Infectious Diseases

Division Data Summary

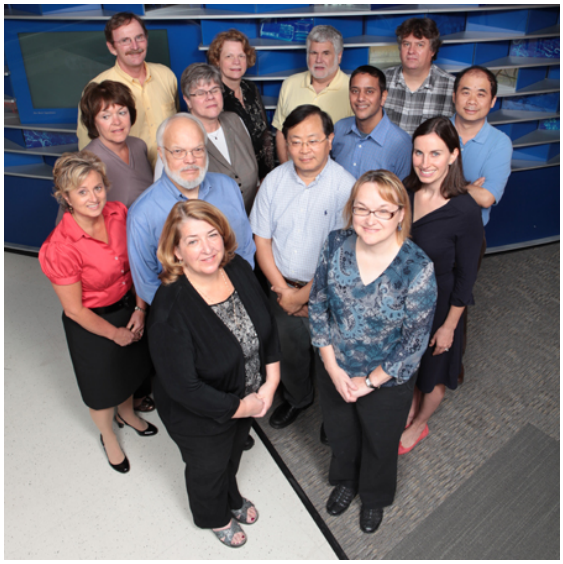
Research and Training Details

Number of Faculty	**19**
Number of Joint Appointment Faculty	**2**
Number of Research Fellows	**3**
Number of Research Students	**2**
Number of Support Personnel	**90**
Direct Annual Grant Support	**$7,837,314**
Direct Annual Industry Support	**$3,178,485**
Peer Reviewed Publications	**48**

Clinical Activities and Training

Number of Clinical Staff	**5**
Number of Clinical Fellows	**3**
Number of Clinical Students	**1**
Number of Other Students	**12**
Inpatient Encounters	**2226**
Outpatient Encounters	**1290**

Division Photo



Row 1: M Staat, R Cardin
Row 2: M Dickey, M Steinhoff, J Jiang, E Schlaudecker
Row 3: N Hutchinson, M McNeal, S Shah, M Tan
Row 4: R Frenck, M Hostetter, D Bernstein, T Farkas

Significant Publications

Morrow AL, Meinzen-Derr J, Huang P, Schibler KR, Cahill T, Keddache M, Kallapur SG, Newburg DS, Tabangin M, Warner BB, Jiang X. **Fucosyltransferase 2 non-secretor and low secretor status predicts severe outcomes in premature infants**. *J Pediatr.* 158(5): p. 745-51 2011.

This landmark paper analyzed secretor gene fucosyltransferase 2 (FUT2) polymorphisms in relation to outcomes of prematurity. Of the 410 study infants, death occurred in 13% of 95 infants who were nonsecretors, 5% of 203 infants who were heterozygotes, and 2% of 96 infants who were secretors. Again by phenotype, 15% of 135 infants with low secretor phenotype died, compared with only 2% of 248 infants with high secretor phenotype. Low secretor phenotype was also associated with necrotizing enterocolitis and gram negative sepsis. This paper provides the first definitive predictive biomarker of adverse outcomes in premature infants.

Staat MA, Stadler LP, Donauer S, Trehan I, Rice M, Salisbury S. **Serologic testing to verify the immune status of internationally adopted children against vaccine preventable diseases**. *Vaccine*. 28(50): p. 7947-55. 2010.

Seven hundred forty-six children presenting to the CCHMC International Adoption Center between 11/1999 through 6/2004 were tested for serologic response to vaccine antigens received in their countries of origin. More than 50% of the children were from Russia, Kazakhstan, or the Ukraine. Another 21% of the children were from China, 12% from Guatemala, and the remaining children from South Korea, Eastern Europe, India, Asian/Pacific Rim, Vietnam, or Africa. For children with 3 or more vaccine doses, overall protection was high

for diphtheria (85%), tetanus (95%), polio (93%), and hepatitis B (77%). Children without immunization documentation had lower immunity. Serologic testing is an important criterion to verify the immunization status of internationally adopted children.

Bravo FJ, Bernstein DI, Beadle JR, Hostetler KY, Cardin RD. **Oral hexadecyloxypropyl-cidofovir therapy in pregnant guinea pigs improves outcome in the congenital model of cytomegalovirus infection**. *Antimicrob Agents Chemother.* 55(1): p. 35-41. 2011.

The authors evaluated the *in vivo* efficacy of an orally bioavailable analogue of cidofovir, hexadecyloxypropyl-cidofovir (HDP-CDV), in a guinea pig model of congenital CMV infection. Pregnant guinea pigs were inoculated with GP-CMV during the second/early third trimester of gestation, and the treatment groups received one of two HD-CDV regimens. All HDP-CDV regimens significantly improved pup survival from 50-60% in untreated animals to 93-100% in treated animals. Treatment with 20 mg/kg HDP-CDV significantly reduced the viral load in pup spleen and liver, while treatment with 4 mg/kg did not. These results indicate that HDP-CDV has promise for treatment of congenital human CMV infection, which can produce both sensorineural hearing loss and mental retardation.

Farkas T, Cross RW, Hargitt E, Lerche NW 3rd, Morrow AL, Sestak K. **Genetic diversity and histo-blood group antigen interactions of rhesus enteric caliciviruses**. *J Virol.* 84(17): p. 8617-25. 2010.

The group examined rhesus macaque stool samples for rhesus caliciviruses (CVs). Approximately 11% of the samples contained recovirus isolates. Phylogenetic analysis classified the recovirus isolates into two genetic groups and at least four genetic types. A single rhesus norovirus isolate was closely related to GII human noroviruses. Neutralizing antibodies against the Tulane virus, a novel rhesus calicivirus, were detected in 88% of serum samples obtained from primate caregivers. Type A and B histo-blood group antigens were involved in Tulane virus infection. These findings indicate the zoonotic potential of primate CVs and bring to light some remarkable similarities between rhesus enteric CVs and human noroviruses.

Tan MX, Jiang X. **Norovirus gastroenteritis, carbohydrate receptors, and animal models**. *PLoS Pathog.* 6(8). 2010.

This invited review in a prestigious journal highlighted the importance of histo-blood group antigens as receptors for noroviruses. Different noroviruses reveal different receptor-binding profiles associated with the ABO, secretor, and Lewis HBGA types. Human volunteer challenge studies of a prototype Norwalk virus provided direct evidence of HBGA receptor recognition. The HBGA-binding interfaces have been identified in the protruding (P) domain of the viral capsid protein, demonstrating that the P domain is the primary site of receptor interaction, which plays an essential role in norovirus infection.

Division Highlights

Margaret K. Hostetter, MD

The Hostetter laboratory focuses on mechanisms and consequences of heparin binding by *Candida albicans*. Binding of heparin by *C. albicans* has been shown by our laboratory to be essential for:
(1) removal of candidal surface proteins that serve as targets for elimination of the organism by innate immunity
(2) exposure of a *C. albicans* superantigen, defined in *J Inf Dis* 2008; 197:981-9
(3) biofilm formation *in vivo*
Collaborators at the University of Cincinnati and CCHMC have helped us to define the mechanism of heparin binding. With Jason Lu, CCHMC Bioinformatics, we evaluated linear heparin binding sites in 400 *C. albicans* surface proteins. Fifty-six *C. albicans* proteins were found to have heparin-binding sites that conformed to the

Cardin, Weintraub, or Sobel motifs. Of these 56, 13 were expressed at the bud neck, the site at which the yeast cell undergoes hyphal morphogenesis. These 13 proteins participated in various functions including chitin synthesis, anti-fungal resistance, GTPase activation, and phosphorylation. The protein with the most heparin binding motifs was Int1, which we had defined in our laboratory (*Science* 1998; 279:1355-8). In collaboration with Alexey Porollo, UC Environmental Health, we identified a cup-like structural motif in at least one of these sites that was conformationally consistent with heparin binding. A collaboration with Apryl Stallcup, UC Chemistry, provided additional information regarding the structure of heparin and possible sites of interaction with positively charged amino acids. Lastly, in a collaboration with Ken Greis, UC Proteomics laboratory, we refined the method of SILAC to examine proteins removed from the *C. albicans* surface after incubation with heparin. Of the top 25 proteins removed (of more than 100), 13 had identifiable heparin binding sites. The proteomics project received core grant funding from the CCTST. These collaborative efforts have provided key insights into the biochemistry of heparin binding.

David I. Bernstein, MD, MA

The pivotal trial for a genital herpes vaccine composed of herpes simplex type 2 glycoprotein D (gD) and adjuvanted with MPL and Alum was completed. Although two large trials showed efficacy in women this trial showed no efficacy for prevention of genital herpes caused by HSV type 2 (HSV-2) but surprisingly demonstrated efficacy against HSV-1 genital herpes. On a more positive note, our preclinical evaluations of vaccines that also contained gB and gH/gL combined with cationic lipid DNA complexes as an adjuvant showed protection, including protection of the dorsal route ganglia, the site of HSV latency.

The large multicenter cytomegalovirus trial that screens infants for congenital CMV has enrolled over 95,000 newborns. We have found that dried blood spots are not suitable for screening (published in *JAMA*) but that saliva was an excellent source for this screen (published in the *NEJM*).

Turning to GI viruses we completed the first human trial of a vaccine for norovirus and found it to be moderately protective (accepted for publication, *NEJM*) while the rotavirus vaccine we developed showed continued efficacy in preventing hospitalizations and deaths around the world.

Rebecca Brady, MD

We published three manuscripts regarding human antibody and T cell responses elicited by influenza vaccines against the hemagglutinin protein.

Rhonda Cardin, PhD

In previous studies, the Cardin lab showed that the viral chemokine receptor M33 encoded by murine cytomegalovirus (CMV) is required for long term latent infection of the bone marrow. In 2010, we identified several cell types in the bone marrow which are latently infected, and importantly, when the virus has a mutation in the M33 gene, some of these cell types do not become latently infected. This is the first identification of bone marrow cells which harbor latent CMV infection and the role that M33 plays during latent CMV infection at the cellular level. In collaboration with Dr. Helen Farrell in Australia, we have shown that the viral chemokine receptor US28 homolog encoded by human CMV rescues the latency defect of a mutant M33 virus, thus suggesting that the human CMV US28 protein plays a similar role in the establishment of CMV latency in humans. Also, in collaboration with Dr. David Bernstein and Dr. Daniel Choo, we have shown that infection of guinea pigs with guinea pig CMV induces hearing loss as measured by Auditory-Evoked Brainstem Analysis (ABR). We find that guinea pig CMV infects the cochleas of newborn guinea pigs which are experimentally infected at 48 hours after birth (neonatal CMV model) or in newborn guinea pigs which were infected *in utero* following infection of the pregnant guinea pig (congenital CMV

model). Both models show that ~50% of the infected pups develop hearing loss. Development of the guinea pig CMV hearing loss models is significant since human CMV is the leading infectious cause of hearing loss, with approximately 0.5-2.0% of newborn infants experiencing hearing loss within the first 2-4 years of life. Studies are underway to determine the underlying mechanisms of CMV-induced hearing loss and to determine if antiviral therapy can prevent the loss.

Tibor Farkas, DVM, PhD, MBA

The Farkas lab studies enteric viral diseases of humans and animals. In 2010 we continued our work on non-human primates (NHP) enteric caliciviruses with the major goal to develop a new disease model for human norovirus (NoV) gastroenteritis. Our work demonstrated remarkable similarities between rhesus enteric caliciviruses (ReCV) and human NoVs including their epidemiology, genetic and antigenic diversity, putative receptor (histo-blood group antigen; HBGA) binding and the ability to induce gastroenteritis in challenged animals. Over15 ReCVs representing different serotypes and HBGA types were tissue culture adapted. Current work is focusing on the development and evaluation of the animal, tissue culture and surrogate model that duplicates the diversity of human NoVs.

In 2010 we described two novel picornavirus groups in turkeys and chickens, including birds with runting stunting syndrome (RSS). RSS of chickens and poult enteritis mortality syndrome (PEMS) of turkeys are the two most significant enteric diseases of poultry. The causative agent(s) of RSS and PEMS are yet unidentified. Establishing the role of picornaviruses identified in our laboratory in enteric diseases of poultry is ongoing.

Robert W. Frenck, MD

We completed the first ever human challenge model with a G2 strain of norovirus. Dr. Bernstein is the IND holder for the virus and Dr. Jiang and Dr Frenck were Principal Investigators on the study. This study has been parlayed into a project with LigoCyte to see if their G2 norovirus vaccine can protect people with subsequent challenge with our G2 strain.

Jason Jiang, PhD

Noroviruses are an important cause of acute gastroenteritis. In the past year we have made significant advancements in understanding the virus/host interaction and receptors for noroviruses. We have resolved the crystal structures of the first non-secretor binding strain (VA207) which would greatly facilitate our future study on the screening and design antivirals against noroviruses. Our preliminary study on silico screening for antivirals against noroviruses based on these crystal structures is ongoing. We have completed the first human volunteer challenge study on a GII.4 norovirus and demonstrated the association of GII.4 infection with the histo-blood types of the volunteers, which concluded one of our projects funded by the DoD. This challenge model is very valuable for future vaccine and antiviral evaluation because it is the first human volunteer challenge with a GII.4 norovirus and the GII.4 noroviruses have been found predominant in many countries around the world. In fact, following the DoD study, we have initiated another study funded by LigoCyte to determine the 50% infectious dosage of the challenge pool. We anticipate a number of vaccine trials will be initiated in the near future using this challenge model, including evaluation of our P particle vaccine licensed to LigoCyte. Our study on the evolution of noroviruses has been summarized in a review article published recently in *Trend in Microbiology*. Our study on the development of norovirus P particles as a candidate vaccine against noroviruses is in the second year of a NIH R01 and we have made excellent progress in the characterization of norovirus antigenic and HBGA receptor binding variations, the establishment of animal model for vaccine efficacy evaluation and scale up production of P particles for

future animal and clinical evaluation. Finally, we have initiated a number of new studies in inactivation/neutralization of Tulane virus replication by silence RNA, screening antivirals against TV protease, diagnosis and passive immunization of norovirus infection with IgY developed in chickens, the study of viral host receptors of rotaviruses, and establishment of TV as a surrogate for human noroviruses in food safety research against norovirus contamination funded by the USDA.

Monica McNeal, MS

The Laboratory for Specialized Clinical Studies continues to supply lab support for a large number of clinical studies involving vaccine trials and vaccine development. Influenza virus vaccines and rotavirus vaccines continue to be important for overall health of children in the US and around the world. The lab is committed to help establish clinical labs in India to support rotavirus vaccine trials in that country. In addition, the lab consults with other labs around the world to provide training and support for establishing quality assays to support vaccine trials.

Nancy Sawtell, PhD

Most of the human population world-wide has been infected by herpes simplex viruses. Following the initial lytic infection, HSVs establish permanent latent infections within sensory neurons. Reactivation of latent virus not only results in viral disease (new infections, blindness and encephalitis) but also contributes to HIV infection, diabetes, cardiovascular and neurodegenerative diseases. No effective vaccine is available and no therapy eliminates latency or prevents reactivation. The long-term goal of ongoing research in the Sawtell lab is to find interventions for recurrent HSV episodes by defining mechanisms that control establishment and reactivation of HSV-1 latency.

The gene expression cascade during HSV-1 lytic infection begins with activation of immediate-early (IE) gene transcription by the virion protein VP16 with host factors Oct-1 and HCF-1. In contrast, the initial events in the reactivation from latency are still poorly defined. Ourcentral hypothesis is that regulation of both VP16 expression and activity underlie the establishment of latency and reactivation from latency. These two levels of control involve multiple positive and negative inputs to allow or inhibit viral replication in the sensory neuron *in vivo*.

Division Collaboration

Bone Marrow Transplantation and Immune Deficiency » Stella M. Davies, MBBS, PhD, MRCP

Dr. Robert Frenck has established a collaboration with Bone Marrow Transplant to evaluate the immunogencity of the 13-valent pneumococcal conjugate vaccine in patients who have undergone bone marrow transplantation.

General and Community Pediatrics » Sheela Rath Geraghty, MD, MS, IBCLC, FAAP; Robert Schaengold , MD; Mary Beth Pero, MD

Dr. Robert Frenck has established a collaboration with General Pediatrics to evaluate a new H. influenzae vaccine in infants.

Immunobiology » Marsha Wills-Karp, PhD

Dr. Margaret Hostetter has established a collaboration with Immunobiology on the role of *Candida albicans* in induction of asthma in murine models.

Perinatal Biology » Alan H. Jobe, MD, PhD

Dr. Margaret Hostetter has established a collaboration with Perinatal Biology on the effects of *Candida*

albicans in amniotic fluid of sheep.

Biomedical Informatics » Long (Jason) Lu, PhD; Jarek Meller, PhD

Dr. Margaret Hostetter has established a collaboration with Biomedial Informatics on informatics approach to identify linear heparin binding motifs on *C. albicans* cell wall proteins with Dr. Lu.

Dr. Jason Jiang has worked with Dr. Meller on structural analysis of noroviruses in interaction with histo-blood group antigen carbohydrates.

Molecular Genetics at the Univeristy of Cincinnati College of Medicine » Malak Kotb, PhD; Richard L. Thompson, PhD

Dr. Nancy Sawtell has worked in collaboration with Drs. Kotb and Thompson to establish a forward genetic approach to identifying host genes modifying herpes simplex virus pathogenic outcomes.

Dr. Nancy Sawtell has also worked in collaboration with Dr. Thompson on HSV latency and herpetic eye disease and transcriptional and posttranscriptional regulation of VP16 in neurons and the control of HSV latency, entry and exit.

Center for Epidemiology and Biostatistics » Ardythe L. Morrow, PhD

Dr. Jason Jiang has collaborated with Dr. Morrow in determining the host receptors for rotavirus based on the approach utilized in the study of receptors of noroviruses.

Center for Acute Care Nephrology » Stuart L. Goldstein, MD

Dr. Rebecca Brady has worked with Dr. Goldstein on a quality improvement project to address the reduction of nephrotoxic medication-associated acute kidney injury and associated costs in hospitalized children.

Experimental Hematology » Maria-Dominique Filippi, PhD

Dr. Rhonda Cardin has worked with Dr. Filippi on the identification of the latent CMV infected cells in the bone marrow.

Otolargygnology » Daniel Choo, MD

Dr. Rhonda Cardin has worked with Dr. Choo in the analysis of hearing loss in the guinea pig CMV models characterized by Drs. Bernstein and Cardin.

Molecular Immunology » Kasper Hoebe, PhD

Dr. Rhonda Cardin has worked on the collaboration to characterize murine CMV infection in various mutant mice generated in Dr. Hoebe's lab and to determine the role of NK cell and innate immunity on latent CMV infection.

Pediatric Surgery » Greg Tiao, MD

Monica McNeal, MS has collaborated with Dr. Tiao using rotavirus to induce a mouse model of biliary atresia. Research involves looking at receptor differences, effects of different rotaviruses to induce the model and cell signaling pathways.

Gastroenerology » Sean Moore, MD

Monica McNeal, MS has collaborated with Dr. Moore on establishing a malnutrion model in mice to use to look at the effects on live rotavirus vaccines.

Human Genetics » Derek Neilson, MD

Monica McNeal, MS, has collaborated with Dr. Neilson on establishing an influenza model in mice to look at a gene that is involved in acute necrotizing encephalopathy.

Molecular Genetics and Chemistry, UC » Alison Weiss, PhD ; Suri Saranathan Iyer, PhD

Monica McNeal, MS has collaborated with Drs. Weiss and Iyer on developing receptor mimics for rapid dection, typing and susceptibility testing of influenza.

Faculty Members

Margaret K. Hostetter, MD, Professor
Director, Division of Infectious Diseases
Albert Sabin Professor of Pediatrics
Research Interests Candida albicans

David I. Bernstein, MD, MA, Professor
Director, Gamble Program for Clinical Studies
Director, VTEU
Research Interests Vaccines, rotavirus, herpes simplex, cytomegalovirus

Steven Black, MD, Adjunct
Research Interests Vaccine safety

Rebecca C. Brady, MD, Associate Professor
Director of Adult Clinical Studies
Research Interests Adult vaccines, influenza

Rhonda D. Cardin, PhD, Assistant Professor
Research Interests Cytomegalovirus, genital herpes vaccines

Beverly L. Connelly, MD, Professor
Director, Pediatric Infectious Diseases Fellowhship Training Program
Director, Infection Control Program
Research Interests Infection control, Healthcare quality improvement

Michelle P. Dickey, MS, CRN, Instructor
Manager, Gamble Program
Research Interests

Tibor Farkas, DVM, PhD, MBA, Assistant Professor
Research Interests Enteric viral diseases

Robert W. Frenck, MD, Professor
Chairman, Institutional Review Board
Director of Clinical Medicine
Research Interests Vaccines

Michael A. Gerber, MD, Professor
Director, Clinical Care and Teaching
Medical Director, Continuing Medical Education
Research Interests

Nancy M. Hutchinson , RN, MSN, CIC, Instructor
Infection Control Program
Research Interests

Xi Jason Jiang, PhD, Professor
Research Interests Caliciviruses. rotavirus, vaccines

Monica M. McNeal, MS, Instructor
Associate Director, LSCS
Research Interests

Nancy M. Sawtell, PhD, Associate Professor

Research Interests Herpes simplex virus

Mary A. Staat, MD, MPH, Professor

Director, International Adoption Center

Research Interests Rotavirus, epidemiology, international adoption, vaccine preventable diseases

Mark C. Steinhoff, MD, Professor

Director, Global Health Center

Research Interests Maternal immunization

Jane E. Strasser, PhD, Adjunct

Director, UC Office of Research Compliance and Regulatory Affairs

Research Interests Shiga like toxins, genetics of susceptibility and resistance

Ramu Subbramanian, PhD, Assistant Professor

Research Interests Influenza, T cell immunity

Ming Tan, PhD, Assistant Professor

Research Interests Calicivirus

Joint Appointment Faculty Members

Steve Black, MD, Adjunct

Center for Global Child Health

Mark C. Steinhoff, MD, Professor

Center for Global Child Health

Clinical Staff Members

- Tracy Byrne, RN, OPAT Clinic, International Adoption Center
- Kelly Hicks, RN, MSN, International Adoption Center
- Jennifer Kelley, APN, OPAT Clinic
- Susan Ruedy, MA, International Adoption Clinic
- Tisha Way, MSSA, LISW-S, International Adoption Clinic

Trainees

- Julianne Green, MD, PhD, PL-5, University of Louisville Collete of Medicine
- Andrew Kreppel, MD, PL-5, St. Louis University School of Medicine
- Elizabeth Schlaudecker, MD, PL-7, University of Cincinnati College of Medicine
- Diana Koch, Graduate Student, PGY-3, Univeristy of Cincinnati College of Medicine
- Ryan Walker, Graduate Student, PGY-1, Univeristy of Cincinnati College of Medicine

Significant Accomplishments

Diarrheal Viruses

Jason Jiang, PhD, and Ming Tan, PhD, have extended their work on the norovirus P particle and its adaptability as a vaccine platform. The norovirus P particle is formed by 24 copies of the protruding (P) domain of the norovirus capsid, which is ideally sized for a subunit vaccine. Their studies have shown that

insertion of the M2e epitope of influenza virus and the VP8 epitope of rotavirus into the three surface loops of each P domain induced high titers of neutralizing antibodies against replication of influenza virus and rotavirus and protected vaccinated mice from infection with these two viruses.

The Rotarix vaccine, invented by David Bernstein, MD, and Richard Ward, PhD, was recently found to be associated with a 42 percent decrease in deaths per 100,000 children aged 11 months or younger in Mexico. Diarrhea-related mortality was 29 percent lower for children between the ages of 12 and 23 months, although these children are typically too old to receive the vaccine. Diarrhea-related mortality among unvaccinated children between the ages 24 and 59 months was not significantly reduced. (Richardson V. et. al., *New England Journal of Medicine,* 2010; 362:299-305).

Herpes Viruses

Nancy Sawtell, PhD, has continued her work on the herpes simplex virus type 1 (HSV-1) virion protein VP16 as a central mediator of latency and reactivation from latency in sensory neurons. Innovative animal models allow testing of the hypothesis that the VP16 gene in the HSV-1 genome can be regulated by action of neuro-specific and stress-responsive promoter elements and corresponding transcription factors to allow the differential responses entailed in initial infection or exit from latency. Sawtell hopes to identify transcription factors or protein-modifying enzymes that regulate VP16 and its differential functions as promising targets for development of therapeutic interventions for HSV reactivation.

Rhonda Cardin, PhD, has developed a guinea pig model that accurately recapitulates transmission of cytomegalovirus (CMV) from mother to fetus and is accompanied by attendant hearing loss. Since CMV infection in humans is the major cause of nonhereditary deafness, this critically important animal model will allow dissection of each step of pathogenesis and serve as an important tool for testing or therapeutic interventions.

Expansion of Clinical Services

Effective Jan. 1, 2011, Robert Frenck, MD, has assumed the position of chief of the Clinical Service after the departure of Michael Gerber, MD. Under Frenck's leadership, divisional revenues from inpatient consults have increased by 37 percent, and the outpatient antibiotic service has had an increase of more than 40 percent in patient encounters over the past two years. Frenck's plans call for the opening of a travel clinic at the Cincinnati Children's Burnet Campus and a general infectious disease clinic at Liberty Campus within the next 12 months.

In continuing to refine their model of services for internationally adopted children, Mary Staat, MD, and the International Adoption Center have added mental health services and family counseling to help internationally adopted children overcome abusive backgrounds and to facilitate families' adjustment to the emotional and educational needs of internationally adopted children.

Division Publications

1. Abdulla RY, Rice MA, Donauer S, Hicks KR, Poore D, Staat MA. **Hepatitis A in internationally adopted children: screening for acute and previous infections**. *Pediatrics*. 2010; 126:e1039-44.
2. Allen SR, Fiorini P, Dickey M. **A streamlined clinical advancement program improves RN participation and retention**. *J Nurs Adm*. 2010; 40:316-22.
3. Basha S, Hazenfeld S, Brady RC, Subbramanian RA. **Comparison of antibody and T-cell responses elicited by licensed inactivated- and live-attenuated influenza vaccines against H3N2 hemagglutinin**.

Hum Immunol. 2011; 72:463-9.

4. Bernstein DI, Earwood JD, Bravo FJ, Cohen GH, Eisenberg RJ, Clark JR, Fairman J, Cardin RD. **Effects of herpes simplex virus type 2 glycoprotein vaccines and CLDC adjuvant on genital herpes infection in the guinea pig**. *Vaccine*. 2011; 29:2071-8.
5. Black S. **Travelers' protection against meningococcal disease: a new vaccine option**. *J Travel Med*. 2010; 17 Suppl:18-25.
6. Black S, Della Cioppa G, Malfroot A, Nacci P, Nicolay U, Pellegrini M, Sokal E, Vertruyen A. **Safety of MF59-adjuvanted versus non-adjuvanted influenza vaccines in children and adolescents: an integrated analysis**. *Vaccine*. 2010; 28:7331-6.
7. Boppana SB, Ross SA, Shimamura M, Palmer AL, Ahmed A, Michaels MG, Sanchez PJ, Bernstein DI, Tolan RW, Jr., Novak Z, Chowdhury N, Britt WJ, Fowler KB. **Saliva polymerase-chain-reaction assay for cytomegalovirus screening in newborns**. *N Engl J Med*. 2011; 364:2111-8.
8. Brady R. **Zygomycosis (Mucormycosis)**. *Rudolph's Pediatrics.* New York: McGraw-Hill; 2011.
9. Brady RC. **Influenza**. *Adolesc Med State Art Rev*. 2010; 21:236-50, viii.
10. Bravo FJ, Bernstein DI, Beadle JR, Hostetler KY, Cardin RD. **Oral hexadecyloxypropyl-cidofovir therapy in pregnant guinea pigs improves outcome in the congenital model of cytomegalovirus infection**. *Antimicrob Agents Chemother*. 2011; 55:35-41.
11. Campbell JD, Chambers CV, Brady RC, Caldwell MC, Bennett NL, Fourneau MA, Jain VK, Innis BL. **Immunologic non-inferiority of a newly licensed inactivated trivalent influenza vaccine versus an established vaccine: A randomized study in US adults**. *Hum Vaccin*. 2011; 7:81-8.
12. El-Kamary SS, Pasetti MF, Mendelman PM, Frey SE, Bernstein DI, Treanor JJ, Ferreira J, Chen WH, Sublett R, Richardson C, Bargatze RF, Sztein MB, Tacket CO. **Adjuvanted intranasal Norwalk virus-like particle vaccine elicits antibodies and antibody-secreting cells that express homing receptors for mucosal and peripheral lymphoid tissues**. *J Infect Dis*. 2010; 202:1649-58.
13. Fairbrother G, Cassedy A, Ortega-Sanchez IR, Szilagyi PG, Edwards KM, Molinari NA, Donauer S, Henderson D, Ambrose S, Kent D, Poehling K, Weinberg GA, Griffin MR, Hall CB, Finelli L, Bridges C, Staat MA. **High costs of influenza: Direct medical costs of influenza disease in young children**. *Vaccine*. 2010; 28:4913-9.
14. Farkas T, Cross RW, Hargitt E, 3rd, Lerche NW, Morrow AL, Sestak K. **Genetic diversity and histo-blood group antigen interactions of rhesus enteric caliciviruses**. *J Virol*. 2010; 84:8617-25.
15. Farrell HE, Abraham AM, Cardin RD, Sparre-Ulrich AH, Rosenkilde MM, Spiess K, Jensen TH, Kledal TN, Davis-Poynter N. **Partial Functional Complementation between Human and Mouse Cytomegalovirus Chemokine Receptor Homologues**. *J Virol*. 2011; 85:6091-5.
16. Fuller CA, Pellino CA, Flagler MJ, Strasser JE, Weiss AA. **Shiga toxin subtypes display dramatic differences in potency**. *Infect Immun*. 2011; 79:1329-37.
17. Gerber MA, Brown HW, Lee G, Tanz RR, Temte JL, Van Beneden CA. **Physicians' opinions about critical attributes of a potential group A streptococcal vaccine**. *Vaccine*. 2010; 28:7155-60.
18. Henkle E, Steinhoff MC, Omer SB, Roy E, Arifeen SE, Raqib R, McNeal M, Breiman RF, Moss WJ, Zaman K. **Incidence of influenza virus infection in early infancy: a prospective study in South Asia**. *Pediatr Infect Dis J*. 2011; 30:170-3.
19. Knipping K, McNeal MM, Crienen A, van Amerongen G, Garssen J, Van't Land B. **A gastrointestinal rotavirus infection mouse model for immune modulation studies**. *Virol J*. 2011; 8:109.
20. Matson DO, Abdel-Messih IA, Schlett CD, Bok K, Wienkopff T, Wierzba TF, Sanders JW, Frenck RW, Jr.. **Rotavirus genotypes among hospitalized children in Egypt, 2000-2002**. *J Infect Dis*. 2010; 202 Suppl:S263-5.
21. McNeil SA, Dodds LA, Fell DB, Allen VM, Halperin BA, Steinhoff MC, MacDonald NE. **Effect of respiratory**

hospitalization during pregnancy on infant outcomes. *Am J Obstet Gynecol*. 2011; 204:S54-7.

22. Morrow AL, Meinzen-Derr J, Huang P, Schibler KR, Cahill T, Keddache M, Kallapur SG, Newburg DS, Tabangin M, Warner BB, Jiang X. **Fucosyltransferase 2 non-secretor and low secretor status predicts severe outcomes in premature infants**. *J Pediatr*. 2011; 158:745-51.
23. Omer SB, Goodman D, Steinhoff MC, Rochat R, Klugman KP, Stoll BJ, Ramakrishnan U. **Maternal influenza immunization and reduced likelihood of prematurity and small for gestational age births: a retrospective cohort study**. *PLoS Med*. 2011; 8:e1000441.
24. Poehling KA, Fairbrother G, Zhu Y, Donauer S, Ambrose S, Edwards KM, Staat MA, Prill MM, Finelli L, Allred NJ, Bardenheier B, Szilagyi PG. **Practice and child characteristics associated with influenza vaccine uptake in young children**. *Pediatrics*. 2010; 126:665-73.
25. Poehling KA, Szilagyi PG, Staat MA, Snively BM, Payne DC, Bridges CB, Chu SY, Light LS, Prill MM, Finelli L, Griffin MR, Edwards KM. **Impact of maternal immunization on influenza hospitalizations in infants**. *Am J Obstet Gynecol*. 2011; 204:S141-8.
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Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct / Project Period Direct
BERNSTEIN, D		
The Natural History of CMV-Related Hearing Loss		
National Institutes of Health(University of Alabama-Birmingham)		
	07/01/05-06/30/12	$121,037
Mouse and Guinea Pig Models for Herpesviruses		
National Institutes of Health		
	09/27/10-09/26/11	$371,610
EMMES/VRC700/Bernstein		
National Institutes of Health(The Emmes Corporation)		
	11/15/10-12/31/11	$180,000
Vaccine and Treatment Evaluation Units (VTEUs)		
National Institutes of Health		
	11/01/07-10/31/14	$1,761,446
HOSTETTER, M		
Pediatric Physician Scientist Program Award		
National Institutes of Health		
K12 HD 000850	09/01/10-06/30/12	$1,895,140
PSDP American Academy of Pediatrics Commitment		
American Academy of Pediatrics		
	09/01/10-06/30/11	$57,375
PSDP March of Dimes Funding Commitment		
March of Dimes National		
	09/01/10-06/30/11	$6,823
PSDP American Pediatric Society Funding Commitment		
American Pediatric Society		

	09/01/10-06/30/12	$44,955

JIANG, X

Characterization of Human Caliciviruses
National Institutes of Health
R01 AI 037093 09/01/09-08/31/11 $284,943

Norovirus and Their Receptors
National Institutes of Health
R56 AI 055649 09/07/10-08/31/11 $261,891

Novel Vaccine Against Norovirus
National Institutes of Health
R01 AI 089634 05/15/10-04/30/15 $761,012

Novel Broad Spectrum Therapeutic Glycans Against Category B Pathogens
National Institutes of Health(Boston College)
U01 AI 075563 09/01/10-08/31/11 $75,154

MCNEAL, M

Hyaluronan Regulation of Microbial Host Defense of the Intestine
National Institutes of Health(Cleveland Clinic Lerner College of Medicine of Case Western Reserve University)
R01 HD 061918 09/15/09-07/31/11 $30,497

Subagreement GAT.1334-07574-SUB
PATH Vaccine Solutions
11/15/07-10/31/11 $64,637

Laboratory Services
Serum Institute of India LTD
03/21/11-03/20/12 $144,000

SAWTELL, N

Unbiased Forward Genetic Analysis of Virus/Host Interactions
National Institutes of Health
RC1 AI 087336 09/26/09-08/31/11 $339,996

Ocular HSV Infection-Latency and Pathogenesis
National Institutes of Health(University of Cincinnati)
R01 EY 013168 05/01/08-04/30/12 $96,499

STAAT, M

Enhanced Surveillance for New Vaccine Preventable Diseases
Ctr for Disease Control and Prevention
U01 IP 000147 08/31/07-08/30/11 $1,340,299

Current Year Direct **$7,837,314**

Industry Contracts

BERNSTEIN, D

LigoCyte Pharmaceuticals, Inc	$177,716
MedImmune Inc.	$102,616
EMMES	$71,610

BRADY, R

Accelovance, Inc.	$10,420

CARDIN, R

Novartis Pharmaceuticals	$170,214
REPLICor, Inc.	$15,215
Genocea Biosciences, Inc.	$107,489

DAWODU, A		
Procter & Gamble China Scholars Program		$240,000
FRENCK, R		
Wyeth Pharmaceuticals		$186,324
GlaxoSmithKline		$30,008
GERBER, M		
Hoffman-LaRoche, Inc.		$12,962
MCNEAL, M		
Liquida Technologies, Inc		$9,424
MORROW, A		
Bristol-Myers Squibb		$14,207
STAAT, M		
GlaxoSmithKline		$1,196,879
STEINHOFF, M		
Wyeth Pharmaceuticals		$84,992
WARD, R		
Merck & Company, Inc.		$428,816
Sanofi Sythelabo		$64,680
Wyeth Pharmaceuticals		$1,099
Protein Sciences Corporation		$106,519
Research Triangle Institute		$147,295
	Current Year Direct Receipts	**$3,178,485**
	Total	**$11,015,799**