has distinguished herself as one of the few lung biologists within Pediatrics that has successfully navigated the physician-scientist path."

Reviewer F: "Dr. Popova's area of research expertise is evaluating molecular mechanisms that contribute to the development of BPD. This is an important area of research, as there are currently no good therapies to prevent or minimize the development of BPD. She has used both animal models, as well as samples from human infants, successfully obtaining NIH RO1 funding for her research…In summary, Dr. Popova has an excellent reputation as a researcher, having made important contributions to our under understanding of the molecular mechanisms that contribute to chronic lung disease following premature birth."

Summary of Recommendations:
Dr. Popova is a physician-scientist who is nationally recognized for her pioneering work in the field of bronchopulmonary dysplasia. She continues to make new discoveries in evaluating molecular mechanisms that contribute to the development of bronchopulmonary dysplasia. She is also an outstanding mentor and clinician who has performed valuable service at Michigan Medicine and the field at large. I am pleased to recommend Antonia Popova, M.D. for promotion to associate professor of pediatrics, with tenure, Department of Pediatrics, Medical School.

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

May 2022