2013 Research Annual Report
Infectious Diseases

Division Details

Division Data Summary

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Significant Accomplishments

Top-funded Research Division

Our division became the top-funded research division at Cincinnati Children’s this year. Our total external funding reached $10.5 million, from diverse sources that include the NIH, CDC, Burroughs Wellcome, Bill and Melinda Gates Foundation, NASA, and industry. We also had the highest increase in grant funding among all Cincinnati Children’s research divisions - at 25 percent. Our projects include studies of the pathogenesis of cytomegalovirus, herpes simplex virus, norovirus/calicivirus, and Candida infections; vaccine response; macrophage biology; normal and aberrant immune responses in pregnancy; and surveillance for community-acquired infections.

Transplant Infectious Disease Program Launched

We launched the Transplant Infectious Disease program this year under the direction of Lara Danziger-Isakov, MD, who was recruited from the Cleveland Clinic. Danziger-Isakov collaborates with clinicians and investigators in solid organ transplant and the bone marrow transplant unit. Overall, our clinicians provided consultative expertise to 691 inpatients and 1,695 outpatient visits in 2012. Billings hit $1.49 million. These numbers represent a three-fold rise in clinical activity since 2010.

Inventions That Improve Child Health
Jason Jiang, PhD, and Ming Tan, PhD, have licensed the technology for a norovirus vaccine to Ligocyte. The Center for Technology Commercialization also patented an antibody from the Hostetter laboratory that prevents *Candida albicans* biofilm formation.

**Research Highlights**

Margaret K. Hostetter, MD

Research in the Hostetter laboratory has expanded into three main areas. 1) Heparin binding motifs in *Candida albicans* and their role in biofilm. After identifying 34 *C. albicans* proteins that contain putative heparin binding motifs, Kris Orsborn and Julianne Green showed that alanine mutation of a particular motif decreased heparin binding. An antibody made to a peptide encompassing the most potent heparin binding motif inhibited binding to heparin *in vitro* and abolished biofilm formation *in vivo* in a rat model of biofilm formation in central venous catheters. A patent has been submitted for this invention. 2) Role of candidal vaginal colonization in preterm birth. John Paluszynski, PhD, has shown that colonization with *Candida albicans* skews the cytokines response of vaginal epithelial cells by augmenting the release of pro-inflammatory cytokines that are damaging to pregnancy and by inhibiting the release of cytokines that preserve pregnancy. 3) Genetics of disseminated staphylococcal infection after osteomyelitis. Exome sequencing of parent/child trios identified *de novo* mutations implicating two novel pathways for susceptibility to disseminated staphylococcal disease. *

David I. Bernstein, MD, MA

Despite the failure of the herpes simplex type 2 glycoprotein D vaccine that we recently published in the *NEJM*, there has been continued interest in the development of HSV vaccines. We are currently evaluating several new approaches to vaccination including live attenuated vaccines and various vector strategies of gD and other novel antigens, funded through our NIH contract and industrial sources. Similarly we have been evaluating two new vaccine strategies for congenital CMV in our guinea pig model. We have also extended our animal studies of an immunotherapeutic HSV sub unit vaccine into a clinical trial, highlighting our unique capabilities to move from translational to clinical evaluations. Other clinical trials included the first human efficacy trial of a bi-valent norovirus vaccine that utilized our recently characterized GII.4 challenge model. Further, we evaluated new vaccination schedules for an anthrax vaccine, a DNA prime and TIV boost strategy for influenza, utilization of a full dose of TIV in young children, the effects of delayed HPV vaccine dosing on the immune response, and a meningococcal b vaccine in children and adolescents.

Rebecca C. Brady, MD

Dr. Brady was the Cincinnati Children’s lead investigator for two NIH, DMID-sponsored clinical trials. The first trial compared the safety and immunogenicity of inactivated versus live-attenuated influenza vaccine in post-partum breastfeeding women and their infants. The second trial assessed the immunogenicity of the 13-valent pneumococcal vaccine in elderly adults. Dr. Brady also served as co-investigator for many clinical studies performed at the Gamble Program for Clinical Studies, Cincinnati Children’s Infectious Diseases Division.

Rhonda D. Cardin, PhD

The Cardin lab previously showed that the viral chemokine receptor M33 encoded by murine cytomegalovirus (CMV) is required for long term latent infection. In order to understand the function of M33 in CMV latency, in 2012, we sought to identify the cell types in the bone marrow and spleen of latently-infected mice which harbor
We have identified several myeloid lineage cells which harbor latent viral DNA and are in the process of demonstrating that virus can be recovered from these populations. In collaboration with Dr. Helen Farrell in Australia, we continue to characterize the role of the cytomegalovirus-encoded chemokine receptors during infection. Also, in collaboration with Dr. David Bernstein, we are characterizing several new guinea pig cytomegalovirus (GPCMV) isolates which will be useful for understanding multi-strain congenital CMV infection in newborn infants as well as for evaluation of vaccine strategies in our GPCMV model. We have shown that the isolates cross the placenta and infect the developing fetus as well as brain and cochleas, similar to our laboratory GPCMV strain. One strain, however, appears to be defective in congenital infection and molecular studies are underway to characterize this defect. Our next studies will determine whether co-infection of pregnant guinea pigs with multiple strains of guinea pig cytomegalovirus leads to increased hearing loss in the newborn guinea pigs, similar to that seen during symptomatic congenital human CMV infection. Lastly, we have characterized two promising anti-HSV drugs (N-MCT and TCP) in our guinea pig model of genital herpes. N-MCT shows superior activity in reducing both acute and recurrent genital herpes compared to ACV when administered during acute HSV-2 infection and therapeutic administration indicates that N-MCT reduces recurrent lesions as well as ACV. The second drug, TCP, targets chromatin complex proteins and disrupts immediate-early HSV-2 gene expression, thus possibly targeting the virus during lytic infection and during reactivation from latency. Both drugs are promising new anti-HSV candidates for treating neonatal and adult HSV-2 infection in humans.

Beverly L. Connelly, MD

Through the Infection Control Program, Dr. Connelly has built collaborations with a variety of programs. For example, she has collaborated with General Pediatrics and Hospital Medicine to improve hand hygiene and with Surgery and Hospital Medicine to implement a care continuum to reduce surgical site infections. She co-sponsored a QI project to implement staphylococcal screening of surgical patients, a practice that feeds into the continuum. In addition, Dr. Connelly has collaborations with Global Child Health to assess influenza tracking by methods other than traditional laboratory based strategies, e.g. Google Flu.

Lara Danziger-Isakov, MD, MPH

Dr. Lara Danziger-Isakov continues her role as protocol chair for two studies in the Clinical Trials in Organ Transplantation in Children funded by the National Institute of Allergy and Infectious Diseases. One study evaluates the interaction between respiratory viral infections and the development of allo- and autoimmunity after pediatric lung transplantation. The second study assesses perceived barriers to adherence after pediatric solid organ transplantation. She was recently re-appointed to the Steering Committee to CTOTC and was named as co-chair of the Adherence, Growth & Development and QOL Subcommittee. Further, Dr. Danziger-Isakov will be the protocol chair for a new study under development to assess the impact of B-cell induction on the development of allo- and autoimmunity and early graft dysfunction that was recently funded.

Dr. Danziger-Isakov has expanded her work in solid organ transplantation (SOT) in a collaboration with the Studies in Pediatric Liver Transplantation (SPLIT) to evaluate current practices for cytomegalovirus prevention. In addition, in collaboration with the VTEU and the solid organ transplant teams, a study to evaluation HPV vaccination in adolescents after SOT is proposed.

Michelle P. Dickey, MS, CRN

Dickey’s interest is in the area of clinical vaccine trials in infants, children, adolescents, adults, elderly, pregnant and breast-feeding populations. Additional interests in clinical research include the areas of informed consent and quality management. This past year, Ms. Dickey presented workshops on clinical research quality
management both regionally and internationally and is currently part of a multidisciplinary team researching simplified informed consent and assent.

Tibor Farkas, PhD, DVM

In 2012, Dr. Farkas and his lab continued their studies of human norovirus surrogate model development. Based on our large collection of tissue culture adapted recovirus strains we developed a tissue culture and animal model with human norovirus-like genetic, antigenic and HBGA binding diversity. Additionally, in collaboration with UC Davis Primate Center we developed a real time PCR method for molecular ABO phenotyping in cynomolgus macaques (Tissue Antigens. 2012). And finally, as part of a collaborative project, targeting the evaluation of laboratory rodents for enteric viral infections we discovered and partially characterized several novel RNA viruses in laboratory and wild mice (Veterinary Microbiology, 2012; Virus Genes, 2012).

Robert W. Frenck, MD

Dr. Frenck, along with Dr. David Bernstein, completed an inpatient challenge study evaluating a vaccine against norovirus. Additionally, he initiated a Phase I study funded by DMID to evaluate a vaccine against Shigella sonnei. The study has completed two of the planned five cohorts with the remaining three cohorts on schedule to be finished by early 2014.

Dr. Frenck has been asked by DMID to develop the protocol and conduct a study to evaluate the dose response curve of infection with norovirus. The protocol is nearing completion with a target to enroll the first cohort by the end of the calendar year.

Dr. Frenck also submitted the re-competition for the VTEU contract with the NIH with Dr. Bernstein.

Dr. Frenck continues to maintain a research focus on clinical trials with special interest in enteric diseases.

Jason Jiang, PhD

Dr. Jiang and his lab continued working on norovirus (NV) and rotavirus (RV) research, mainly focusing on the virus-host interaction related to human HBGAs as receptors. For NVs, we continued characterization of the diversity of NVs in recognition of different HBGAs by different genotypes of NVs. Our work on the characterization of the Tulane virus as a surrogate for human NVs is going well. In addition, we participated in a vaccine trial of recombinant VLP vaccine against NVs using the human volunteer challenge model developed in our group. This study is funded by LigoCyte. We also initiated a study to develop humanized monoclonal antibodies against NVs in collaboration with Institut für Biochemie, Biotechnologie und Bioinformatik in German. Our collaboration with Virginia Tech on the evaluation of NV P particle vaccine and collaboration with OSU on evaluation of influenza (M2e) vaccine are going well. Finally, our study on human NV replication in human intestinal organoids is ongoing well and we submitted a R21 to seek further support for this study. For rotavirus, we discovered a new receptor binding pattern of P[11] RVs recognizing the disaccharide LacNAc, a precursor of human HBGA. P[11] RVs mainly infect neonates and young children and the VP8* of P[11] RVs binding to saliva of neonates and infants but not of adults. Our study suggests that LacNAc could be an age-specific receptor for P[11] RVs infecting neonates and young children. This work will be continued next year. In the meantime, we expanded study to characterize the host receptors for other genotypes and genogroups of RVs causing human or animal infection. We hypothesize that RVs are also diverse in recognizing different host receptors like NVs. An elucidation of receptor binding patterns for all major human and animal RVs is fundamental. The study of RV diversity in host interaction will be continued in the near future.

Monica M. McNeal, MS
Ms. McNeal is the Associate Director for the Laboratory for Specialized Clinical Studies which provides 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. Additional projects include using animal models to investigate the effects of malnutrition on oral rotavirus vaccines.

We have continued to support rotavirus vaccine trials conducted in numerous countries around the world. We have completed analyzing clinical samples collected from a rotavirus trial conducted in a developing country aimed at increasing the effectiveness of rotavirus vaccines. The first ever Phase I trial of a non-living rotavirus vaccine was conducted this year. We developed and qualified the assays to analyze samples from this trial. During this past year, we have supported the testing of a *Shigella* vaccine by establishing the assays in the lab and supporting the inpatient vaccine study. We have continued our support of influenza vaccine trials by developing assays to support studies on the H3 variant strain in addition to the seasonal vaccine strains.

Joseph E. Qualls, PhD

Macrophages are vital immune cells involved in tissue homeostasis, wound healing, and recognizing (and then fighting) infection. Our studies in mycobacteria infection show an intimate relationship between L-arginine availability and anti-pathogen control by macrophages. Namely, macrophages in low L-arginine environments are less able to kill/control *M. bovis BCG* *in vitro* compared to macrophages with a surplus of L-arginine. This phenotype can be rescued by adding L-citrulline – a process that requires intra-macrophage L-citrulline to L-arginine synthesis. Adding L-citrulline to macrophages that have a surplus of L-arginine has no additional effect on BCG control than L-arginine alone. Importantly, mice that lack the ability to convert L-citrulline to L-arginine in immune cells only are also more susceptible to *M. bovis BCG* and *M. tuberculosis* *in vivo* – suggesting L-arginine is limiting during infection. Our interests are to determine the regulation of L-citrulline metabolism in macrophages and other immune cells, and the consequences on mycobacterial infection in vitro and *in vivo*. In addition to rescuing nitric oxide production, we have found that L-citrulline rescues protein loss due to low L-arginine availability. Our goals for this project are to 1) identify regulatory pathways involved in L-citrulline metabolism that can be manipulated to enhance anti-pathogen responses, and 2) to demonstrate if supplemental L-citrulline is a useful immune-stimulant that can provide additional protection against mycobacterial infection.

Nancy M. Sawtell

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 neurons in both the peripheral and central nervous systems. 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. Our central hypothesis is that a specialized region of the VP16 promoter regulates its de novo expression in neurons and thereby controls the establishment of, and reactivation from latency. A second layer of stress responsive regulation entails post translational structural modification of the VP16 proteins, which influences its
interaction with its binding partners HCF-1 and Oct-1. Our studies will have a major impact on vaccine and gene transfer vector design, and may lead to a new class of therapeutics. Through the use of a mouse genetic reference population we have identified a locus on mouse chromosome 16 that regulates HSV neurovirulence as well as the severity of herpetic stromal keratitis. Our studies are the first to demonstrate that the virus’ interaction with the nervous system contributes to its ability to cause corneal opacity and blindness and have led to a novel hypothesis regarding the initiation of stromal disease. In related studies we have initiated a “genomics squared” analysis to explore the interaction of both viral and host genetics in herpetic disease. A new project recently funded by NASA seeks to determine the effect of deep space (cosmic) radiation on damage induced in the brain by latent HSV. These studies will define risks to astronauts and may model HSV induced CNS damage (potentially increasing dementia risks) occurring in the aging population.

Elizabeth P. Schlaudecker, MD, MPH

Dr. Schlaudecker’s research continues to focus on the immunologic responses to maternal immunization. After completing a comprehensive epidemiologic study of the etiology and seasonality of viral respiratory infections in rural Honduras, she has shifted to prevention of these infections with maternal immunization. Her recent work has demonstrated antibody persistence in mothers one year after pneumococcal immunization in pregnancy, as well as a significantly decreased antibody response to influenza immunization in pregnant women. In collaboration with Dr. Mark Steinhoff and Monica McNeal, she evaluated influenza-specific IgA levels in breast milk and demonstrated that they were significantly higher in influenza vaccines compared to pneumococcal controls for at least six months postpartum. She also demonstrated that greater exclusivity of breastfeeding in the first six months of life significantly decreased the expected number of respiratory illness with fever episodes in infants of influenza-vaccinated mothers, but not in infants of pneumococcal-vaccinated mothers.

Dr. Schlaudecker continues to study the immunologic response to influenza immunization in pregnant women with the support of a Procter Scholars Award. Because hemagglutination inhibition titers were significantly decreased in pregnant women compared to non-pregnant women after immunization, Dr. Schlaudecker is currently investigating the IgG isotype responses to influenza immunization in Dr. Sing Sing Way’s laboratory with the mentorship of Dr. Fred Finkelman in the Division of Cellular and Molecular Immunology. She is also investigating immunologic responses to immunization in breast milk and maternal pertussis immunization with Cincinnati Children’s Vaccine and Treatment Evaluation Unit (VTEU).

Mary A. Staat, MD, MPH

Through Dr. Staat’s large epidemiology and surveillance program developed in 1997, she has been able to develop optimal methods of detecting the changes and manifestations of infectious diseases of children within Cincinnati Children’s and for the population of Hamilton County, and to compare these findings to national trends. Recognizing that Cincinnati Children’s captures essentially all Hamilton County children requiring hospitalization or care in the emergency department has allowed Dr. Staat to conduct studies to determine the population-based rates of Hamilton County hospitalizations and emergency department visits for many pediatric infectious diseases using unique methods such as capture-recapture methods to determine disease burden and case-cohort and case-control designs to determine the post-licensure effectiveness of rotavirus and influenza vaccines. Studies published last year included the effectiveness of rotavirus vaccines, pre- and post-licensure costs of rotavirus disease, epidemiology of norovirus infections in children and the epidemiology and disease burden of RSV.

Dr. Staat has also utilized data from her large international adoption center to publish studies to assist in the development of evidence-based guidelines for internationally adopted children. In addition to studies in the field
of infectious diseases, Dr. Staat and her colleagues have begun to explore the differences in neurological function between adopted and birth children using neuroimaging and psychological testing. This past year, the first study in this area was published in collaboration with researchers from the Neuroimaging Center and the Division of Physical Medicine and Pediatric Rehabilitation. This study examined functional magnetic resonance imaging and language function in Eastern European and Chinese adoptees.

Ming Tan, PhD

Dr. Tan's research focused on two directions: 1) development of norovirus P domain-based complexes into useful vaccines and vaccine platforms and 2) elucidation of complex interactions between between diverse noroviruses or rotaviruses and their HBGA (histo-blood group antigen) receptor. For the first direction, we have demonstrated the norovirus P particle as a capable vaccine against noroviruses and useful vaccine platform for antigen presentation. Chimeric P particles containing the spike protein VP8* of rotavirus and M2e epitope of influenza virus, respectively, have been shown to be effective dual vaccine candidates against both norovirus/rotavirus and norovirus/influenza virus. Based on the knowledge that we learnt from the P particle formation, we have further developed three new polyvalent vaccine platforms, the lineage, network, and agglomerate complexes. Epitopes and antigens from different pathogens can be presented by these vaccine platforms for increased immunogenicity for multivalent vaccine development against different infectious diseases. For norovirus/rotavirus-receptor interactions, we elucidated the crystal structures of the HBGA binding sites of GII.13 NoVs, which showed a new binding site distinct from the conserved GII binding sites. This new finding indicated GII.13 as a unique genotype that has emerged from the GII noroviruses through an as-yet unknown evolution path. Further study of the GII.13 will shed light into the complex interactions between the diverse NoV and polymorphic HBGAs. Rotavirus, another important enteric virus causing gastroenteritis, like norovirus, was also found to recognize HBGA in a way similar to norovirus-HBGA interaction, suggesting HBGAs may be a common niche in the evolution of the two viruses. A number of papers have been published in the past year and a new patent has been applied due to above works. Our research outcomes provide valuable data and strategies for future development of vaccine and antivirals against norovirus, rotavirus and other infectious pathogens.

Sing Sing Way, MD, PhD

Dr. Way's group has continued ongoing investigation on the immune pathogenesis of prenatal infection and persistent infections. In particular, results from publications in the past year show overriding maternal regulatory T cell suppression required for maintaining fetal tolerance may dictate the immune pathogenesis of pregnancy complications with maternal infection during pregnancy. Other related publications have uncovered fundamental immune aspects of T cell biology including the formation of memory for the regulatory CD4 T cell subset, and selective differentiation process for antigen specific CD4 T cells on a single cell basis.

Significant Publications


This paper reports the results of population surveillance for acute respiratory illness in three US counties from 2003 to 2009, with a focus on human metapneumovirus (HMPV) infection. HMPV was detected in 6% of hospitalized children, 7% of children in outpatient clinics or the emergency department, and 1% of asymptomatic controls. Children hospitalized with HMPV infection were older and more likely to receive a
diagnosis of pneumonia or asthma, to require supplemental oxygen, and to have a longer stay in the intensive care unit as compared to those hospitalized without HMPV infection.


Human challenge models have shown the association of human histo-blood group antigens (secretors) and susceptibility to infection with Norwalk virus (GI.1) norovirus, but GII.4 is the predominant norovirus genotype worldwide. Human challenge study using GII.4 norovirus again showed that 70% of the secretors were infected with the virus and only one nonsecretor (5.9%) became ill. Thus, secretor status determined the susceptibility to norovirus GII.4 challenge.


Respiratory syncytial virus is a significant contributor to morbidity in adult lung transplant recipients. In a retrospective analysis of 21 adult lung transplant patients infected with RSV, no significant differences were detected in six-month outcomes such as progressive disease between oral and inhaled ribavirin therapy for RSV infection after lung transplantation.


During infection, macrophages import extracellular arginine to synthesize nitric oxide. Citrulline is generated as a byproduct and is surprisingly exported from macrophages during the early stages of nitric oxide production. Less than 2% is retained for recycling via the Ass1-Asl pathway. As a result, extracellular arginine is depleted, and Ass1 expression enables macrophages to synthesize arginine from imported citrulline to sustain nitric oxide output.


In pregnant women the bacterium Listeria monocytogenes causes disseminated infection that can result in spontaneous abortion or stillbirth. In a murine model, the investigators demonstrate that maternal Listeria infection during pregnancy is associated with reductions in maternal Foxp3+ regulatory T cells, along with reciprocal expansion and activation of maternal fetal-specific effector T cells. These infection-induced reductions in maternal Foxp3+ regulatory T cell suppression disrupt fetal tolerance and lead to immune-mediated fetal wastage.

Division Publications


Faculty, Staff, and Trainees

Faculty Members

Margaret K. Hostetter, MD, Professor

Leadership Director, Division of Infectious Diseases; Albert Sabin Professor of Pediatrics

Research Interests Candida albicans - heparin binding motifs and biofilm, Candida albicans - role of vaginal colonization in preterm birth, genetics of disseminated Staphylococcus aureus infection

David I. Bernstein, MD, MA, Professor
Leadership Director, Gamble Program for Clinical Studies; Director, VTEU

Research Interests Vaccines, rotavirus, herpes simplex, cytomegalovirus

Rebecca C. Brady, MD, Associate Professor
Leadership Director of Adult Clinical Studies
Research Interests Vaccines for adults; Influenza

Rhonda D. Cardin, PhD, Assistant Professor
Research Interests Cytomegalovirus, Herpes Simplex type 2, antivirals, vaccines

Beverly L. Connelly, MD, Professor
Leadership Director, Pediatric Infectious Diseases Fellowship Training Program; Director, Infection Control Program
Research Interests Understanding and preventing healthcare associated infections

Lara Danziger-Isakov, MD, MPH, Associate Professor
Leadership Director, Transplant ID
Research Interests Transplantation, immunocompromised hosts, respiratory viruses, vaccines

Michelle P. Dickey, MS, CRN, Instructor
Leadership Manager, Gamble Program
Research Interests Clinical vaccine trials

Tibor Farkas, DVM, PhD, MBA, Assistant Professor
Research Interests Human and animal enteric viral infections

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

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

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

Monica M. McNeal, MS, Instructor
Leadership Associate Director, LSCS
Research Interests Rotavirus, influenza and Shigella vaccine research

Joseph E. Qualls, PhD, Assistant Professor
Research Interests Macrophage biology, intracellular pathogenesis, amino acid metabolism and immune function

Nancy M. Sawtell, PhD, Professor
Research Interests Herpes simplex virus: a) Molecular mechanisms regulating viral latency and reactivation and recurrence; b) Host gene variants and molecular pathways affecting the outcome of infection; c) Regulation of disease severity by the intersection of viral and host genetics; d) Short and long-term consequences of simulated deep space radiation on latent herpes simplex virus infection of the central nervous system

Elizabeth P. Schlaudecker, MD, MPH, Assistant Professor
Research Interests Immunologic responses to maternal immunization in serum and breast milk

Mary A. Staat, MD, MPH, Professor
Leadership Director, International Adoption Center
Research Interests Rotavirus, epidemiology, international adoption, vaccine preventable diseases

Jane E. Strasser, PhD, Assistant Professor
Leadership Director, UC Office of Research Compliance and Regulatory Affairs
Research Interests Shiga like toxins, genetics of susceptibility and resistance

Ming Tan, PhD, Assistant Professor
Research Interests Calicivirus, rotavirus, multivalent vaccine development

Way Sing Sing, MD, PhD, Associate Professor
Leadership Pauline and Lawson Reed Chair
Research Interests Protective immunity, host defense, prenatal infection, maternal fetal tolerance, immune pathogenesis of infection

Joint Appointment Faculty Members

Steve Black, MD, Adjunct (Global Health Center)
Research Interests Vaccine Safety

Samir Shah, MD, MSCE, Associate Professor (Hospital Medicine)
Research Interests Health services research, community infections

Mark C. Steinhoff, MD, Professor (Global Health Center)
Research Interests Global vaccines, vaccine in pregnancy

Clinical Staff Members

Samantha Blum, RN,
ID Transplant Clinic

Andrea Bohlen, MSW, LISW-S,
International Adoption Center

Cathy Boyce, RN,
OPAT Clinic, International Adoption Center

Kelly Hicks, RN, MSN,
International Adoption Center

Tisha Way, MSSA, LISW-S,
International Adoption Center

Trainees

Kevin Downes, MD, PL-5, University of Pennsylvania
Andrea Hahn, MD, PL-5, Ohio State University
Julianne Green, MD, PhD, PL-7, University of Louisville College of Medicine
Andrew Kreppel, MD, PL-7, St. Louis University School of Medicine
Shannon Rapovy, PG1, University of Cincinnati
Xufu Zhang, PG2, China
Vivian Mao, Columbia University
Sara Oliver, MD, University of Alabama
Division Collaboration

Center for Autoimmune Genomics and Etiology (CAGE); Cancer and Blood Diseases Institute

John Harley, MD, PhD: Professor, Ken Kaufman, PhD: Professor, and Susanne Wells, PhD: Associate Professor

Dr. Margaret Hostetter has collaborated with John Harley, MD, PhD and Ken Kaufman, PhD of CAGE to perform exome sequencing of parent/child trios for de novo mutations that contribute to disseminated staphylococcal osteomyelitis. De novo mutations identified in the first two trios implicated a new pathway for osteomyelitis susceptibility. In vitro studies of the biology of this disease will be conducted in collaboration with Susanne Wells, PhD.

Division of Biomedical Informatics; Division of Rheumatology/CAGE

Jason Lu, PhD: Assistant Professor, Richard Ittenbach, PhD: Professor, and Alexey Porollo, PhD: Field Service, Assistant Professor

Dr. Hostetter has also collaborated with Jason Lu, PhD and Alexey Porollo, PhD to identify heparin binding motifs in several pathologic microorganisms and their structural correlates.

Michelle Dickey, MS, CRN has collaborated with Dr. Richard Ittenbach on the development of protocols researching understanding of informed consent and assent in clinical research.

Proteomics and Mass Spectroscopy, UC Department of Cancer Biology

Ken Greis, PhD: Associate Professor

Dr. Hostetter has collaborated with Ken Greis, PhD, to identify proteins released from the surface of Candida albicans after treatment with heparin.

Joseph Qualls is in collaboration with Dr. Greis utilizing peptide mass spectrometry. Dr. Greis is analyzing the incorporation of the L-citrulline carbon backbone into newly synthesized protein in macrophages. These findings support the potential for L-citrulline as an immune-stimulating supplement during intracellular pathogenesis.

Division of Adolescent Medicine

Jessica Kahn, MD: Professor and Lea Widdice, MD: Assistant Professor

Dr. David Bernstein as co-investigator successfully re-competed Dr. Kahn's R0-1 evaluating the effect of HPV vaccination on circulating strains of HPV: Behavioral and Virologic Impact of HPV Immunization.

Dr. Bernstein is co-investigator with Dr. Widdice on a VTEU project to assess the impact of off schedule HPV vaccination.

Michelle Dickey, MS, CRN is in collaboration with Lea Widdice, MD on two NIH VTEU projects; HPV and Bacterial Vaginosis.

Division of Gastroenterology

Sean Moore, MD: Assistant Professor and Mitchell B. Cohen, MD: Professor

Dr. Bernstein is also in collaboration with Sean Moore, MD in the development of a malnourished mouse model for evaluation of rotavirus vaccines.

Monica McNeal is in collaboration with Dr. Moore on a project to generate a mouse model of environmental enteropathy to study rotavirus vaccines.

Michelle Dickey, MS, CRN is in collaboration with Mitch Cohen, MD on developing a cholera vaccine study.

Division of General and Community Pediatrics

Sheela Rath Geraghty, MD, MS, IBCLC, FAAP

Michelle Dickey, MS, CRN is in collaboration with Sheela Geragherty, MD on the recruitment of pediatric participants from the Cincinnati Children's Pediatric clinics for inclusion in clinical vaccine trials.

Division of Rheumatology; Global Health

Jennifer Huggings, MD: Associate Professor, Rina Mina, MD: Fellow,
and Steven Black, MD: Professor
Dr. Steve Black and Dr. Rebecca Brady collaborated with Jennifer Huggins, MD and Rina Mina, MD in the Division of Rheumatology and received funding for Cincinnati Children’s to be a member of the CDC Clinical Immunization Safety Assessment network.

Division of Neurology » Brenda Wong, MD: Professor and Michael Williams, PhD: Associate Professor
Dr. Rebecca Brady is in collaboration with Dr. Brenda Wong on a clinical trial which showed that the immunogenicity of trivalent inactivated influenza vaccine among individuals with neuromuscular diseases was similar when administered by either the intramuscular or subcutaneous route.

Dr. Nancy Sawtell is collaborating with Dr. Michael Williams to determine the acute and long term outcomes of simulated deep space radiation exposure on latent viral CNS infection and CNS pathology.

Experimental Hematology » Maria-Dominique Filippi, PhD: Associate Professor
Dr. Rhonda Cardin is in collaboration with Dr. Filippi in the identification of the latent CMV infected cells in the bone marrow.

Division of Otolaryngology/Head and Neck Surgery » Daniel Choo, MD: Professor
Dr. Cardin is in collaboration with Dr. Choo in the analysis of hearing loss in the guinea pig CMV models characterized by Drs. Bemstein and Cardin.

Division of Cellular and Molecular Immunology » Kasper Hoebe, PhD: Assistant Professor
Dr. Cardin is in collaboration with Dr. Hoebe 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.

Division of Immunobiology ; Division of Molecular Immunology » David Hildeman, PhD: Associate Professor and Claire Chougnet, PhD: Associate Professor
Dr. Cardin is in collaboration with Drs. Hildeman and Chougnet on the role of regulatory T cell in control of murine CMV infection.

Pediatric Liver Care Center; Division of Nephrology; Small Bowel Transplantation Program; Pediatric Lung Transplant Program ; Gastroenterology, Hepatology, & Nutrition; Heart Institute » John Bucuvalas, MD: Professor, Rohit Kohli, MBBS, MS: Associate Professor, Jens Goebel, MD: Associate Professor, Marc Schecter, MD: Associate Professor, Samuel Kocoshis, MD: Professor, and Chesney Castleberry, MD: Assistant Professor
Dr. Lara Danziger-Isakov is in collaboration on the integrated solid organ transplant (ISOT)–performed evidence-based guideline development for the prevention of cytomegalovirus in conjunction with liver (Rohit Kohli, John Bucuvalas), kidney (Jens Goebel), heart (Chesney Castleberry), lung (Marc Schecter) and small bowel (Sam Kocoshis) teams.

Dr. Danziger-Isakov is also collaborating on SPLIT survey in CMV prevention in conjunction with John Bucuvalas in Liver Transplantation.

Division of Physical Medicine and Rehabilitation » Douglas G. Kinnett: Associate Professor
Michelle Dickey, MS, CRN has collaborated with Douglas Kinnett, MD on a research study examining the infectious complications of intrathecal baclofen pump devices in pediatrics.

Division of Veterinary Services » Gary Keller, DVM: Field Service Professor
Dr. Tibor Farkas is in collaboration with Dr. Keller on the evaluation of laboratory rodents for enteric viral infections.

Division of Neonatology and Pulmonary Biology » Ardythe Morrow, PhD: Professor and Beena Kamath-Rayne, MD, MPH: Assistant Professor
Dr. Tibor Farkas is in collaboration with Dr. Morrow under the human milk grant.

Dr. Elizabeth Schlaudecker is in collaboration with Dr. Morrow on the immunologic response in breast milk after influenza immunization.

Dr. Mary Staat is in collaboration with Ardythe Morrow, PhD under the New Vaccine Surveillance Network examining the association of blood group antigens and acute gastroenteritis due to norovirus.

Dr. Schlaudecker is also in collaboration with Dr. Kamath-Rayne on a neonatal resuscitation program, “Helping Babies Breathe”, in Honduras.

Division of Rheumatology; Division of Infectious Diseases, Global Health » Michael Barnes, PhD: Assistant Professor and Mark Steinhoff, MD: Professor
  Dr. Tibor Farkas is in collaboration Drs. Barnes and Steinhoff on the evaluation of recovirus zoonosis.

UC Molecular Genetics, Biochemistry & Microbiology » Andy Herr, PhD: Assistant Professor
  Dr. Jason Jiang is in collaboration with Dr. Herr on structural analysis (by resolving Chrystal structures) of human rotaviruses interaction with human histo-blood group antigens.

Division of Human Genetics » Derek Neilson, MD: Assistant Professor
  Monica McNeal is in collaboration with Dr. Neilson to develop an animal model of influenza induced acute necrotizing encephalopathy.

Division of Pediatric General and Thoracic Surgery » Greg Tiao, MD: Associate Professor
  Monica McNeal is in collaboration with Dr. Tiao on a project that involves using the animal model of rotavirus induced biliary atresia to determine the mechanism of the disease.

Director of the Mass Spectrometry Lab, Division of Pathology » Ken Setchell, PhD: Professor
  Dr. Joseph Qualls is in collaboration with Dr. Setchell on small molecule mass spectrometry. Dr. Setchell is identifying and quantifying the downstream metabolites generated from imported L-citrulline in macrophages. These findings help define the utilization of L-arginine derived from L-citrulline, and its importance in anti-pathogen macrophage function.

Division of Cellular and Molecular Biology » Fred Finkelman, MD: Professor
  Dr. Elizabeth Schlaudecker is in collaboration with Dr. Finkelman on IgG isotype and cytokine analysis after influenza immunization in pregnant women.

Grants, Contracts, and Industry Agreements

<table>
<thead>
<tr>
<th>Grant and Contract Awards</th>
<th>Annual Direct</th>
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<tr>
<td><strong>BERNSTEIN, D</strong></td>
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<tr>
<td>Vaccine and Treatment Evaluation Units (VTEUs): Evaluation of Control Measures Against Diseases Other Than AIDS</td>
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<td>HHSN272201000008I/HHSN27200001</td>
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<tr>
<td>The Natural History of CMV-Related Hearing Loss</td>
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<tr>
<td>National Institutes of Health(University of Alabama-Birmingham)</td>
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<td>VRC 701/702</td>
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<td>NIH(The Emes Corporation)</td>
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<td>CARDIN, R</td>
<td>Role of Viral Chemokine Receptors in Cytomegalovirus Latency</td>
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<td>DANZIGER-ISAKOV, L</td>
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<td>DOWNES, K</td>
<td>Urinary Biomarkers for Aminoglycoside-Associated Acute Kidney Injury in Cystic Fibrosis</td>
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<td>HOSTETTER, M</td>
<td>Balance of Th17 Cells and Regulatory T Cells in Candidal Vaginal Colonization in Pregnant Macaques and Humans</td>
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<td>GAPPS, Seattle Children's Hospital</td>
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<td>Pediatric Physician Scientist Program Award</td>
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<td>K12 HD 000850</td>
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<td>JIANG, J</td>
<td>Immune Responses to Norovirus after Natural Infection in Vietnamese Children and Correlation with Blood Group Antigen Secretor Status</td>
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<td>Fogarty International Center</td>
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<td>Inactivation of Enteric Foodborne Viruses in High Risk Foods by Non-Thermal Processing Technologies</td>
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<td>Newcastle Disease Virus Vectored Vaccines for Norovirus</td>
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<td>Universal Flu Vaccine by a Norovirus P Particle Platform</td>
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<td>The Role of Human Milk in Infant Nutrition and Health (Project 2 and Core D)</td>
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<td>Hyaluronan Regulation of Microbial Host Defense of the Intestine</td>
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<td>Receptor Mimics for Rapid Detection, Typing, and Susceptibility Testing</td>
<td>PATH Vaccine Solutions</td>
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<td>Enhanced Surveillance for New Vaccine Preventable Disease-Patient Protection-ACA</td>
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<td>Enhanced Surveillance for New Vaccine Preventable Disease-Patient Protection - Supplement</td>
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<td>HSV Latency and Reactivation and the Novel Neuronal Regulation of VP16 In Vivo</td>
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<td>Enhanced Surveillance for New Vaccine Preventable Disease-Patient Protection</td>
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<td>The Immune Pathogenesis of Prenatal Listeria Monocytogenes Infection</td>
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*MCNEAL, M*

*SAWTELL, N*

*STAAT, M*

*WAY, S*
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<tr>
<th>Industry Contracts</th>
<th>Current Year Direct Receipts</th>
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<td>Genocea Biosciences, Inc</td>
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<td>LigoCyte Pharmaceuticals, Inc</td>
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<td>FrieslandCampina Nederland BV Research Project</td>
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<td>Aga Kahn University</td>
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<td>GlaxoSmithKline</td>
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<td>Ortho-Clinical Diagnostics, Inc</td>
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<td><strong>Total</strong></td>
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Current Year Direct Receipts: $3,570,562