

# **Critical Care Medicine**





First Row: K Page, J Kaplan Second Row: S. Poynter, B Zingarelli Third Row: L Doughty, R Chima

Fourth Row: D Wheeler, H Wong, K Tegtmeyer

Not present: E Al-Khadra

# **Division Data Summary**

Research and Training Details		
Number of Faculty	11	
Direct Annual Grant Support	\$1,474,555	
Direct Annual Industry Support	\$26,347	
Peer Reviewed Publications	22	
Clinical Activities and Training		
Number of Clinical Staff	23	
Number of Clinical Fellows	11	
Inpatient Encounters	8855	

# **Significant Publications**

Chima RS, Hake PW, Piraino G, Mangeshkar P, Denenberg A, Zingarelli B. Ciglitazone ameliorates lung inflammation by modulating the inhibitor kappaB protein kinase/nuclear factor-kappaB pathway after hemorrhagic shock. Crit Care Med. 2008 Oct;36(10):2849-57.

This manuscript demonstrates that ciglitazone ameliorates lung injury in a model of hemorrhagic shock. Ciglitazone is currently FDA approved for type II diabetes, thus increasing the feasibility of bringing this therapeutic strategy to the bedside in the near future.

Wheeler DS, Lahni PM, Denenberg AG, Poynter SE, Wong HR, Cook JA, Zingarelli B. Induction of endotoxin

tolerance enhances bacterial clearance and survival in murine polymicrobial sepsis. Shock. 2008 Sep;30(3):267-73.

This manuscript demonstrates that the concept of endotoxin tolerance functions is an unexpected manner in the context of bacterial infection. Animals rendered endotoxin tolerant are not immune-suppressed. Rather, these animals have an enhanced capacity to clear bacterial infection.

Page K, Lierl KM, Hughes VS, Zhou P, Ledford JR, Wills-Karp M. TLR2-mediated activation of neutrophils in response to German cockroach frass. J Immunol. 2008 May 1:180(9):6317-24.

This manuscript demonstrates that cockroach frass contains a TLR2 agonist and is the first report of an allergen directly activating the innate immune system via TLR2.

Wong HR, Cvijanovich N, Allen GL, Lin R, Anas N, Meyer K, Freishtat RJ, Monaco M, Odoms K, Sakthivel B, Shanley TP; Genomics of Pediatric SIRS/Septic Shock Investigators. Genomic expression profiling across the pediatric systemic inflammatory response syndrome, sepsis, and septic shock spectrum. Crit Care Med. 2009 May;37(5):1795-6.

This manuscript demonstrates takes a genomic approach to pediatric septic shock and demonstrates that children with septic shock have early, persistent, and wide spread repression of gene programs relevant to zinc-related biology and the adaptive immune system.

Wong HR, Cvijanovich N, Wheeler DS, Bigham MT, Monaco M, Odoms K, Macias WL, Williams MD. Interleukin-8 as a stratification tool for interventional trials involving pediatric septic shock. Am J Respir Crit Care Med. 2008 Aug 1;178(3):276-82. Epub 2008 May 29.

This manuscript derived and validated the ability of interleukin-8 to serve as an outcome stratification biomarker in children with septic shock. The data have led to the submission of a patent application by CCHMC.

# **Division Highlights**

Ranjit S. Chima, MD

Junior faculty member received K-level funding.

Jennifer M. Kaplan, MD

Junior faculty member received K-level funding.

Lesley A. Doughty, MD

Received a first time R01 grant.

The T32 training grant that is co-directed with the Department of Surgery at the University of Cincinnati was re-funded for an additional 5 years.

# **Faculty Members**

Hector Wong, MD, Professor; Director

Research Interests: Septic shock, Genomics, Biomarkers

Eman Al-Khadra, MD, Assistant Professor Research Interests: Bacterial Pneumonia

Richard Brilli, MD, Professor Clinical

Research Interests: Quality Improvement BSI, VAP

Ranjit Chima, MD, Research Assistant Professor; Lung injury/inflammation/Hemorrhagic Shock

Research Interests: Lung Injury/Inflammation, Hemorrhagic Shock

Lesley Doughty, MD, Associate Professor; Fellowship Director

Research Interests: Sepsis

Jennifer Kaplan, MD, Assistant Professor

Research Interests: Sepsis

Kristen Page, PhD, Associate Professor

Research Interests: Asthma, airway inflammation, inflammatory mediators

Sue E. Poynter, MD, Assistant Professor; Medical Director Division of Respiratory Care;

Research Interests: Acute lung injury, resident education

Ken Tegtmeyer, MD, Associate Professor Clinical Research Interests: Multimedia Medical Education

Derek S. Wheeler, MD, Assistant Professor Clinical; Clinical Director

Research Interests: Sepsis, Stress preconditioning, Quality Improvement

Basilia Zingarelli, MD, Associate Professor

Research Interests: Sepsis, hemorrhage and ischemia and reperfusion injury

## **Trainees**

- · Jeffrey Nowak, , PL-9, University of Minnesota
- Erika Stalets, , PL-8, University of Tennessee Health Sciences Center
- o Scottie Day, , PL-7, Indiana University
- Elizabeth Mack, , PL-6, Palmetto Richland University
- o Donna Claes, , PL-5, CCHMC & University of Missouri
- Rodney Daniels, , PL-5, Albany Medical Center
- Derrick Dauplaise, , PL-5, CCHMC & University of South Florida
- o Sarah Norris, , PL-5, Medical College of Georgia
- Stephen Standage, , PL-4, Childrens Hospital of Philadalphia
- Sandeep Tripathi, , PL-4, Suny Downstate
- Erik Mikkelsen, , PL-5, Children's Mercy Hospital

# **Significant Accomplishments**

#### Overview

This year, we opened a renovated pediatric intensive care unit (PICU) with a 36-bed capacity, an increase from 25 beds. We cared for a record number of admissions to the PICU. We changed coverage in the PICU this year to a two-team system, which includes coverage by two attending-level faculty per day. This new coverage system, along with the larger capacity PICU, should serve us well in meeting the needs of all critically ill children admitted to Cincinnati Children's. Derek Wheeler, MD, FAAP, became medical director of the division and of the Pediatric Intensive Care Unit and was promoted to associate Professor. Basilia Zingarelli, MD, PhD, became a standing member of the SAT study section at the NIH; Lesley Doughty, MD, successfully transitioned her K-level funding to a first time R01; and Ranjit Chima, MD, and Jennifer Kaplan, MD, received K-level funding for their respective research programs.

### **Division Publications**

- 1. Wheeler DS, Zingarelli B, Wheeler WJ, Wong HR. <u>Novel pharmacologic approaches to the management of sepsis: targeting the host inflammatory response</u>. *Recent Pat Inflamm Allergy Drug Discov.* 2009; 3: 96-112.
- 2. Bigham MT, Amato R, Bondurrant P, Fridriksson J, Krawczeski CD, Raake J, Ryckman S, Schwartz S, Shaw J, Wells D, Brilli RJ. <u>Ventilator-associated pneumonia in the pediatric intensive care unit: characterizing the problem and implementing a sustainable solution</u>. *J Pediatr.* 2009; 154: 582-587 e2.
- 3. Stalets E, Wong HR. Critically associating. Crit Care Med. 2009; 37: 1492-3.
- 4. Giuliano JS, Jr., Wheeler DS. Excess circulating angiopoietin-2 levels in sepsis: harbinger of death in the intensive care unit?. Crit Care. 2009; 13: 114.
- Mack EH, Wheeler DS, Embi PJ. <u>Clinical decision support systems in the pediatric intensive care unit</u>. Pediatr Crit Care Med. 2009; 10: 23-8.
- Zingarelli B, Hake PW, O'Connor M, Burroughs TJ, Wong HR, Solomkin JS, Lentsch AB. <u>Lung injury after</u> <u>hemorrhage is age dependent: role of peroxisome proliferator-activated receptor gamma</u>. *Crit Care Med.* 2009; 37: 1978-87.
- Huber N, Sakai N, Eismann T, Shin T, Kuboki S, Blanchard J, Schuster R, Edwards MJ, Wong HR, Lentsch AB. <u>Agerelated decrease in proteasome expression contributes to defective nuclear factor-kappaB activation during hepatic ischemia/reperfusion</u>. *Hepatology*. 2009; 49: 1718-28.
- 8. Wheeler DS, Chase MA, Senft AP, Poynter SE, Wong HR, Page K. <u>Extracellular Hsp72, an endogenous DAMP, is released by virally infected airway epithelial cells and activates neutrophils via Toll-like receptor (TLR)-4</u>. Respir Res. 2009; 10: 31.
- 9. Wong HR, Cvijanovich N, Allen GL, Lin R, Anas N, Meyer K, Freishtat RJ, Monaco M, Odoms K, Sakthivel B, Shanley

- TP. <u>Genomic expression profiling across the pediatric systemic inflammatory response syndrome, sepsis, and septic shock spectrum</u>. *Crit Care Med.* 2009; 37: 1558-66.
- 10. Al-Khadra E. **"Disorders of the acid-base status."** *Pediatric nephrology in the ICU.* Berlin; London: Springer; 2008: 19-34.
- 11. Wong HR, Shanley TP. **"Genetic basis of acute lung injury."** *Mechanical ventilation : clinical applications and pathophysiology.* Philadelphia: Saunders/Elsevier; 2008: 207-215.
- 12. Galloway E, Shin T, Huber N, Eismann T, Kuboki S, Schuster R, Blanchard J, Wong HR, Lentsch AB. <u>Activation of hepatocytes by extracellular heat shock protein 72</u>. *Am J Physiol Cell Physiol*. 2008; 295: C514-20.
- 13. Wong HR, Cvijanovich N, Wheeler DS, Bigham MT, Monaco M, Odoms K, Macias WL, Williams MD. <u>Interleukin-8 as a stratification tool for interventional trials involving pediatric septic shock</u>. *Am J Respir Crit Care Med.* 2008; 178: 276-82.
- Fan H, Zingarelli B, Harris V, Tempel GE, Halushka PV, Cook JA. <u>Lysophosphatidic acid inhibits bacterial</u> <u>endotoxin-induced pro-inflammatory response: potential anti-inflammatory signaling pathways</u>. *Mol Med.* 2008; 14: 422-8.
- 15. Page K, Lierl KM, Hughes VS, Zhou P, Ledford JR, Wills-Karp M. <u>TLR2-mediated activation of neutrophils in response to German cockroach frass</u>. *J Immunol.* 2008; 180: 6317-24.
- 16. Brilli RJ, Sparling KW, Lake MR, Butcher J, Myers SS, Clark MD, Helpling A, Stutler ME. <u>The business case for preventing ventilator-associated pneumonia in pediatric intensive care unit patients</u>. *Jt Comm J Qual Patient Saf.* 2008; 34: 629-38.
- 17. Wheeler DS, Beckers T, Miller RR. <u>The effect of subadditive pretraining on blocking: limits on generalization</u>. *Learn Behav.* 2008; 36: 341-51.
- 18. Chima RS, Hake PW, Piraino G, Mangeshkar P, Denenberg A, Zingarelli B. <u>Ciglitazone ameliorates lung inflammation by modulating the inhibitor kappaB protein kinase/nuclear factor-kappaB pathway after hemorrhagic shock</u>. *Crit Care Med.* 2008; 36: 2849-57.
- 19. Giuliano JS, Jr., Lahni PM, Bigham MT, Manning PB, Nelson DP, Wong HR, Wheeler DS. <u>Plasma angiopoietin-2</u> <u>levels increase in children following cardiopulmonary bypass</u>. *Intensive Care Med.* 2008; 34: 1851-7.
- 20. Anderson J, Leonard D, Braner DA, Lai S, Tegtmeyer K. <u>Videos in clinical medicine</u>. <u>Umbilical vascular catheterization</u>. *N Engl J Med*. 2008; 359: e18.
- 21. Abboud PA, Lahni PM, Page K, Giuliano JS, Jr., Harmon K, Dunsmore KE, Wong HR, Wheeler DS. <u>The role of endogenously produced extracellular hsp72 in mononuclear cell reprogramming</u>. *Shock.* 2008; 30: 285-92.
- 22. Wheeler DS, Lahni PM, Denenberg AG, Poynter SE, Wong HR, Cook JA, Zingarelli B. <u>Induction of endotoxin</u> <u>tolerance enhances bacterial clearance and survival in murine polymicrobial sepsis</u>. *Shock.* 2008; 30: 267-73.

# **Grants, Contracts, and Industry Agreements**

### **Grant and Contract Awards**

## **Annual Direct / Project Period Direct**

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0111		

#### C-peptide a Novel Anti-inflammatory Peptide Inhibitor of Lung Injury

Shock Society

09/01/08 - 08/31/10

\$30,000 / \$60,000

#### DAY. S

#### Host Response to Trauma Research Training Program

National Institutes of Health (University of Cincinnati)

T32 GM 008478 07/01/08 - 06/30/09 \$48,852 / \$48,852

#### DOUGHTY. L

### Viral Modulation of the Inflammatory Response

National Institutes of Health

K08 GM 071568 03/01/05 - 06/30/09 \$111,200 / \$488,968

### Interferon-Mediated Reprogramming of Toll-like Receptor

National Institutes of Health

#### **NOWAK. J**

	Current Year Direct Receipts	\$26,347
Wheeler, D Discovery Laboratories, Inc.		\$ 167
Poynter, S Pneuman Pharmaceuticals		\$ 26,180
dustry Contracts		
	Current Year Direct	\$1,474,555
Role of Eicosanoids In Shock National Institutes of Health (Medical Univ	versity of South Carolina) 07/03/08 - 06/30/14	\$24,561 / \$122,80
Role of PPARgamma and PPARgamma National Institutes of Health R01 GM 067202	07/01/08 - 06/30/13	\$247,080 / \$1,235,400
ZINGARELLI, B  Mechanisms of Age-Related Inflammat National Institutes of Health R01 AG 027990	09/01/07 - 08/31/12	\$200,900 / \$1,025,000
R01 GM 064619	09/01/07 - 08/31/10	\$219,299 / \$677,67
WONG, H.  Genomic Analysis of Pediatric SIRS  National Institutes of Health		
National Institutes of Health R03 HD 058246	07/01/08 - 06/30/10	\$50,000 / \$100,00
The Immunomodulatory Effects of HSF National Institutes of Health K08 GM 077432	04/01/06 - 03/31/11	\$111,991 / \$561,25
WHEELER, D		
Role of Cockroach Proteases in Airwa National Institutes of Health R01 HL 075568	y Inflammation 12/15/04 - 11/30/09	\$189,636 / \$800,00
PAGE, K		

National Institutes of Health (University of Cincinnati)