Infectious Diseases

Division Details

RESEARCH AND TRAINING DETAILS	
Faculty	**20**
Joint Appointment Faculty	**7**
Research Fellows and Post Docs	**4**
Research Graduate Students	**6**
Total Annual Grant Award Dollars	**$17,984,009**
Total Annual Industry Award Dollars	**$1,898,869**

CLINICAL ACTIVITIES AND TRAINING	
Clinical Fellows	**6**
Inpatient Encounters	**4,540**
Outpatient Encounters	**2,158**

Row 1: K Singh, J Wang, M Staat, N Sawtell, L Danziger-Isakov

Row 2: X Jiang, R Brady, M McNeal, S Shah, E Schlaudecker

Row 3: M Tan, A Herr, SS Way, J Schaffzin, P Spearman, G Paulsen

Row 4: J Hammonds, D Haslam, R Frenck, B Connelly, J Qualls

Visit Infectious Diseases

Division Highlights

The Division of Infectious Diseases at Cincinnati Children's Hospital conducts broad-based research focused on the diagnosis, prevention, and treatment of childhood infections. Vaccine development and evaluation in both children and adults is a prominent focus of the division, highlighted by the National Institutes of Health (NIH)-funded Vaccine and Treatment Evaluation Unit (VTEU) and other sponsored trials within the Gamble Program for Clinical Studies, led by Drs. Robert Frenck, Jr., MD, and David Bernstein, MD, MA. Epidemiology and surveillance of pediatric infections and vaccine safety are additional strengths, led by Dr. Mary Staat, MD, MPH, and her research group. Clinical research in transplant populations is a growing strength, headed by Dr. Lara Danziger-Isakov, MD, MPH, and colleagues. Basic science laboratories in the division have made great progress in the past year, with the highlights from each laboratory outlined below. Notably, Dr. Sing Sing Way's groundbreaking research into maternal-fetal immunologic tolerance and prenatal infections has received extensive national and local recognition, including the 2016 E. Mead Johnson Award for Pediatric Research, a Howard Hughes Medical Institute Faculty Scholar appointment and the Research Achievement Award from Cincinnati Children's in 2017. Details of individual research highlights and discoveries of our faculty are below.

Paul Spearman, MD

Dr. Paul Spearman, MD, joined the Division of Infectious Disease as division chief this past year. His laboratory focuses on HIV biology, in particular the interactions of viral components with cellular pathways required for particle assembly. One of the highlights of the past year from this work was the discovery that Siglec-1, a cell surface molecule that captures HIV-1 particles, plays an important role in forming an internal compartment (the virus-containing compartment) in infected macrophages, and this contributes to HIV transmission to T cells

(PLoS Pathogens 2017; 13:e1006181). A second major area of work focuses on the role of Rab11-FIP1C on HIV envelope glycoprotein incorporation into particles. In addition to basic laboratory studies, Dr. Spearman is contributing to vaccine studies within the VTEU and collaborating in systems biology studies designed to elucidate basic aspects of responses to vaccines in humans.

David Bernstein, MD, MA

The National Institutes of Health (NIH) funded vaccine treatment evaluation unit (VTEU), led by Dr. David Bernstein, MD, MA, and Dr. Robert Frenck, MD, is very active in evaluating vaccines, antivirals, and the development of novel challenge models for infectious diseases. Clinical studies recently completed include: evaluations of altered dosing schedules for the human papillomavirus (HPV) vaccine in adolescent girls, a study of an enterotoxigenic Escherichia coli (ETEC) vaccine provided by several routes of administration, a study of a Shigella vaccine, and a new treatment for bacterial vaginosis (BV). Another priority area for the NIH, and the VTEUs, has been influenza vaccines including a study of bird flu vaccines and attempts to develop more broadly protective vaccines that could eliminate the need for yearly vaccinations. Current trials are underway for H7N9 influenza vaccine, a novel RSV vaccine, several candidate Shigella vaccines, a DNA vaccine for Andes virus, and others.

Dr. Bernstein's interest in herpes vaccines also continued with both preclinical and clinical studies of a therapeutic vaccine for genital herpes. This vaccine, originally shown by our group to reduce recurrences and recurrent virus shedding in an animal model was also effective in a clinical trial. The manuscript, recently submitted by Dr. Bernstein, described a trial in subjects with recurrent genital herpes that showed vaccine induced reductions in clinical recurrences and for the first time recurrent HSV-2 shedding, the most common source for the spread of this virus. Additioanl published work by us describes an animal model evaluation of a vaccine for congenital cytomegalovirus (CMV) that utilized LCMV as a vector for two CMV proteins.

Rebecca Brady, MD

Dr. Rebecca Brady, MD, is the medical director of the Ohio American Academy of Pediatrics Maximizing Office Based Immunization (MOBI) Program. The expansion of this program now includes specialized modules and quality improvement activities. She continues as the contributing section editor for the *American Academy of Pediatrics Grand Rounds* publication, and is a question writer for PREP-ID. Dr. Brady serves as co-investigator for many clinical studies performed at the Gamble Program for Clinical Studies. Together with Dr. Jennifer Huggins, MD, within the Division of Rheumatology, she has grant funding from Pfizer for the project, "Connecting the Silos: A Partnership to Improve Immunization Rates among Adolescents with High-Risk Chronic and Immunocompromising Conditions". She serves as the division's representative for the education of medical students and residents.

Beverly Connelly, MD

FY17 was a banner year for the collaborative partnerships of the infection prevention and control program under the directorship of Dr. Beverly Connelly, MD, with the institution reaching a targeted 95% compliance with observed opportunities for hand hygiene. Program partnerships with the improvement group to reduce central line associated bloodstream infections (CLABSIs) realized a significant improvement with > 20% reduction. Other collaborations continue to work to reduce other healthcare associated infections. Air and water safety programs continue in development throughout the medical center and its satellites. Two additional Cu/Ag water treatment systems brought on line are a part of the water safety program. An air sampling program put in place at the Burnet campus, establishes baseline data for future surveillance activities related to construction and renovation activities. Partnership with environmental services resulted in a heightened cleanliness through the campus and a great start to program to UV treat discharge rooms of patients with clostridium difficile infections, and infections with multi-drug resistant organisms in order to interrupt transmission opportunities. Collaborative research opportunities this year resulted in publications in *Biology of Blood and Marrow Transplantation, Journal of Neurosurgery: Pediatrics*, *Infection Control and Hospital Epidemiology*, and *Clinical Infectious Diseases*.

Lara Danziger-Isakov, MD, MPH

Dr. Lara Danziger-Isakov, MD, MPH, continues her role as protocol chair for studies in the Clinical Trials in Organ Transplantation in Children (CTOT-C) funded by the National Institute of Allergy and Infectious Diseases (NIAID). One study evaluates the interaction between respiratory viral infections and the development of allo–and autoimmunity after pediatric lung transplantation including long-term follow-up in this cohort; while the second assesses the impact of B-cell induction on the development of allo- and autoimmunity and early graft dysfunction in pediatric lung transplant recipients. She was re-appointed to the steering committee of CTOT-C, and named as co-chair

of the Adherence, Growth & Development and QOL subcommittee that is launching, and currently enrolling, a new study to assess the impact of post-traumatic stress symptoms on adherence and outcomes after solid organ transplantation (SOT).

Dr. Danziger-Isakov expanded her work in SOT in collaboration with the Studies in Pediatric Liver Transplantation (SPLIT) to evaluate current practices for cytomegalovirus prevention in collaboration with a multi-center pediatric infectious disease collaborative to evaluate the epidemiology and impact of respiratory viral infections and clostridium difficile infections after SOT and hematopoietic stem cell transplantation (HSCT). Further, her team is actively enrolling patients in NIAID-funded studies evaluating: 1) influenza vaccination responses after HSCT, 2) adenovirus infection after HSCT, and 3) norovirus infections after SOT. A focus on quality improvement continues efforts to improve post-transplant vaccination rates after SOT.

Michelle Dickey, MS, APRN, CNFP, CPNP, CCRC

Ms. 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. With collaborators, Ms. Dickey has undertaken an innovative approach to simplified informed consent and assent.

Robert W. Frenck, MD

Dr. Robert Frenck, MD, is the director for the National Institutes of Health (NIH)-funded Vaccine Treatment Evaluation Unit (VTEU), a contract designed to evaluate new vaccines and therapeutics in the continual quest to eliminate infectious diseases from the world. A major focus of the VTEU has been evaluation of improved vaccines against influenza as well as testing candidate vaccines against potential pandemic strains of influenza. The NIH recently awarded the Cincinnati Children's VTEU a $5.5 million contract to evaluate vaccines against an evolving strain of influenza in birds (H7N9) that has potential to cause pandemics in humans. In addition to the VTEU, Dr. Frenck maintains an active clinical research portfolio with emphasis on enteric diseases including Shigella, E. coli and norovirus. He recently completed testing of candidate vaccines against Shigella, as well as developed and tested a human challenge model for Shigella. The combination of these projects resulted in an industry partner choosing Dr. Frenck to lead a multi-million dollar project to test their Shigella vaccine. The Department of Defense (DoD) recently contacted Dr. Frenck to use the model to test a Shigella vaccine they developed, the the hope that the study will begin later in the year. A norovirus challenge model developed by Dr. Frenck in collaboration with Dr. Jason Jiang, PhD, of our division is being completed, and will be available for testing of vaccines and therapeutics against norovirus, the leading cause of diarrhea among children in the U.S.

David Haslam, MD

Along with Josh Courter, PharmD, the stewardship program has implemented VigiLanz clinical decision support software which performs real-time monitoring of antimicrobial use and resistance, facilitating audit and feedback of antimicrobial use at Cincinnati Children's. Dr. Haslam's research laboratory is using metagenomic sequencing to identify patients at risk of infection with antibiotic-resistant bacteria.

Margaret K. Hostetter, MD

Research in the Hostetter laboratory has expanded into three main areas: 1) Obtained a patent for the use of antibodies against heparin binding motifs in Candida albicans to inhibit their role in biofilm. After publishing the paper on the effects of an antibody against heparin binding motifs in inhibiting Candida albicans biofilm production in the *Journal of Infectious Diseases*, the laboratory has found that the antibody also inhibits biofilms due to other Candida species as well as bacteria; 2) Role of candidal vaginal colonization in preterm birth. The laboratory 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. The in vitro data have sparked a clinical study of pregnant women in Bangladesh and Zimbabwi, funded by the Global Alliance to Prevent Prematurity and Stillbirth (GAPPS), an arm of the Bill & Melinda Gates Foundation; and 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. In vitro experiments to identify the functional correlates of these mutations are underway.

Xi Jason Jiang, PhD

Dr. Jiang's lab focuses on norovirus (NV) and rotavirus (RV) research, mainly the virus-host interaction related to human histo-blood group antigen (HBGAs) as receptors. For NVs, work continues on characterization of newly emerged genotypes of human NVs that cause major epidemics in different regions. The goal is to elucidate the mechanism of the emergence in associated with their host HBGA binding property variations for knowledge in future surveillance and disease control and prevention. For RVs, the focus is on characterization of HBGA-associated host ranges of different RV genotypes and genogroups causing diseases in different human population, as well as some animal species for better understanding of RV evolutions, zoonosis, epidemiology and disease burden; and therefore for development strategy against RVs. The research on the development, and evaluation of vaccines against NVs and RVs, is ongoing in the laboratory.

Monica M. McNeal, MS

Ms. Monica McNeal, MS, is the associate director for the Laboratory for Specialized Clinical Studies (LSCS) in the Division of Infectious Diseases, which provides lab support for clinical studies involving vaccine trials, vaccine development and surveillance studies. The laboratory was, and continues to be, the central laboratory supporting the development of past and present live oral rotavirus vaccines. Rotavirus vaccines continue to be an important aspect in improving child health worldwide. Ms. McNeal continues to support rotavirus vaccine trials conducted in numerous countries around the world in association with nonprofit organizations and industrial sponsors. Some of those studies involve determining how to improve efficacy of rotavirus vaccines in developing countries in Asia and Africa by looking at vaccination schedules, booster doses and the effect of breast feeding.

The laboratory is also involved in supporting influenza vaccines, analyzing samples from clinical trials conducted in the US. Additional projects include using animal models to investigate the effects of malnutrition on oral rotavirus vaccines, detecting the pathogens causing community acquired pneumonia presenting to the emergency department, rotavirus vaccine effectiveness in conjunction with the Center for Disease Control and Prevention (CDC) and establishing assays to quantitate norovirus shedding in immunocompromised patients. Ms. McNeal continues to support the clinical trials run by the Gamble Program for Clinical Studies, including Shigella and Escherichia coli (ETEC) vaccine trials, by establishing new assays and providing laboratory support.

Grant Paulsen, MD

Dr. Grant Paulsen, MD, maintains a focus on clinical research and trials, with a special interest in prevention of post-transplant infections, vaccination following organ transplant, and treatment and prevention of viral infections in immunocompromised patients. Aimed research to determine the effect of screening in pre-transplant methicillin resistant staphylococcus aureus (MRSA) screening, and use of targeted peri-operative prophylactic antibiotics on early post-transplant infections continues as an area of focus. He is also investigating the safety and efficacy of live viral vaccines, such as varicella and MMR, following liver transplantation. Dr. Paulsen currently serves as principal investigator on a Phase I trial of an investigational hantavirus vaccine with Cincinnati Children's Vaccine and Treatment Evaluation Unit (VTEU). In addition, Dr. Paulsen is a sub-investigator for a number of ongoing clinical trials with the VTEU and further collaborative studies in immunocompromised patients.

Joe Qualls, PhD

What do immune cells "eat" when they are hungry? Research in the Qualls laboratory addresses how amino acid uptake and metabolism regulates immune cell function. L-arginine is a semi-essential amino acid required for microbicidal nitric oxide (NO) production by macrophages, and for T cell proliferation. When L-arginine is limiting, these cells rely on its synthesis from a related amino acid, L-citrulline, to sustain their respective functions. Mice whose immune system is unable to convert L-citrulline to L-arginine are more susceptible to mycobacterial infection in vivo. One project in our lab involves exploring the necessity of L-citrulline metabolism during anti-mycobacterial T cell function. These studies suggest that proliferation of mycobacterial-specific CD4+ T cells in vivo might not depend on L-citrulline, yet their accumulation in relevant tissues of infected mice is regulated by L-citrulline metabolism. Another project explores the metabolic consequences of L-citrulline in mycobacteria-infected macrophages. Our data show control of mycobacteria in vivo is dependent on macrophage L-citrulline metabolism, and supplementing mice with commercially available L-citrulline enhances host defense during infection. These exciting findings have led to a new five-year R01 grant from the NIH/NIAID to study the implication and therapeutic potential of L-citrulline metabolism in models of virulent tuberculosis disease.

Nancy Sawtell, PhD

Recent discoveries funded, by the National Institutes of Health (NIH), identify several key features underpinning the establishment of latency in sensory neurons and subsequent reactivation in vivo. Dr. Sawtell, PhD, determined both host and viral genes play important roles in these processes. Using advanced recombinant inbred (ARI) strains of mice, they identified a quantitative host locus on mouse chromosome 16 that influences the ability of the virus to invade the nervous system and return to the surface of the eye to cause herpetic keratitis, the leading cause of infectious blindness in the U.S. A paradigm shifting finding of the lab is that the viral protein 16 (VP16), normally expressed late during virus infection, is first expressed in neurons that reactivate from latency. This expression of VP16 is essential for the very early stages in virus reactivation from latency. More recent publications from her lab demonstrate that VP16 expressed de novo in sensory neurons during the acute stage of infection gates entry into replication in neurons, the VP16 promoter functioning as a specialized sensor integrating key aspects of the neuronal environment to viral genome transcriptional activity.

Recent, yet unpublished work, show the importance of HSV-1 encoded regulatory RNAs in the balance between lytic and latent infections; findings indicate that manipulating their expression can protect from lethal viral encephalitis. In a project, funded by NASA, the Sawtell lab is conducting studies to determine the long term outcomes of latent HSV in the central nervous system, and the effects of stress and exposure to galactic cosmic radiation on HSV related pathology in the brain. Unexpectedly, these studies have revealed that long term latent infection can have significant impact on learning and memory, and this effect exacerbates in the presence of the human APOE4 allele.

Elizabeth Schlaudecker, MD, MPH

Dr. Elizabeth Schlaudecker's research continues to focus on the immunologic responses to maternal immunization. Her recent work with Cincinnati Children's Hospital Medical Center's Vaccine and Treatment Evaluation Unit (VTEU) has demonstrated increased innate immune signaling responses in breast milk lymphocytes after live-attenuated influenza vaccine. These findings suggest that breastfeeding extends the innate response to live-attenuated influenza vaccine via mucosal immunity. With the mentorship and support of Dr. Sing Sing Way, MD, PhD, Dr. Schlaudecker has revealed an altered isotype profile in pregnant women compared to non-pregnant women consistent with a decreased response to the vaccine. She continues to investigate sequential versus simultaneous administration of influenza and tetanus, diphtheria, and acellular pertussis (Tdap) vaccines in pregnant women with the Centers for Disease Control and Prevention (CDC).

Mary A. Staat, MD, MPH

Through Dr. Mary Allen Staat's large epidemiology and surveillance program developed in 1997; optimization of methods of detecting the changes and manifestations of infectious diseases of children within Hamilton County allow her to compare local findings to national trends. Using unique methods, Dr. Staat conducted studies to determine the population-based rates of Hamilton County hospitalizations, and emergency department visits, for many pediatric infectious diseases. These studies determined disease burdens as well as effectiveness of vaccines including rotavirus and influenza. Dr Staat currently is heading a trial funded by the Center for Disease Control and Prevention (CDC) to examine intussusception associated with rotavirus vaccine.

Dr. Staat 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.

Ming Tan, PhD

Dr. Ming Tan, PhD, has two major research focuses: 1) elucidation of complex norovirus-host interactions, and 2) development of combinational subunit vaccines against enterically transmitted viruses. Dr. Tan demonstrated that histo-blood group antigens (HBGAs) are critical host attachment factors affect the host susceptibility and host ranges of noroviruses. He discovered the mechanisms by which noroviruses enhance their HBGA binding capabilities, which in turn results in the expansion of norovirus target populations. These studies led to the finding that human noroviruses changed their host factors from human HBGAs to porcine-specific glycans thus shifting host specificity from humans to pigs.

Utilizing his discovery that norovirus protruding (P) domains self-assemble into P particles, Dr. Tan has developed three P domain-based polymers and used them as combinational vaccines and vaccine platforms. Development of several promising vaccine candidates uses this technology, and three have moved to preclinical animal trials. In summary, Dr. Tan research outcomes shed light onto norovirus-host interactions and norovirus evolution and offer new strategies for vaccine development against noroviruses and other infectious pathogens.

Sing Sing Way, MD, PhD

Dr. Way's research team investigates fundamental aspects of microbial infection, host antimicrobial immunity and developmental immunology by asking why individuals are particularly susceptible to infection during defined developmental windows. Given direct translational implications for the health of infants and children, we focus on infection during pregnancy and the early newborn period along with maternal-fetal immunological tolerance. For newborn infants, we overturned the dogma of immunological immaturity in this vulnerable population by demonstrating a greater necessity for active immune silencing that mitigates aberrant inflammation from abrupt exposure to commensal microbes (*Nature*, 2013). Interestingly, immunological suppression also causes infection susceptibility during pregnancy that reflects, in mothers, a more essential need for averting fetal rejection (*Cell Host & Microbe*, 2011). Infection during pregnancy overrides fetal tolerance – unmasking genetically foreign fetal tissues and rendering them susceptible to rejection that instigates fetal wastage and congenital invasion (*Journal of Clinical Investigation*, 2015). Applying antigen-specific tools for tracking maternal CD4 T cells, researchers identified protective “memory” features for fetal-specific regulatory T cells that persist in mothers after parturition, which reconciles human partner-specific protective benefits of prior pregnancy against complications in future pregnancies (*Nature*, 2012). Memory CD4 T cells require ongoing antigen exposure, and the team showed “microchimeric” maternal cells retained in offspring as an essential depot of maternal antigen that enforces fetal tolerance during next-generation pregnancies (*Cell*, 2015). Our ongoing work further extends these analysis by investigating how our immune system distinguishes commensal from pathogenic microbes, and why a pathogen is a pathogen in each developmental window.

Division Publications

1. Isanaka S; Guindo O; Langendorf C; Seck AM; Plikaytis BD; Sayinzoga-Makombe N; McNeal MM; Meyer N; Adehossi E; Djibo A. **Efficacy of a Low-Cost, Heat-Stable Oral Rotavirus Vaccine in Niger.** *The New England journal of medicine*. 2017; 376:1121-1130.

2. Marigo I; Zilio S; Desantis G; Mlecnik B; Agnellini AHR; Ugel S; Sasso MS; Qualls JE; Kratochvill F; Zanovello P. **T Cell Cancer Therapy Requires CD40-CD40L Activation of Tumor Necrosis Factor and Inducible Nitric-Oxide-Synthase-Producing Dendritic Cells.** *Cancer Cell*. 2016; 30:377-390.

3. Mohanty SK; Donnelly B; Lobeck I; Walther A; Dupree P; Coots A; Meller J; McNeal M; Sestak K; Tiao G. **The SRL Peptide of Rhesus Rotavirus VP4 Protein Governs Cholangiocyte Infection and the Murine Model of Biliary Atresia.** *Hepatology*. 2017; 65:1278-1292.

4. Haslam DB. **Nonalcoholic Steatohepatitis and the Intestinal Microbiota.** *Hepatology*. 2017; 65:401-403.

5. Lee S; Nguyen MT; Currier MG; Jenkins JB; Strobert EA; Kajon AE; Madan-Lala R; Bochkov YA; Gern JE; Roy K. **A polyvalent inactivated rhinovirus vaccine is broadly immunogenic in rhesus macaques.** *Nature Communications*. 2016; 7:12838.

6. Hampton CM; Strauss JD; Ke Z; Dillard RS; Hammonds JE; Alonas E; Desai TM; Marin M; Storms RE; Leon F. **Correlated fluorescence microscopy and cryo-electron tomography of virus- infected or transfected mammalian cells.** *Nature Protocols*. 2017; 12:150-167.

7. Payne DC; Sulemana I; Parashar UD; Curns AT; Esona MD; Mijatovic-Rustempasic S; Tate JE; Wikswo ME; Harrison CJ; Moffatt ME. **Evaluation of effectiveness of mixed rotavirus vaccine course for rotavirus gastroenteritis.** *JAMA Pediatrics*. 2016; 170:708-710.

8. Cox JW; Ballweg RA; Taft DH; Velayutham P; Haslam DB; Porollo A. **A fast and robust protocol for metataxonomic analysis using RNAseq data.** *Microbiome*. 2017; 5:7.

9. Kahn JA; Widdice LE; Ding L; Huang B; Brown DR; Franco EL; Bernstein DI. **Substantial Decline in Vaccine-Type Human Papillomavirus (HPV) Among Vaccinated Young Women During the First 8 Years After HPV Vaccine Introduction in a**

Community. *Clinical Infectious Diseases*. 2016; 63:1281-1287.

10. Navabi N; Whitt J; Wu SE; Woo V; Moncivaiz J; Jordan MB; Vallance BA; Way SS; Alenghat T. **Epithelial Histone Deacetylase 3 Instructs Intestinal Immunity by Coordinating Local Lymphocyte Activation.** *Cell Reports*. 2017; 19:1165-1175.
11. Jiang TT; Martinov T; Xin L; Kinder JM; Spanier JA; Fife BT; Way SS. **Programmed Death-1 Culls Peripheral Accumulation of High-Affinity Autoreactive CD4 T Cells to Protect against Autoimmunity.** *Cell Reports*. 2016; 17:1783-1794.
12. Johnson LR; Weizman OE; Rapp M; Way SS; Sun JC. **Epitope-Specific Vaccination Limits Clonal Expansion of Heterologous Naive T Cells during Viral Challenge.** *Cell Reports*. 2016; 17:636-644.
13. Goldstein SL; Mottes T; Simpson K; Barclay C; Muething S; Haslam DB; Kirkendall ES. **A sustained quality improvement program reduces nephrotoxic medication-associated acute kidney injury.** *Kidney international*. 2016; 90:212-221.
14. Hammonds JE; Beeman N; Ding L; Takushi S; Francis AC; Wang JJ; Melikyan GB; Spearman P. **Siglec-1 initiates formation of the virus-containing compartment and enhances macrophage-to-T cell transmission of HIV-1.** *PLoS pathogens*. 2017; 13:e1006181.
15. Sawtell NM; Thompson RL. **De Novo Herpes Simplex Virus VP16 Expression Gates a Dynamic Programmatic Transition and Sets the Latent/Lytic Balance during Acute Infection in Trigeminal Ganglia.** *PLoS pathogens*. 2016; 12:e1005877.
16. He Z; Liu B; Tao Y; Li C; Xia M; Zhong W; Jiang X; Liu H; Tan M. **Norovirus GII.17 Natural Infections in Rhesus Monkeys, China.** *Emerging infectious diseases*. 2017; 23:316-319.
17. Bernstein DI; Wald A; Warren T; Fife K; Tyring S; Lee P; Van Wagoner N; Magaret A; Flechtner JB; Tasker S. **Therapeutic vaccine for Genital herpes simplex virus-2 infection: Findings from a randomized trial.** *Journal of Infectious Diseases*. 2017; 215:856-864.
18. Kazi AM; Cortese MM; Yu Y; Lopman B; Morrow AL; Fleming JA; McNeal MM; Steele AD; Parashar UD; Zaidi AKM. **Secretor and Salivary ABO Blood Group Antigen Status Predict Rotavirus Vaccine Take in Infants.** *Journal of Infectious Diseases*. 2017; 215:786-789.
19. Hoft DF; Lottenbach K; Goll JB; Hill H; Winokur PL; Patel SM; Brady RC; Chen WH; Edwards K; Creech CB. **Priming Vaccination With Influenza Virus H5 Hemagglutinin Antigen Significantly Increases the Duration of T cell Responses Induced by a Heterologous H5 Booster Vaccination.** *Journal of Infectious Diseases*. 2016; 214:1020-1029.
20. Bowen MD; Mijatovic-Rustempasic S; Esona MD; Teel EN; Gautam R; Sturgeon M; Azimi PH; Baker CJ; Bernstein DI; Boom JA. **Rotavirus Strain Trends During the Postlicensure Vaccine Era: United States, 2008-2013.** *Journal of Infectious Diseases*. 2016; 214:732-738.
21. Yu G; Li K; Huang P; Jiang X; Jiang W. **Antibody-Based Affinity Cryoelectron Microscopy at 2.6-Å Resolution.** *Structure*. 2016; 24:1984-1990.
22. Yuan Z; Fan X; Staitieh B; Bedi C; Spearman P; Guidot DM; Sadikot RT. **HIV-related proteins prolong macrophage survival through induction of Triggering receptor expressed on myeloid cells-1.** *Scientific Reports*. 2017; 7:42028.
23. Zhang XF; Long Y; Tan M; Zhang T; Huang Q; Jiang X; Tan WF; Li JD; Hu GF; Tang S. **P[8] and P[4] Rotavirus Infection Associated with Secretor Phenotypes Among Children in South China.** *Scientific Reports*. 2016; 6:34591.
24. Xia M; Wei C; Wang L; Cao D; Meng XJ; Jiang X; Tan M. **Development and evaluation of two subunit vaccine candidates containing antigens of hepatitis E virus, rotavirus, and astrovirus.** *Scientific Reports*. 2016; 6:25735.
25. Lei S; Ryu J; Wen K; Twitchell E; Bui T; Ramesh A; Weiss M; Li G; Samuel H; Clark-Deener S. **Increased and prolonged human norovirus infection in RAG2/IL2RG deficient gnotobiotic pigs with severe combined immunodeficiency.** *Scientific Reports*. 2016; 6:25222.

Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
David I Bernstein, MD	Vaccine and Treatment Evaluation Units (VTEU)	National Institutes of Health	HHSN272200800006C	11/01/2007 - 09/30/2017	$1,496,206.20
David I Bernstein, MD	Mouse and Guinea Pig Models for Herpesviruses	National Institutes of Health	HHSN272201000008I	09/27/2010 - 08/30/2017	$754,237
Nancy M Sawtell, PhD	Acute and Long-term Outcomes of Simulated Deep Space Radiation Exposure on Latent Viral CNS Infection and CNS Pathology.	National Aeronautics and Space Admin (National Aeronautics and Space Admin)	NNX13AO47G	01/01/2014 - 12/31/2017	$76,000
David I Bernstein, MD	Vaccine and Treatment Evaluation Unites (VTEU).	National Institutes of Health	HHSN272201300016I	09/16/2013 - 09/15/2023	$416,516.24
Lara Danziger-Isakov, MD, MPH	B-Cell Targeted Induction to Improve Outcomes in Pediatric Lung Tranpslantation	National Institutes of Health (Washington University)	U01 IA077810	03/01/2013 - 02/28/2018	$109,253.10
Xi Jason Jiang, PhD	HBGA Receptors in Host Cell Entry and Infection of Norovirus.	National Institutes of Health (Purdue University)	R01 AI111095	12/01/2014 - 11/30/2019	$252,533
Nancy M Sawtell, PhD	Revealing Networks Targeted by HSV-1 ncRNAs with In Vivo Gain-of-function Studies	National Institutes of Health (University of Cincinnati)	R21 AI116389	01/01/2015 - 12/31/2016	$97,500
Joseph Edward Qualls, PhD	L-citrulline and Host Defenses to Mycobacteria	American Heart Association - National	15SDG21550007	01/01/2015 - 12/31/2017	$77,000
Sing Sing Way, MD, PhD	Pregnancy Induced Maternal Regulatory T Cells	March of Dimes - Ohio	6-FY15-254	06/01/2015 - 05/31/2018	$210,649.34
Xi Jason Jiang, PhD	Human Monoclonal Antibodies against Norovirus.	National Institutes of Health	R21 AI122132	04/01/2016 - 03/31/2018	$195,000
Sing Sing Way, MD, PhD	Maternal Regulatory T cell Antigen-specificity	National Institutes of Health	R01 AI120202	11/05/2015 - 10/31/2020	$390,000
Xi Jason Jiang, PhD	A Novel Lactic Acid Bacteria-based Norovirus Vaccine.	National Institutes of Health (Ohio State University)	R01 AI123661	03/10/2016 - 02/28/2021	$113,493

Heidi Mills Andersen, MD	NIEHS funded Training Program: Molecular Epidemiology in Children's Environmental Heath (MECEH)	National Institutes of Health (University of Cincinnati)	T32 ES010957	05/01/2015 - 04/30/2018	$45,180
Lara Danziger-Isakov, MD, MPH	Comparison of High vs. Standard Dose Flu Vaccine in Pediatric Stem Cell Transplant Recipients.	National Institutes of Health (Vanderbilt University)	U01 AI125135	08/19/2016 - 07/31/2019	$76,527
Sing Sing Way, MD, PhD	Immunological Identity Redefined by Genetically Foreign Microchimeric Cells	National Institutes of Health	DP1 AI131080	09/01/2016 - 07/31/2021	$1,092,000
Joseph Edward Qualls, PhD	L-citrulline and Anti-tuberculosis Host Defense	National Institutes of Health	R01 AI116668	07/01/2016 - 06/30/2021	$390,000
Sing Sing Way, MD, PhD	Systemic Immune Modulation by Enteric Commensal Fungi.	National Institutes of Health	R21 AI123089	03/01/2016 - 02/28/2018	$234,000
Xi Jason Jiang, PhD	Receptors of Rotaviruses	National Institutes of Health	R56 AI114831	08/20/2016 - 07/31/2018	$528,037
Sing Sing Way, MD, PhD	Commensal Fungi Positively Calibrate Asthma Susceptibility	National Institutes of Health	R21 AI128932	12/01/2016 - 11/30/2018	$195,000
Margaret K Hostetter, MD	Pediatric Scientist Development Program (PSDP) [K12]	National Institutes of Health	K12 HD000850	07/01/2016 - 06/30/2017	$1,683,906
Sing Sing Way, MD, PhD	The Immune Pathogenesis of Prenatal Listeria Monocytogenes Infection.	National Institutes of Health	R01 AI100934	07/01/2016 - 06/30/2017	$457,872
Nancy M Sawtell, PhD	HSV Latency and Reactivation and the Novel Neuronal Regulation of VP16 In Vivo.	National Institutes of Health	R01 AI093614	07/01/2016 - 06/30/2018	$503,931
Xi Jason Jiang, PhD	Prevalence of P[6] and P[11] Rotaviruses in Developing Countries	National Institutes of Health	R21 AI130631	02/15/2017 - 01/31/2019	$188,360
David Haslam, MD	Metagenomic Predictors of Infection and Transmission of Antibiotic Resistant Organisms.	Ctr for Disease Control and Prevention	200-2016-91939	09/30/2016 - 09/29/2017	$643,450
Robert W Frenck, MD	Prospective Observational	National Institutes of	HHSN275201000003I	09/16/2016	$58,800

	Study of the Risk Factors for Hospital-Acquired and Ventilator-Associated Bacterial Pneumonia (HABP/VABP)	Health (Duke University)		- 03/28/2017	
Sing Sing Way, MD, PhD	HHMI Faculty Scholar Award	Howard Hughes Medical Institute	55108587	11/01/2016 - 10/31/2021	$120,000
Sing Sing Way, MD, PhD	Functional Immune Tolerance to Non-inherited Maternal Antigen	National Institutes of Health	R01 AI124657	02/09/2017 - 01/31/2022	$390,000
Mary Allen Staat, MD	Enhanced Surveillance for New Vaccine Preventable Diseases	Ctr for Disease Control and Prevention	U01 IP001059	09/01/2016 - 08/31/2021	$214,285
Lara Danziger-Isakov, MD, MPH	B-Cell Targeted Induction to Improve Outcomes in Pediatric Lung Transplantation.	National Institutes of Health (Washington University)	U01 AI077810	03/01/2016 - 02/28/2017	$10,219
Lara Danziger-Isakov, MD, MPH	Multi-center Studies to Improve Diagnosis and Treatment of Pediatric Candidiasis.	National Institutes of Health (Duke University)	R01 AI103315	01/01/2014 - 12/31/2017	$20,000
Lara Danziger-Isakov, MD, MPH	Fungal Biomarkers for Diagnosis and Response to Therapy for Pediatric Candidemia.	National Institutes of Health (Duke University)	R01 HD081044	08/12/2015 - 05/31/2019	$25,596
Mary Allen Staat, MD	Enhanced Surveillance for New Vaccine Preventable Diseases	Ctr for Disease Control and Prevention	U01 IP001059	09/01/2016 - 04/30/2018	$1,985,712
David I Bernstein, MD	Vaccine and Treatment Evaluation Unites (VTEU) - H5 Virus	National Institutes of Health	15-0066.B1C1D141	09/16/2016 - 12/31/2018	$762,539
David I Bernstein, MD	Vaccine and Treatment Evaluation Unites (VTEU) - Flu	National Institutes of Health	14-0112.B1C1D129	01/15/2016 - 06/05/2018	$512,034
Lara Danziger-Isakov, MD, MPH	Comparison of High vs. Standard Dose Flu Vaccine in Pediatric Stem Cell Transplant Recipients	National Institutes of Health (Vanderbilt University Medical Center)	U01 AI125135	08/19/2016 - 07/31/2019	$50,625
Paul W Spearman, MD	Mucosal Protection Against HIV Generated by PIV5 Priming and VLP Boosting	National Institutes of Health	R01 AI111863	04/01/2017 - 03/31/2018	$597,176
Robert W Frenck, MD	Dose Finding Study of	PATH Vaccine	GAT.1957-01033590-	10/01/2016	$1,732,050

	Lyophilized Shigella Sonnei 53G Challenge Strain	Solutions	CT	- 03/31/2018	
David I Bernstein, MD	Vaccine and Treatment Evaluation Units (VTEU) Protocol Development, Implementation and Assays - HHSN272201300023I	National Institutes of Health	16-0119.B1C1D10065	06/12/2017 - 03/28/2020	$1,278,322
Total Annual Grant Award Dollars					**$17,984,008.88**

Annual Industry Award Dollars

Investigator	Industry Sponsor	Amount
David I Bernstein, MD	Genocea Biosciences, Inc.	$199,430
David I Bernstein, MD	PAXVAX, INC.	$810,478
David I Bernstein, MD	Regeneron Pharmaceuticals, Inc.	$60,031
Grant Paulsen, MD	Merck & Company, Inc.	$113,851
Lara Danziger-Isakov, MD, MPH	Genentech, Inc.	$144,967
Mary Allen Staat, MD	DART Therapeutics	$99,330
Rebecca C Brady, MD	Pfizer, Inc. (University of Cincinnati Physicians Co.)	$398,182
Robert W Frenck, MD	Accelovance, Inc.	$72,600
Total Annual Industry Award Dollars		**$1,898,869**