Approved by the Regents
May 14, 2009

PROMOTION RECOMMENDATION
UNIVERSITY OF MICHIGAN
MEDICAL SCHOOL
DEPARTMENT OF PEDIATRICS AND COMMUNICABLE DISEASES

Thomas P. Shanley, M.D., associate professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, Medical School, is recommended for promotion to professor of pediatrics and communicable diseases, with tenure, Department of Pediatrics and Communicable Diseases, Medical School.

Academic Degrees:

M.D.	1989	University of Chicago
B.A.	1985	Carleton College

Professional Record:

2004-present	Associate Professor of Pediatrics and Communicable Diseases, University of Michigan
2002-2004	Associate Professor of Pediatrics, University of Cincinnati
1997-2002	Assistant Professor of Pediatrics, University of Cincinnati

Summary of Evaluation:

Teaching: Dr. Shanley has always made his teaching responsibilities a very high priority in his academic practice. Since his arrival at the University of Michigan, he has continued to place a high priority on his teaching responsibilities and maintained a strong reputation among trainees. As director of the Fellowship Program in PCCM (Pediatric Critical Care Medicine), he has had excellent evaluations from fellow trainees. He has given a number of lectures to the Pediatric house staff including two lectures each month to those rotating through the PICU. His teaching evaluations from the house staff have been uniformly excellent and he has been named a Top 10 Teacher in the department for the past three years. His teaching skills are recognized at the national level. He has co-edited the most recent, comprehensive pediatric critical care text entitled, "*Pediatric Critical Care Medicine: Basic Science and Clinical Evidence.*" On six separate occasions, he has either co-chaired or chaired the two most prominent national, educational meetings targeted to pediatric intensivists that are sponsored by the Society of Critical Care Medicine: the Pediatric Multiprofessional Critical Care Review Course and the Current Concepts in Pediatric Critical Care Course. In the laboratory setting, Dr. Shanley has and continues to, mentor a number of trainees ranging from undergraduate students to post-doctoral fellows, many of whom have secured academic pediatric positions and secured mentored or independent funding.

Research: Dr. Shanley has maintained an active and productive research program. Having been trained in the laboratory of Dr. Peter Ward under the auspices of the Pediatric Scientist Development Program, he began examining the regulation of acute lung inflammation in models of lung injury. Among the findings from this work, he established that IL-10 was a crucial anti-inflammatory cytokine that down regulated other pro-inflammatory mediators. After transitioning to Cincinnati Children's Hospital Research Foundation, he was supported on a Departmental CHRC and AHA Young Investigator Grant prior to submitting a competitive KO8 application sponsored by Dr. Jeffrey Whitsett. The aims of the grant included the development of a unique transgenic mouse capable of externally regulated (via doxycycline chow), lung-specific (via a Clara Cell promoter-driven expression of the reverse tetracycline transactivator gene) human IL-10 over-expression. The role of IL-10 in regulating cytokine and chemokine expression via suppression of NF-□B signaling led Dr. Shanley to examine additional signal transduction pathways and additional endogenous regulators of these pathways. One of the key family of molecules identified through this work were phosphatases--enzymes capable of dephosphorylating and thus, typically deactivating kinases. Two key phosphatases he has studied most recently include the Serine/Threonine phosphatase, PP2A and the Dual Specific Phosphatase, MKP-1 and this work has been funded via NIH/NIGMS R01 mechanism. Dr. Shanley's laboratory has identified PP2A as a key negative regulator of the c-jun N-terminal kinase (JNK1) and p38 MAP kinases. The mechanism by which p38 is regulated involves upstream targets, MK2 and TTP, with a consequent effect on destabilizing cytokine mRNA.

This basic science work complimented with his clinical observations in the PICU led to a strong interest in translational investigations in pediatric critical care that ultimately focused on gene expression patterns in sepsis and so-called "immunophenotyping" patients following exposure to extracorporeal circuits (e.g. ECMO, CPB and CRRT). He was a co-investigator for the R01-supported grant, Gene Expression Profiling in Pediatric Systemic Inflammatory Response Syndrome/Sepsis. Results from this multi-center study have been reported in three seminal manuscripts reporting on: the ability to measure substantial gene expression changes in pediatric sepsis with insight into novel mechanisms (e.g. zinc metabolism), kinetic changes from day one to day three and validation of the experimental approach. One of the challenges involved in treating critically ill children has been determining whether their immune systematic response needs to be attenuated (to prevent organ injury) or "boosted" because of a functional immunosuppression that attenuates pathogen clearance. Current work is aimed at being able to phenotype this immune responsiveness and determine the molecular mechanism by which circulating monocytes become less responsive to activation by pathogen associated molecular patterns. Further, within the context of a randomized trial of tight glycemic control in infants following cardiac surgery, Dr. Shanley's laboratory has obtained funding to determine whether this approach alters the immune response of the children, preserves pathogen clearance and thus, reduces post-operative infection complications. Therefore, in combination with his basic science efforts synergizing with a clinical/translational effort, Dr. Shanley has led a productive research program making important contributions to our understanding of signal transduction, gene expression and clinical outcomes. He remains one of the very few NIH-funded physician-scientists in his medical sub-specialty of Pediatric Critical Care Medicine. He continues to lead a number of national, multi-center studies and is the site PI for C.S. Mott Children's Hospital's participation in other network-sponsored trials. He has recently been appointed director of Clinical Research for the Department with the responsibility of enhancing and growing the clinical and translational research infrastructure, activity and funding.

Recent and Significant Publications:

Zhao B, Sun L, Haas M, Denenberg A, Wong HR, Shanley TP: PP2A regulates upstream members of the c-jun N-terminal kinase mitogen-activated protein kinase signaling pathway. *SHOCK* 29(2):181-188, 2008.

Shanley TP, Cvijanovich N, Lin R, Allen GL, Thomas NJ, Doctor A, Kalyanaraman M, Tofil NM, Penfil S, Monaco M, Odoms K, Barnes M, Sakthivel B, Aronow BJ, Wong HR: Genome-level longitudinal expression of signaling pathways and gene networks in pediatric septic shock. *Mol Med* 13(9-10):495-508, 2007.

Sun L, Stoecklin G, Vanway SM, Hinkovska-Galcheva V, Guo R-F, Shanley TP: The role of phosphatase 2A on the post-transcriptional regulation of TNF alpha secretion in alveolar macrophages. *J Biol Chem* 282(6):3766-3777, 2007.

Wong HR, Shanley TP, Bhuvaneswari S, Cvijanovich N, Lin R, Allen GL, Thomas NJ, Doctor A, Kalyanaraman M, Tofil NM, Penfil S, Monaco M, Tagavilla MA, Odoms K, Dunsmore K, Barnes M, Aronow BJ for the Genomics of Pediatric SIRS/Septic Shock Investigators: Genome level expression profiles in pediatric septic shock indicate a role for altered zinc homeostasis in poor outcome. *Physiol Genomics* 30(2):146-155, 2007.

Spight D, Zhao B, Haas M, Denenberg AG, Shanley TP: Immunoregulatory effects of regulated, lung-targeted expression of IL-10 in vivo. *Am J Physiol Lung Cell Mol Physio*l 288(2):L251-65, 2005.

Service: Dr. Shanley has held an increasing number of departmental service positions over the course of his academic career. Since transitioning to the University of Michigan, he has continued to be active in service roles at the divisional, departmental and national level. As director of Pediatric Critical Care Medicine, Dr. Shanley oversees all clinical, training and research activities of the Division. He is the program director for the PCCM Fellowship Program and has navigated the program through its most recent external RRC review. He is a standing member of the PCCM PICU Joint Practice Committee responsible for all policies and procedures regulating the PICU clinical activities. He was instrumental in starting the COPS (Committee on Pediatric Sedation), a multidisciplinary effort to optimized sedation practices in the PICU. This activity has resulted in the PICU's participation as one of 17 centers in an NHLBI-sponsored clinical trial on pediatric sedation. At the departmental level, he has been re-elected by peers to serve a second term on the Research Advisory Committee and also sits on the Mott Executive Committee and the Grand Rounds Committee. He has been actively involved in resident, fellow and faculty recruitment and sat on the search committee for division chief of Pediatric Hematology-Oncology and chaired the search committee for division chief of Pediatric Cardiology. At the Hospital level, he has served on the C.S. Mott Children's and Women Hospitals Replacement Project, the Pandemic Flu Ventilator Triage Sub-Committee, and the Nextel Phone Project. Finally, he has served a three-year term on the Medical School's Biomedical Research Council. At the national level, he was most recently reappointed to the Pediatric Subcommittee a Study Section of the NICHD and was elected as treasurer of the Society for Pediatric Research.

Professional Work: Dr. Shanley is responsible for attending in the 16 bed pediatric intensive care unit of C. S. Mott Children's Hospital for approximately nine weeks of clinical service per year. In this capacity he is responsible for supervising and directing the clinical management of all patients in the PICU excepting pediatric surgery patients. His areas of clinical expertise include: management of hypoxemic respiratory failure and the use of non-conventional strategies (e.g. High Frequency Oscillatory Ventilation); management of sepsis and application of extracorporeal modes of renal replacement therapies (e.g. Continuous Renal Replacement Therapy and Total Plasma Exchange) in critically ill children. In his role as division chief, he is also responsible for overseeing the quality initiatives that impact patient care in the PICU. Remarkable progress has been gained in creating a culture of patient safety in the PICU (substantiated by objective data from Safety Attitudes Questionnaire) with significant impact on important patient outcomes including: severity adjusted mortality, incidence of catheter-associated bloodstream infections and incidence of ventilator-associated pneumonia. As a testament to these efforts, the PICU was named the 2007 UMHS Clinical Program of the year under his clinical leadership.

External Review:

Reviewer A: "Dr. Shanley has an outstanding national reputation in pediatric critical care, and is recognized as one of the premier scientists in this field....In short, the University of Michigan is lucky to have Dr. Shanley, as he is truly one of the most outstanding scientists in our field."

Reviewer B: "I will characterize Dr. Shanley as one of the two or three most prominent mid-career figures in pediatric critical care nationally based on his scientific impact in the field and his leadership of outstanding academic programs."

Reviewer C: "...he is an outstanding teacher at a national and international level....His scholarly niche is in mechanisms of signal transduction in sepsis and his professional niche is as one of the leading academic pediatric intensive care clinician scientists in the world."

Reviewer D: "Tom is highly respected in our field as reflected by his many invited presentations and is also building a strong international reputation....Tom Shanley is richly deserving of promotion....Having served on the promotions committee for many years at [my institution], he would certainly meet our standards for Professor."

Reviewer E: "...I can simply say that he is one of a very small number of pediatric physicians in the field of critical care who have also been able to establish a credible presence in the research arena and have sustained that through extramural support and peer review."

Reviewer F: "...Dr. Shanley's scholarship and science has clearly impacted the field of Pediatic Critical Care Medicine, as well as adult critical care with regards to sepsis....Dr. Shanley is clearly involved in significant national peer organizational work including study sections, manuscript review for major journals as well as activities relating to mentorship and board review courses by the Society of Critical Care Medicine. His educational skills and

achievements have been of the highest quality and he has demonstrated continuing productivity in these various areas."

Summary of Recommendation:

Dr. Shanley has proven his commitment to excellence in all areas of patient care, research and education. He continually seeks to be an active participant in the advancement and success of the Department as well as the Medical School and Hospital. He is an outstanding leader, researcher, and educator and I give this nomination my strongest recommendation.

James O. Woolliscroft, M.D.
Dean
Lyle C. Roll Professor of Medicine

May 2009