

Infectious Diseases

Division Details

RESEARCH AND TRAINING DETAILS

Faculty	16
Joint Appointment Faculty	7
Research Fellows and Post Docs	2
Research Graduate Students	4
Total Annual Grant Award Dollars	\$10,375,273
Total Annual Industry Award Dollars	\$1,826,951
Total Publications	63

CLINICAL ACTIVITIES AND TRAINING

Clinical Fellows	6
Inpatient Encounters	4,579
Outpatient Encounters	1,921



Row 1: J Jiang, M Hostetter, L Danziger-Isakov, M Tan, S Shah, R Brady, N Sawtell, G Paulsen, M Staat

Row 2: S S Way, A Herr, R Frenck, J Qualls, B Connelly, D Haslam, M McNeal

Research Highlights

Robert W. Frenck, MD

[Dr. Robert Frenck](#), along with [Dr. David Bernstein](#), directs the [NIH](#) funded Vaccine Treatment Evaluation Unit (VTEU) contract. Over the past year, the VTEU has focused largely on improving vaccines against influenza, and Dr. Frenck has helped oversee the conduct of these trials.

Dr. Frenck received a [DoD](#)-sponsored grant to develop a challenge model of *Shigella sonnei*. The model is a first step in a program to test vaccines to prevent *S. sonnei* infections, a major cause of shigellosis in industrialized nations. The first cohort of the study is complete and the remainder of the study has a projection completion date of early 2017. Once the model is developed, Dr. Frenck has plans to use the model to test various vaccines against *S. sonnei*.

Dr. Frenck has received various grants from vaccine manufacturers to test their vaccines as part of the path to licensure. Included among the vaccines are influenza, pathogenic *E. coli*, *C. difficile* and *S. aureus*.

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

David I. Bernstein, MD, MA

The [NIH](#) funded vaccine treatment evaluation unit (VTEU), led by [Dr. David Bernstein](#) continued to be active. Clinical studies recently completed included 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 the

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 an H5N1 and an H7N9 influenza vaccine as well as prime boost strategies designed to induce broadly protective antibodies.

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. Work was also published by us describing an animal model evaluation of a vaccine for congenital cytomegalovirus (CMV) that utilized LCMV as a vector for two CMV proteins.

Rebecca C. Brady, MD

[Dr. Rebecca Brady](#) 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 *Infectious Diseases*, an [American Academy of Pediatrics Grand Rounds](#) publication. Dr. Brady also served as co-investigator for many clinical studies performed at the [Gamble Program for Clinical Studies](#), Cincinnati Children's Division of Infectious Diseases. She led the Division of Infectious Diseases in a quality improvement project to improve review of immunization records for all new patients seen in the infectious diseases clinics. This project provided American Board of Pediatrics Maintenance of Certification Part IV credit. Together with [Jennifer Huggins \(Division of Rheumatology\)](#), 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 Cincinnati Children's Division of Infectious Diseases representative for the education of medical students and residents.

Beverly L. Connelly, MD

The collaborative efforts of the infection control program, directed by [Dr. Beverly Connelly](#), aligned with the institutional strategic goals to reduce healthcare associated infections (HAIs). Hand hygiene activities focused on incorporating the [World Health Organization's "My 5 Moments of Hand Hygiene"](#) into everyday practice throughout the medical center and on further developing teams for monitoring and improvement. The program also partnered with the central line associated bloodstream infections (CLABSIs) improvement group to identify opportunities for simplification of protocols and standardization of care surrounding central line use across all units. With successful implementation of the CLABSI One Standard during FY 16, we expect to see reduced variation in practice and reductions in CLABSI rates. Collaborative efforts and standardization of processes helped maintain a low rate of surgical site infections (SSIs) in FY 16. The program partnered with Emergency Preparedness, Occupational Safety and Environmental Health (OSEH), Employee Health, and the Divisions of [Emergency Medicine](#) and [Critical Care Medicine](#) to capitalize on "ebola learnings" to meet the [Ohio Department of Health](#) requirements for Assessment Hospitals. This work moves Cincinnati Children's toward a more universal preparedness model. During FY 16, the program established stronger collaborative relationships with OSEH and Plant Engineering in the area of water safety. The institution moved toward a more robust water safety plan with the assistance of an outside consultant. We look to add additional Cu/Ag legionella prevention at select satellite locations in FY17. Our air quality and safety program moved forward in FY 16, bringing sampling capabilities in-house. This program can now expand surveillance activities in FY 17 to better support state-of-the-art prevention programs with our construction contractors.

Lara Danziger-Isakov, MD, MPH

[Dr. Lara Danziger-Isakov](#) continues her role as protocol chair for three studies in the Clinical Trials in Organ Transplantation in Children (CTOTC) 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, 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. The final study assesses perceived barriers to adherence after pediatric solid organ transplantation. She was re-appointed to the Steering Committee to CTOTC and named as co-chair of the Adherence, Growth & Development and QOL Subcommittee that is launching a new study to assess the impact of post-traumatic stress symptoms on adherence and outcomes after solid organ transplantation (SOT).

Dr. Danziger-Isakov has expanded her work in SOT in collaboration with the Studies in Pediatric Liver Transplantation ([SPLIT](#)) to evaluate current practices for cytomegalovirus prevention and in collaboration with a multi-center pediatric infectious disease collaborative to evaluate the epidemiology and impact of respiratory viral infections after SOT and hematopoietic stem cell transplantation. A focus on quality improvement has led to significant improvements in pre-transplant infectious disease risk assessment and post-transplant vaccination rates.

Monica M. McNeal, MS

Ms. McNeal 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 has been, 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 has continued 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 continues to support the development of non-living rotavirus vaccines by developing and validating assays for clinical trials. The first ever human vaccine trial using a non-living rotavirus vaccine in children and infants, took place in Africa with a publication ready for submission. 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 ED, 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 including Shigella and Escherichia coli (ETEC) vaccine trials, by establishing new assays and providing laboratory support.

Grant C. Paulsen, MD

[Dr. Grant Paulsen](#) 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. Research in pre-transplant Methicillin Resistant Staphylococcus aureus ([MRSA](#)) screening is aimed at determining the effect of screening, and use of targeted peri-operative prophylactic antibiotics on early post-transplant infections. He is also investigating the safety and efficacy of live viral vaccines, such as varicella and MMR, following liver transplantation. In addition, Dr. Paulsen serves as sub-investigator for a number of ongoing clinical studies in immunocompromised patients as well as clinical trials with Cincinnati Children's Vaccine and Treatment Evaluation Unit (VTEU).

Joseph E. Qualls, PhD

Research in the Qualls laboratory has focused on the contribution of intracellular L-arginine synthesis on immune cell function. L-arginine is a semi-essential amino acid, meaning it isn't synthesized to sufficient amounts in our bodies during "stressful" conditions – including infection and other disease states. In addition to serving as a building block for protein synthesis, microbicidal nitric oxide (NO) production by macrophages and for T lymphocyte proliferation requires this amino acid. When L-arginine is limiting, these cells rely on L-arginine synthesis from L-citrulline, to sustain their respective functions. Mice that cannot convert L-citrulline to L-arginine in immune cells of hematopoietic lineage are impaired at clearing *M. bovis* BCG and *M. tuberculosis* infection in vivo. One project, funded by the [American Heart Association](#), aims to define the metabolic consequences of L-citrulline in mycobacteria-infected macrophages. We published the first study stemming from this award, defining differential metabolic pathways of imported L-arginine, and L-arginine synthesized from intracellular L-citrulline in macrophages ([Rapovy et al. The Journal of Immunology. 2015](#)). Additionally, the preliminary data from these studies suggest control of mycobacterial is dependant on macrophage L-citrulline metabolism, and supplementing mice with commercially available L-citrulline enhances host defense to mycobacteria infection. These exciting findings resulted in a pilot award from Cincinnati Children's, and led to a new five-year grant from the [NIH/NIAID](#) (1 R01 AI116668-01A1) to study the implication and therapeutic potential of L-citrulline metabolism in models of virulent tuberculosis disease.

A doctoral candidate in the laboratory, Shannon (Rapovy) Lange, is studying the necessity of L-citrulline metabolism during T cell function. Although previous studies have shown that L-citrulline can rescue T cell proliferation in L-arginine scarce environments in vitro,

the contribution of L-citrulline on T cell function in vivo is not addressed. Shannon has recently established a novel mouse model to probe the necessity and mechanism of L-citrulline metabolism in T cells, and experiments testing this during homeostasis and disease in vivo are underway. Preliminary data from these studies suggest that proliferation of mycobacterial-specific CD4+ T cells might not depend on L-citrulline. However, the survival of mycobacterial-specific CD4+ T cells with intact L-citrulline metabolism is far superior compared to those unable to metabolize L-citrulline. This project was partially funded by the [American Association of Immunologists](#), which supported Mrs. Lange's stipend for 2015-2016.

Nancy M. Sawtell, PhD

Most of the human population world-wide is and will remain infected with herpes simplex virus (HSV). At its core, this relationship hinges on the ability of the virus to aggressively replicate in the epithelial cells at the site of infection, transport into the nervous system through the axons innervating the infection site, and enter a repressed state called latency. Periodically, the latent viral program in rare neurons switches to the lytic cycle and infectious progeny and transport back to the body surface followed by rounds of replication in mucosal epithelium and virus shedding with the potential for transmission to new hosts. This facet of the viral life cycle, called reactivation, results in inflammation in the nervous system and serious outcomes including blindness and encephalitis. In addition, HSV infection contributes to diabetes, cardiovascular, neurodegenerative diseases and increases the probability of HIV infection.

No effective vaccine is available, and no therapy eliminates latency or prevents the early stages of reactivation. One long-term goal of ongoing research in the [Sawtell lab](#) is to find interventions for recurrent HSV episodes by defining the host and viral mechanisms that control the establishment and reactivation of HSV-1 latency. Interaction between the virus and the sensory neuron represents a pivot point where largely unknown mechanisms lead to a latent or a lytic infection in the neuron. Recent discoveries in the lab have identified several key features as to how to establish latency in vivo. Their studies could 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, they have identified a locus on mouse chromosome 16 that regulates HSV neurovirulence as well as the severity of herpetic stromal keratitis. Their 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, "genomics squared" analysis to explore the interaction of both viral and host genetics in herpetic disease have been initiated. 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. These studies will not only define risks to astronauts and but also model HSV induced CNS damage (potentially increasing dementia risks) occurring in the aging population. Finally, a new [NIH](#) funded project exploits virally encoded miRNAs to regulate HSV reactivation in vivo.

Elizabeth P. Schlaudecker, MD, MPH

[Dr. Elizabeth Schlaudecker's](#) research continues to focus on the immunologic responses to maternal immunization. Her recent work has demonstrated shifts in antibody isotype responses after influenza vaccination during pregnancy. With the mentorship and support of [Dr. Sing Sing Way](#) in the Division of Infectious Diseases, and [Dr. Fred Finkelman](#) in the [Division of Immunology](#), she has revealed an altered isotype profile in pregnant women compared to non-pregnant women consistent with a decreased response to the vaccine. She is also investigating a 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](#)), as well as immunologic responses to immunization in breast milk with Cincinnati Children's Vaccine and Treatment Evaluation Unit (VTEU).

Samir S. Shah, MD, MSCE

[Dr. Shah's](#) research team focuses on improving efficiency and effectiveness of care of hospitalized children with a particular emphasis on respiratory tract infections. Several ongoing studies will determine the comparative effectiveness of different antibiotic regimens for community-acquired pneumonia and identify biomarkers that predict illness severity in children with community-acquired pneumonia and bronchiolitis. Recently published research identified factors associated a higher risk of treatment failure in children hospitalized with pneumonia. Dr. Shah is also PI on a parallel group randomized trial determining the efficacy of home nursing visits in improving outcomes after hospitalization for acute illnesses such as pneumonia and bronchiolitis.

Mary A. Staat, MD, MPH

Through [Dr. Staat's](#) large epidemiology and surveillance program developed in 1997; she has optimized methods of detecting the changes and manifestations of infectious diseases of children within Hamilton County which has allowed her to compare local findings to national trends. Using unique methods, Dr. Staat has conducted studies to determine the population-based rates of Hamilton County hospitalizations and emergency department visits for many pediatric infectious diseases. These studies have resulted the determination of 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 as well as two studies funded through the Vaccine and Treatment Evaluation Unit (VTEU) contract to evaluate the ability of mupiricin to decrease colonization of *S aureus* in infants, and to evaluate the treatment of children with community acquired pneumonia.

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.

Ming Tan, PhD

[Dr. Tan](#) 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 attachment factors that 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 the target populations for norovirus. 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 the "P" particle that he discovered in norovirus, Dr Tan has developed three P domain-based polymers used as combinational vaccines and vaccine platforms. Several promising vaccine candidates were developed using the "P" particle technology, and three have moved to preclinical animal trials. In summary, Dr. Tan research outcomes shed light onto virus-host interactions and evolution of norovirus and offer new strategies for vaccine development against noroviruses and other infectious pathogens.

Sing Sing Way, MD, PhD

[singsing-way](#)Dr. Way's group investigates host defense, and the immune pathogenesis of infectious disease, using representative models of human infection. We have a particular focus on prenatal infection, infection during the early neonatal period and maternal-fetal immunological tolerance. Results from our work over the past few years have uncovered a critical need for immune suppression in the first few days following birth that protects against pathological inflammation triggered by colonization with commensal microbes. This immune suppression within newborn infants also makes them susceptible to disseminated infection. Other related publications have uncovered fundamental new aspects of T cell biology including differentiation into immune suppressive regulatory T cells and antigen-specificity each required for maintaining maternal immune tolerance to the developing fetus during pregnancy.

Jason Jiang, PhD

[Dr. Jiang's](#) lab continued working on norovirus (NV) and rotavirus (RV) research, mainly focusing on the virus-host interaction related to human histo-blood group antigen (HBGAs) as receptors. The current focus is on the characterization of newly emerged genotype, the GII.17 of human NVs that caused major epidemics in China, and spread to several countries around world in collaboration with two groups in China. The goal is to elucidate the mechanism of the emergence responsible for the increased epidemics for knowledge in future surveillance and disease control and prevention. For rotavirus, they continue to expand their understanding on the diversity of RVs recognizing different HBGAs in association with the host ranges, evolution, cross-species transmission of RVs between humans and animals. In these studies they have identified a unique evolutionary lineage connecting RVs in two major genogroups, P[*I*] and P[*II*], that mainly infect animals and humans, respectively. The elucidation of the molecular basis in controlling host ranges by the HBGA binding specificity of individual genotypes in the evolutionary lineage provided valuable insight of the epidemiology of RV: why some of the P[*II*] RVs, such as [4] and P[8] mainly infect humans, while others, such as P[6] and P[19], also infect animal and why the majority of P[*I*] RVs mainly infect animals, while a few of others, such as P[10] also infect humans. Planned further study to verify the precise carbohydrate structures responsible for such host range variations is important for better understanding the 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.

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 publishing the paper on the effects of an antibody against heparin binding motifs in inhibiting *Candida albicans* biofilm production (*Journal of Infectious Diseases*, 2013; 208:1695-1704), the laboratory is now testing the efficacy of the antibody to inhibit biofilms formed by other organisms; 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, also 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.

Michelle P. Dickey, MS, CRN

[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.

David B. Haslam, MD

[Dr. David Haslam](#) joined the Division of Infectious Diseases in the summer of 2013 as the medical director of the Antimicrobial Stewardship Program. 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 Hospital. Dr. Haslam's research laboratory is investigating the mechanisms of defense against *Clostridium difficile* infection. In particular, the laboratory is investigating how normal intestinal bacteria (the 'microbiome') prevent *C. difficile* disease. In addition, the laboratory is using metagenomics and whole bacterial genome sequencing to identify patients colonized and infected with antibiotic-resistant bacteria.

Significant Publications

Atmar RL, [Bernstein DI](#), Lyon GM, Treanor JJ, Al-Ibrahim MS, Graham DY, Vinjé J, Jiang X, Gregoricus N, [Frenck RW](#), Moe CL, Chen WH, Ferreira J, Barrett J, Opekun AR, Estes MK, Borkowski A, Baehner F, Goodwin R, Edmonds A, Mendelman PM. [Serological Correlates of Protection against a GII.4 Norovirus](#). *Clin Vaccine Immunol*. 2015 Aug;22(8):923-9.

Currently the correlate of protection against Norovirus is unclear. Having a good correlate will enhance our ability to determine the predicted efficacy of a vaccine candidate. This study furthers our understanding of protection against norovirus and may lead to improved ability to evaluate candidate vaccines.

[Bernstein DI](#), Munoz FM, Callahan ST, Rupp R, Wootton SH, Edwards KM, Turley CB, Stanberry LR, Patel SM, [McNeal MM](#), Pichon S, Amegashie C, Bellamy AR. [Safety and efficacy of a cytomegalovirus glycoprotein B \(gB\) vaccine in adolescent girls: A randomized clinical trial](#). *Vaccine*. 2016 Jan 12;34(3):313-9.

Cytomegalovirus (CMV) continues to be a significant cause of morbidity in neonates. Developing a vaccine to protect mothers against CMV could significantly improve the health of mothers and their offspring. This trial reports the experience of a large trial to evaluate the protective effect of a candidate vaccine against CMV.

Chen WH, Cohen MB, Kirkpatrick BD, [Brady RC](#), Galloway D, Gurwith M, Hall RH, Kessler RA, Lock M, Haney D, Lyon CE, Pasetti MF, Simon JK, Szabo F, Tennant S, Levine MM. [Single-dose Live Oral Cholera Vaccine CVD 103-HgR Protects Against Human Experimental Infection With *Vibrio cholerae* O1 El Tor](#). *Clin Infect Dis*. 2016 Jun 1;62(11):1329-35.

Cholera remains a common cause of severe diarrhea in many parts of the world resulting in an estimated 1.5 million cases annually and approximately 100,000 deaths/year. At the present, there is no vaccine licensed against cholera in the US. This trial was instrumental in the vaccine receiving approval from the FDA for use in travelers

Danziger-Isakov L, Frazier TW, Worley S, Williams N, Shellmer D, Dharnidharka VR, Gupta NA, Ikle D, Sweet SC; CTOTC-05 Consortium. **Perceived barriers to medication adherence in pediatric and adolescent solid organ transplantation.** *Pediatr Transplant.* 2016 Mar;20(2):307-15.

Non-adherence to medical recommendations has shown to be a major cause for failure of the graft. This project examined potential barriers to adherence and ways to improve adherence.

Fix AD, Harro C, **McNeal M**, Dally L, Flores J, Robertson G, Boslego JW, Cryz S. **Safety and immunogenicity of a parenterally administered rotavirus VP8 subunit vaccine in healthy adults.** *Vaccine.* 2015 Jul 17;33(31):3766-72.

In the US, currently licensed rotavirus (RV) vaccines have resulted in a markedly reduction in RV disease. However, the vaccines have not been as effective in parts of the developing world. This study provides us information to move us closer to testing in children of a new candidate vaccine against RV.

Division Publications

1. Armah G, Lewis KD, Cortese MM, Parashar UD, Ansah A, Gazley L, Victor JC, McNeal MM, Binka F, Steele AD. **A Randomized, Controlled Trial of the Impact of Alternative Dosing Schedules on the Immune Response to Human Rotavirus Vaccine in Rural Ghanaian Infants.** *J Infect Dis.* 2016; 213:1678-85.
2. Atmar RL, Bernstein DI, Lyon GM, Treanor JJ, Al-Ibrahim MS, Graham DY, Vinje J, Jiang X, Gregoricus N, Frenck RW, Moe CL, Chen WH, Ferreira J, Barrett J, Opekun AR, Estes MK, Borkowski A, Baehner F, Goodwin R, Edmonds A, et al. **Serological Correlates of Protection against a GII.4 Norovirus.** *Clin Vaccine Immunol.* 2015; 22:923-9.
3. Bernstein DI, Munoz FM, Callahan ST, Rupp R, Wootton SH, Edwards KM, Turley CB, Stanberry LR, Patel SM, McNeal MM, Pichon S, Amegashie C, Bellamy AR. **Safety and Efficacy of a Cytomegalovirus Glycoprotein B (G_B) Vaccine in Adolescent Girls: A Randomized Clinical Trial.** *Vaccine.* 2016; 34:313-9.
4. Bowen M, Mijatovic-Rustempasic S, Esona M, Teel E, Gautam R, Sturgeon M, Azimi P, Baker C, Bernstein D, Boom J. **Rotavirus Strain Trends During the Post-Licensure Vaccine Era: United States, 2008-2013.** *J Infect Dis.* 2016.
5. Brady RC, Crawford AH. **Case 1: Clavicular Pain of 2 Months' Duration in a 9-Year-Old Girl.** *Pediatr Rev.* 2015; 36:545-7.
6. Bryant KA, Frenck R, Gurtman A, Rubino J, Treanor J, Thompson A, Jones TR, Sundaraiyer V, Baxter LM, Gruber WC, Emini EA, Scott DA, Schmoele-Thoma B. **Immunogenicity and Safety of a 13-Valent Pneumococcal Conjugate Vaccine in Adults 18-49 Years of Age, Naive to 23-Valent Pneumococcal Polysaccharide Vaccine.** *Vaccine.* 2015; 33:5854-60.
7. Cardin RD, Bravo FJ, Pullum DA, Orlinger K, Watson EM, Aspoeck A, Fuhrmann G, Guirakhoo F, Monath T, Bernstein DI. **Replication-Defective Lymphocytic Choriomeningitis Virus Vectors Expressing Guinea Pig Cytomegalovirus G_B and Pp65 Homologs Are Protective against Congenital Guinea Pig Cytomegalovirus Infection.** *Vaccine.* 2016; 34:1993-9.
8. Carpenter S, Nunes-Alves C, Booty M, Way S, Behar S. **A Higher Activation Threshold of Memory Cd8(+) T Cells Has a Fitness Cost That Is Modified by Tcr Affinity During Tuberculosis.** *PLoS Pathog.* 2016; 12.
9. Chen WH, Cohen MB, Kirkpatrick BD, Brady RC, Galloway D, Gurwith M, Hall RH, Kessler RA, Lock M, Haney D, Lyon CE, Pasetti MF, Simon JK, Szabo F, Tennant S, Levine MM. **Single-Dose Live Oral Cholera Vaccine Cvd 103-Hgr Protects against Human Experimental Infection with Vibrio Cholerae O1 El Tor.** *Clin Infect Dis.* 2016; 62:1329-35.
10. Danziger-Isakov L, Frazier TW, Worley S, Williams N, Shellmer D, Dharnidharka VR, Gupta NA, Ikle D, Sweet SC, CTOTC-05 Consortium. **Perceived Barriers to Medication Adherence in Pediatric and Adolescent Solid Organ Transplantation.** *Pediatr*

Transplant. 2016; 20:307-15.

11. Davis J, Kreppel A, Brady R, Jones B, Stevenson C, Fouladi M, Hummel T. **Nocardia Farcinica Meningitis Masquerading as Central Nervous System Metastasis in a Child with Cerebellar Pilocytic Astrocytoma.** *J Pediatr Hematol Onc.* 2015; 37:482-85.
12. Elaish M, Kang KI, Xia M, Ali A, Shany SA, Wang L, Jiang X, Lee CW. **Immunogenicity and Protective Efficacy of the Norovirus P Particle-M2e Chimeric Vaccine in Chickens.** *Vaccine.* 2015; 33:4901-9.
13. Elaish M, Kang KI, Xia M, Ali A, Shany SA, Wang L, Jiang X, Lee CW. **Immunogenicity and Protective Efficacy of the Norovirus P Particle-M2e Chimeric Vaccine in Chickens.** *Vaccine.* 2015; 33:4901-9.
14. El-Bietar J, Nelson A, Wallace G, Dandoy C, Jodele S, Myers K, Teusink A, Lane A, Davies S, Danziger-Isakov L. **Rsv Infection without Ribavirin Treatment in Pediatric Hematopoietic Stem Cell Transplantation.** *Bone Marrow Transplant.* 2016.
15. Farkas T, Singh A, Le Guyader FS, La Rosa G, Saif L, McNeal M. **Multiplex Real-Time Rt-Pcr for the Simultaneous Detection and Quantification of Gi, Gil and Giv Noroviruses.** *J Virol Methods.* 2015; 223:109-14.
16. Fix AD, Harro C, McNeal M, Dally L, Flores J, Robertson G, Boslego JW, Cryz S. **Safety and Immunogenicity of a Parenterally Administered Rotavirus Vp8 Subunit Vaccine in Healthy Adults.** *Vaccine.* 2015; 33:3766-72.
17. Freedman SB, Lee BE, Louie M, Pang XL, Ali S, Chuck A, Chui L, Currie GR, Dickinson J, Drews SJ, Eltoriki M, Graham T, Jiang X, Johnson DW, Kellner J, Lavoie M, MacDonald J, MacDonald S, Svenson LW, Talbot J, et al. **Alberta Provincial Pediatric Enteric Infection Team (Appetite): Epidemiology, Emerging Organisms, and Economics.** *BMC Pediatr.* 2015; 15:89.
18. Frenck RW, Jr., Fiquet A, Gurtman A, van Cleeff M, Davis M, Rubino J, Smith W, Sundaraiyer V, Sidhu M, Emini EA, Gruber WC, Scott DA, Schmoele-Thoma B, B. Study Group. **Immunogenicity and Safety of a Second Administration of 13-Valent Pneumococcal Conjugate Vaccine 5 Years after Initial Vaccination in Adults 50 Years and Older.** *Vaccine.* 2016; 34:3454-62.
19. Galloway D, Danziger-Isakov L, Goldschmidt M, Hemmelgarn T, Courter J, Nathan JD, Alonso M, Tiao G, Fei L, Kocoshis S. **Incidence of Bloodstream Infections in Small Bowel Transplant Recipients Receiving Selective Decontamination of the Digestive Tract: A Single-Center Experience.** *Pediatr Transplant.* 2015; 19:722-9.
20. Griffin SM, Converse RR, Leon JS, Wade TJ, Jiang X, Moe CL, Egorov AI. **Application of Salivary Antibody Immunoassays for the Detection of Incident Infections with Norwalk Virus in a Group of Volunteers.** *J Immunol Methods.* 2015; 424:53-63.
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Grants, Contracts, and Industry Agreements

Annual Grant Award Dollars

Investigator	Title	Sponsor	ID	Dates	Amount
Heidi Mills Andersen, MD	NIEHS funded Training Program: Molecular Epidemiology in Children's Environmental Health (MECEH)	National Institutes of Health (University of Cincinnati)	T32 ES010957-14	5/1/2015 - 4/30/2018	\$60,132
David I Bernstein, MD	Mouse and Guinea Pig Models for Herpesviruses	National Institutes of Health	HHSN2722010000081	9/27/2010 - 8/30/2016	\$734,332
David I Bernstein, MD	Vaccine and Treatment Evaluation Unites (VTEU).	National Institutes of Health	HHSN2722013000161	9/16/2013 - 9/15/2023	\$1,802,382
Rhonda Cardin, PHD	Role of Viral Chemokine Receptors in Cytomegalovirus Latency	National Institutes of Health	R01 AI087683	7/5/2012 - 3/31/2016	\$341,649
Lara Danziger-Isakov, MD-MPH	Multi-center Studies to Improve Diagnosis and Treatment of Pediatric Candidiasis	National Institutes of Health (Duke University)	R01 AI103315	1/1/2014 - 12/31/2017	\$5,000
Lara Danziger-Isakov, MD-MPH	Fungal Biomarkers for Diagnosis and Response to Therapy for Pediatric Candidemia	National Institutes of Health (Duke University)	R01 HD081044	8/12/2015 - 8/6/2020	\$6,401
Lara Danziger-Isakov, MD-MPH	B-Cell Targeted Induction to Improve Outcomes in Pediatric Lung Transplantation	National Institutes of Health (Washington University)	U01 IA077810	3/1/2013 - 2/28/2018	\$248,611
Margaret K Hostetter, MD	Pediatric Scientist Development Program	National Institutes of Health	K12 HD000850	7/3/2012 - 6/30/2016	\$1,488,680

(PSDP) [K12]

Robert W Frenck, MD	Dose-Finding Study of Lyophilized Shigella Sonnei 53G Challenge Strain	Department of Defense	W911QY-16-2-0002	1/19/2016 - 11/1/2016	\$1,340,405
Margaret K Hostetter, MD	March Of Dimes Administrative Grant	March of Dimes	4-FY14-504	10/1/2014 - 9/30/2019	\$108,540
Margaret K Hostetter, MD	PSDP American Academy of Pediatrics Funding	American Academy of Pediatrics	PSDP AAP	9/1/2010 - 6/30/2017	\$196,257
Xi Jason Jiang, PHD	Inactivation of Enteric Foodborne Viruses in High Risk Foods by Non-thermal Processing Technologies	University of Delaware	2.01E+12	2/1/2011 - 1/31/2017	\$162,287
Xi Jason Jiang, PHD	Universal Flu Vaccine by a Norovirus P Particle Platform	US Department of Agriculture (Ohio State University)	2013-87015-20476	2/1/2013 - 1/31/2018	\$186,784
Xi Jason Jiang, PHD	HBGA Receptors in Host Cell Entry and Infection of Norovirus	National Institutes of Health (Purdue University)	R01 AI111095	12/1/2014 - 11/30/2019	\$255,793
Xi Jason Jiang, PHD	Human Monoclonal Antibodies Against Norovirus	National Institutes of Health	R21 AI122132	4/1/2016 - 3/31/2018	\$234,000
Tony Jiang	Antifungal Immunity Controlled by Commensal Bacteria	National Institutes of Health	F30 DK107199	5/1/2015 - 4/30/2020	\$37,544
Ming Tan	Norovirus Capsid: A Novel Drug Target	National Institutes of Health (University of Cincinnati)	R21 AI097936	8/6/2013 - 7/31/2016	\$5,936
Joseph Edward Qualls, PHD	L-citrulline and Host Defenses to Mycobacteria	American Heart Association	15SDG21550007	1/1/2015 - 12/31/2017	\$77,000
Joseph Edward Qualls, PHD	Careers in Immunology Fellowship Application	American Association of Immunologists	Qualls_AAI	9/1/2015 - 8/31/2016	\$22,920
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	NNX13AO47G	1/1/2014 - 12/31/2016	\$94,889
Nancy M Sawtell, PHD	HSV Latency and Reactivation and the Novel Neuronal Regulation of VP16 In Vivo	National Institutes of Health	R01 AI093614	7/1/2012 - 6/30/2016	\$503,930

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	1/1/2015 - 12/31/2016	\$117,000
Mary Allen Staat, MD	EV-D68 Outbreak: Spectrum of Illness Risk and Disease Burden	Ctr for Disease Control and Prevention	200-2015-M-61640	1/20/2015 - 12/31/2016	\$135,000
Mary Allen Staat, MD	Enhanced Surveillance for New Vaccine Preventable Disease	Ctr for Disease Control and Prevention	U01IP000458	8/1/2014 - 7/31/2016	\$1,166,929
Sing Sing Way, MD-PHD	The Immune Pathogenesis of Prenatal Listeria Monocytogenes Infection	National Institutes of Health	R01 AI100934	9/6/2012 - 6/30/2016	\$457,872
Sing Sing Way, MD-PHD	Maternal Regulatory T Cell Antigen-specificity	National Institutes of Health	R01 AI120202	11/5/2015 - 10/31/2020	\$390,000
Sing Sing Way, MD-PHD	Systemic Immune Modulation by Enteric Commensal Fungi	National Institutes of Health	R21 AI123089	3/1/2016 - 2/28/2018	\$195,000
Total Annual Grant Award Dollars					\$10,375,273

Annual Industry Award Dollars

Investigator	Industry Sponsor	Amount
David I Bernstein, MD	Genocea Biosciences, Inc.	\$100,398
David I Bernstein, MD	Takeda Global Res & Development Ctr, Inc	\$149,389
Robert W Frenck, MD	Janssen Research & Development, LLC	\$577,480
Robert W Frenck, MD	Pfizer, Inc.	\$643,552
Monica Malone McNeal	PATH Vaccine Solutions	\$356,133
Total Annual Industry Award Dollars		\$1,826,951