## 2014 Research Annual Report

# Gastroenterology, Hepatology and Nutrition

#### **Division Summary**

RESEARCH AND TRAINING DETAILS	
Number of Faculty	34
Number of Joint Appointment Faculty	2
Number of Research Fellows	3
Number of Research Students	5
Number of Support Personnel	47
Direct Annual Grant Support	\$5,088,852
Direct Annual Industry Support	\$2,999,809
Peer Reviewed Publications	131

#### CLINICAL ACTIVITIES AND TRAINING

Number of Clinical Staff	62
Number of Staff Physicians	1
Number of Clinical Fellows	13
Number of Other Students	3
Inpatient Encounters	8,829
Outpatient Encounters	18,606

#### **Division Photo**



Cincinnati Children's

Row 1: S Huppert, C Yin Row 2: V Mukkada, M Cohen, K Campbell, B Balistreri Row 3: J Palermo, R Kohli, C Cole, T Denson, J Bezerra, C Wetzel, J Heubi Row 4: M Leonis, A Miethke, S Gandhi, M Rosen, M Farrell, S Moore, C Dykes

## Significant Accomplishments

## Digestive Health Center (DHC): A catalyst for research on digestive disease

The DHC is one of only 17 Silvio O. Conte Digestive Diseases Research Core Centers supported by the NIH, and the only one dedicated to pediatric diseases. With 101 investigators, the DHC contributes to the research goals of faculty from 21 divisions in the Department of Pediatrics and nine other Departments in the University of Cincinnati, College of Medicine. Our successful Pilot and Feasibility Program has distributed \$1.3 million among 32 junior investigators since 2007. These investigators have since attracted \$25.4 million in extramural grant funding.

## Pediatric Liver Care Center (PLCC): New insights into biliary atresia

Despite the limited understanding of the pathogenesis of biliary atresia, steroids have been widely combined with surgery. To conclusively examine whether steroid therapy is an effective treatment, Jorge Bezerra, MD, led a multi-center study funded by the NIH. The study found that steroid treatment did not offer an advantage over placebo and the use of steroids was associated with an increased risk for post-operative complications (*Journal of the American Medical Association*, 2014, 311:1750). In patients with biliary atresia, PLCC investigators found an unexpected increase in the cytokine interleukin-33 (IL-33). The administration of this cytokine into newborn mice with experimental biliary atresia healed the lining of injured ducts and allowed for growth of extrahepatic bile ducts (*Journal of Clinical Investigations*, 2014, 124:3241). These findings have

major implications for potential new therapies for biliary atresia and for the future engineering of bile ducts.

## Schubert Martin Inflammatory Bowel Disease (IBD) Center: Leading the Way

This year, more than 700 patients IBD were seen in our center, including 100 newly diagnosed and 90 secondopinion patients from 25 states and abroad. The center is an integral and leading participant in collaborative consortia, ie, ImproveCareNow, and Crohn's and Colitis Foundation's (CCFA's) PRO-KIDS. This role is reflected in superior outcomes for our patients with 80 percent of IBD patients in remission, 64 percent in sustained remission, and 84 percent having a good quality of life. These outcome measures are shared transparently on the center's website. Our Annual IBD Family Education Day, co-hosted by CCFA, continues to be one of the largest educational events of its kind in the country.

## **Research Highlights**

Cincinnati Children's Steatohepatitis Center (CCSC): Understanding and treating NAFLD and NASH The Cincinnati Steatohepatitis Center (CCSC), led by Drs. Xanthakos and Kohli, is a multidisciplinary program that provides care to a growing population of pediatric patients with nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). NAFLD, the hepatic consequence of obesity and metabolic syndrome, affects about 10% of children and ranges from fatty liver alone (NAFLD) to fatty liver with varying degrees of liver inflammation and fibrosis (NASH). NASH has become the third leading cause for liver transplantation in adults over the last decade. NAFLD and NASH often begin in childhood and progressive severe fibrosis can occur in early adolescence. Early identification and intervention is critical to prevent progression to end-stage liver disease.

Since its inception in 2007, the CCSC has evaluated over 260 children and adolescents with NAFLD and NASH. Dr. Kristin Bramlage joined our program as a third physician in 2013 further increasing access to the program. We collaborate clinically with other obesity-related programs at Cincinnati Children's, including the Center for Better Health and Nutrition, Sleep, Hypertension and Lipid, and Diabetes Clinics, and the Surgical Weight Loss Program for Teens. We monitor our outcomes quarterly using our clinical NASH Registry and have shown that our multidisciplinary clinical program is effective in improving ALT.

Seminal research highlights from the CCSC in fiscal year 2014 include publications on the requirement of bile acid-mediated signaling to reduce body weight and improve glucose tolerance after sleeve gastrectomy (*Nature* 2014;509:183) and the use of magnetic resonance elastography to non-invasively assess hepatic fibrosis in children with chronic liver disease (*J Pediatr* 2014;164:186). We continue to maintain a robust biospecimen repository (serum, plasma, DNA and liver tissue) from participants enrolled in our local NASH Registry to facilitate translational work. Our research program has been supported by grants from Ethicon Endosurgery Inc., the Cincinnati Diabetes and Obesity Center, the North American Society for Pediatric Gastroenterology and Hepatology Foundation and the National Institutes of Health. The CCSC is a leading pediatric site in the NIDDK-funded NASH Clinical Research Network (NASH CRN), a multi-center study investigating the natural history and determinants of NASH in adults and children. A NASH CRN clinical trial investigating cysteamine versus placebo for the treatment of pediatric NASH (CyNCH) is ongoing and in the follow-up phase with estimated completion in early 2015. In 2014, we also anticipate beginning a prospective clinical trial comparing the effectiveness of comprehensive lifestyle intervention versus bariatric surgery in treating NASH in severely obese adolescents.

In the past fiscal year, the CCSC has published key papers in the area of steatohepatitis and obesity research in the following journals: Nature, Endocrinology, Gut, Hepatology, American Journal of Physiology, Endocrinology and Metabolism, Obesity, JAMA Pediatrics, Journal of Pediatrics, and the Journal of Pediatric Gastroenterology, Hepatology and Nutrition.

#### Pancreas Care Center

Our mission is to provide comprehensive multidisciplinary management of pancreatic disorders that strives to improve patient outcomes through focused expertise, standardization of care and clinical research. The program is led by Joseph Palermo, MD, PhD; Tom Lin, MD; and Maisam Abu-EI-Haija, MD. With its recent inception, the program has already completed a survey of Cincinnati Children's providers to better understand the variation in management of acute pancreatitis, assembled a multidisciplinary care team to evaluate and treat complex pancreatic disorders, established a REDCap database for patient registry and instituted an evidence based order set for the management of acute pancreatitis. Our current research projects include the development of a prognostic tool to stratify pediatric patients at risk for severe acute pancreatitis; determining how standardization of care for acute pancreatitis. In addition, the program participates in the INSPPIRE consortium for pediatric pancreatitis and is one the few children's hospitals able to offer pediatric patients with chronic pancreatitis the option of total pancreatectomy with islet autotransplantation (TPIAT).

#### Intestinal Transplantation

The small intestinal transplantation program has become a national and international leader in transplantation. Our outcomes with regard to one year and now three year survival are the best in North America. Since 2009, our one year survival for the past 12 transplants is 100% and our three year survival between 2009 and 2012 is also 100%. We have accepted referrals from Texas, Arkansas, Alabama, Georgia, Tennessee, Indiana, Michigan, South Carolina, and Kentucky. We have also accepted international referrals from Israel, Saudi Arabia, Qatar, and Kuwait. We have been recognized by referring physicians for our circumspect, thoughtful approach to transplantation and our willingness to employ state of the art non-transplant medical or surgical therapies to facilitate intestinal adaptation among short bowel syndrome patients. We have initiated ethanol lock dwells for patients with central venous catheters and previous blood stream infections. This and other line care strategies have reduced the blood stream infection rate in our patient population from nearly 12/1000 catheter days.

The bone marrow transplantation service is currently developing an ethanol lock strategy for their patients based upon our own strategy. In addition we have adopted a low lipid TPN regimen to prevent and ameliorate the intestinal failure-associated cholestasis seen in patients receiving soy based parenteral lipid which contains high quantities of phytosterols. When lipid reduction fails to ameliorate cholestasis, we have available Omegaven®, a fish-oil based parenteral lipid. Its mechanism of action is two-fold. First, administration avoids phytosterol exposure, and second, it reduces inflammation in the liver by providing eicosapentaenoic acid (EPA). We also have enrolled out of state patients in another investigational protocol designed to optimize pediatric dosing for teduglutide. Teduglutide is a stable analog of glucagon like polypeptide 2 (GLP2) which enhances intestinal epithelial proliferation and facilitates bowel adaptation. In the four patients enrolled in our open trial, it has reduced TPN requirements by 20% to date. Beyond employing medical therapies, we have also been willing to embark upon non-transplant surgical strategies for improving intestinal function. We now have a series of four patients who had undergone previous serial transverse enteroplasties at other institutions for bowel lengthening. Those surgeries were followed by ongoing vomiting among the patients. Because the bowel remained dilated postoperatively, the patients were referred to us for transplantation. Because of radiographic or endoscopic discovery of a fixed, partial mechanical obstruction, we performed re-exploration upon those patients. We have discovered two obstructions at enteroplasty staple lines and two obstructions at jejunocolonic anastomoses. Upon relief of those obstructions, patients are once again making progress toward achieving enteral autonomy.

Programmatic refinements have taken place as well. We have streamlined our patient "passport," a valuable tool for documenting significant post-transplant events that have clinical implications for physicians in emergency departments or other institutions called upon to see our patients on an urgent basis. We have established an easily accessible time line on the passport that enables those other physicians to obtain a thorough snapshot of our patients' histories and current clinical situations. We are also in the process of establishing an EPIC "Phoenix" platform for easy electronic access of all pertinent transplant information. By doing so, we will have at our fingertips, the data necessary for compliance with regulatory mandates. Hence, we are more likely to remain in compliance with UNOS regulations.

An important clinical initiative has been the implementation of an initiative to document that all of our patients are adequately immunized against childhood diseases, pneumococcus, varicella, hepatitis A and B, and HPV.

We have been actively engaged in several research initiatives. We maintain our collaboration with Dr. Sandra Cortina of behavioral science in investigating psychosocial factors responsible for parental or patient non-adherence to therapeutic regimens. This ongoing prospective study is still very active and likely to be a landmark study regarding the psychosocial aspects of post-transplant care. We intend to expand the study to include pre-transplant candidates and to identify predictors of post-transplant non-adherence.

In addition, we maintain our collaboration with Dr. Pierre Russo of Children's Hospital of Philadelphia in order to ascertain whether antienterocyte antibodies or anti tissue transglutaminase antibodies are expressed in blood of post-transplant patients with allograft crypt hyperplastic villous atrophy.

Our initial observational paper regarding the value of incorporating routine psychosocial assessment and intervention following transplantation is in press.

We have presented an abstract at the International Small Bowel Transplant Symposium in Oxford, England regarding the value of limited resection for treatment of complications of exfoliative rejection in our patients.

In addition, we have written a review article for Current Opinion in Gastroenterology on intestinal physiology following small intestinal transplantation.

Finally, we have published a paper regarding micronutrient deficiencies among patients having undergone intestinal transplantation.

Along with the intestinal rehabilitation program, we are recipients of \$167,146.07 from NPS Pharmaceuticals to conduct an open trial of teduglutide in pediatric patients.

#### Neurogastroenterology and Motility

Under the leadership of Ajay Kaul, MD, the Neurogastroenterology and Motility Disorders Program at Cincinnati Children's continues to expand with 495 outpatient encounters over the last year, an increase of 200% in the last three years. Patients came from 29 states and seven countries. The majority of the growth came from children referred for second opinion from outside of our primary service area seeking our expertise in evaluation and management of motility disorders. With the addition of Sandra Wright, MD, to our program, we are starting an interdisciplinary clinic with Jason Frischer, MD, and Belinda Hsi Dickie, MD, of Colorectal Surgery. The goal of this clinic is to evaluate and treat children with complex colorectal and motility disorders such as Hirschprung's disease and severe idiopathic chronic constipation and improve patient outcomes through standardization of practice and clinical research. Future areas of expansion include gastric pacing for refractory gastroparesis and sacral nerve stimulation for intractable severe idiopathic chronic constipation.

Digestive Health Center: A catalyst for research on digestive disease

The Digestive Health Center (DHC) directed by Jorge Bezerra, MD, and managed by Cynthia Wetzel, PhD, is one of only 17 Silvio O. Conte Digestive Diseases Research Core Centers in the U.S., and the only one dedicated to pediatric diseases. The center seeks to improve diagnosis, treatments and outcomes for chronic liver disease, inflammatory and diarrheal diseases and obesity. The DHC catalyzes studies on pediatric digestive diseases by enabling investigators to have timely access to state-of-the-art technologies at four Cores: Integrative Morphology, Gene and Protein Expression, Bioinformatics, and Pluripotent Stem Cell and Organoid Cores. With 101 investigators, the DHC contributes to the research goals of faculty from 21 divisions in the Department of Pediatrics and nine other departments of the University of Cincinnati, College of Medicine. This year, we welcomed five new center investigators; collectively, DHC investigators have \$35.6 million in extramural research funds. Our successful Pilot and Feasibility Program also distributed \$1.3 million among 32 junior investigators since 2007. These investigators have since attracted \$25.4 million in extramural grant funding. In addition to an outstanding record of publications with 176 peer-reviewed articles during the past 12 months, the following Center investigators received national and international recognition for their clinical, research, and educational accomplishments:

- Mitchell Cohen, MD, received the Shwachman Award of the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition and was elected to the American Association of Physicians.
- Gurjit Hershy, MD, PhD, and Sing-Sing Way, MD, were elected to the American Society for Clinical Investigation.
- Alexander Miethke, MD, received a Travel Award from American Society for Pediatric Gastroenterology, Hepatology and Nutrition and European Society for Pediatric Gastroenterology, Hepatology and Nutrition.
- Marc Rothenberg, MD, PhD, was named a Fellow of the American Association of the Advancement of Science.
- Rohit Kohli, MBBS, and Jessica Woo, MHSA, PhD, were selected to the Society for Pediatric Research.

#### The Outpatient Liver Disease Program

The Outpatient Liver Disease Program provides comprehensive care for children with liver diseases. Staffed by seven pediatric hepatologists, the Program serves a national and international referral population via a comprehensive evaluation of all medical and surgical aspects of liver disease. The evaluation includes a full spectrum of metabolic analysis, inflammatory processes, and sequencing techniques to diagnose mutations that cause clinical phenotypes. It is multidisciplinary, with timely consultation with surgeons, pathologists, radiologists, and nutritionists with expertise in pediatric liver disease. This coordinated approach enables a thorough evaluation of the impact of the illness on the child's well being. For children with advanced stages of liver disease, evaluation for liver transplantation and close follow-up minimize complications, improve post-transplant course, and optimizes outcomes.

Recognizing that research is critical to improvement in child care, the Clinic Staff leads multi-center studies sponsored by the National Institutes of Health to understand mechanisms of pediatric liver disease, to develop new diagnostic tests, and to perform clinical trials. Ongoing projects include: 1) the development of the *LiverChip* to diagnose genetic mutations, 2) mitochondrial and immunologic diseases as causes of liver failure, 3) causes and new treatments for biliary atresia, 4) biomarkers and new therapies for fatty liver disease, 5) biomarkers of fibrosis, and 6) new therapies for bile acid disorders, 7) new treatments for viral hepatitis. The clinical and research programs create an outstanding environment for the training of future leaders in the field via a fellowship-training program in Advanced and Transplant Hepatology.

Dr. Bezerra and investigators in the Pediatric Liver Care Center completed a clinical trial for children with biliary atresia and discovered a novel cellular crosstalk that repairs the epithelium of injured bile ducts. Biliary

atresia is a disease that typically progresses to end-stage cirrhosis, and patients require liver transplantation for long-term survival. Despite the limited understanding of pathogenesis of disease, steroids have been widely used to improve the surgical outcome for biliary atresia. To conclusively examine whether this is an effective treatment, Dr. Bezerra led a multi-center study funded by the National Institutes of Health. The study found that steroid treatment did not offer advantage over placebo, as demonstrated by no improvement in bile drainage or transplant-free survival. In addition to the lack of benefit, the use of steroids was associated with an increased risk for post-operative complications. Based on the impact of the results to clinical practice, the study was a featured presentation at the annual meeting of the American Association for Studies of Liver Disease (Boston, November 2013) and was published in the prestigious Journal of the American Medical Association (*JAMA*) in May 2014.

To understand why steroids do not improve surgical and clinical outcomes, Dr. Bezerra, Dr. Shivakumar, and collaborators performed studies in liver biopsy samples obtained at the time of diagnosis and found molecular profiles specific for biliary atresia. One of the molecular signatures clearly differentiates biliary atresia from other types of liver disease (published in the *Journal of Hepatology*), and may enable the design of new treatments that take into account the biological makeup of the patient. Another signature showed an unexpected increase in the cytokine interleukin-33 (IL-33). Most notably, the administration of this cytokine into newborn mice with experimental biliary atresia healed the lining of injured ducts and allowed for growth of extrahepatic bile ducts (published in the *Journal of Clinical Investigation*). These findings have major implications for potential new therapies for biliary atresia and for the future engineering of bile ducts.

#### Schubert-Martin IBD Center

More than 700 patients with IBD are seen in the division of Gastroenterology, Hepatology and Nutrition and the IBD Center. Close to 100 new patients are diagnosed annually and close to 90 second opinion patients are seen by the physicians of the Schubert-Martin Pediatric IBD Center from more than 25 states and abroad. These numbers reflect a 33% increase in total patient volume, and a 347% increase in second opinions over the last five years. The Center is an integral and leading participant in collaborative consortia like ImproveCareNow, and Crohn's and Colitis Foundation's PRO-KIDS. This role is reflected in superior outcomes for our patients with more than 80% of IBD patients within the center being in remission, 64 % in sustained remission, and 84% having a good quality of life. These outcome measures are shared transparently on the center's website.

Our Annual IBD Family Education Day, co-hosted by local chapter of Crohn's and Colitis Foundation continues to be one of the largest educational events of its kind in the country. A rejuvenated and energized Parent Advisory Board has been established to partner with center providers and identify priority areas for improvement, education, increased awareness and community involvement with an active Facebook page. Physicians within the center continue to develop and lead basic, translational and clinical research in identifying key etiopathogenic mechanisms for inflammatory bowel diseases, minimally invasive biomarkers for predicting disease flares and remission, development of mobile phone apps for patient engagement and self management, transition of patients to adult providers, and pilot testing of eVisits. Collaborations within the institution with the Anderson Center for Health System Excellence, Behavioral Medicine and Adherence Center, Pediatric Surgery, Allergy and Immunology, Adolescent Medicine, and Radiology continue to make significant contributions to finding a cure as well as improving outcomes and self-management skills for children suffering from IBD

#### Cincinnati Center for Eosinophillic Disorders

The Cincinnati Center for Eosinophilic Disorders is a well-established and recognized multidisciplinary referral

center for evaluation and treatment of eosinophilic gastrointestinal disorders in children. It is comprised of clinicians and physicians from the Divisions of Gastroenterology, Allergy, Immunology, Pathology and Behavioral Medicine. We are supported by experienced nurses, dieticians, and social worker. We evaluate more than 100 new patients per year, most of whom are referred from outside the local catchment area.

Most of our patients agree to participate in our clinical and basic science research programs. Our clinical research has included important studies of both dietary and pharmacologic management of eosinophilic esophagitis (EoE). Dr. Rothenberg's lab has been responsible for many of the seminal investigations into the genetic and immunologic underpinnings of the disease, and has a substantial biorepository of tissue and blood for ongoing studies.

As a direct result of those studies, a team of Researchers from the Divisions of Gastroenterology and Allergy and Immunology reported a key paper (Wen, et al; Molecular diagnosis of eosinophilic esophagitis by gene expression profiling. *Gastroenterology*. 2013 Dec;145(6):1289-99) focused on developing a molecular diagnostic panel for eosinophilic esophagitis (EoE). The investigators have translated their prior finding, concerning the EoE transcriptome, to a reliable test that can be performed with fresh biopsy tissue or with formalin fixed paraffin embedded tissue. They show that the test, referred to as the EoE Diagnostic Panel (EDP), is accurate and reliable in distinguishing EoE from control biopsies including patients with reflux disease, can quantitatively measure the degree of disease activity, identify patients exposed to topical glucocorticoids and can be done within hours after biopsy procurement. This tested has been recently licensed to Diagnovus, LLC and is now commercially available as Enguage™.

We are collaborating with Endocrinology (Drs. Backlejauw and Golekoh) and currently enrolling patients in the first prospective assessment of adrenal axis function in children who take steroids chronically for Eosinophilic Esophagitis.

In addition, we started enrollment in the first trial to look at treating EoE with losartan, a novel concept based on its impact on transforming growth factor beta, which is a major contributor to the disease and its complications.

We hosted a conference last fall focused on current concepts in EoE, supported by CURED (a patient advocacy and research fundraising organization). The conference included lectures on clinical and research aspects of eosinophilic disease for both a CME course and subsequent parent/patient conference.

## Interdisciplinary Feeding Team (IFT)

This multi-disciplinary team provides comprehensive evaluation of children with swallowing/feeding disorders. It includes members from gastroenterology, otolaryngology, human genetics, speech therapy, occupational therapy, social work, and nutrition. Doctors Scott Pentiuk and Vincent Mukkada serve as the pediatric gastroenterologists on the team. The IFT continues to grow with over 320 new patients and 1200+ patient visits over the last year. The team also has extensive outpatient treatment programs including multi-disciplinary treatment sessions and Parent-Child Interaction Training for families. Current IFT research projects include the use and development of a pureed by G-tube diet, quality of life assessment of feeding therapies, methods to evaluate children with swallowing dysfunction, and the creation of a prospective database in order to track the effectiveness of therapies and patient outcomes. This year the Feeding Team also successfully completed a Quality Improvement project to decrease patient wait time during clinic visits.

#### Diarrhea and Malnutrition

Our mission is to improve the prevention and treatment of childhood diarrhea and undernutrition in low- and middle-income countries by implementing best practices and creating new knowledge through bench-to-

bedside research collaborations between Cincinnati Children's Hospital Medical Center and global partners. Drs. Cole, Huppert, Moore, and Saeed have established individual partnerships with investigators in Brazil, Ghana, Nigeria and Pakistan focused on micronutrient deficiencies (zinc and iron), undernutrition, diarrheal diseases, and environmental enteropathy.

Dr. Moore's laboratory is engaged in understanding and reversing the "vicious cycle" of malnutrition and enteric infections in developing countries. Current areas of focus include: 1) IMAGINE (Interventions and Mechanisms of Alanyl-Glutamine for Inflammation, Nutrition, and Enteropathy), a clinical dose-response trial of alanyl-glutamine supplementation in 140 Brazilian children with environmental enteropathy (Fogarty International Center (FIC)/NIH, The Bill & Melinda Gates Foundation (BMGF)), 2) Human biomarkers of environmental enteropathy (BMGF), 3) Novel mouse models of environmental enteropathy (FIC/NIH, BMGF), and 4) Mouse enteroid models of intestinal epithelial homeostasis (DARPA).

In a related program, Dr. Cohen completed phase I studies on a new candidate vaccine with potential efficacy against enterotoxigenic *E. coli* and and \$4M pivotal phase III study of a candidate cholera vaccine.

## Pediatric Liver Transplantation

The Pediatric Liver Transplant Program, led by Kathleen Campbell, MD, (medical director) continues its' mission of advancing the care of liver transplant recipients by improving the health care delivery system, providing unparalleled clinical care, and addressing gaps in knowledge through patient-based and basic laboratory research. Our program remains one of the largest pediatric liver transplant programs in the country, with clinical outcomes at or above the national average. In addition to providing care for the most common pediatric liver disorders leading to transplantation, we are able to leverage institutional strengths in other Divisions to provide care, and the best outcomes available, to a number of patients with rare diseases and extremely complex needs, including those with advanced liver tumors and patients with primary immune defects. Clinically, the Cincinnati Children's Hospital Medical Center Pediatric Liver Transplant Program has maintained its' overall transplant volume and has continued to build expertise in transplantation for primary hepatic tumors.

Since 2007, we have performed more pediatric liver transplants for primary hepatic tumors than any other program in the United States. Members of the Liver Transplant Program continue to act as leaders in national quality improvement efforts and multicenter clinical and translational research studies. These include: the pediatric Acute Liver Failure Study Group (PALF), Medication Adherence in Children who had a Liver Transplant (MALT), Immunosuppression Withdrawal for Stable Pediatric Liver Transplant Recipients (iWITH), the Studies in Pediatric Liver Transplantation (SPLIT) quality improvement community and clinical registry, the Clinical Trials in Organ Transplantation in Children (CTOT-C) project, and Impact of Everolimus on Renal Function in Pediatric Liver Transplantation.

## Intestinal Rehabilitation Program

The Intestinal Rehabilitation Program continues in its mission to provide the best possible care for children at risk and with intestinal failure through innovation. We are the lead center in a 17 center pediatric clinical trial, evaluating the safety and efficacy of Teduglutide (Gattex®) for use in children ages 1-17 years dependent on parenteral nutrition. Teduglutide is a glucagon-like protein 2 (GLP-2) analogue which was recently approved for use in adults on long term parenteral nutrition. This demonstrates our commitment to improving the patient experience and optimizing outcome. Our NIH/Emmaus Inc. funded multicenter clinical trial evaluating the safety and efficacy of enteral glutamine in the infants with short bowel syndrome continues to enroll patients. We also continue to enroll patients with persistent intestinal failure associated liver disease in an efficacy and safety trial using fish-oil derived lipid (Omegaven®) to prevent chronic liver disease and liver

failure in this population.

We are experiencing considerable growth, and our program continues to be one of the largest intestinal rehabilitation programs nationally. Drs. Cole and Kocoshis in collaboration with surgery (Dr. Michael Helmrath) and neonatology (Dr. Andrew South) managed patients from 24 states and 6 countries in the past year. The multidisciplinary model to standardize care, facilitate research and implement therapy among the three disciplines (gastroenterology, neonatology and surgery) providing care to infants and children with intestinal failure continues to be successful with our patients experiencing one of the highest rates of survival without significant liver disease (as measured by cholestasis) nationally. The incidence of outpatient acquired central line bloodstream infections in this population is also one of the lowest rates nationally.

## Significant Publications

Ryan KK, Tremaroli V, Clemmensen C, Kovatcheva-Datchary P, Myronovych A, Karns R, Wilson-Perez HE, Sandoval DA, **Kohli R**, Backhed F, Seeley RJ. FXR is a molecular target for the effects of vertical sleeve gastrectomy. *Nature* 2014 8;509(7499):183-8.

Weight loss surgeries such as vertical sleeve gastrectomy (VSG) are associated with sustained weight loss and reduced overall mortality in patients. Weight-loss and metabolic outcomes after VSG is in part dependent on a metabolic signaling cascade (FXR) triggered by increased circulating bile acids. These results were reported in Nature by a team of researchers including Dr. Rohit Kohli. Bariatric surgery has become an important therapeutic option for morbid obesity and nonalcoholic fatty liver disease. Still, the invasive nature of bariatric surgery – which involves altering the gastrointestinal anatomy of patients – also comes with significant medical risks. This paper used mice lacking the bile acid target molecule FXR and report that it is a critical molecular target for the success of VSG. Thus, highlighting the fact the FXR and bile acid signaling could be potential therapeutic targets for replicating the effects of bariatric procedures without actual surgery.

**Bezerra JA**, Spino C, Magee JC, Shneider BL, Rosenthal P, Wang KS, Erlichman J, Haber B, Hertel PM, Karpen SJ, Kerkar N, Loomes KM, Molleston JP, Murray KF, Romero R, Schwarz KB, Shepherd R, Suchy FJ, Turmelle YP, Whitington PF, Moore J, Sherker AH, Robuck PR, Sokol RJ. Use of corticosteroids after hepatoportoenterostomy for bile drainage in infants with biliary atresia: the START randomized clinical trial. *JAMA*. 2014 7;311(17):1750-9.

Biliary atresia is a disease that typically progresses to end-stage cirrhosis, and patients require liver transplantation for long-term survival. Despite the limited understanding of pathogenesis of disease, steroids have been widely used to improve the surgical outcome for biliary atresia. To conclusively examine whether this is an effective treatment, Dr. Bezerra led a multi-center study funded by the National Institute of Health. The study found that steroid treatment did not offer advantage over placebo, as demonstrated by no improvement in bile drainage or transplant-free survival. In addition to the lack of benefit, the use of steroids was associated with an increased risk for post-operative complications. Based on the impact of the results to clinical practice, the study was a featured presentation at the annual meeting of the American Association for Studies of Liver Disease (Boston, November 2013) and was published in JAMA in May 2014.

Gevers D, Kugathasan S, **Denson LA**, Vazquez-Baeza Y, Van Treuren W, Ren B, Schwager E, Knights D, Song SJ, Yassour M, Morgan XC, Kostic AD, Luo C, Gonzalez A, McDonald D, **Haberman Y**, Walters T, Baker S, Rosh J, Stephens M, Heyman M, Markowitz J, Baldassano R, Griffiths A, Sylvester F, Mack D, Kim S, Crandall W, Hyams J, Huttenhower C, Knight R, Xavier RJ. The treatment-naive microbiome in new-onset Crohn's disease. *Cell Host Microbe*. 2014 12;15(3):382-92.

This multi-center collaborative effort represents the largest study to date to define the mucosal microbiome in

children with Crohn Disease at diagnosis, and pediatric controls without gastrointestinal disorders. A composite description of the mucosal microbial community, the microbial dysbiosis index, was defined, and shown to be associated with clinical disease severity. Remarkably, the rectal microbial community distinguished children with Crohn Disease from healthy controls, regardless of the degree of local inflammation. This study has implications for targeted microbial therapy to reduce symptoms, and novel diagnostics based upon the rectal microbial profile.

Wen T, Stucke EM, Grotjan TM, Kemme KA, Abonia JP, **Putnam PE, Franciosi JP, Garza JM, Kaul A**, King EC, Collins MH, Kushner JP, Rothenberg ME. Molecular diagnosis of eosinophilic esophagitis by gene expression profiling. *Gastroenterology*. 2013 145(6):1289-99.

The investigators have translated their prior finding, concerning the EoE transcriptome, to a reliable test that can be performed with fresh biopsy tissue or with formalin fixed paraffin embedded tissue. They show that the test, referred to as the EoE Diagnostic Panel (EDP), is accurate and reliable in distinguishing EoE from control biopsies including patients with reflux disease, can quantitatively measure the degree of disease activity, identify patients exposed to topical glucocorticoids and can be done within hours after biopsy procurement. This tested has been recently licensed to Diagnovus, LLC and is now commercially available as Enguage<sup>™</sup>.

**Xanthakos SA**, Podberesky DJ, Serai SD, Miles L, King EC, **Balistreri WF, Kohli R**. Use of magnetic resonance elastography to assess hepatic fibrosis in children with chronic liver disease. *J Pediatr*. 2014 164(1):186-8.

In 2014, we demonstrated that magnetic resonance elastrogaphy (MRE) is both feasible and accurate in detecting significant hepatic fibrosis in a cohort of 35 children aged 4 to 20 years with chronic liver disease. This non-invasive technique measures liver tissue stiffness without the need for intravenous contrast and takes only a few minutes. It has proven especially useful for children who have non-alcoholic fatty liver disease (NAFLD), as many of these patients are severely obese and ultrasound-based elastography methods are less reliable in obese patients. We now plan to validate our findings in a larger prospective clinical trial to evaluate whether MRE can reduce dependence on percutaneous needle liver biopsies, currently the standard practice for evaluating liver fibrosis.

## **Division Publications**

- Abonia JP, Wen T, Stucke EM, Grotjan T, Griffith MS, Kemme KA, Collins MH, Putnam PE, Franciosi JP, von Tiehl KF, Tinkle BT, Marsolo KA, Martin LJ, Ware SM, Rothenberg ME. High prevalence of eosinophilic esophagitis in patients with inherited connective tissue disorders. *J Allergy Clin Immunol.* 2013; 132:378-86.
- 2. Abu-El-Haija M, Lin TK, Palermo J. Update to the management of pediatric acute pancreatitis: highlighting areas in need of research. *J Pediatr Gastroenterol Nutr.* 2014; 58:689-93.
- Abu-El-Haija M, Schultz J, Rahhal RM. Effects of 70% ethanol locks on rates of central line infection, thrombosis, breakage, and replacement in pediatric intestinal failure. *J Pediatr Gastroenterol Nutr*. 2014; 58:703-8.
- Alonso EM, Martz K, Wang D, Yi MS, Neighbors K, Varni JW, Bucuvalas JC, Studies of Pediatric Liver Transplantation Functional Outcomes G. Factors predicting health-related quality of life in pediatric liver transplant recipients in the functional outcomes group. *Pediatr Transplant*. 2013; 17:605-11.
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## Faculty, Staff, and Trainees

#### **Faculty Members**

#### Mitchell B Cohen, MD, Professor

**Leadership** Gastroenterology Endowed Chair; Vice-Chair of Pediatrics for Clinical Affairs; Director, Division of Gastroenterology, Hepatology and Nutrition; Associate Director, Digestive Health Center

Research Interests Diarrheal Diseases

Maisam Abu-El-Haija, MD, Assistant Professor

#### Research Interests Pancreatitis and Cystic Fibrosis

## William F Balistreri, MD, Professor

**Leadership** Dorothy M.M. Kersten Endowed Chair; Director Emeritus, Pediatric Liver Care Center; Medical Director Emeritus, Liver Transplantation; Program Director, Advanced Hepatology Fellowship; Editor, Journal of Pediatrics

## Research Interests Chronic Liver Disease

## Jorge A Bezerra, MD, Professor

**Leadership** William and Rebecca Balistreri Chair in Pediatric Hepatology; Director of Research, Division of Gastroenterology, Hepatology and Nutrition; Director, Biliary Atresia Center; Director, Digestive Health Center; Medical Director, Pediatric Liver Care Center; Director, Trustee and Procter Scholar Award Program

## Research Interests Biliary Atresia and Chronic Liver Disease

## John C Bucuvalas, MD, Professor

**Leadership** Endowed Chair in Pediatric Transplant Hepatology; Director, Integrated Solid Organ Transplant Center; Editorial Board, Hepatology; Associate Editor, Clinical Liver Disease; Associate Medical Director, Pediatric Liver Care Center

Research Interests Liver Failure and Liver Transplantation

## Kathleen M Campbell, MD, Associate Professor

Leadership Medical Director, Pediatric Liver Transplant Program

**Research Interests** Pediatric Liver Transplantation, Post-transplant Renal Dysfunction, Liver Disease Associated With Congenital Heart Disease

## Conrad R Cole, MD, Associate Professor

Leadership Medical Director, Intestinal Rehabilitation Program/Intestinal Care Center

Research Interests Intestinal Failure

## Lee A Denson, MD, Professor

Leadership M. Susan Moyer Chair in Pediatric IBD; Director, Schubert-Martin Pediatric IBD Center

Research Interests Inflammatory Bowel Diseases

## Dana "Chelly" Dykes, MD, Assistant Professor Research Interests Inflammatory Bowel Disease, Clinical and Quality Improvement Research

## Michael K Farrell, MD, Professor

Leadership Chief of Staff

Research Interests Nutrition

## Shekhar Gandhi, PhD, Professor

Research Interests Liver Transplantation Immunology, Liver Regeneration, Hepatic Stellate Cells

## Xiaonan Han, PhD, Assistant Professor

Research Interests Inflammatory Bowel Diseases

## James E Heubi, MD, Professor

**Leadership** Associate Chair for Clinical Investigation of Pediatrics; Associate Dean for Clinical and Translational Research; Co-Director, Center of Clinical and Translational Science & Training

## Research Interests Chronic Liver Disease

#### Stacey Huppert, PhD, Associate Professor

#### Research Interests Hepatic Development and Regeneration

#### Ajay Kaul, MD, Professor

Leadership Director, Neurogastroenterology and Motility Disorders Program; Director, GI Operations at Liberty Campus

Research Interests Intestinal Motility Disorders

#### Samuel A Kocoshis, MD, Professor

Leadership Medical Director, Pediatric Nutritional and Intestinal Care Center; Medical Director, Small Bowel Transplantation Program

#### Research Interests Intestinal Failure and Intestinal Transplantation

#### Rohit Kohli, MD, Associate Professor

Leadership Medical Director, Complex Surgery and Transplant Inpatient Unit; Co-Director, Steatohepatitis Center; Associate Medical Director, Liver Transplant Program

Research Interests Non-alcoholic Steatohepatitis

Mike A Leonis, MD, PhD, Associate Professor

Leadership Director, GI Fellowship Program

Research Interests Liver Failure and Liver Transplantation; Liver Tumors

#### Tom K Lin, MD, Assistant Professor

**Research Interests** Pancreatitis and Other Pancreas Disorders, Pancreaticobiliary Disorders, Therapeutic Endoscopy

Alexander Miethke, MD, Assistant Professor

Research Interests Biliary Atresia and Primary Sclerosing Cholangitis

## Phillip Minar, MD, Assistant Professor

Research Interests Inflammatory Bowel Disease

#### Sean Moore, MD, Assistant Professor

Research Interests Diarrheal Diseases and International Health

#### Vincent Mukkada, MD, Assistant Professor

Research Interests Eosinophilic Gastrointestinal Disorders and Pediatric Feeding Disorders

## Joseph Palermo, MD, PhD, Assistant Professor

Research Interests Disorders of the Bile Ducts

## Scott Pentiuk, MD, Assistant Professor

**Leadership** Associate Clinical Director, GI; Associate Medical Director, A4S; Associate Director, Fellowship Program

## Research Interests Feeding Disorders; Medical Education

## Philip E Putnam, MD, Professor

Leadership Director, Endoscopy Services; Medical Director, Cincinnati Center for Eosinophilic Disorders

Research Interests Eosinophilic Gastrointestinal Disorders

## Michael Rosen, MD, MSCI, Assistant Professor

Research Interests Inflammatory Bowel Disease, Mucosal Immunology

#### Shehzad A Saeed, MD, Professor

Leadership Clinical Director, GI Service; Medical Director, A4S; Clinical Director of the Schubert-Martin IBD Center

Research Interests Inflammatory Bowel Disease

Pranav Shivakumar, PhD, Assistant Professor Research Interests Biliary Atresia

## Noah Shroyer, PhD, Adjunct

Research Interests Intestinal Development

#### Kris Steinbrecher, PhD, Assistant Professor Research Interests Diarrheal diseases; Inflammatory Bowel Diseases

#### Cynthia C Wetzel, PhD, Assistant Professor

Leadership Program Manager, Digestive Health Center; Program Manager, Trustee and Procter Scholar Award Program

Research Interests Research Administration

#### Stavra Xanthakos, MD, Associate Professor

**Leadership** Medical Director, Surgical Weight Loss Program for Teens; Co-Director, Steatohepatitis Center; Physician Leader for the Clinical Research Coordinators; Associate Director, Fellowship Program

Research Interests Obesity; Non-alcoholic Steatohepatitis

## Chunyue Yin, PhD, Assistant Professor Research Interests Liver Biology

Joint Appointment Faculty Members

Lin Fei, PhD, Associate Professor (Biostatistics and Epidemiology)

## Anjaparavanda Naren, PhD, Professor (Pulmonary)

#### **Clinical Staff Members**

• Kristin Bramlage, MD

## Trainees

- Monique Choquette, MD, PL-7, Cincinnati Children's Hospital Medical Center
- Ashish Dhawan, MD, PL-4, B.J. Medical College, University of Pune
- David Galloway, MD, PL-5, Phoenix Children's Hospital Maricopa Medical Center
- Yael Haberman, MD, PL-6, Tel Hashomer Medical Center, Tel Hashomer, Ramat Gan, Israel
- Einar Hafberg, MD, PL-4, University of Iceland
- Karla Hicks, MD, PL-5, Cincinnati Children's Hospital
- Alexanderia (Ali) Menchise, MD, PL-6, University of South Florida College of Medice, Tampa
- Ethan Mezoff, MD, PL-5, Children's National Medical Center
- Tatsuki Mizuochi, PhD, PL-14, Nagasaki University School of Medicine, Japan
- Andriy Myronovych, MD, PhD, PL-3, University of Tsukuba, Tsukuba, Ibaraki, Japan
- Stephanie Oliveira, MD, PL-4, Universidade Federal Do Ceara Faculdade
- James Squires, MD, PL-6, Cincinnati Children's Hospital Medical Center
- Flora Szabo, MD, PL-5, University of Kentucky

- Amy Taylor, MD, PL-4, Northwestern Un, Feinberg School of Medicine
- Sandra Wright, MD, PL-5, University of Alabama at Birmingham
- Changwen Zhang, PhD, PL-1, Fudan University, China

## **Division Collaboration**

Computational science and systems biology in Pediatric Digestive Disease: *Bioinformatics Core* of The Digestive Health Center (Jorge A. Bezerra, MD)

Biomedical Informatics » Bruce Aronow, PhD and Anil Jegga, DVM, MRes

Molecular phenotypes of biliary atresia (Jorge A. Bezerra, MD)

Biomedical Informatics » Bruce Aronow, PhD and Anil Jegga, DVM, MRes

Gene interaction as modifiers of chronic liver diseases in children (Jorge A. Bezerra, MD)

Biomedical Informatics » Bruce Aronow, PhD and Anil Jegga, DVM, MRes

Embryogenesis and tissue organoids in Pediatric Digestive Disease: The Digestive Health Center (Jorge A. Bezerra, MD)

Developmental Biology » S. Steven Potter, MD, James Wells, PhD, and Aaron Zorn, PhD

Development and function of the neonatal biliary system (Jorge A. Bezerra, MD) Developmental Biology » S. Steven Potter, MD, James Wells, PhD, and Aaron Zorn, PhD

Development and function of liver organoids from iPSCs (Jorge A. Bezerra, MD) Developmental Biology » S. Steven Potter, MD, James Wells, PhD, and Aaron Zorn, PhD

Pathobiology of Pediatric Digestive Disease: *Integrative Morphology Core* of The Digestive Health Center (Jorge A. Bezerra, MD)

Pathology » Kevin Bove, MD, Kumar Shanmukhappa, DVM, Rachel Sheridan, MD, and David P. Witte, MD

Molecular staging of liver injury in biliary atresia (Jorge A. Bezerra, MD) **Pathology** » Kevin Bove, MD, Kumar Shanmukhappa, DVM, Rachel Sheridan, MD, and David P. Witte, MD

The neonatal immune system and pathogenesis of biliary atresia (Jorge A. Bezerra, MD) Immunobiology » Claire Chougnet, PhD

Mechanisms of auto-immune liver disease (Jorge A. Bezerra, MD) Immunobiology » Claire Chougnet, PhD

Mechanisms of virus-induced biliary atresia (Jorge A. Bezerra, MD) **Pediatric Surgery** » Jaimie Nathan, MD and Greg Tiao, MD

Gut-biliary axis and pathogenesis of cholangiopathies (Jorge A. Bezerra, MD) **Pediatric Surgery** » Jaimie Nathan, MD and Greg Tiao, MD To define strategies for CMV prevention strategies for at-risk pediatric liver transplant recipients as a foundation for future comparative effectiveness studies within SPLIT. (John Bucuvalas, MD)

Infectious Disease » Lara Danziger, MD

To ensure appropriate immunization for transplant candidates and recipients based on existing guidelines and best evidence. (John Bucuvalas, MD)

Infectious Disease » Lara Danziger, MD

A NIH funded multi-center study to define reliable markers to detect nonadherence: this will open the way to research about predictors for nonadherence and interventions to improve it (John Bucuvalas, MD)

## Behavioral Medicine » Denny Drotar, PhD

Conduct pilot of a standard approach to assess risk for failure of self-management in solid organ transplant candidates and recipients, and target pilot interventions to improve self-management preemptively based on risk assessment. (John Bucuvalas, MD)

Behavioral Medicine » Sandra Cortina, PhD

Multi-center NIH funded study to Assess proposed viral (EBV) and immunologic biomarkers associated with development and progression of PTLD after transplantation. (John Bucuvalas, MD)

Heart Institute » Clifford Chin, MD

To decrease overall LOS and ICU LOS following liver transplantation by identifying and subsequently developing individualized pretransplant and perioperative care plans for liver transplant patients. (John Bucuvalas, MD)

Heart Institute » Angela Lorts, MD

A pilot study focusing designed to improve conflict resolution, trust and accountability among the non-physician members of the liver transplant interprofessional health care team. (John Bucuvalas, MD)

Human Resources » Carl Allison

Safety and Immunogenicity of a Single Oral Dose of Recombinant Double-Mutant Heat-Labile Toxin (dmLT) Derived from Enterotoxigenic Escherichia coli (ETEC) (Mitchell B. Cohen, MD)

Infectious Diseases » David Bernstein, MD and Rebecca C. Brady, MD

A Phase III Randomized, Double-Blind, Placebo-Controlled, Efficacy Trial of a Single Dose of Live Oral Cholera Vaccine Candidate, PXVX0200 CVD 103-HgR Strain, in Preventing Cholera following Challenge with Vibrio cholerae O1 El Tor Inaba 10 Days or 3 Months after Vaccination (Mitchell B. Cohen, MD)

Infectious Diseases » David Bernstein, MD and Rebecca C. Brady, MD

The importance of addressing anxiety in youth with functional abdominal pain (Mitchell B. Cohen, MD)

**Behavioral Medicine and Clinical Psychology** » Natoshia Raishevich Cunningham, PhD, Anne Lynch-Jordan, PhD, and Susmita Kashikar-Zuck, PhD

LAUNCH Study (Mitchell B. Cohen, MD)

#### Behavioral Medicine and Clinical Psychology » Lori Stark, PhD

Translational and outcomes research in patients with and at risk for intestinal failure (Conrad R. Cole, MD, Samuel A. Kocoshis, MD)

Section of Neonatology, Perinatal and Pulmonary Biology » Andrew P. South, MD Pediatric General and Thoracic Surgery » Michael A. Helmrath, MD, MS

A Pharmacokinetic, Safety, and Pharmacodynamic Study of Teduglutide in Pediatric Subjects With Short Bowel Syndrome (Conrad R. Cole, MD, Samuel A. Kocoshis, MD)

Pediatric General and Thoracic Surgery » Michael A. Helmrath MD

Efficacy of enteral glutamine in pediatric SBS (Conrad R. Cole, MD, Samuel A. Kocoshis, MD) **Biostatistics and Epidemiology** » Eileen C. King, PhD **Pediatric General and Thoracic Surgery** » Michael A. Helmrath, MD **Section of Neonatology, Perinatal and Pulmonary Biology** » Andrew P. South, MD

Radiologic changes in patients on prolonged parenteral nutrition receiving suboptimal micronutrients (Conrad R. Cole, MD)

Radiology » Alan E. Oestreich, MD

Shared Decision Making in Pediatric Chronic Conditions: Biologics in IBD and JIA (Lee A Denson, MD) **Adolescent and Transition Medicine** » Maria Britto, MD and Ellen Lipstein, MD

Eosinophil:M2 macrophage:CCL11 axis in experimental colitis and pediatric corticosteroid-dependent UC. (Lee A Denson, MD)

Allergy and Immunology » Simon P. Hogan, PhD

Telehealth Enhancement of Adherence to Medication in Pediatric IBD (TEAM Study) (Lee A Denson, MD, Shehzad A. Saeed, MD)

Behavioral Medicine and Clinical Psychology » Kevin A. Hommel, PhD

Predicting Response to Standardized Pediatric Colitis Therapy: The PROTECT Study (Lee A Denson, MD) Behavioral Medicine and Clinical Psychology » Kevin A. Hommel, PhD

Risk stratification and identification of immunogenetic and microbial markers of rapid disease progression in children with Crohn's disease. (Lee A Denson, MD)

Biomedical Informatics » Bruce Aronow, PhD

Ileal transcriptome analysis as a diagnostic and prognostic tool in Inflammatory Bowel Disease (Lee A Denson, MD)

Biomedical Informatics » Bruce Aronow, PhD

Risk stratification and identification of immunogenetic and microbial markers of rapid disease progression in children with Crohn's disease. (Lee A Denson, MD)

#### Biostatistics and Epidemiology » Mi-Ok Kim, PhD

Innate Dysregulation and Growth Failure in Pediatric Crohn's Disease (Lee A Denson, MD) **Endocrinology** » David Klein, MD

Human IgG-Mediated Anaphylaxis (Lee A Denson, MD) Immunobiology » Fred Finkelman, MD

Predicting Response to Standardized Pediatric Colitis Therapy: The PROTECT Study (Lee A Denson, MD) **Pathology and Laboratory Medicine** » Margaret Collins, MD

Risk stratification and identification of immunogenetic and microbial markers of rapid disease progression in children with Crohn's disease. (Lee A Denson, MD)

Section of Neonatology, Perinatal and Pulmonary Biology » Bruce C. Trapnell, MD

Causes and Consequences of Neutrophil Dysfunction in Early Onset Crohn Disease (Lee A Denson, MD)

Section of Neonatology, Perinatal and Pulmonary Biology » Bruce C. Trapnell, MD

Risk stratification and identification of immunogenetic and microbial markers of rapid disease progression in children with Crohn's disease. (Lee A Denson, MD)

Radiology » Dan Podberesky, MD, Alex Towbin, MD, and Dan Wallihan, MD

Regulation of Adult Stem Cell Homeostatic Response to Infectious and Inflammatory Injury (Lee Denson, MD, Xiaonan Han, PhD, Noah Shroyer, PhD)

**Developmental Biology** » Christopher N. Mayhew, PhD and James M. Wells, PhD **Infectious Diseases** » David Haslam, MD and Sing Sing Way, MD **Pediatric Surgery** » Michael A. Helmrath, MD

Inborn Errors of Bile Acid Metabolism (James E. Heubi, MD) Mass Spectrometry Laboratory » Kenneth D Setchell, PhD

Studies of Bone Disease (James E. Heubi, MD) General and Community Pediatrics » Heidi J. Kalkwarf, PhD, RD

Impact of age and chronic cholestasis on cholangiocyte secretion (Stacey S. Huppert, PhD) **Pediatric General and Thoracic Surgery** » Gregory M. Tiao, MD **Pulmonary Medicine** » Anjaparavanda P. Naren, PhD

Transcriptional complexes governing hepatoblast cell fate decisions (Stacey S. Huppert, PhD) **Developmental Biology** » Aaron M. Zorn, PhD **Pediatric Urology** » Joo-Seop Park, PhD

Using mouse models to understand the cerebrovascular abnormalities associated with Alagille syndrome – developmental or stress induced? (Stacey S. Huppert, PhD)

Pediatric Interventional Neuroradiology » Todd Abruzzo, MD

Pediatric General and Thoracic Surgery » Sudhakar Vadivelu, DO

FIC1 disease modeling using induced pluripotent stem cells (Stacey S. Huppert, PhD, Alexander G. Miethke, MD) **Developmental Biology** » James M. Wells, PhD and Christopher N. Mayhew, PhD

Murine models of environmental enteropathy and effects of global and hepatobiliary-specific deletion of the polymeric immunoglobulin receptor (Stacey S. Huppert, PhD, Sean R. Moore, MD)

Allergy and Immunology » Simon P. Hogan, PhD

Hepatic Immune Activation in Pediatric Liver Disease (Jorge A. Bezerra, MD, Stacey S. Huppert, PhD, Alexander G. Miethke, MD)

**Pathology** » Kevin E. Bove, MD, Anita Gupta, MD, and Rachel Sheridan, MD **Pediatric Surgery** » Gregory M. Tiao, MD,

Mitochondrial ultrastructure changes in NASH (Rohit Kohli, MD, Stavra Xanthakos, MD) Pathology and Laboratory Medicine » Kevin Bove, MD

Bile acids in animal models of bariatric surgery (Rohit Kohli, MD) Pathology and Laboratory Medicine » Kevin Bove, MD

Hepatic histology in NASH animal models (Rohit Kohli, MD) Pathology and Laboratory Medicine » Lili Miles, MD

Coenzyme Q as a biomarker for NASH (Rohit Kohli, MD) Pathology and Laboratory Medicine » Michael Miles, PharmD

Developmental Outcome of Urea Cycle Defect Liver Transplant Recipients (Rohit Kohli, MD) Radiology » Marcia Kukreja, MD

The types of Inflammatory Bowel Disease (IBD) predispose to distinct clinical phenotypes of Primary Sclerosing Cholangitis (PSC) in children (Alexander Miethke, MD)

Pathology and Laboratory Medicine » Rachel Sheridan, MD Radiology » Daniel Wallihan, MD

Collaborating with Bradley Keller, PhD of Lumena Pharmaceutical, Inc to research Pharmacological inhibition of intestinal bile acid re-uptake changes bile composition and blocks progression of liver disease in a murine model of progressive familial intrahepatic cholestasis (PFIC) type 3. (Alexander Miethke, MD, Amy Taylor, MD)

**Pathology and Laboratory Medicine** » Kenneth Setchell, PhD, Wujuan Zhang, PhD, and Shiva Kumar Shanmukhappa BVSc, PhD, DACVP

Myeloid dendritic cells maintain Th17 lymphocyte responses during the obstructive phase of experimental biliary atresa. (Alexander Miethke, MD, Celine Silva-Lages, PhD)

Immunobiology » Claire Chougnet, PhD

Pathology and Laboratory Medicine » Shiva Kumar Shanmukhappa BVSc, PhD, DACVP Pediatric General and Thoracic Surgery » Sujit Mohanty, PhD and Gregory Tiao, MD

Heterozygosity for deleterious mutations in *Abcb4* is associated with a pro-inflammatory hepatic transcriptome predisposing neonatal mice to cholestatic liver injury (Jorge A Bezerra, MD, Alexandra Menchise, MD, Alexander Miethke, MD, Celine Silva-Lages, PhD, Julia Simmons)

Biomedical Informatics » Rebekah Karns, PhD

Pathology and Laboratory Medicine » Wujuan Zhang, PhD and Kenneth Setchell, PhD

Initiation of biliary injury in murine sclerosing cholangitis involves hepatic effector and regulatory lymphocytes (Alexandra Menchise, MD, Alexander Miethke, MD, Celine Silva-Lages, PhD, Julia Simmons)

Immunobiology » Claire Chougnet, PhD

Pathology and Laboratory Medicine » Shiva Kumar Shanmukhappa BVSc, PhD, DACVP

Targeted next-generation sequencing (ngs) reveals novel genotype and phenotype correlations for mitochondrial dna depletion syndromes in pediatric acute liver failure (alf). (Alexander Miethke, MD, Anna Peters, MD)

Human Genetics » Taosheng Huang, MD, PhD and C. Alexander Valencia, PhD

Pathology and Laboratory Medicine » Kevin Bove, MD and Rachel Sheridan, MD

Network dynamics of circadian rhythms, cell cycle, and DNA damage response in mouse enteroids.(Sean R Moore, MD)

Cellular and Molecular Physiology/Systems Biology » Christian Hong, PhD

Murine models of environmental enteropathy and effects on oral rotavirus vaccine immunogenicity (Sean R Moore, MD)

Infectious Diseases » Monica Malone McNeal, MS

Murine models of environmental enteropathy (Sean R. Moore, MD) Pediatric General and Thoracic Surgery » Michael A. Helmrath, MD

Twin and Family Risk from Environment and Epigenetics (FREE) Studies Reveal Strong Environmental and Weaker Genetic Cues That Explain High Heritability of Eosinophilic Esophagitis (Vincent Mukkada, MD)

**Biostatistics and Epidemiology** » Lisa Martin, PhD **Biomedical Informatics** » Eileen Alexander, MS, BSN, RN

Eileen Alexander's PhD Dissertation Committee (Vincent Mukkada, MD) **Biomedical Informatics** » Eileen Alexander, MS, BSN, RN

Stricture development in Eosinophilic Gastrointestinal Diseases (Vincent Mukkada, MD) **Pathology and Laboratory Medicine** » Margaret Collins, MD

New pilot therapeutic trial of losartan in patients with Eosinophilic Esophagitis (Vincent Mukkada, MD) Allergy and Immunology » Marc Rothenberg, MD, PhD and Pablo Abonia, MD

Therapeutic trial of oral viscous budesonide in Eosinophilic Esophagitis (Vincent Mukkada, MD) Allergy and Immunology » Marc Rothenberg, MD, PhD and Pablo Abonia, MD

Therapeutic trial of novel dietary therapy in Eosinophilic Esophagitis (Vincent Mukkada, MD)

Allergy and Immunology » Pablo Abonia, MD and Marc Rothenberg, MD, PhD

Consortium of Eosinophilic Gastrointestinal Disease Researchers (Vincent Mukkada, MD) **Allergy and Immunology** » Pablo Abonia, MD and Marc Rothenberg, MD, PhD **Biomedical Informatics** » Lin Fei, PhD and Eileen King, PhD **Pathology and Laboratory Medicine** » Margaret Collins MD

Comparative Effectiveness of Therapies for Eosinophilic Esophagitis (Vincent Mukkada, MD) **Allergy and Immunology** » Pablo Abonia, MD and Marc Rothenberg, MD, PhD **Biostatistics** » Lin Fei, PhD and Eileen King, PhD **Pathology** » Margaret Collins MD

Multidisciplinary evaluation and treatment of children and adults who have Eosinophilic Gastrointestinal Disorders (Vincent Mukkada, MD, Philip E. Putnam, MD)

Allergy and Immunology » Pablo Abonia, MD and Marc Rothenberg, MD, PhD Cardiology » Human Genetics » Derek Neilson, MD and Elizabeth Schorry, MD Neurology » Otolaryngology » Mike Rutter, MD Pathology » Margaret Collins MD Pediatric General and Thoracic Surgery » Rebeccah Brown, MD and Victor Garcia, MD Behavioral Medicine and Clinical Psychology » Nicole Zahka, PhD Rheumatology » Tracey Ting, MD

Evaluation and treatment of children who have complex airway disorders. (Vincent Mukkada, MD, Scott Pentiuk, MD, Philip E. Putnam, MD)

**ADSC Team (Aero Digestive Sleep Center)** » Alessandro dr Alarcon, MD, Daniel von Allmen, MD, R. Paul Boesch, DO, Robin T. Cotton, MD, Victor F. Garcia, MD, Thomas H. Inge, MD, PhD, Michael J. Rutter, MD, J. Paul Willging, MD, and Robert E. Wood, MD, PhD

**Interdisciplinary Feeding Team** » Alessandro dr Alarcon, MD, Daniel von Allmen, MD, Dan Benscoter, DO, Robin T. Cotton, MD, Victor F. Garcia, MD, Thomas H. Inge, MD, PhD, Michael J. Rutter, MD, Charles Monroe Myer III, MD, Charles M. Myer IV, MD, Cherie Torres-Silva, MD, J. Paul Willging, MD, and Robert E. Wood, MD, PhD

Otolaryngology » Mike Rutter, MD

Pathology and Laboratory Medicine » Margaret Collins MD

Pediatric General and Thoracic Surgery » Rebeccah Brown, MD and Victor Garcia, MD

Social Work »

Speech and Language »

A Phase 1b, Randomized, Double-Blind, Placebo-Controlled, Dose Escalation Study of N6022 to Evaluate Safety and Pharmacokinetics in Subjects with Cystic Fibrosis Homozygous for the F508del-CFTR Mutation (Joe Palermo, MD, PhD)

Pulmonary Medicine » John P. Clancy, MD and Gary L. McPhail, MD

Detection of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Expression and Activity in

Gastrointestinal Tissue from Pediatric Patients with and without Severe Constipation (Joe Palermo, MD, PhD)

Pulmonary Medicine » John P. Clancy, MD and Gary L. McPhail, MD

A Phase 2, Randomized, Multicenter, Double-Blind, Placebo-Controlled Study to Evaluate Safety, Efficacy, Pharmacokinetics, and Pharmacodynamics of VX-661 in Combination With Ivacaftor for 12 Weeks in Subjects With Cystic Fibrosis, Homozygous for the F508del-CFTR Mutation (Joe Palermo, MD, PhD)

Pulmonary Medicine » John P. Clancy, MD and Gary L. McPhail, MD

First prospective assessment of adrenal axis function in children who take steroids chronically for Eosinophilic Esophagitis (Philip E. Putnam, MD)

Endocrinology » Philippe F. Backeljauw, MD and Marjorie C. Golekoh, MD

First trial to look at treating EoE with losartan, a novel concept based on its impact on transforming growth factor beta, which is a major contributor to the disease and its complications(Philip E. Putnam, MD) **Endocrinology** » Philippe F. Backeljauw, MD and Marjorie C. Golekoh, MD

Myeloid Cell-Derived IL-33 in Chronic IL-10-Deficient Colitis (Michael J. Rosen, MD, MSCI) Allergy and Immunology » Simon P Hogan, PhD

Anti-TNF Therapy for Refractory Colitis in Hospitalized Children (Michael J. Rosen, MD, MSCI)
 Biostatistics and Epidemiology » Mi-Ok Kim, PhD
 Clinical Pharmacology » Sander A. Vinks, PharmD, PhD, FCP

The ImageKids study: Developing the Pediatric Crohn's Disease Intestinal Damage Score (PECDID score) and the Pediatric MRE-Based Activity Index (P-MECAI) (Shehzad A. Saeed, MD)

Radiology » Daniel Podberesky, MD

Anatomical variants of the duodenum and their clinical implications (Shehzad A. Saeed, MD) Radiology » Alex Towbin, MD

The Utility of Psychosocial Screening Measures for Referral to Psychological Services in Children Diagnosed with Inflammatory Bowel Disease (IBD) (Shehzad A. Saeed, MD)

Behavioral Medicine and Clinical Psychology » Kevin Hommel, PhD

Telehealth Enhancement of Adherence to Medication in Pediatric IBD (TEAM Study) (Shehzad A. Saeed, MD)

Behavioral Medicine and Clinical Psychology » Kevin Hommel, PhD

Self-Management Assistance for Recommended Treatment (SMART) Portal (Shehzad A. Saeed, MD) Behavioral Medicine and Clinical Psychology » Kevin Hommel, PhD

Longitudinal Examination of Adherence and Disease Severity in IBD (LEAD study) (Shehzad A. Saeed, MD)

Behavioral Medicine and Clinical Psychology » Kevin Hommel, PhD

Understanding needs and barriers to transition to adult IBD care: Patient, parent and clinician perspectives. (Shehzad A. Saeed,

MD)

## Behavioral Medicine and Clinical Psychology » Kevin Hommel, PhD

Evaluating the Effectiveness of Parent Activation Tools on Clinical Interactions. The E<sup>3</sup>Healthcare Study (Engaged, Empowered, Electronic) (Shehzad A. Saeed, MD)

## James M. Anderson Center for Health Systems Excellence » Lisa Opipari-Arrigan, PhD

Developing and Testing Systems to Support Patient, Physician and Researcher Collaboration to Conduct Individual "N of 1" Trials (Shehzad A. Saeed, MD)

James M. Anderson Center for Health Systems Excellence » Peter Margolis, MD, PhD

Enhancing Patient-Provider Partnerships: Development and Feasibility Testing of the Orchestra Platform modifications work best for specific individuals. (Shehzad A. Saeed, MD)

James M. Anderson Center for Health Systems Excellence » Peter Margolis, MD, PhD

Passive PROs: Using mobile sensing technology to measure outcomes in patients with IBD (Shehzad A. Saeed, MD)

James M. Anderson Center for Health Systems Excellence » Michael Seid, PhD

Ileal and Ileocecal Resection in Pediatric Crohn's Disease (IRCD) (Shehzad A. Saeed, MD) **Pediatric General and Thoracic Surgery** » Jason Frischer, MD

Age Related Surgical Management Trends and Outcomes in Pediatric Inflamamtory Bowel Disease (Shehzad A. Saeed, MD)

Pediatric General and Thoracic Surgery » Jason Frischer, MD

Hemostatic Factors in Colitis and Colitis-Associated Colon Cancer (Kris A. Steinbrecher, PhD) Cancer and Blood Diseases Institute » Joseph Palumbo, MD

Analysis of PDZ domain interaction between guanylate cyclase C and CFTR (Kris A. Steinbrecher, PhD) **Pulmonary Medicine** » AP Naren, PhD

Intestinal microflora and mucosal immunity (Kris A. Steinbrecher, PhD) Infectious Disease » Sing Sing Way MD, PhD

Outcome of NASH in adolescents after bariatric surgery versus lifestyle intervention (Stavra A. Xanthakos, MD) **Behavioral Medicine and Clinical Psychology** » Megan Ratcliff, PhD **Biostatistics and Epidemiology** » Eileen C. King, PhD

Magnetic Resonance Elastography in children with chronic liver disease (Stavra A. Xanthakos, MD)
 Biostatistics and Epidemiology » Eileen C. King, PhD
 Pathology and Laboratory Medicine » Lili Miles, MD
 Radiology » Kim M. Cecil, PhD, Daniel J. Podberesky, MD, and Suraj Serai, PhD

Biological determinants of steatohepatitis (Stavra A. Xanthakos, MD)

Pediatric General and Thoracic Surgery » Thomas H. Inge, MD and Todd M. Jenkins, PhD

Teen LABS U01 (Stavra A. Xanthakos, MD)

Pediatric General and Thoracic Surgery » Thomas H. Inge, MD and Todd M. Jenkins, PhD

Surgical Weight Loss Program for Teens (Stavra A. Xanthakos, MD) **Pediatric General and Thoracic Surgery** » Thomas H. Inge, MD and Todd M. Jenkins, PhD

The role of IL-17 in NASH (Stavra A. Xanthakos, MD) Allergy and Immunology » Senad Divanovic, PhD

TSH elevation and severity of pediatric NASH (Stavra A. Xanthakos, MD)
 Biostatistics and Epidemiology » Lin Fei, PhD
 Endocrinology » Nancy A. Crimmins, MD

Advanced Metabolic Clinic, a monthly multidisciplinary clinic for children with multiple obesity-related complications (Stavra A. Xanthakos, MD)

Cardiology » Holly M. Ippisch, MD and Robert M. Siegel, MD

NASH Clinical Research Network (Stavra A. Xanthakos, MD) **Radiology** » Kim M. Cecil, PhD, Daniel J. Podberesky, MD, and Suraj Serai, PhD

Determination of Liver Stiffness in Chronic Liver Disease Patients by Acoustic Radiation Force Imaging (ARFI-US - Stavra A. Xanthakos, MD) **Radiology** » Kim M. Cecil, PhD, Daniel J. Podberesky, MD, and Suraj Serai, PhD

Improving the consultation process at a large tertiary care children's hospital (Stavra A. Xanthakos, MD) **Emergency Medicine** » Joseph W. Luria, MD **Hospital Medicine** » Stephen A. Spooner, MD, MS and Christine M. White, MD, MAT

## Grants, Contracts, and Industry Agreements

Grant and Contract Awards		Annual Direct
BEZERRA, J		
Digestive Health Center: Ben National Institutes of Health	nch to Bedside Research in Pediatric Digestive Dis	ease
P30 DK 078392	06/01/12-05/31/17	\$711,923
Bezerra, J	Administrative Core	\$404,368
Potter, S	Gene Expression Core	\$22,822
Mayhew, C	Stem Cell Core	\$25,590
Keddache, M	Sequencing Core	\$42,618

Witte, D	Integrative Morphology Core	\$80,122
		<b>2</b> 22 22 <i>4</i>
Aronow, B	Bioinformatics Core	\$98,924
Bezerra, J	Flow Cytometery/Luminex Core	\$37,479
Haslam, D	Pilot & Feasibility Grant	\$50,000
Sherrill, J	Pilot & Feasibility Grant	\$10,000
Weaver, T	Pilot & Feasibility Grant	\$50,000
Immunologic Dysfunction in Biliar	y Atresia	
R01 DK 064008	02/01/13-01/31/17	\$266.617
The LiverChip - A Diagnostic Tool	for Genetic Liver Diseases	<i> </i>
National Institutes of Health(P2D, Ir	ic.)	
R44 DK 093214	04/01/14-02/28/16	\$85,493
BUCUVALAS, J		
·		
Immunosuppression Withdrawal f	or Stable Pediatric Liver Transplant Recipients	
		\$150 AEZ
Mediaction Adherence in Children		\$150,457
National Institutes of Health (Mount	Sinai Medical Center)	
	12/22/09-06/30/15	\$42.484
Polyclonal Tracs to Promote Tolo	ranco in Podiatric Livor Transplant Patients	ψτ2,τ0τ
National Institutes of Health(The Re	egents of the University of California)	
U01 AI 104347	02/01/13-01/31/14	\$11,273
CHOQUETTE, M		
2013 AASI D Advanced/Transpla	nt Henatology Followshin	
American Association for the Study	of Liver Diseases	
	07/01/13-06/30/14	\$60,000
COHEN, M / DENSON, L (MPI)		
Pediatric Gastroenterology and N	utrition Training Grant	
National Institutes of Health		
T32 DK 007727	07/01/10-06/30/15	\$398,428
DENSON, L		

Causes and Consequences of Neutrophil Dysfunction in Early Onset Crohn's Disease

National Institutes of Health(Emory University)

R01 DK 098231	09/17/13-07/31/18	\$101,657
Characterizing the Gut Microbial Eco	system for Diagnosis and Therapy in IBD	
National Institutes of Health(Broad Me	dical Research Program)	
U54 DE 023798	09/06/13-08/31/16	\$85,491
Innate Dysregulation and Growth Fai	lure in Pediatric Crohn's Disease	
Crohn's & Colitis Foundation of Americ	a	
CCFA Ref#3189	07/01/11-06/30/14	\$108,609
Predicting Response to Standard Pe	diatric Colitis Therapy: The PROTECT Study	
National Institutes of Health(Connection	ut Children's Medical Center)	
U01 DK 095745	05/01/12-06/30/17	\$188,798
Predicting Response to Standard Pe	diatric Colitis Therapy: The PROTECT Study	
National Institutes of Health(Connection	ut Children's Medical Center)	
U01 DK 095745	05/01/12-06/30/17	\$8,035
Risk Stratification and Identification	of Immunogenetic and Microbial Markers of Compli ca(Emory University)	cated Disease Course
CCFA Ref#2920	07/01/13-06/30/17	\$129 764
Risk Stratification and Identification	of Immunogenetic and Microbial Markers of Compli	cated Disease Course
Crohn's & Colitis Foundation of Americ	ca(Emory University)	
CCFA Ref#292052	07/01/13-06/30/17	\$18,634
Human IgG-Mediated Anaphylaxis		
National Institutes of Health(University	of Cincinnati)	
R21 AI 103816	07/01/12-06/30/15	\$56,735
Ulcerative Colitis Genetics Initiative		
Crohn's & Colitis Foundation of Americ	ca(Washington University)	
CCFA Ref #326556	04/15/14-04/14/17	\$231,138
A Multidisciplinary Human Study on Inflammatory Bowel Disease	the Genetic, Environment and Microbial Interactions	s that Cause
Crohn's & Colitis Foundation of Canad	a(Mount Sinai Hospital, Toronto)	
	01/01/12-03/31/16	\$3,059
HAN, X		
Development of Somatic Cell Therap	y for Infection-Induced Gut Barrier Dysfunction: Ro	ble of Intestinal Stem Cell
in Barrier Regeneration		
Department of Defense		
W81XWH-13-1-0437	09/30/13-03/29/15	\$84,374
Regulation of Adult Stem Cell Homeo	ostatic Response to Inflammatory Injury	
National Institutes of Health		
R21 AI 103388	02/04/13-01/31/15	\$113,148
HEUBI, J		
Sterol and Isoprenoid Diseases Rare	Diseases Consortium	
National Cancer Institute(Oregon Hea	th Sciences University)	
U54 HD 061939	09/29/09-07/31/14	\$49,492

KOHLI, R

NHE1 Ablation Protects Against L University of Cincinnati	liver Steatosis	
	10/01/13-06/13/14	\$5,000
Role of Bile Acid-FGF19 Signaling NASPGHAN Foundation	in NASH Improvement After Bariatric Surgery	
	11/15/13-11/14/15	\$75,000
LEONIS, M		
A Multi-Center Group to Study Ac National Institutes of Health(Univer	<b>ute Liver Failure in Children</b> sity of Pittsburgh)	
U01 DK 072146	09/01/10-08/31/15	\$112,737
A Multi-Center Group to Study Ac National Institutes of Health(Univer	<b>ute Liver Failure in Children</b> sity of Pittsburgh)	
U01 DK 072146	09/01/13-08/31/14	\$1,000
MENCHISE, A		
<b>Regulation of Adaptive Immune R</b> National Institutes of Health(The Ch	esponses in a Murine Model of Chronic Cholestatsis nildren's Hospital of Denver)	& MDR2 Deficiency
U01 DK 062453	06/01/13-05/31/14	\$56,702
MIETHKE, A		
<b>Prevalence of Mitochondrial DNA</b> National Institutes of Health(The Ch	Depletion Syndromes in Pediatric Acute Liver Failur nildren's Hospital of Denver)	re
U01 DK 062453	06/01/13-05/31/14	\$25,000
Regulation of Hepatic Lymphocyt	e Responses in Sclerosing Cholangitis	
PSC Partners Seeking a Cure		
	11/13/13-11/12/15	\$30,000
The Role of Regulatory T Cells in National Institutes of Health	Biliary Atresia	
R01 DK 095001	08/15/12-06/30/17	\$210,550
MOORE, S		
Global and Liver-Specific Knocko Bill & Melinda Gates Foundation	ut of Pigr to Generate Environmental Enteropathy in	Mice
OPP1092957	09/27/13-08/31/15	\$75,000
BAA 11-66 Biochronicity Department of Defense(University of	of Cincinnati)	
D12 AP00005	01/01/12-12/31/15	\$70,689
<b>Cellular Molecular Mechanisms o</b> Fogarty International Center	f Alanyl-Glutamine Oral Rehyrdration and Nutrition	
K02 TW 008767	09/16/11-07/31/16	\$116,070

Novel Metabonomic Biomarkers of Gut Function and Health: Modeling Enteropathy (EE) and Field Validation

Bill & Melinda Gates Foundation(Unive	rsity of Virginia)	
GF12746-141813	11/01/12-10/31/14	\$76,200
PALERMO, J		
Longitudinal Study of Cystic Fibrosis	Liver Disease	
Cystic Fibrosis Fdn Therapeutics, Inc(T	he Children's Hospital of Denver)	
NARKEW07A0	01/01/11-12/31/14	\$40,894
Longitudinal Study of Cystic Fibrosis	Liver Disease	
Cystic Fibrosis Fdn Therapeutics, Inc(T	he Children's Hospital of Denver)	
NARKEW07A0	01/01/11-12/31/14	\$10,150
ROSEN, M		
Th2 Cytokines and Signaling in Pediat National Institutes of Health	tric Inflammatory Bowel Disease	
K23 DK 094832	12/01/13-03/31/18	\$166,100
SAEED, S		
The ImageKids Study: Developing the Pediatric MRE-Based Activity Index (	Pediatric Crohn's Disease Intestinal Damage Sc P-MECA)	ore (PECDID) and the
Shaare Zedek Medical Center(Abbott L	aboratories)	
	11/07/12-11/06/14	\$5,947
SHIVAKUMAR, P		
Innate and Adaptive Immune System	s in Biliary Atresia	
American Liver Foundation		
	07/01/11-06/30/14	\$75,000
SHROYER, N		
KLF5 Regulation of Intestinal Develop	oment and Stem Cell Homeostasis	
National Institutes of Health		
R01 DK 092306	07/05/11-06/30/16	\$246,439
The Role of ATOH1 as a Tumor Suppr	ressor in Colorectal Cancer	
National Institutes of Health		
R01 CA 142826	02/23/10-01/31/15	\$181,148
SHROYER, N / WELLS, J (MPI)		
Human Endocrine Cell Development		
National Institues of Health		
R01 DK 092456	04/07/12-02/28/17	\$297,412
STEINBRECHER, K		
cGMP Metabolism in Resistance to B	acterial Infection	
National Institutes of Health		

WILLOUGHBY, J			
Patient Education Prototypes: Constipation	on Folders		
	11/15/13-11/15/14		\$2,000
XANTHAKKOS, S			
Pediatric Adverse Reaction in NASH National Institutes of Health(Arizona Board	of Regents)		
R01 HD062589	06/01/12-11/30/14		\$27,090
YIN, C			
Regulation of Hepatic Stellate Cells in Dev National Institutes of Health	velopment and Alcoholic Live	er Injury	
R00 AA 020514	03/01/14-02/28/17		\$159,615
		Current Year Direct	\$5,088,852
Industry Contracts			
COHEN, M			
PaxVax, Inc.			\$2,587,911
HEUBI, J			
Asklepion Pharmaceuticals, LLC			\$69,037
Nordmark Arzneimittel GmbH & Co.KG			\$199,244
KOCOSHIS, S			
NPS Pharmaceuticals, Inc.			\$54,041
KOHLI, R			
Ethicon Endo-Surgery, Inc			\$43,313
LEONIS, M			
Novartis Pharmaceuticals Corporation			\$9,625
MIETHKE, A			
Lumena Pharmaceuticals Inc.			\$3,850
MUKKADA, V			
Meritage Pharma, Inc.			\$32,788

Service Collaborations		
KOHLI, R		
PPD Global Central		\$16,520
STEINBRECHER, K		
Ironwood Pharma		\$37,923
	Current Year Direct	\$54,443
	Total	\$8,143,104