Dear Friends

This has been another exciting year for Children’s of Alabama and the Department of Pediatrics. Our research report details these accomplishments by division.

In the Department of Pediatrics, we seek to discover new knowledge to improve the health of the children of Alabama, the region and, the world.

The clinical advances and research discoveries we describe here have an impact on children’s lives. That impact will be our legacy. We present in this report some early signs of that impact as measured by major research accomplishments and publications. In FY 2015, the Department of Pediatrics faculty had over 200 publications, research funding from the NIH of $15 million, and total research funding of $25 million.

We aim to build on these successes and expand the size and, importantly, the impact of this research funding in the coming year. We anticipate growth not only in our core areas of significant accomplishment – virology, therapeutic drug development, and cancer and rheumatology outcomes – but also in newer areas where the recruitment of talented young researchers will ensure continued and expanded success.

Children’s is the only medical center in Alabama dedicated solely to the care and treatment of children. It is a private, not-for-profit medical center that serves as the primary site of the University of Alabama at Birmingham (UAB) pediatric medicine, surgery, psychiatry, research and residency programs. Children’s of Alabama built the Benjamin Russell campus, a world class physical facility, three years ago. We are now partnering with Children’s of Alabama to continue to build the world class clinical and research programs that belong in this building and that the children of Alabama deserve.

Sincerely,

Mitchell B. Cohen, MD
Katharine Reynolds Ireland Professor
Chair, Department of Pediatrics
University of Alabama at Birmingham
Physician in Chief, Children’s of Alabama
The UAB Department of Pediatrics at Children’s of Alabama is comprised of 16 Subspecialty Divisions each with a research, educational, and clinical focus. To find research initiatives, areas of clinical excellence, educational efforts and learn more about the faculty, click on the division of interest below.

**PEDIATRIC DIVISIONS:**
1. Pediatric Allergy & Immunology
2. Pediatric Cardiology
3. Pediatric Critical Care
4. Pediatric Emergency Medicine
5. Pediatric Endocrinology
6. Pediatric Gastroenterology, Hepatology & Nutrition
7. General Pediatrics and Adolescent Medicine
8. Pediatric Hematology and Oncology
9. Pediatric Hospital Medicine
10. Pediatric Infectious Diseases
11. Neonatology
12. Pediatric Nephrology
13. Pediatric Neurology
14. Pediatric Pulmonology and Sleep Medicine
15. Pediatric Rehab Medicine
16. Pediatric Rheumatology

**CONTENT PER DIVISION INCLUDES:**
- Pediatric Faculty
- Featured Research
- Significant Publications
- Division Awards & Recognition
The division of Pediatric Allergy and Immunology engages in a broad range of research in primary immune deficiencies, autoimmunity, and disease-specific pathogens. Current pharyngitis guidelines focus solely on group A β-hemolytic streptococcal infection. European data suggest that in patients aged 15 to 30 years, *Fusobacterium necrophorum* causes at least 10% of cases of pharyngitis; however, few U.S. data exist. In a report in the Annals of Internal Medicine, Prescott Atkinson, M.D., Ph.D., and co-authors demonstrated that *Fusobacterium necrophorum*-positive pharyngitis occurs more frequently than group A β-hemolytic streptococcal-positive pharyngitis in a student population drawn from The University of Alabama at Birmingham (UAB), and *F. necrophorum*-positive pharyngitis clinically resembles streptococcal pharyngitis. These findings suggest that physicians should consider *F. necrophorum* when treating pharyngitis in young adults and adolescents. Importantly, *F. necrophorum* can cause a life-threatening illness known as Lemierre’s syndrome, further highlighting the importance of this work. See publication.

Studies continue on the epidemiology and microbiology of mycoplasma. *Mycoplasma pneumoniae* is a common pathogen that causes upper and lower respiratory tract infections in people of all ages, responsible for up to 40% of community-acquired pneumonias. It also is linked to a wide array of extra-pulmonary infections and autoimmune phenomena. To better understand the physiology and pathogenicity of this important human pathogen, Dr. Atkinson and colleagues analysed 15 strains of *M. pneumoniae* isolated between the 1940s to 2009 from respiratory specimens and cerebrospinal fluid originating from the USA, China, and England. These data indicate that the *M. pneumoniae* genome is extraordinarily stable over time and geographic distance across the globe. See publication.

Macrolide-resistant *Mycoplasma pneumoniae* (MRMP) is highly prevalent in Asia and is now being reported from Europe. Few data on MRMP are available in the United States. Dr Atkinson participated in a study that demonstrated high-level MRMP in 13.2% of *M. pneumoniae*-positive specimens in the US. See publication.

At present the most effective means for detection and strain-typing for *M pneumoniae* is qPCR, which has limited practicality for widespread, point-of-care use. Dr. Atkinson had previously developed a sensitive and specific assay for diagnosing *M pneumoniae* (NA-SERS). In a recent study, they demonstrated that NA-SERS correctly identified *M. pneumoniae* with a high level of sensitivity and specificity. See publication.

**Significant Publications**


Pediatric Allergy & Immunology Awards & Recognition

Prescott Atkinson, M.D. Ph.D, Pediatric Allergy and Immunology, has been appointed vice chair of the American Board of Allergy and Immunology.

The Accreditation Council for Graduate Medical Education (ACGME) announced the appointment of Prescott Atkinson, M.D., Ph.D., Pediatric Allergy and Immunology, to the ACGME Review Committee for Allergy and Immunology.
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PEDIATRIC CARDIOLOGY

Pediatric Faculty

Dr. Yung R. Lau  Professor
Dr. Jeffery Alten CVICU  Professor
Dr. Santiago Borasino CVICU  Associate Professor
Dr. Wally F. Carlo  Associate Professor
Dr. Edward V. Colvin  Professor
Dr. Kimberly Jackson CVICU  Assistant Professor
Dr. Walter H. Johnson  Professor
Dr. Yuvraj Kalra CVICU  Assistant Professor
Dr. Mark Law  Associate Professor
Dr. William S. McMahon  Professor
Dr. F. Bennett Pearce  Professor
Dr. Leslie Rhodes CVICU  Assistant Professor
Dr. Robb L. Romp  Associate Professor
Dr. Hayden Zaccangi CVICU  Assistant Professor

Featured Research

The division of Pediatric Cardiology and the section of Cardiovascular Intensive Care feature one of the nation’s only comprehensive pediatric cardiac intensive care unit repositories for biological samples from patients. With the approval of the UAB Institutional Review Board, blood, urine, chest tube samples, and peritoneal and other samples are stored from every consenting cardiac surgery patient, and annotated with clinical details. Pilot data from this valuable resource will lay the foundation for translational research grant proposals and multi-center research collaborations in the years to come.

Division members presented 15 oral and poster presentations at scientific conferences, and received four conference abstract awards.

The division was the lead institution for the first multicenter evaluation of nutritional requirements and approaches, along with associated outcomes, following neonatal cardiac surgery. See publication.

Significant Publications


**Cardiology Awards & Recognition**

William S. McMahon, M.D., and Mark Law, M.D., Pediatric Cardiology, were recently certified to implant a new device used for closure of patent ductus arteriosus (PDA). This new device, specifically designed for percutaneous PDA closure, facilitates non-surgical closure of PDA in infants and children.
A major research interest within Pediatric Critical Care Medicine involves approaches and decisions for acute pediatric traumatic brain injuries (TBI). The investigators are measuring standard practices across the various sites, performing outcomes testing, and determining which therapies are associated with the best outcomes. Completion of this study will provide evidence for change in clinical practices, provide evidence for new Level II recommendations for future guidelines, and lead to improved research protocols that would limit variability in treatment of TBI.

The study known as Age of Blood (used for transfusion) in Children (ABC) in Pediatric Intensive Care Units (PICU) is a double blind, randomized controlled trial at multiple international centers, which compares the clinical consequences of red blood cell (RBC) storage duration for critically ill children to determine whether the transfusion of RBCs of reduced storage duration improves outcomes. The ABC PICU trial will compare development of new or progressive multiple organ dysfunction syndrome in critically ill children transfused with RBCs stored for less than eight days or with standard issue RBCs. This is a unique collaboration between Children’s of Alabama and UAB Pediatric Intensive Care Unit (PICU), blood bank, and the research team in a partnership that ultimately has significant likelihood of benefitting our patients. This study is funded by the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health and by the Canadian Institutes of Health Research.

Among other research highlights of the division is the prospective clinical trial of azithromycin treatment in RSV-Induced Respiratory Failure in Children, which is funded by the UAB Center for Clinical and Translational Science (CCTS) with Michele Kong, M.D., as the principal investigator.

Additionally, Pediatric Critical Care has a research focus on Genetic Epidemiology of Life-Threatening Influenza in Children.

**Significant Publications**

**RESEARCH ANNUAL REPORT**


**Division Awards & Recognition**

**Michele Kong, M.D.,** Pediatric Critical Care, received the Junior Faculty 2015 Dean’s Excellence Award in Service, University of Alabama at Birmingham.
Marjorie Lee White, M.D., and colleagues in the division of Pediatric Emergency Medicine have developed a significant research program involving the UAB Simulation Center. An example of this is the Impact of Just-in-Time and Just-in-Place Simulation on Intern Success with Infant Lumbar Puncture, published in Pediatrics. This prospective study enrolled pediatric and emergency medicine interns from 2009 to 2012 at 34 centers and included review of 436 infant lumbar punctures (LPs). The study explored the impact of just-in-time and just-in-place training (JIPT) on pediatric interns’ infant LP success. JIPT produced improved early stylet removal and pain control. See publication.

Building upon research in education and training, Dr. White also co-authored in Academic Medicine a six-step pedagogical framework for procedural skills training composed of the following parameters: Learn, See, Practice, Prove, Do, and Maintain. Evidence in support of each component of the framework contributes to a potential paradigm shift in procedural skill training. See publication.
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A JAMA Pediatrics publication titled, “Improving Cardiopulmonary Resuscitation with a CPR Feedback Device and Refresher Simulations,” studied the effects of cardiopulmonary resuscitation (CPR) on hemodynamics, survival, and neurological outcomes following pediatric cardiopulmonary arrest (CPA). Again using novel and practical technology, JIT training was found to improve compliance with American Heart Association guidelines for CPR that are associated with better outcomes. See publication.

Significant Publications


Division Awards & Recognition

Kathy Monroe, M.D., Pediatric Emergency Medicine, has been elected to serve as a member on the AAP’s Executive Committee of the Council on Injury, Violence and Poison Prevention.

David Smith, M.D., Pediatric Emergency Medicine, received the 2015 Society for Pediatric Research Clinical Fellows Research Award.

Peter W. Glaeser, M.D., Pediatric Emergency Medicine, received the 2015 Rocco V. Morando Lifetime Achievement Award, recognizing a lifetime of commitment and contributions to Emergency Medical Services (EMS). The award is the National Association of Emergency Medical Technicians (NAEMT)’s most prestigious award.

Christopher Pruitt, M.D., Pediatric Emergency Medicine, received the Southern Society for Pediatric Research 2015 Young Faculty Award.
Christopher Pruitt, M.D., Pediatric Emergency Medicine, has been elected to the Executive Council of the Southern Society for Pediatric Research.

Michele H. Nichols, M.D., Pediatric Emergency Medicine, received the Senior Faculty 2015 Dean’s Excellence Award in Teaching, University of Alabama at Birmingham.
Division of Pediatric Endocrinology highlights from 2015 include research in conditions such as cystic fibrosis and type 1 diabetes.

Research in cystic fibrosis (CF), conducted by Michael Stalvey, M.D., has assessed the frequency of endocrine co-morbidities in CF patients. Specifically, the reduced growth and osteoporosis seen in CF patients are multifactorial but interrelated. Reduced growth in CF is associated with reduced lung health and life expectancy. In addition, poor bone health and CF-related bone disease can lead to increased fractures and decrease the likelihood for lung transplantation. Ongoing research by Dr. Stalvey’s laboratory suggests an intrinsic defect exists in CF that predisposes to problems with bone metabolism and normal growth. These pathogenic abnormalities can be noted even in the absence of other CF complications. Preliminary studies indicate that correction of the fundamental CF defect improves growth in CF children.

The pathogenesis of type 1 diabetes mellitus (T1DM) involves autoimmune destruction of pancreatic beta cells. Once hyperglycemia appears, more than 70% of islet beta cell mass has been destroyed; surviving beta cells represent the only reservoir for potential regeneration. Recent studies suggest that gamma aminobutyric acid (GABA) plays important metabolic roles in the pancreas through: (1) promotion of insulin secretion by beta cells, (2) suppression of glucagon secretion by alpha cells, (3) activation of cell survival pathways, (4) protection against apoptosis, and (5) decrease in inflammation. GABA has been shown both to prevent and to reverse diabetes in animal models. GABA also has an excellent safety profile, with virtually no serious side effects. The endocrinology division has designed and is conducting the first clinical trial of GABA in children with T1DM to assess the hypothesis that GABA will improve endogenous insulin secretion, improve metabolic/glycemic control, and alter the autoimmune milieu involved in the pathogenesis of this disease. To date, the vast majority of studies aiming to cure T1DM have focused on immune suppression to halt autoimmune pancreatic destruction. Studies of GABA avoid the toxicities and risks associated with immunosuppressive regimens, thus potentially improving the quality of life for T1DM patients.
Placental DNA methylation of peroxisome-proliferator-activated receptor-γ co-activator-1α promoter is associated with maternal gestational glucose level. Xie X, Gao H, Zeng W, Chen S, Feng L, Deng D, Qiao FY, Liao L, McCormick K, Ning Q, Luo X.


RESEARCH ANNUAL REPORT

PEDIATRIC GASTROENTEROLOGY, HEPATOLOGY & NUTRITION

Pediatric Faculty

Dr. Reed Dimmitt  Professor
Dr. Erin Bhatia  Instructor
Dr. Mitchell Cohen  Professor
Dr. David Galloway  Assistant Professor
Dr. Traci Jester  Assistant Professor
Dr. Jeanine Maclin  Associate Professor
Dr. Jose Mestre  Professor
Dr. Janaina Nogueira  Assistant Professor

Significant Publications


Division Awards & Recognition

Traci Jester, M.D., Pediatric Gastroenterology, has been selected to join the Crohn’s and Colitis Foundation of America’s Pediatric Affairs Committee.

Mitch Cohen, M.D., Pediatric Gastroenterology, has been selected to participate in Leadership Birmingham.

Mitch Cohen, M.D., Pediatric Gastroenterology, has been appointed to Alabama Health Care Improvement Task Force.
The UAB Division of General Pediatrics and Adolescent Medicine performs an array of investigations that include outcomes research as well as assessments of physiologic changes during growth and development. Krista Casazza, Ph.D., has assessed the correlation between bone mineralization and energy expenditure prior to adolescents. She has found that bone mineral content is a determinant of circulating insulin and basal metabolic rate, and a co-dependent relationship with body fat may contribute in a race-specific manner. See publication.

Myriam Peralta, M.D., worked with Waldemar A. Carlo, M.D., Neonatology, among other investigators, assessing the long-term pulmonary outcomes among infants who participated in the National Institute of Child Health and Human Development’s Surfactant Positive Airway Pressure and Pulse Oximetry Randomized Trial (SUPPORT). Utilizing a factorial design that randomized extremely preterm infants to lower vs higher oxygen saturation targets and delivery room continuous positive airway pressure (CPAP) vs intubation/surfactant, the study determined that treatment with early CPAP rather than intubation/surfactant is associated with less respiratory morbidity by 18-22 months chronologic age. See publication.

Another research area within the division utilizing outcomes measurements is led by
Elizabeth Cason Benton, M.D., director of the Alabama Child Health Improvement Alliance (ACHIA). Dr. Benton is the ACHIA liaison to the National Improvement Partnership, and focuses on fostering a culture of quality improvement through partnerships with practitioners, payers, families, and organizations that deliver care to Alabama to improve health outcomes of children in the state.

**Significant Publications**


**Division Awards & Recognition**

**Crayton A. Fargason, Jr., M.D.,** General Pediatrics, serves on the Healthcare Safety & Quality Improvement Research study section of the Agency for Healthcare Research and Quality.

**Myriam Peralta, M.D., M.P.H., FAAP,** General Pediatrics and Adolescent Medicine, has been elected to serve as a member of the Section on Developmental and Behavioral Pediatrics Executive Committee for a three-year term.

**Elizabeth Cason Benton, M.D.,** General Pediatrics and Adolescent Medicine, has been selected as a member for the Association of Maternal and Child Health Program (AMCHP) Medicaid Managed Care Learning Collaborative.

**Elizabeth Cason Benton, M.D.,** General Pediatrics and Adolescent Medicine, was elected to serve as a board member for the American Academy of Pediatrics – Alabama Chapter.

**Elizabeth Cason Benton, M.D.,** General Pediatrics and Adolescent Medicine, received a Special Achievement Award for her dedication to promoting quality healthcare for all children in Alabama.
Tina Simpson, M.D., Krista Casazza, M.D., and Jasmine Pagan, M.D., General Pediatrics and Adolescent Medicine, received The 2015 Association of Teachers of Maternal and Child Health Innovative Teaching Award.
Pediatric Hematology and Oncology faculty have focused their efforts on discovery in the following areas: novel targeted approaches to treat brain tumors, pathogenesis of kidney disease in patients with sickle cell disease, and understand the landscape of the burden of morbidity borne by childhood, adolescent and young adult cancers.

Gregory Friedman, M.D., has demonstrated that the most deadly subgroup of medulloblastoma is highly sensitive to a genetically modified herpes simplex virus. He is leading a highly innovative targeted approach at killing brain tumor cells while sparing normal brain cells; this bench-to-bedside translation of engineered herpes simplex virotherapy, is FDA approved and supported by the NIH. To further advance this therapy in the lab, Dr. Friedman received funding from the Department of Defense to develop a novel route of delivering the virus to target metastatic pediatric brain tumors.

Jeffrey Lebensburger, D.O., received a K23 mentored career development grant from the NIH/NHLBI and an American Society of Hematology Scholar Award to better understand the progression to chronic kidney disease among adolescent patients with sickle cell disease. He has developed a longitudinal cohort of patients with sickle cell disease to develop biomarkers of progression of kidney injury. Patients identified as at risk for progression are eligible to participate in a pilot study of losartan.
Five-year survival rates for childhood cancer survival now exceed 85%. However, this progress has come at a price – the survivors carry a high burden of morbidity and are at risk for premature mortality. One of these adverse outcomes is the increased risk of HPV-related malignancies. Given that this is a preventable outcome, Wendy Landier, Ph.D., is conducting an R01-funded study (funded by the NCI) to understand the factors responsible for HPV vaccine non-initiation among childhood cancer survivors, as well as the safety and immunogenicity in these survivors. Findings from this study will be used to develop the next phase of the study – i.e., targeted intervention to improve vaccination rates.

Acute lymphoblastic leukemia is the most common cancer in children. While over 95% of the children enter into remission, 20% relapse within five years. Durable remissions require two years of daily oral chemotherapy (6-mercaptopurine) in order to sustain remissions. Smita Bhatia, M.D., MPH, has (through an R01-funded mechanism from the NCI) demonstrated that a large proportion of children do not adhere to oral chemotherapy and that non-adherence is associated with an increased risk of relapse. She and Dr. Landier are now co-leading a national phase III trial to improve adherence to oral chemotherapy.

The adverse events encountered by childhood cancer survivors are directly related to the chemotherapy and radiation used to treat the children for their primary cancer. Dr. Bhatia is leading a national NCI-funded study to understand the molecular pathogenesis of these adverse outcomes and develop prediction models to identify those at highest risk. She is leading a large multi-institutional trial (funded by the NCI) to study pharmacologic interventions to reduce the risk of radiation-related breast cancer in childhood cancer survivors.

While progress has been made over the past five decades in cancer treatment for young children, far less progress has been made in improving survival rates for adolescents and young adults (AYAs) diagnosed between the ages of 15 to 39. In fact, cancer is the leading cause of death in people ages 15-39, so it is important to understand why the outcome in these patients has not seen the same improvement as that in young children or older adults. Julie Wolfson, M.D., and her team’s work has revealed that care at an NCI-designated Comprehensive Cancer Center (CCC) or Children’s Oncology Group (COG) site mitigates the poor outcome in AYAs, compared with children. Potential barriers to accessing these CCC or COG sites for AYAs include age, non-private insurance, low socioeconomic status, and distance from the nearest age-appropriate site. Dr. Wolfson’s group currently is evaluating a comprehensive approach to acute lymphoblastic leukemia disparities in AYAs that encompasses these sociodemographic elements along with clinical and biological factors.

**Significant Publications**


RESEARCH ANNUAL REPORT


Division Awards & Recognition

Smita Bhatia, M.D., MPH, Pediatric Hematology and Oncology, elected to the at-large position of the Children’s Oncology Group executive committee.

Gregory Friedman, M.D., Pediatric Hematology and Oncology, participated in an NIH-sponsored advanced training course, “Frontiers in Stem Cells in Cancer,” in Ponce, Puerto Rico. He spoke on “Pediatric Cancer Stem Cells: Biologic Strategies with Oncolytic Virotherapy” and taught a lab, “Pediatric Cancer Stem Cells: Intracranial Injections and Immunofluorescent Staining.”

Avi Madan-Swain, Ph.D., Pediatric Hematology and Oncology, received the Senior Faculty 2015 Dean’s Excellence Award in Service, University of Alabama at Birmingham.
The Division of Hospital Medicine draws upon its significant clinical expertise to ask important research questions relating to standardization of pediatric care throughout Children’s of Alabama and across the state. One such area relates to utilization of laboratory testing that is unlikely to be utilized in the clinical management of hospitalized patients. Sri Narayanan, M.D., and Paul Scalici, M.D., have investigated the utility of testing serum magnesium concentrations in children hospitalized at Children’s of Alabama. In a retrospective trial, these investigators found that 83% of tests for serum magnesium likely were unnecessary because they were ordered on patients who were not at risk for low serum magnesium and did not require any changes in management based on the test results. Outside of a select few populations, such as children receiving chemotherapy and those who have undergone solid organ transplants or major abdominal surgery, abnormal magnesium levels or levels that require supplementation are very uncommon and testing serum magnesium is not needed. Their findings are at the forefront of a larger movement within pediatric hospital medicine to target resources where they have the greatest likelihood of improving the health of children, and in the process reduce laboratory overuse. See publication.

Another area of focus for the division centers upon parental behaviors that impact the health of the children of Alabama. An example of this is the work done by Susan Walley, M.D., with second hand tobacco smoke. Approximately 25% of children in the state are exposed to second hand tobacco smoke. In approaching this health risk, Dr. Walley first investigated whether or not patients hospitalized at Children’s of Alabama are exposed to second hand tobacco smoke by incorporating those questions as part of the standard intake evaluation at the time of admission to the hospital. In addition, she produced a seven minute video on smoking cessation (See video) that is offered for viewing to all parents or caregivers of hospitalized children. Dr. Walley then completed a research project aimed at determining whether or not the hospitalization of a child with respiratory disease could be used as an opportunity to instruct caregivers on methods to decrease their child’s exposure to second hand smoke. Her results show that the interventions offered during hospitalization (e.g., watching the video, brief counseling, offer of starter nicotine replacement, and
referral to the Quit Line, 1-800-quit-now) are beneficial. Results from caregiver interview by phone three months after hospitalization showed that a significant number of caregivers had adopted practices that would decrease the child’s exposure to second hand tobacco smoke and a modest number had given up smoking. Dr. Walley’s research has been supported by the American Academy of Pediatrics Julius Richmond Center of Excellence, which is devoted to preventing exposure of children to tobacco smoke. In December 2015, Dr. Walley was awarded a grant from the Alabama Department of Health aimed at decreasing tobacco use and initiation among middle and high school students in Birmingham. See publication.

Another state-wide challenge in Alabama relates to rural residence as a determinant of health and healthcare utilization. Nearly one in five children in the United States resides in a rural area. Compared with non-rural children, children living in rural areas often experience worse health outcomes. Little is known about differences in children’s hospital utilization between rural and non-rural children. Chang Wu, M.D., is examining the disparities in healthcare delivered to various patient populations. Using national data from the Pediatric Health Information System, or PHIS, database (which is a large clinical database from the major children’s hospitals across the United States, including Children’s of Alabama), Dr. Wu collaborated with investigators from Yale University, Boston Children’s Hospital, Children’s Hospital of Philadelphia, Children’s Hospital of Colorado, and the Children’s Hospital Association in a study aimed at comparing demographic characteristics and healthcare utilization of hospitalized rural children compared with non-rural children. He found that rural children hospitalized at children’s hospitals have high rates of medical complexity and often reside in low-income and medically underserved areas. Compared with non-rural children, rural children experience more expensive hospitalizations and more frequent readmissions. Results suggest that better integration of care between children’s hospitals and healthcare providers in rural areas is needed, especially for patients with complex medical needs, and that additional study is needed to identify specific approaches to improve the quality of care and outcomes for children residing in rural areas. Highlighting the collaborative nature of research within the Department of Pediatrics, Dr. Marjorie Lee White (UAB Pediatric Emergency Medicine) worked closely with Dr. Wu and the team of investigators on this project. (Peltz, A. Wu, CL. White, ML. Wilson, K. Lorch, S. Thurm, C. Hall, M. Berry, J. Characteristics of rural children admitted to pediatric hospitals. Pediatrics, In Press.)

**Significant Publications**


**Division Awards & Recognition**

Susan Walley, M.D., Pediatric Hospital Medicine, has been selected as a member of the Executive Committee of the national AAP Section on Tobacco Control (SOTC) and currently serves as the AAP SOTC Publications Chair and Newsletter Editor. She has also been selected to author the AAP Policy Statement on Electronic Nicotine Delivery Systems (i.e., electronic cigarettes).
A major focus of research in the Division of Pediatric Infectious Diseases is the study of perinatal infections that impact the health and development of infant and children. Multiple projects, including completion of patient follow-up and data analysis of the NIDCD-funded CHIMES study, are providing new insight into the natural history of congenital cytomegalovirus infection. This study enrolled over 100,000 infants from six hospitals in the US and was organized and administered by Suresh Boppana, M.D., and Karen Fowler, Ph.D. Findings from the CHIMES study represent the benchmarks for the prevalence of congenital CMV infections in the U.S. and the long term outcome from this infection. Important new findings include the development of a highly sensitive and specific PCR-based assay for testing newborn saliva samples to identify babies infected with CMV, failure of testing of blood spots collected from newborns for routine screening for detecting CMV-infected babies, a significantly higher prevalence of congenital CMV infection in African American women and teens, and the failure of newborn hearing screening to identify significant proportion (~40%) of infants with CMV-associated hearing loss at birth. Many of these have been detailed in major publications in recent years (New England Journal of Medicine, Journal of the American Medical Association, Journal of Infectious Diseases, and the Pediatric Infectious Diseases Journal). The findings from the CHIMES study have also been presented at a number of international and national meetings. Many of these findings are being used in the development of new guidelines on caring for infants and children here in Alabama, nationally, and internationally.

Dr. Fowler is conducting a CDC-funded study to determine the effectiveness of a cognitive-behavioral intervention to reduce the transmission of CMV to babies of young pregnant women in Birmingham. This study provides a short video about CMV along with prevention text messages sent to the women during their pregnancy. If successful, this intervention will be available for adaption by obstetricians and pediatricians in their practices. Additionally, a grant from the NIH was awarded to Dr. Boppana assesses mechanism of transmission of CMV through breast milk, a very common
route of transmission of CMV. These studies will lead to further understanding of the role of viral diversity and acquisition of virus on the epithelial surface as well as determining the activities of antiviral antibodies in limiting virus infection of epithelium, and will complement the technologies and findings provided by studies of viral genetic diversity in viruses isolated from infants with congenital CMV infections by Shannon Ross, M.D. Utilizing next generation sequencing technologies and informatics, Dr. Ross is investigating the contribution of genetic heterogeneity in the distribution of viruses in different areas of viral shedding in infected infants, in hopes of identifying a biomarker for the development of hearing loss. To further explore the overall contribution of CMV to hearing loss in children, Dr. Ross is collaborating with Children’s of Alabama otolaryngologist Audie Woolley, M.D., and is examining the frequency and importance of CMV detected in the inner ear in patients undergoing cochlear implantation for sensorineural hearing loss. Although the studies described above have focused on populations in the US, Bill Britt, M.D., and Drs. Boppana and Fowler have ongoing projects in Brazil and South Africa (supported by the NIH). In Brazil over 20,000 women and their newborn infants are being enrolled in studies to define the natural history of congenital CMV infection in a population of women with universal immunity to CMV, a critical question in the design of prophylactic vaccines for this infection. Utilizing specimens from this population and in collaboration with investigators at the University of Massachusetts, Drs. Britt and Boppana are analyzing the origin of populations of viruses from individual patients. These projects have resulted in two comprehensive studies of genetic diversity and population drifts of CMV virus families in individual patients (submitted to *PNAS* and *Molecular Biology and Evolution*). Studies conducted by Drs. Boppana and Fowler in South Africa will help understand the relationship between HIV infection in women and the natural history of congenital CMV infection.

The antiviral drug development programs of Mark Prichard, Ph.D., Debra Quenelle, Ph.D., and Scott James, M.D., assess novel antiviral agents that have activity against herpesviruses. These studies not only advance knowledge of drugs that can treat viral infections, but by inhibiting viral replication also yield insights into the natural history of CMV infections (*PLOS One*, 2014). Mechanisms of resistance for drugs such as maribavir have been defined (*Journal of Virology*, 2014), and novel agents such as serpin antithrombin III and methylenecyclopropane analogs have been assessed (*Antimicrobial Agents and Chemotherapy*, 2014). Dr. James received a K08 career development award to explore novel mechanisms of antiviral resistance in specimens from subjects enrolled in multicenter studies conducted by the NIAID Collaborative Antiviral Study Group (CASG), described below. And investigations of helicase-primase inhibitors for HSV (*Clinical Pharmacology and Therapeutics*, 2015), new small molecule entry inhibitors for influenza (*Journal of Virology*, 2014), and retinazone for Ebola (*Antiviral Chemistry and Chemotherapy*, 2014) have been published. This group has had additional publications in *New England Journal of Medicine* and *Science Translational Medicine* over the past year as well.

Major clinical trials of the treatment of life-threatening viral infections also has been undertaken by David Kimberlin, M.D., and Richard Whitley, M.D. Building upon their previous body of work that had established intravenous ganciclovir and oral valganciclovir as the standard of care for the management of babies with symptomatic congenital CMV disease, Drs. Kimberlin and Whitley conducted a major NIAID-funded trial of longer-term oral valganciclovir therapy in this population through their multicenter network known as the Collaborative Antiviral Study Group (CASG). Trial results were published in the *New England Journal of Medicine in March 2015*, demonstrating improved audiologic and, for the first time, improved neurodevelopmental outcomes among those babies treated for six months as compared with babies treated for six weeks. This
major advance will again establish a new standard of care for the management of this disease. Over the past year, CASG data have directly led to new indications being issued for valganciclovir from the European Medicines Agency (their version of the FDA), and for oseltamivir from the U.S. Food and Drug Administration. These regulatory accomplishments represent significant advancements worldwide in the treatment of viral infections, based upon CASG data from UAB and Children’s of Alabama.

Mary Ballestas, Ph.D., Veronica Sanchez, Ph.D., and Drs. Boppana, Britt, and Ross all lead robust laboratory research as well. Studies in basic molecular virology and virus:host interactions describe multiple ongoing projects. A significant effort has been focused on understanding the role of virus-induced inflammation and brain development in a small animal model of CMV infection of the developing central nervous system that has been developed in collaboration with investigators at the University of Rijeka in Croatia. This system has pointed to the role of inflammation in altered cell positioning in the developing brain, a finding that recapitulates aspects of the pathology of brain disease in infants with congenital CMV infection (PLOS Pathogens, 2013). Interestingly, many of the findings in this system have also been described in infants with autism, and as a result division investigators are developing a specific research program in collaboration with investigators in the Department of Neurobiology at UAB to investigate links between brain inflammation and autism. A second major focus of this project is defining mechanisms of hearing loss in infants with congenital CMV infections. This small animal model closely recapitulates the findings of hearing loss in infants with congenital CMV infection and findings generated from studies in this system have identified mechanisms of hearing loss, which include virus-induced inflammation (in revision, PLOS Pathogens, 2014). These studies are mature and a collaborative project involving investigators at Washington University in St. Louis and the University of Washington will be submitted for funding this year. Drs. Britt and Boppana have additional projects underway to determine if antiviral antibodies can prevent CMV infection at an epithelial surface, a critical question for development of prophylactic vaccines to prevent CMV infection. Finally, utilizing findings from in vitro studies that have been developed as part of long standing collaborative studies with investigators in the Department of Medicine at UAB, division investigators have begun to understand the relationship between CMV infection of monocytes in inflammation of the intestinal mucosa of patient with inflammatory bowel disease (Journal of Immunology, 2014).

A second component of laboratory studies in virology are directed at understanding fundamental aspects of virus replication and virus:host interactions. These studies include several projects directed at dissecting the role of the functional components of the infected cell in the efficient production of infectious virus from an infected cell, a project that can be translated into the identification of novel targets for antiviral agents. In addition, these studies have developed new and previously unknown function of novel modes of regulation of cellular function, viral micro RNA molecules. Collaborative studies with investigators at Oregon Health Science University demonstrated that these non-coding RNA molecules can regulate the cellular endocytic pathway to facilitate virus assembly and to block the cellular secretion of anti-viral molecules (Cell Host Microbe, 2014). Additional structural studies of CMV with collaborators at University of Nuremberg/Erlangen in Germany have identified binding sites of antiviral antibodies that can limit virus infection, requisite information for vaccine design (Journal of Virology, 2014). Dr. Ballestas has conducted innovative studies in basic virus:host interactions include projects to decipher the role of the tissue microenvironment in the biology of Kaposi Sarcoma, a virus induced cancer seen in immunocompromised patients and in children in sub-Saharan Africa. This project includes
collaborators from the Mass Spectroscopy facility at UAB and the Department of Dermatology at UAB and has identified proteins in the microenvironment that could serve target for drug development for treatment of this malignancy. Newly initiated projects in the division include studies of the role of CMV regulation of cholesterol metabolism, a potential link between virus-induced inflammation and heart disease and the regulation of the cellular cytoskeleton by viral micro RNAs to optimize virus replication, a process that could represent a target for antiviral drug development.

Maaike Everts, Ph.D., and Dr. Whitley lead the UAB Drug Discovery Program. Awarded in March 2014, this U19 grant funds a multi-institutional program under the Centers for Excellence in Translational Research program. UAB is the operational center for the five year, $34.3 million dollar award that is focused on antiviral drug discovery and development. Already a lead has been identified against MERS and SARS. Preclinical toxicology and pharmacokinetic assessments in normal human volunteers have been completed. The molecule is positioned for studies against MERS in Saudi Arabia. The Drug Discovery Library also has been screened for Ebola and Zika viruses, with promising molecules being identified for these emerging pathogens as well. In collaboration with Southern Research, the Alabama Drug Discovery Alliance is also developing molecules for Parkinson Disease, a variety of cancers, and tuberculosis, among others. These accomplishments promise to further advance therapeutic opportunities for diseases across the spectrum of age and pathology.

Significant Publications


RESEARCH ANNUAL REPORT


RESEARCH ANNUAL REPORT

Michaels MG, Sánchez PJ, Stewart A, Bernstein DI, Feja K, Novak Z, Fowler KB, Boppana SB; National Institute on Deafness and Other Communication Disorders CHIMES Study.


Prevalence of congenital cytomegalovirus infection in Nigeria: a pilot study. Olusanya BO, Slusher TM, Boppana SB.

Helicase-primase as a target of new therapies for herpes simplex virus infections. James SH, Larson KB, Acosta EP, Prichard MN.

Division Awards & Recognition

David W. Kimberlin, M.D., Pediatric Infectious Diseases, received the American Academy of Pediatrics – Alabama Chapter Special Achievement Award. He also presented the Philip Porter Lecture at Massachusetts General Hospital for Children and Harvard University.

Richard Whitley, M.D., Pediatric Infectious Diseases, has been named as Co-Chair of the NIH Recombinant DNA Advisory Committee’s Biosafety Committee.

Suresh Boppana, M.D., Pediatric Infectious Diseases, received the inaugural Congenital CMV Award at the 5th annual International Congenital CMV Conference in Brisbane, Australia in April.
The UAB Division of Neonatology is a founding member of the Eunice Kennedy Shriver NICHD Neonatal Research Network, or NRN. Over its 30 years of existence, the NRN has defined the standards of multi-institutional collaborative research that directly has resulted in the increased survival rates of extremely low birth weight infants in the United States. The UAB Division of Neonatology is consistently one of the top centers in developing, leading, enrolling, and analyzing the important studies conducted by the NRN. For example, Neonatology Division members recently have led three major innovative NRN studies: the SAVE Factorial Trial, Cytokine, and the SUPPORT Factorial Trial.

The UAB Division of Neonatology also has conducted seminal investigations of resuscitation and essential newborn care in 100 communities in six countries, which included almost 200,000 infants. These trials established the effectiveness of these interventions in reducing stillbirths and neonatal mortality, and led to worldwide implementation of training, including the globally-implemented Helping Babies Breathe Program and the Essential Care for Every Baby Program introduced in 2014. See publication 1, 2.

The Neonatology Division also conducts groundbreaking basic research in the LungMAP project. Namasivayam Ambalavanan, M.D., is the Principal Investigator of the UAB Research Center, which along with Yale University, University of California San Diego, and Carnegie Mellon University comprise the LungMAP consortium. LungMAP seeks to improve lung health by providing the research community with a web-based resource to support investigations into the processes that
regulate lung development. The use of cutting-edge technologies upon the many cell types from prenatal and postnatal mouse and human tissues will generate a novel map of where and when the lung cells differentiate and the alveoli form. LungMAP is making this knowledge accessible and freely available to the public through novel imaging and web-based tools. See publication.

**Significant Publications**


**Division Awards & Recognition**

The Society for Pediatric Research has named **Waldemar Carlo, M.D.**, Neonatology, the 2015 recipient of the Douglas K. Richardson Award in Perinatal and Pediatric Healthcare Research.

**Prem Fort, M.D.**, Neonatology, received the 2015 Fellows’ Section Clinical Research Award from the Society for Pediatric Research as well as the Southern Society of Pediatric Research Clinical Science Young Investigator Award.

**Namasivayam Ambalavanan, M.D.**, Neonatology, has been selected as the Southern Society of Pediatric Research 2015 Founders’ Award recipient.

**Waldemar A. Carlo, M.D.**, Neonatology, is a Southern Society for Pediatric Research (SSPR) Founders Award recipient for 2016 in recognition of his work in promoting the SSPR and research in pediatric health.
RESEARCH ANNUAL REPORT

PEDiatric NEPHroLOGY

Pediatric Faculty

Dr. Daniel Feig  Professor
Dr. David Askenazi  Associate Professor
Dr. Sahar Fathallah-Shaykh  Associate Professor
Dr. Michael Seifert  Assistant Professor
Dr. Monica Tucci-Cramer  Assistant Professor

Featured Research

The Division of Pediatric Nephrology leads research efforts in drug discovery and pharmacokinetics, as well as the assessment, progression, and treatment of chronic kidney disease in children.

The Pediatric and Infant Center for Acute Care Nephrology (PICAN) is directed by David Askenazi, M.D. Seeking to develop novel management options for pediatric patients with renal impairment, PICAN studied a new dialysis device called Aquadex. Designed to remove excess accumulated water in elderly individuals with heart failure, the Aquadex was adapted to treat neonates and premature infants with kidney failure who were too small for hemodialysis. As a result of this work, children as small as 1500gm can now receive this life-saving therapy. With the publication of these results, this technology now is being used at other major children’s hospitals across the country, including Cincinnati Children’s, Boston Children’s and Seattle Children’s. See publication.

The Pediatric Renal Transplant Program is another area of expertise for the division. Michael Seifert, M.D., who recently joined the Pediatric Nephrology Division from Washington University, investigates ways to improve long term kidney function in children who receive kidney transplants. (Predictors of Early Rejection and Allograft Failure in Pediatric Kidney Transplantation: Impact of Histology and Behavior. Seifert ME, Yanik MV, Mannon RB. In Press.) In a study that will alter how children with kidney transplants are evaluated, he has demonstrated that early immunologic activation, seen on surveillance renal transplant biopsies, predicts long term complications even before changes in laboratory values. His current NIH funded studies are aimed identification of biomarkers of chronic transplant dysfunction and new therapeutic targets to mitigate chronic allograft nephropathy.

Daniel Feig’s, M.D., Childhood Hypertension Program provides critical insights into the role of serum uric acid in the development of adolescent onset essential hypertension. Previous clinical trials have demonstrated that elevated serum uric acid causes vascular damage and activation of the renin angiotensin system resulting in high blood pressure that can be mitigated by uric acid lowering therapy. The SURPHER (Serum Uric acid Reduction to Prevent HypERTension) trial is an ongoing study to assess the effectiveness of uric acid reduction in lowering blood pressure in young adults. This study has found that even mild hyperuricemia results in increased risk for development of hypertension and chronic kidney disease in patients with type 2 diabetes through vascular injury associated mechanisms similar to those causing hypertension. See publication.
Significant Publications


The UAB Division of Pediatric Neurology is leading the assessment of studies examining the natural history, safety, and tolerability of oral cannabidiol in childhood epilepsy that is not controlled by existing treatments. Cannabidiol is a light, oily liquid derived from the cannabis plant, and research conducted by Drs. Goyal, Kankirawatana, and Harsanyi-Jilling has received support from the State of Alabama to improve the lives of its youngest citizens with intractable seizure disorders. This degree of expertise also is being applied to multicenter studies of the treatment of Lennox-Gastaut Syndrome and Dravet Syndrome.

**Significant Publications**


Cognitive Outcomes in Febrile Infection-Related Epilepsy Syndrome Treated With the Ketogenic Diet. Singh RK, Joshi SM, Potter DM, Leber SM, Carlson MD, Shellhaas RA.
RESEARCH ANNUAL REPORT

PEDIATRIC PULMONOLOGY AND SLEEP MEDICINE

Pediatric Faculty

Dr. Hector Gutierrez  Professor
Dr. Kristin Avis  Associate Professor
Dr. Jennifer Guimbellot  Instructor
Dr. William Harris  Assistant Professor
Dr. Wyn Hoover  Associate Professor
Dr. Claire Lenker  Associate Professor
Dr. Isabel Lowell  Associate Professor
Dr. David Lozano  Associate Professor
Dr. Mary Halsey Maddox  Assistant Professor
Dr. Teri Magruder  Associate Professor
Dr. Madhuri Penugonda  Assistant Professor
Dr. Valerie Tarn  Assistant Professor
Dr. Brad Troxler  Assistant Professor
Dr. Charles Judy  Associate Professor
Dr. Vinit Mahesh  Associate Professor

Featured Research

The Pediatric Pulmonary Division remains active in research, with focus areas in asthma, sleep, and cystic fibrosis.

The Cystic Fibrosis Center continued its active participation as a Cystic Fibrosis Foundation-sponsored Therapeutic Development Network research site. Clinical trials for new cystic fibrosis therapeutics continued with significant activity with over a dozen studies ongoing.

Steve Rowe, M.D., is the director of the UAB Cystic Fibrosis (CF) Center, and is a member of the Division of Pediatric Pulmonary Medicine. UAB leads the GOAL and PROSPECT studies in cystic fibrosis, which are two large multi-center clinical trials supported by the CF Foundation to evaluate the efficacy of CFTR modulators and their mechanistic basis. This also supports a biorepository of clinical samples and human cells to enable precision based therapeutics in the future. Additionally, pediatric researchers in the CF Center recently obtained a large ($7.5 million) grant from the CF Foundation (in conjunction with Southern Research) to identify compounds that will suppress CFTR nonsense mutations and partially inhibit Nonsense-Mediated mRNA Decay (NMD) of CFTR nonsense-containing mRNAs. Additional efforts include NIH funded research evaluating the effect of a novel mucolytic on respiratory and gastrointestinal healthy, including prevention of meconium ileus in CF rats, and generating the first humanized F508del and G551D CFTR rats for translational studies evaluating CFTR modulators. The CF researchers also have NIH support to investigate acquired CFTR dysfunction as a proximate cause of COPD in ferrets, as well as developing a pilot clinical study in humans evaluating CFTR modulators in COPD patients with chronic bronchitis.

The Pediatric Sleep Disorders Center investigates the relationship between sleep disorders/sleep deprivation and injury risk in children using a virtual reality pedestrian environment. Led by Kristin Avis, Ph.D., and David Lozano, M.D., the Center has developed and validated a virtual reality pedestrian environment (VRPE) that evaluates risk but without exposure to true risk. This methodology permits the investigation of effects of sleep loss on children’s safety in a
real-world immersive environment, and the application of known consequences of sleep loss to the real world. The Center’s researchers have established that obstructive sleep apnea and narcolepsy significantly increase children’s pedestrian injury risk compared with matched healthy peers, and have documented that treating these two separate sleep disorders significantly reduces pedestrian injury risk in children. This research provides a unique opportunity to identify a real world, ecologically valid impact of sleep deprivation in pre-adolescent children who have a high rate of both unintentional injury and sleep deprivation.

Research in the division also involves development of minimally invasive, personalized models for predicting the effectiveness of CFTR modulators in cystic fibrosis patients and those with acquired CFTR dysfunction. Small molecules that mitigate CFTR malfunction (modulators) have shown great promise in clinical trials, but their effectiveness is limited to a subset of patients with specific mutations. In addition, genetic and environmental heterogeneity seem to impair the function of these drugs in the target population. Therefore, strategies determining a priori the efficacy of CFTR modulators on an individualized basis is absolutely essential. Jennifer Guimbellot, M.D., and colleagues have developed a rapid cell culture-based model of epithelial cells from the nose as a screening method to assess efficacy of small molecule therapies from individual patients ex vivo, which will provide a unique and innovative tool to predict corrector activity in any candidate for CFTR modulators. This tool involves the culture of respiratory “organoids”, three dimensional cultures of nasal epithelial cells that may be evaluated for modulator-induced responses using functional measurements, microscopy, and biochemical analysis. These culture techniques may be applied to other cell types, including that of sweat gland epithelia, to compare and study CFTR modulation. This model systems has the potential for use as a clinical outcome tool, as well as overcome certain limitations of existing cell culture-based models for studying cystic fibrosis, including the basic defect of CFTR and related proteins.

The new Primary Ciliary Dyskinesia (PCD) Clinic at Children’s of Alabama is run in conjunction with the PCD Program at the University of Alabama at Birmingham (UAB) focusing on the inherited disorder of moving cilia – structures lining the airways, ears and sinuses.

Pulmonary faculty will be collaborating in developing new clinical research tools to assess these disorders using micro-optical coherence tomography (microOCT) for in human subjects to determine the functional epithelial microanatomy concerning ciliary movement.

Significant Publications

J Clin Sleep Med. 2014 Nov 8. pii: jc-00244-14. Sleep Patterns, Sleep Instability, and Health Related Quality of Life in Parents of Ventilator-Assisted Children. Lisa J. Meltzer, PhD; Maria M. Sanchez-Ortuno, PhD; Jack D. Edinger, PhD; Kristin T. Avis, PhD.


RESEARCH ANNUAL REPORT


RESEARCH ANNUAL REPORT

PEDIATRIC REHAB MEDICINE

Pediatric Faculty

Dr. Drew Davis  Associate Professor
Dr. Paola "Lala" Mendoza  Assistant Professor
Dr. Erin Swanson  Assistant Professor

Featured Research

The UAB Division of Pediatric Rehabilitation Medicine at Children’s of Alabama seeks to generate new knowledge related to disabling conditions of childhood through close collaboration with the UAB Lakeshore Research Collaborative. Efforts being led by the division include assessments of obesity and physical impairment in childhood, a major problem in the state of Alabama. Additionally, division members are collaborating with the Children’s of Alabama Concussion Work Group and other UAB collaborators to identify biomarkers and risk factors for prolonged concussion recovery in children and adolescents. Their work is at the forefront of efforts nationally to learn more about the serious consequences of traumatic brain injury. The division also is developing new applications for constraint induced movement therapy in the pediatric population, building upon close collaborations with leaders in this area in the adult population here at UAB.

Division Awards & Recognition

Drew Davis, M.D., Pediatric Rehabilitation Medicine, will serve a three-year term as vice chair of education for the Pediatric Rehabilitation/Developmental Disabilities Council of the American Academy of Physical Medicine and Rehabilitation.

Drew Davis, M.D., Pediatric Rehabilitation Medicine, has been selected by the American Board of Physical Medicine and Rehabilitation to serve a three-year term as an item writer for the Pediatric Rehabilitation Medicine Board Examination.
Featured Research

Members of the Division of Pediatric Rheumatology excel in research into macrophage activation syndrome (MAS), in the pediatric population. This includes the novel recognition that a group of patients with fatal H1N1 flu died after their viral infections triggered this serious hyperinflammatory disorder. Randy Cron, M.D., Ph.D., led a group of investigators from across the country to determine that the reason for this increased mortality was related to gene mutations in these susceptible individuals. His data suggest that people with other types of infections and identical gene mutations also may be prone to the disorder, known as reactive HLH (rHLH), or hemophagocytic lymphohistiocytosis. See publication. Perhaps more importantly, these findings raise the question of whether HLH gene mutations (potentially up to 10% of the population) should be screened for at birth to identify those carrying risk alleles for developing severe H1N1, or other, infections.

Dr. Cron’s work in this area also includes a retrospective re-analysis of the results from a large clinical trial of IL-1 blockade using Anakinra for the treatment for sepsis. When sepsis patients were divided based on the presence of macrophage activation syndrome (MAS), it was found that Anakinra doubled survival of those sepsis patients with features of MAS. Anakinra had no effect on survival of sepsis patients without MAS. See publication.

In recognition of his leadership in this area, Dr. Cron led a group of experts who developed and published classification criteria for macrophage activation syndrome (MAS) complicating systemic juvenile idiopathic arthritis (sJIA). See publication.

Tim Beukelman, M.D., continues his efforts as the Scientific Director of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. CARRA is the North American pediatric rheumatology research organization, founded in 2002 to improve the care of children with rheumatic diseases. The CARRA Registry a multi-center prospective observational registry for children with arthritis. It became operational in 2015 and currently has over 40 clinical sites enrolling patients. The primary aim of the Registry is to evaluate the safety of therapeutic agents used to treat pediatric rheumatic diseases, and the secondary aim is to evaluate clinical outcomes and their determinants, including treatment. Dr. Beukelman has worked tirelessly with other members of the Registry Executive Committee to bring the Registry to fruition and encourage the performance of Phase IV safety surveillance studies that satisfy FDA requirements. Current work is focused on expanding the capabilities of the Registry to allow investigator-initiated observational and interventional substudies to be layered on the existing Registry infrastructure.
Dr. Beukelman also has NIH funding for the development of a research plan to assess the treatment of children newly diagnosed with juvenile idiopathic arthritis (JIA) that involves fewer than five joints and does not affect the eyes. Patients with this JIA phenotype are currently treated with NSAIDs and steroid joint injections as the standard of care. However, more than 50% of these children will develop arthritis in five or more joints (polyarthritis) or inflammation of the eyes (uveitis). When this occurs, children are typically treated with methotrexate, but they often have suboptimal clinical outcomes. The aim of his current efforts is to determine whether the use of methotrexate earlier in the disease course can prevent the occurrence of polyarthritis and uveitis and improve clinical outcome overall.

Dr. Beukelman is the PI of a pharmacoepidemiology project as part of the AHRQ-funded UAB Center for Education and Research on Therapeutics (CERTs). This project aims to use administrative claims data, such as Medicaid billing data, to further evaluate the safety of medications used to treat JIA with emphasis on serious infection and malignancy risk. These studies build upon this team’s prior successful publications and will allow for longer-term follow-up of patients, as well as the examination of newer biologic agents.

**Significant Publications**


Division Awards & Recognition

Randy Cron, M.D., Ph.D., Pediatric Rheumatology, has been selected to serve a three-year term on the Society for Pediatric Research (SPR) Fellows Basic Research Awards Selection Committee.

Tim Beukelman, M.D., MSCE, Pediatric Rheumatology, was selected as a visiting professor to the Florida Hospital Medical Center in Orlando as part of the American College of Rheumatology’s Rheumatology Research Foundation Pediatric Visiting Professor program.

Randy Cron, M.D., Ph.D, Pediatric Rheumatology, has been selected to serve on the editorial board for Arthritis Care & Research.