

## Division Data Summary

### Research and Training Details

|                                     |             |
|-------------------------------------|-------------|
| Number of Faculty                   | 13          |
| Number of Joint Appointment Faculty | 2           |
| Number of Support Personnel         | 20          |
| Direct Annual Grant Support         | \$1,039,599 |
| Direct Annual Industry Support      | \$42,541    |
| Peer Reviewed Publications          | 23          |

### Clinical Activities and Training

|                            |      |
|----------------------------|------|
| Number of Clinical Staff   | 10   |
| Number of Clinical Fellows | 12   |
| Inpatient Encounters       | 8369 |

## Division Photo



Row 1: K Page, J Kaplan, E Stalets  
Row 2: R Chima, L Doughty, B Varisco  
Row 3: D Wheeler, H Wong, K Tegtmeyer, R Basu

## Significant Publications

## Faculty Members

**Hector Wong, MD**, Professor

*Director*

**Research Interests** Septic shock, Genomics, Biomarkers

**Ranjit Chima, MD**, Assistant Professor

**Research Interests** Lung Injury/Inflammation, Hemorrhagic Shock

**Lesley Doughty, MD**, Associate Professor

*Fellowship Director*

**Research Interests** Sepsis

**Jennifer Kaplan, MD, MS**, Assistant Professor

**Research Interests** Sepsis and obesity

**Kristen Page, PhD**, Associate Professor

**Research Interests** Asthma, airway inflammation, inflammatory mediators, innate and adaptive immune response

**Sue E. Poynter, MD**, Assistant Professor

*Medical Director Division of Respiratory Care*

*Associate Director Pediatric Residency Training Program*

**Research Interests** Acute lung injury, resident education

**Erika Stalets, MD**, Instructor

**Research Interests** Quality Improvement and Patient Safety

**Ken Tegtmeyer, MD**, Associate Professor

**Research Interests** Multimedia Medical Education

**Rajit Basu, MD**, Instructor

**Research Interests** The role of kidney injury in distal organ function

**Derek S. Wheeler, MD**, Associate Professor

*Clinical Director PICU*

**Research Interests** Sepsis, Stress preconditioning, Quality Improvement

**Basilgia Zingarelli, MD, Ph.D.**, Associate Professor

**Research Interests** Sepsis, hemorrhage and ischemia and reperfusion injury

## Joint Appointment Faculty Members

**Bradley Marino, MD**, Associate Professor

Cardiology

**Research Interests** Long-term outcomes in children and adolescents with CHD, Resuscitation of children with CHD

## Trainees

- Gabriela Botez, MD, PL4, Universitatea de Medicină "GR.T.Popa"
- Ma-Bernardita Gamallo, MD, PL4, Jersey Shore University Medical Center
- Rodney Daniels, MD, PL6, Eastern Virginia Medical School
- Michael Hobson, MD, PL5, Indiana University School of Medicine
- Riad Lutfi, MD, PL6, University of Damascus
- Carrie Morgan, MD, PL5, University of Kentucky College of Medicine
- Carley Riley, MD, PL5, Children's Hospital of Los Angeles
- Ravi Ramraj, MD, PL4, Driscoll Children's Hospital
- Stephen Standage, MD, PL6, The Children's Hospital of Philadelphia
- Shilpa Shah, MD, PL4, The University of Texas Medical Branch
- Siahei Slinko, MD, PL5, University of Buffalo
- John Whitt, MD, PL4, University of Alabama School of Medicine at Birmingham

## Significant Accomplishments

### Studying pediatric septic shock

Jennifer Kaplan, MD, MS, received an Investigational New Drug approval from the Food and Drug Administration to conduct a Phase-1 trial of PPAR-gamma agonism in pediatric septic shock. This study reflects a natural progression of basic science research efforts in the division. The concept of PPAR-gamma agonism as therapeutic strategy in sepsis was demonstrated in pre-clinical studies led by Basilgia Zingarelli, PhD. Kaplan's Phase-1 study is the first direct translation of our basic science research to the bedside of critically ill children.

### New director for basic research

Zingarelli, a nationally recognized researcher who has been with our Division since it formed in 1994, has been appointed director of basic research to provide expanded oversight for our growing research portfolio. She also has been named president - elect of the Shock Society, an international organization dedicated to improving the care of victims of trauma, shock, and sepsis.

### **Mechanisms of chronic lung disease**

Brian Varisco, MD, who was recruited to Cincinnati Children's to serve as a physician-scientist in pediatric critical care medicine, has secured K-level funding to continue his studies of the mechanisms of chronic lung disease. He achieved this milestone under the mentorship of Jeffrey Whitsett, MD, director of the Division of Pulmonary Biology and Chief of the Section of Neonatology, Perinatal and Pulmonary Biology.

## **Division Publications**

1. Aneja RK, Sjodin H, Gefter JV, Zingarelli B, Delude RL. **Small interfering RNA mediated Poly (ADP-ribose) Polymerase-1 inhibition upregulates the heat shock response in a murine fibroblast cell line.** *J Inflamm (Lond)*. 2011; 8:3.
2. Basu RK, Devarajan P, Wong H, Wheeler DS. **An update and review of acute kidney injury in pediatrics.** *Pediatr Crit Care Med*. 2011; 12:339-47.
3. Basu RK, Hubchak S, Hayashida T, Runyan CE, Schumacker PT, Schnaper HW. **Interdependence of HIF-1alpha and TGF-beta/Smad3 signaling in normoxic and hypoxic renal epithelial cell collagen expression.** *Am J Physiol Renal Physiol*. 2011; 300:F898-905.
4. Basu RK, Wheeler D. **Effects of ischemic acute kidney injury on lung water balance: nephrogenic pulmonary edema?** *Pulm Med*. 2011; 2011:414253.
5. Basu RK, Wheeler DS, Goldstein S, Doughty L. **Acute renal replacement therapy in pediatrics.** *Int J Nephrol*. 2011; 2011:785392.
6. Chima RS, LaMontagne T, Piraino G, Hake PW, Denenberg A, Zingarelli B. **C-peptide, a novel inhibitor of lung inflammation following hemorrhagic shock.** *Am J Physiol Lung Cell Mol Physiol*. 2011; 300:L730-9.
7. Chima RS, Maltese G, Lamontagne T, Piraino G, Denenberg A, O'Connor M, Zingarelli B. **C-peptide ameliorates kidney injury following hemorrhagic shock.** *Shock*. 2011; 35:524-9.
8. Fan H, Bitto A, Zingarelli B, Luttrell LM, Borg K, Halushka PV, Cook JA. **Beta-arrestin 2 negatively regulates sepsis-induced inflammation.** *Immunology*. 2010; 130:344-51.
9. Fan H, Li P, Zingarelli B, Borg K, Halushka PV, Birnbaumer L, Cook JA. **Heterotrimeric Galpha(i) proteins are regulated by lipopolysaccharide and are anti-inflammatory in endotoxemia and polymicrobial sepsis.** *Biochim Biophys Acta*. 2011; 1813:466-72.
10. Istaphanous GK, Wheeler DS, Lisco SJ, Shander A. **Red blood cell transfusion in critically ill children: A narrative review.** *Pediatr Crit Care Med*. 2011; 12:174-183.
11. Kaplan JM, Hake PW, Denenberg A, Nowell M, Piraino G, Zingarelli B. **Phosphorylation of extracellular signal-regulated kinase (ERK)-1/2 is associated with the downregulation of peroxisome proliferator-activated receptor (PPAR)-gamma during polymicrobial sepsis.** *Mol Med*. 2010; 16:491-7.
12. Le TM, Willis AS, Barr FE, Cunningham GR, Canter JA, Owens SE, Apple RK, Ayodo G, Reich D, Summar ML. **An ethnic-specific polymorphism in the catalytic subunit of glutamate-cysteine ligase impairs the production of glutathione intermediates in vitro.** *Mol Genet Metab*. 2010; 101:55-61.
13. Mack EH, Wheeler DS, Hirsch R. **Endovascular treatment of near-fatal neonatal superior vena cava syndrome.** *Pediatr Crit Care Med*. 2010; .
14. Mahabeleshwar GH, Kawanami D, Sharma N, Takami Y, Zhou G, Shi H, Nayak L, Jeyaraj D, Grealy R, White M, McManus R, Ryan T, Leahy P, Lin Z, Haldar SM, Atkins GB, Wong HR, Lingrel JB, Jain MK. **The**

**Myeloid Transcription Factor KLF2 Regulates the Host Response to Polymicrobial Infection and Endotoxic Shock.** *Immunity*. 2011; 34:715-28.

15. Ortega RA, Andreoli MT, Chima RS. **Is there a place for music in medical school?**. *Med Teach*. 2011; 33:76-7.
16. Smith HA, Boyd J, Fuchs DC, Melvin K, Berry P, Shintani A, Eden SK, Terrell MK, Boswell T, Wolfram K, Sopfe J, Barr FE, Pandharipande PP, Ely EW. **Diagnosing delirium in critically ill children: Validity and reliability of the Pediatric Confusion Assessment Method for the Intensive Care Unit.** *Crit Care Med*. 2011; 39:150-7.
17. Solan PD, Piraino G, Hake PW, Denenberg A, O'Connor M, Lentsch A, Zingarelli B. **Liver X receptor alpha activation with the synthetic ligand T0901317 reduces lung injury and inflammation after hemorrhage and resuscitation via inhibition of the nuclear factor kappaB pathway.** *Shock*. 2011; 35:367-74.
18. Standage SW, Wong HR. **Biomarkers for pediatric sepsis and septic shock.** *Expert Rev Anti Infect Ther*. 2011; 9:71-9.
19. Varisco BM. **The pharmacology of acute lung injury in sepsis.** *Adv Pharmacol Sci*. 2011; 2011:254619.
20. Varisco BM, Palmatier CM, Alten JA. **Reversal of intractable hypoxemia with exogenous surfactant (calfactant) facilitating complete neurological recovery in a pediatric drowning victim.** *Pediatr Emerg Care*. 2010; 26:571-3.
21. Wheeler DS, Giuliano JS, Jr., Lahni PM, Denenberg A, Wong HR, Zingarelli B. **The immunomodulatory effects of albumin in vitro and in vivo.** *Adv Pharmacol Sci*. 2011; 2011:691928.
22. Wong HR, Wheeler DS, Tegtmeyer K, Poynter SE, Kaplan JM, Chima RS, Stalets E, Basu RK, Doughty LA. **Toward a clinically feasible gene expression-based subclassification strategy for septic shock: proof of concept.** *Crit Care Med*. 2010; 38:1955-61.
23. Zingarelli B, Piraino G, Hake PW, O'Connor M, Denenberg A, Fan H, Cook JA. **Peroxisome proliferator-activated receptor {delta} regulates inflammation via NF-{kappa}B signaling in polymicrobial sepsis.** *Am J Pathol*. 2010; 177:1834-47.

## Grants, Contracts, and Industry Agreements

|                           |                                       |
|---------------------------|---------------------------------------|
| Grant and Contract Awards | Annual Direct / Project Period Direct |
|---------------------------|---------------------------------------|

### WHEELER, D

**Therapeutic Hypothermia after Pediatric Cardiac Arrest**

National Institutes of Health(University of Michigan)

|               |                   |          |
|---------------|-------------------|----------|
| U01 HL 094345 | 09/01/09-02/28/11 | \$21,334 |
|---------------|-------------------|----------|

**Therapeutic Hypothermia after Pediatric Cardiac Arrest (per patient)**

National Institutes of Health(University of Michigan)

|               |                   |         |
|---------------|-------------------|---------|
| U01 HL 094345 | 07/01/10-06/30/11 | \$2,579 |
|---------------|-------------------|---------|

### WONG, H

**Pediatric Sepsis Biomarker Risk Model**

National Institutes of Health

|               |                   |           |
|---------------|-------------------|-----------|
| RC1 HL 100474 | 09/30/09-08/30/11 | \$333,062 |
|---------------|-------------------|-----------|

**MMP-8 as a Novel Therapeutic Target in Sepsis**

National Institutes of Health

|               |                   |           |
|---------------|-------------------|-----------|
| R01 GM 096994 | 04/01/11-03/31/15 | \$190,000 |
|---------------|-------------------|-----------|

### ZINGARELLI, B

**PPARgamma and PPARgamma Agonists in Septic Shock**

National Institutes of Health

|               |                   |           |
|---------------|-------------------|-----------|
| R01 GM 067202 | 07/01/08-06/30/12 | \$244,609 |
|---------------|-------------------|-----------|

|                                                                             |                   |                    |
|-----------------------------------------------------------------------------|-------------------|--------------------|
| <b>Role of Eicosanoids in Shock</b>                                         |                   |                    |
| National Institutes of Health(Medical University of South Carolina)         |                   |                    |
| R01 GM 027673                                                               | 07/03/08-06/30/13 | \$49,124           |
| <b>Mechanisms of Age-Related Inflammatory Response in Hemorrhagic Shock</b> |                   |                    |
| National Institutes of Health                                               |                   |                    |
| R01 AG 027990                                                               | 09/01/07-08/31/12 | \$198,891          |
| <b>Current Year Direct</b>                                                  |                   | <b>\$1,039,599</b> |
| Industry Contracts                                                          |                   |                    |
| <b>BARR, F</b>                                                              |                   |                    |
| Asklepion Pharmaceuticals, LLC                                              |                   | \$25,322           |
| Bayer HealthCare Pharmaceuticals, Inc.                                      |                   | \$17,219           |
| <b>Current Year Direct Receipts</b>                                         |                   | <b>\$42,541</b>    |
| <b>Total</b>                                                                |                   | <b>\$1,082,140</b> |