Division Details

Division Data Summary

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<th>RESEARCH AND TRAINING DETAILS</th>
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Significant Accomplishments

Digestive Health Center One of 17 Core Research Centers Nationwide

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. Our center engages 102 investigators from 21 divisions within the Department of Pediatrics and eight other departments within the University of Cincinnati College of Medicine. This year, we added nine investigators from Gastroenterology, Hepatology and Nutrition, Allergy and Immunology, Oncology, Endocrinology, Infectious Diseases, and Experimental Hematology and Cancer Biology. Alexander Miethke, MD, a member of our Division, was among those joining the center after receiving NIH funding to study the role of regulatory T cells in biliary atresia. Noah Shroyer, PhD, a DHC member from our Division, was elected Vice Chair of the Growth, Development and Child Health Section of the American Gastroenterological Association. Also in 2013, the DHC started the Pluripotent Stem Cell and Organoid Core, under the leadership of James Wells, PhD, and Chris Mayhew, PhD, which uses state-of-the-art technology to advance translational research in digestive diseases. Collectively, DHC investigators have received $32.5 million in extramural research funds and have published more than 140 peer-reviewed articles during the past 12 months. Our successful Pilot and Feasibility Program also distributed $1.15 million among 29 junior investigators since 2007. These investigators have since attracted $20.1 million in extramural grant...
Liver Transplant Program Reducing Immunosuppression Dose Levels

Immunosuppression is a critical component of the care of children following liver transplantation. The goal is to administer the lowest possible dosage to prevent rejection, both in the short- and long-term phases of life after transplant. John Bucuvalas, MD, is our site principal investigator for the IWITH trial, a multi-center study of immunosuppression withdrawal in children with stable graft function. The trial addresses key conclusions of the NIH-sponsored 2007 consensus conference on long-term outcomes in pediatric liver transplantation, which states that long-term immunosuppression can lead to substantial complications and that identifying biomarkers to predict therapy tolerance could lessen the risk. The overriding goal of the IWITH trial is to guide clinical decision-making to achieve safe withdrawal of immunosuppression. The 12-center study is jointly funded by NIDDK and NIAID. Sandy Feng MD, PhD, from the University of California San Francisco is the trial principal investigator. In addition to his local role, Bucuvalas serves as the study’s protocol chair.

Inflammatory Bowel Disease Services Continue to Grow

More than 700 children with inflammatory bowel disease (IBD) from 25 states visited Cincinnati Children’s in the past year to receive primary IBD care and second opinions. Many families are seeking our state-of-the art services, which include diagnostic imaging without radiation exposure and targeted psychology interventions for non-adherence. Many others are seeking expert advice. Our volume of second opinion patients has quadrupled in the past three years. In February, more than 300 families attended our annual Family Education and Support day, which continues to grow in collaboration with the local Crohn’s and Colitis Foundation of America chapter. Our research efforts this year included contributing to international genome-wide association studies to identify susceptibility genes for pediatric-onset disease, and prospective cohort studies to develop personalized models of disease behavior and response to therapy. In collaboration with the Broad Institute, MIT, we have characterized the gut microbial community and host response in 1,600 children with IBD and have used this information to define novel pathogenic mechanisms and patient sub-groups. Our investigators are deeply involved in launching the PROTECT study, the first NIH-funded multi-center clinical trial to test a model for predicting therapeutic responses and clinical outcomes among newly diagnosed children with ulcerative colitis. The project will incorporate clinical, genomic, microbial and immune biomarkers that we have developed. At Cincinnati Children’s, this study includes Bruce Trapnell, MD, Pulmonary Biology; Mi-Ok Kim, PhD, Epidemiology and Biostatistics; and Bruce Aronow, PhD, Biomedical Informatics. Meanwhile, Kevin Hommel, PhD, is leading the first randomized controlled multi-center trial of a telemedicine intervention to improve medication adherence in children with IBD. Knowledge gained from these studies will be rapidly translated into practice through our collaborations with Peter Margolis, MD, PhD, in Clinical Effectiveness, via his leadership of the ImproveCareNow (ICN) pediatric IBD quality improvement network. The IBD Center has played a leading role in ICN, which has achieved significant improvement in patient remission rates by implementing consensus patient care guidelines and practices. At Cincinnati Children’s, we have reached a sustained 67 percent remission rate among our IBD patients, up 20 percent over the past two years.

Research Highlights

Cincinnati Center for Eosinophilic Disorders (CCED)

Research at the Cincinnati Center for Eosinophilic Disorders (CCED) includes basic, clinical and translational studies. Phil Putnam, MD, has led projects including epidemiology, quality of life research, descriptive research...
databanks, specimen databanks, translational studies and clinical trials. In the past year, the CCED team participated in the publication of more than 10 manuscripts on aspects of eosinophilic disorders, including a major revision of the Consensus Recommendations for Diagnosis of Eosinophilic Esophagitis in children and adults. Marc Rothenberg, MD, PhD, continues basic science research to understand the genetic and immunologic bases for eosinophilic gastrointestinal disorders. As a continuation of our $1.5 million NIH stimulus research grant awarded in 2009, the first national Registry for Eosinophilic Gastrointestinal Disorders (www.regid.org) was launched in 2010 and has begun enrolling patients. The CCED is leading a multi-center registry collaboration with eight pediatric and adult hospitals with plans for further expansion. This year, Vincent Mukkada, MD, joined the CCED. He has recently published manuscripts on microRNA profiling of esophageal biopsies in EoE and the use of novel immunohistochemical biomarkers in pediatric EoE. In the coming year, the CCED will join a multicenter trial on the use of a new viscous budesonide product in EoE as well as initiate new trials on the use of losartan in EoE as well as novel dietary management strategies.

Cincinnati Children's Steatohepatitis Center

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 is estimated to progress to cirrhosis and liver failure in an estimated 25% of adult individuals and has become the third leading cause for liver transplantation in adults. NAFLD and NASH often begin in childhood and progressive severe fibrosis can occur in early adolescence. Early identification and intervention is critical to minimize progression to end-stage liver disease. Since its inception in 2007, the CCSC has evaluated over 200 children and collaborates 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. Research highlights from the CCSC in fiscal year 2013 include publications of the effects of innovative animal models of bariatric surgery on NASH and bile acid physiology, including sleeve gastrectomy. The pre-clinical research program has further been supported by grants from Ethicon Endosurgery Inc. and Cincinnati Diabetes and Obesity Center. In clinical research, 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 anticipated to finish enrollment by December 2013. In the past year, the CCSC has published clinical and pre-clinical papers in the area of steatohepatitis research in the following journals: Endocrinology, Obesity, Journal of Pediatric Gastroenterology, Hepatology and Nutrition, Clinical Liver Disease, Journal of Clinical Endocrinology and Metabolism, and the Indian Journal of Pediatrics.

Diarrhea and Malnutrition

Our goal is to advance the quality of care for children with diarrhea and malnutrition by creating new knowledge through robust research and clinical collaborations between Cincinnati Children's Hospital Medical Center and international partners. Drs. Moore, Cole and Saeed have established and are evolving collaborations with colleagues in Brazil, Ghana, Nigeria and Pakistan focused on micronutrient deficiencies (zinc and iron), undernutrition, diarrheal diseases, and tropical/environmental enteropathy.

Sean Moore’s laboratory is broadly interested in understanding and reversing the “vicious cycle” of malnutrition and enteric infections in developing countries. Current areas of focus are: 1) laboratory and clinical studies of glutamine supplementation in enteroids, murine models of weanling malnutrition, and underweight children in
Northeast Brazil (supported by the NIH and NASPGHAN Foundation), 2) human biomarkers and murine models of environmental enteropathy (supported by The Bill & Melinda Gates Foundation), and 3) intestinal epithelial cell signaling networks linking cell cycle, metabolism, DNA damage response, and circadian rhythms (supported by the DARPA Biochronicity Program).

In a related program, Dr. Cohen completed phase I studies on a new candidate vaccine with potential efficacy against enterotoxigenic E. coli and cholera, two important causes of diarrhea in developing countries.

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. Dr. Vincent Mukkada recently joined Scott Pentiuk, MD, as the second pediatric gastroenterologist on the team. The IFT continues to grow with over 1200 patient visits over the last year. The team has also had extensive outpatient treatment programs including co-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.

Intestinal Rehabilitation Program

The Intestinal Rehabilitation Program continues in its mission to provide the best possible care through innovation for patients to experience optimal outcome. We continue to experience considerable growth, and our program is one of the largest intestinal rehabilitation programs nationally, with active basic scientific, translational and clinical research. Drs. Kocoshis and Cole managed patients from 26 states and three countries in the past year. The multidisciplinary model to standardize care and facilitate research among the three disciplines (gastroenterology, neonatology and surgery) providing care to infants and children with intestinal failure continues to be successful. Currently the rate of survival without significant liver disease (as measured by cholestasis) of our patients with intestinal failure is among the highest nationally due to this initiative and rapid translation of research into clinical care. Specific initiatives, including active event analysis with the home healthcare services, have contributed to the significant reduction in the incidence of outpatient acquired central line bloodstream infections and we now have one of the lowest rates nationally.

Ongoing translational and clinical trials research initiatives include developing in vitro culture methods to grow and expand both normal and diseased intestinal tissue from patients with intestinal failure; validating the use of bomb calorimetry as a measure of enteral energy balance among intestinal failure patients; and feeding advancement trial in patients with gastroschisis to identify the method that optimally decreases the duration of TPN. An 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 participants. 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.

Intestinal Transplantation Program

Under the leadership of Dr. Samuel Kocoshis, the Intestinal Transplant Program continues to implement quality improvement initiatives. The program, as the first within our medical center to utilize medical passports for patients, continues to use them with great success. The medical passport gives a snapshot of each patient’s medical history from pretransplant medical issues, the technical details of the transplant itself, to the unique
postoperative problems faced by each patient. Individual drug reactions, organ dysfunction of other organ systems, and clinical quirks of each patient are highlighted in a cogent story which provides caregivers with insights to our patients that they would never have otherwise acquired. These insights facilitate the care of our patients wherever they travel, or whenever they are seen by either other divisions or by emergency physicians. Numerous physicians and other healthcare providers continue to commend us for providing such a comprehensive view of our patients. The medical passport focuses not only upon medical complications but also upon psychosocial issues that impact adversely upon outcomes.

Our program remains an active participant in hospital-wide QAPI initiatives. Our “dashboard” continues to show good outcomes in complying with regulatory procedures and in patient survival. Hence we are developing metrics for nutritional parameters such as BMI, 25-OH vitamin D levels, and other nutritional markers. We maintain a close association with the “adherence” program from the behavioral science department. A psychologist sees all of our patients as inpatients and outpatients in order to analyze and correct barriers to adherence. Moreover, among the 11 most recent patients transplanted between 2009 and 2012, we continue to have 100% one-year survival, making us the most successful program in North America in terms of patient survival for the three year period between 2009 and 2013.

We have embarked upon several research initiatives. We are working with the Behavioral Science Department, and have written an observational paper on the contributions that an adherence program can make within a transplantation program. We have also written an IRB protocol in collaboration with the Behavioral Science Department for a prospective study correlating clinical and psychosocial outcomes and regimen adherence of patients and their families following small bowel or multivisceral transplant. We have initiated a translational project in collaboration with Dr. Pierre Russo of the Pathology Department at Children’s Hospital of Philadelphia. It is a cross sectional study regarding the prevalence and significance of anti-enterocyte antibodies in small bowel transplantation. We hypothesize that anti-enterocyte antibodies may function as sensitive and specific biomarkers for antibody mediated rejection in intestinal transplantation. A third project is an emerging collaboration with Dr. Sander Vinks of the Clinical Pharmacology department to study intestinal metabolism of sirolimus and to study the ontogeny of that metabolism within the small intestine. A final protocol upon which we are about to embark is a collaborative study with Dr. Koji Hashimoto of the Cleveland Clinic. This study explores the role of helper T cells in acute cellular rejection of intestinal allografts. We will provide peripheral blood from patients undergoing intestinal transplant for flow cytometric analysis of T cell subpopulations. The hypothesis is that acute cellular rejection is most likely to occur when helper T cell populations are reconstituted following administration of antithymocyte globulin to intestinal transplant recipients.

The Liver Disease Program

The Liver Disease Program, led by Dr. Jorge Bezerra, 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 and the prompt initiation of conventional and innovative treatments. The evaluation includes a full spectrum of metabolic analysis, inflammatory processes, and state-of-the-art gene sequencing techniques to diagnose mutations known to cause clinical phenotypes, and discover mutations in new genes relevant to liver diseases. In addition to the consultation with expert hepatologists and clinical nurse specialists, the outpatient program includes the 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, an evaluation for liver transplantation and close follow-
up in the pre-transplant clinic enable the implementation of the most comprehensive treatment protocol to minimize complications, improve post-transplant course, and optimizes outcomes.

Recognizing that research is critical to improvement in child care, the Clinical and Research Staff lead patient- and laboratory studies in liver diseases. In patient studies, the staff conduct multi-center studies sponsored by the National Institutes of Health and the American Liver Foundation to advance knowledge on mechanisms of pediatric liver disease, to develop new diagnostic tests, and to perform clinical trials to explore new strategies to recover liver function and increase the short- and long-term outcomes of children with acute and chronic liver diseases. Ongoing projects include: 1) the development of the LiverChip, a new high-throughput blood test that screens for mutations in 13 genes that cause genetic liver diseases, 2) mitochondrial and immunologic diseases as causes of liver failure, 3) an ongoing trial to determine the efficacy of corticosteroids in children with biliary atresia, 4) studies to dissect the causes and develop new treatments for biliary atresia, 5) studies to discover biomarkers and new therapies for fatty liver disease, 6) identification of biomarkers of fibrosis, and 6) the development of new therapies for bile acid disorders.

In the laboratory, Research Staff use innovative models using transgenic technologies in rodents and zebrafish to study fundamental mechanisms of liver development and pathogenic basis of liver injury, repair, autoimmunity, cholestasis, steatohepatitis and tumor formation. Together, 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.

Pancreatic Disorders

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-El-Haija MD. With its inception this year, this 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 and established a REDCap database for patient registry. In addition, the program participates in the INSPIRE consortium for pediatric pancreatitis and are one the few children's hospitals able to offer pediatric patients with chronic pancreatitis the option of total pancreatectomy with islet autotransplantation (TPIAT).

Pediatric Acute Liver Failure Study Group

The Pediatric Acute Liver Failure (PALF) Study Group is a NIH U01-funded consortium of 12 children's hospitals (11 U.S. and one Canadian) whose focus is to study infants and children who develop acute liver failure. Patients with acute liver failure are gravely ill and often require liver transplantation in order to rescue the patient; despite this high morbidity and mortality, very little is known about the etiology of disease initiation or progression, or risk factors that will predict prognosis. Current goals of the PALF Study Group are to comprehensively study these patients' biochemical and clinical management profiles and using this information, to develop models of PALF using statistical modeling techniques augmented with mechanistic models of complex biological systems to inform us of factors impacting prognosis or decision-making regarding liver transplantation.

The Pediatric Liver Care Center at Cincinnati Children's has participated in the PALF Study Group since 2005. This past year, Cincinnati Children's has enrolled nine patients into the study, which is the second highest enrollment of the 12 centers (total PALF Study Group enrollment for 2013 was 70 patients). Dr. Leonis is the Cincinnati Children's site PI for this study, and has recently published an article on behalf of the PALF Study.
Group on chronic acetaminophen exposure in patients with PALF that was published in *Pediatrics*.

**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.

**Significant Publications**


In this study, the authors showed that the transcription factor SPDEF, which is normally part of the cellular differentiation program in the intestine, is silenced in >80% of colorectal tumors. Using transgenic mice, they showed that absence of SPDEF increased tumor formation and progression to invasive carcinoma in several models of colorectal cancer. In complementary studies, they showed that re-expression of SPDEF could block the growth of established tumors. Finally, they discovered that SPDEF directly binds to and interferes with the activity of beta-catenin, a protein that is almost universally oncogenic in colorectal cancer. Together, these studies identify SPDEF as a new target for therapeutic intervention in colorectal cancer.


This collaborative study between the Departments of Pathology, Surgery, and Pediatrics at Cincinnati Children's Hospital identified a novel mechanism of innate dysfunction, local intestinal production of GM-CSF auto-antibodies, in children with aggressive Crohn Disease requiring surgical resection. This provides new insight into a medical approach based upon boosting antimicrobial responses for this sub-group of patients who are refractory to current therapies.


Regulatory T cells have been linked to immunologic immaturity of the newborn and its predisposition to develop
biliary atresia, a life threatening blockage of the bile ducts. This report by Lages et al. elucidated mechanisms by which regulatory T cells modulate dendritic cell dependent costimulation of CD8 lymphocytes causing bile duct obstruction in experimental biliary atresia. The study identified cellular and molecular targets for future immunotherapy to block progression of neonatal bile duct injury.

Division Publications


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, Assistant 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, Associate 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

Jose Garza, MD, Assistant Professor
Research Interests Neurogastroenterological Disorders

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

Research Interests  Non-alcoholic Steatohepatitis

Mike A Leonis, MD, PhD, Assistant 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

Adam G Mezoff, MD, Professor
Leadership  Associate Medical Director, Pediatric Nutritional and Intestinal Care Center; Clinical Director for Gastroenterology

Research Interests  Intestinal Failure and Intestinal Transplantation

Alexander Miethke, MD, Assistant Professor
Research Interests  Biliary Atresia and Primary Sclerosing Cholangitis

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

Shehzad A Saeed, MD, Associate 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, Associate Professor
  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
  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)

Trainees

Frank Dipaola, MD, PL-7, Vanderbilt Children's Hospital
Dana Dykes, MD, PL-7, Children's Hospital at UAB
Kristin Bramlage, MD, PL-7, NS-LIJ Health System
Monique Choquette, MD, PL-6, Cincinnati Children's Hospital Medical Center
Phillip Minar, MD, PL-6, Medical College of Wisconsin
George Zacur, MD, PL-6, University of Miami/Jackson Memorial Hospital
Yael Haberman Ziv, MD, PL-5, Tel Hashomer Medical Center, Tel Hashomer, Ramat Gan, Israel
Alexandra Menchise, MD, PL-5, University of South Florida College of Medicine, Tampa
James Squires, MD, PL-5, Cincinnati Children's Hospital Medical Center
Sandra Wright, MD, PL-5, University of Alabama at Birmingham
David Galloway, MD, PL-4, Phoenix Children's Hospital Maricopa Medical Center
Karla Hicks, MD, PL-4, Cincinnati Children’s Hospital
Ethan Mezoff, MD, PL-4, Children’s National Medical Center
Division Collaboration

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

- Disease activity, behavioral dysfunction, and health-related quality of life in adolescents with inflammatory bowel disease - Lee A. Denson, MD
- Treatment adherence in adolescents with inflammatory bowel disease: the collective impact of barriers to adherence and anxiety/depressive symptoms - Lee A. Denson, MD
- Individually tailored treatment of medication nonadherence - Lee A. Denson, MD
- The Utility of Psychosocial Screening Measures for Referral to Psychological Services in Children Diagnosed with Inflammatory Bowel Disease (IBD) - Shehzad A. Saeed, MD
- Telehealth Enhancement of Adherence to Medication in Pediatric IBD - (TEAM Study) - Shehzad A. Saeed, MD
- PedsQL Gastrointestinal symptoms module for pediatric patients with gastrointestinal disorders: field test - Shehzad A. Saeed, MD
- Longitudinal examination of adherence and disease severity in IBD (LEAD study) - Shehzad A. Saeed, MD

Pulmonary Biology » Bruce C. Trapnell, MD

- Granulocyte-macrophage colony stimulating factor blockade promotes CCR9+ lymphocyte expansion in Nod2 deficient mice - Xiaonan Han, PhD; Lee A. Denson, MD
- Innate dysfunction promotes linear growth failure in pediatric Crohn's disease and growth hormone resistance in murine ileitis - Lee A. Denson, MD

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

- Paediatric parenting stress in inflammatory bowel disease: application of the pediatric inventory for parents - Lee A. Denson, MD
- Evaluation of a group-based behavioral intervention to promote adherence in adolescents with inflammatory bowel disease - Lee A. Denson, MD

Biomedical Informatics; Biostatistics and Epidemiology » Bruce Aronow, PhD and Eileen C. King, PhD

- Differentiation factors as tumor suppressors - Noah F. Shroyer, PhD

Neonatology and Pulmonary Biology; Developmental Biology » Jeffrey A. Whitsett, MD and James M. Wells, PhD

- KLF5 regulation of intestinal development and stem cell homeostasis - Noah F. Shroyer, PhD

Developmental Biology » James M. Wells, PhD
Human endocrine cell development - Noah F. Shroyer, PhD

Developmental Biology; Pediatric Surgery » James M. Wells, PhD and Michael A. Helmrath, MD
In vitro organoid models of the gastrointestinal tract - Noah F. Shroyer, PhD

Developmental Biology; Pediatric Surgery; Allergy and Immunology; Pulmonary Biology » James M. Wells, PhD, Michael A. Helmrath, MD, Simon P. Hogan, PhD, and John P. Clancy, MD
Intestinal organoid models of cystic fibrosis - Noah F. Shroyer, PhD

Hematology/Oncology » Joseph S. Palumbo, MD
Hemostatic Factors in colitis and colitis-associated colon cancer - Kris A. Steinbrecher, PhD

Allergy and Immunology » Simon P. Hogan, PhD
Pathogenic role of the macrophage in ulcerative colitis - Kris A. Steinbrecher, PhD
Effects of weanling undernutrition on intestinal barrier function in mice - Sean R. Moore, MD

Pediatric Surgery; Developmental Biology » Michael A. Helmrath, MD, James M. Wells, PhD, and Christopher N. Mayhew, PhD
Regulation of adult stem cell homeostatic response to inflammatory injury - Xiaonan Han, PhD
Development of somatic cell therapy for inflammation-induced gut barrier dysfunction - Xiaonan Han, PhD

Behavioral Medicine and Clinical Psychology » Yelena Wu, PhD and Sandra Cortina, PhD
Psychosocial risk factors associated with non-adherence in small bowel transplant recipients - Samuel A. Kocoshis, MD

Clinical Pharmacology » Sander A. Vinks, PharmD, PhD, FCP
Gastrointestinal metabolism of rapamycin in children - Samuel A. Kocoshis, MD

Pediatric Surgery » Jaimie D. Nathan, MD
Role of memory T cells in acute cellular rejection after small bowel transplant. - Samuel A. Kocoshis, MD

Biomedical Informatics » Bruce Aronow, PhD and Anil Jegga, DVM, MRes
Computational science and systems biology in Pediatric Digestive Disease: Bioinformatics Core of the Digestive Health Center - Jorge A. Bezerra, MD
Molecular phenotypes of biliary atresia – Jorge A. Bezerra, MD
Genetic synergy as causes of chronic liver diseases in children - Jorge A. Bezerra, MD

Developmental Biology » S. Steven Potter, MD, Aaron M. Zorn, PhD, and James M. Wells, PhD
Embryogenesis and tissue organoids in Pediatric Digestive Disease: The Digestive Health Center – Jorge A. Bezerra, MD
Development and function of the neonatal biliary system - Jorge A. Bezerra, MD

Pathology » David P. Witte, MD, Kumar Shanmukhappa, DVM, Rachel Sheridan, MD, and Kevin E. Bove, MD
Pathobiology of Pediatric Digestive Disease: Integrative Morphology Core of the Digestive Health Center - Jorge A Bezerra, MD
Mechanisms of hepatic tumorigenesis - Jorge A. Bezerra, MD
Molecular staging of liver injury in biliary atresia - Jorge A. Bezerra, MD

Cellular and Molecular Immunology » Claire A. Chougnet, PhD, Kasper Hoebe, PhD, and Jochen Mattner, MD, PhD
The neonatal immune system and pathogenesis of biliary atresia - Jorge A. Bezerra, MD
Liver disease modeling through in vivo mutagenesis - Jorge A. Bezerra, MD
Mechanisms of auto-immune liver disease - Jorge A. Bezerra, MD

**Pediatric Surgery** » Gregory M. Tiao, MD and Jaimie D. Nathan, MD
Mechanisms of virus-induced biliary atresia - Jorge A. Bezerra, MD
Gut-biliary axis and pathogenesis of cholangiopathies - Jorge A. Bezerra, MD

**Allergy and Immunology** » William M. Ridgway, MD, PhD
Mechanisms of auto-immune liver disease - Jorge A. Bezerra, MD

**Cellular and Molecular Physiology** » Marshall Montrose, PhD
In vivo cell monitoring of the digestive system: Integrative Morphology Core - Jorge A. Bezerra, MD

**Pathology; Allergy and Immunology; Psychology; Human Genetics; Rheumatology; Otorhinolaryngology; Neurology; Endocrinology; Cardiology; Pediatric Surgery** » CCED Team (Cincinnati Center for Eosinophilic Disorders), Margaret H. Collins, MD, and Marc E. Rothenberg, MD, PhD
Multidisciplinary evaluation and treatment of children and adults who have Eosinophilic Gastrointestinal Disorders - Philip E. Putnam, MD; Vincent Mukkada, MD

**Pulmonary; Otolaryngology; Social Work; Interdisciplinary Feeding Team; Speech and Language**

**Pathology; Pediatric Surgery** » ADSC Team (Aero Digestive Sleep Center), Robert E. Wood, PhD, MD, R. Paul Boesch, DO, Robin T. Cotton, MD, Michael J. Rutter, MD, Alessandro de Alarcon, MD, J. Paul Willging, MD, Daniel von Allmen, MD, Thomas H. Inge, MD, PhD, and Victor F. Garcia, MD
Evaluation and treatment of children who have complex airway disorders - Philip E. Putnam, MD; Vincent Mukkada, MD

**Otolaryngology; Human Genetics; Speech Therapy; Occupational Therapy; Social Work; Nutrition** »
Interdisciplinary Feeding Team
Multi-disciplinary team provides comprehensive evaluation of children with swallowing/feeding disorders - Scott P. Pentiuk, MD

**Infectious Diseases** » Monica Malone McNeal, MS
Murine models of environmental enteropathy and effects on oral rotavirus vaccine immunogenicity - Sean R. Moore, MD

**Pediatric Surgery** » Michael A. Helmrath, MD
IGF-1 effects in mouse models of undernutrition - Sean R. Moore, MD

**Pathology** » Kevin E. Bove, MD
Mitochondrial ultrastructure changes in NASH - Rohit Kohli, MD; Stavra A. Xanthakos, MD
Bile acid synthetic defect pathology - James E. Heubi, MD

**Pediatric Surgery** » Thomas H. Inge, MD and Todd M. Jenkins, PhD
Biological determinants of steatohepatitis - Stavra A. Xanthakos, MD
Teen LABS U01- Stavra A. Xanthakos, MD
Surgical Weight Loss Program for Teens - Stavra A. Xanthakos, MD

**Endocrinology** » Nancy A. Crimmins, MD
NAFLD in Youth with Type 2 diabetes: An Important but Under-Recognized Co-Morbidity - Stavra A. Xanthakos, MD

**Cardiology** » Robert M. Siegel, MD and Holly M. Ippisch, MD
Advanced Metabolic Clinic, a monthly multidisciplinary clinic for children with multiple obesity-related complications- **Stavra A. Xanthakos, MD**

**Biostatistics and Epidemiology** » Eileen C. King, PhD

- Magnetic Resonance Elastography in children with chronic liver disease - **Stavra A. Xanthakos, MD**

**Radiology** » Kim M. Cecil, PhD, Daniel J. Podberesky, MD, and Suraj Serai, PhD

- NASH Clinical Research Network- **Stavra A. Xanthakos, MD**

- Magnetic Resonance Elastography in children with chronic liver disease- **Stavra A. Xanthakos, MD**

**Cardiology** » Bradley S. Marino, MD

- The association between biochemical markers and post-Fontan cardiac index - **Kathleen M. Campbell, MD**

**Cardiology** » Bradley S. Marino, MD, Chesney Castleberry, MD, Gruschen R. Veldtman, FRCP, MBChB, and Christopher P. Learn, MD

- Clinical protocol for diagnosis and management of liver disease in patients post-Fontan palliation - **Kathleen M. Campbell, MD**

**Radiology** » Daniel J. Podberesky, MD and Daniel B. Wallihan, MD

- Utility of MR elastography in diagnosing and grading hepatic fibrosis - **Kathleen M. Campbell, MD**

**Allergy and Immunology** » Senad Divanovic, PhD

- The role of IL-17 in NASH - **Rohit Kohli, MD**

- Examine mitochondrial dysfunction due to ALR deficiency - **C. Shekhar Gandhi, PhD**

**Mass Spectrometry Laboratory** » Kenneth D. Setchell, PhD

- Bile acids in animal models of bariatric surgery - **Rohit Kohli, MD**

- Inborn errors of bile acid metabolism - **James E. Heubi, MD**

**Pathology** » Lili Miles, MD

- Hepatic histology in NASH animal models - **Rohit Kohli, MD**

**Pathology** » Michael Miles, PharmD

- Coenzyme Q as a biomarker for NASH - **Rohit Kohli, MD**

**Radiology** » Kamlesh U. Kukreja, MD

- Developmental Outcome of Urea Cycle Defect Liver Transplant Recipients- **Rohit Kohli, MD**

**Neonatology; Pediatric Surgery** » Andrew P. South, MD and Michael A. Helmrath, MD

- Transational and outcomes research in patients with and at risk for intestinal failure- **Conrad R. Cole, MD; Samuel A. Kochosis, MD**

**Pediatric Surgery; Neonatology; Biostatistics and Epidemiology** » Michael A. Helmrath, MD, Andrew P. South, MD, and Eileen C. King, PhD

- Efficacy of enteral glutamine in pediatric SBS - **Conrad R. Cole, MD; Samuel A. Kocoshis, MD**

**Radiology** » Alan E. Oestreich, MD

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

**Pathology; Biomedical Informatics** » Kenneth D. Setchell, PhD, Kevin E. Bove, MD, and Rebekah Karns, PhD

- Elucidation of the interrelation between phospholipid homeostasis and immune responses in the neonatal liver.- **Alexander Miethke, MD**

**Human Genetics; Pathology** » Taosheng Huang, MD, PhD, C. Alexander Valencia, PhD, Kevin E. Bove, MD, and
Collaborative study to correlate the molecular diagnosis derived by next generation sequencing technology with clinical data and histopathology in a retrospective cohort of subjects with acute liver failure and suspected mitochondrial DNA depletion syndrome.- Alexander Miethke, MD

Molecular Immunology; Pathology » Claire A. Chougnet, PhD, Kumar Shanmukhappa, DVM, Anita Gupta, MD, and Rachel Sheridan, MD

Determination of the role of Th17 cells in progression of cholestatic liver disease in children with biliary atresia after Kasai portoenterostomy.- Alexander Miethke, MD

Pediatric Surgery » Gregory M. Tiao, MD

Review of treatment and outcomes of patients with IBD and PSC followed at Cincinnati Children’s and at Dr. v Hauner Kinderspital Munich, Germany.- Alexander Miethke, MD

Community Pediatrics » Heidi Kalkwarf, PhD

Bone disease in childhood - James E. Heubi, MD

Immunology » Lisa H. Filipovich, MD

Etiopathogenesis of pediatric acute liver failure - John C. Bucuvalas, MD

Center for Adherence and Self-Management » Dennis Drotar, PhD

Medical adherence in liver transplant recipients - John C. Bucuvalas, MD

Nephrology » Jens W. Goebel, MD and Stuart L. Goldstein, MD

Differing Effects of Rapamycin or Calcineurin Inhibitor on T-Regulatory Cells in Pediatric Liver and Kidney Transplant Recipients - John C. Bucuvalas, MD

Recognition and Prevention of Acute Kidney Injury in Hospitalized Children- John C. Bucuvalas, MD

Pediatric Surgery; Oncology; Pathology; Radiology » Gregory M. Tiao, MD, James I. Geller, MD, Anita Gupta, MD, Kevin E. Bove, MD, Kamlesh Kukreja, MD, and Alexander J. Towbin, MD

Liver Tumor Research Group - Mike A. Leonis, MD, PhD

Anderson Center for Health System Excellence » Peter Margolis, MD, PhD and Michael Seid, PhD

Developing and testing systems to support patient, physician and researcher collaboration to conduct individual "N of 1" trials - Shehzad A. Saeed, MD

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

Evaluating the Effectiveness of Parent Activation Tools on Clinical Interactions. The E³Healthcare Study (Engaged, Empowered, Electronic) - Shehzad A. Saeed, MD

Pediatric Surgery » Jason S. Frischer, MD

Diverting ileostomy in Crohn's disease: analysis of benefits, trends, and complications in the pediatric population - Shehzad A. Saeed, MD

Radiology » Daniel J. Podberesky, MD

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

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

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
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

Pediatric Surgery; Pathology » Gregory M. Tiao, MD, Kevin E. Bove, MD, Rachel Sheridan, MD, and Anita Gupta, MD
Hepatic Immune Activation in Pediatric Liver Disease - Alexander G. Miethke, MD; Jorge A. Bezerra, MD; Stacey S. Huppert, PhD

Experimental Hematology and Cancer Biology » Yi Zheng, PhD
Modulating neutrophil reactive oxygen species in Inflammatory Bowel Disease - Phil Minar, MD

Radiology » Sara M. O’Hara, MD
Pediatric normograms for the common bile duct – Tom K. Lin, MD

Pathology » Margaret H. Collins, MD
Stricture development in Eosinophilic Gastrointestinal Diseases - Vincent A. Mukkada, MD

Allergy and Immunology » Marc E. Rothenberg, MD, PhD and J. Pablo Abonia, MD
New pilot therapeutic trial of losartan in patients with Eosinophilic Esophagitis - Vincent A. Mukkada, MD
Therapeutic trial of oral viscous budesonide in Eosinophilic Esophagitis - Vincent A. Mukkada, MD
Therapeutic trial of novel dietary therapy in Eosinophilic Esophagitis - Vincent A. Mukkada, MD

Grants, Contracts, and Industry Agreements

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<td>Digestive Health Center: Bench to Bedside Research in Pediatric Digestive Disease</td>
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Mayhew, C  Stem Cell Core  $28,261
Keddache, M  Sequencing Core  $31,790
Witte, D  Integrative Morphology Core  $78,134
Aronow, B  Bioinformatics Core  $99,872
Bezerra, J  Flow Cytometry/Luminex Core  $43,954
Zheng, Y  Pilot & Feasibility Grant  $47,983
Palumbo, J  Pilot & Feasibility Grant  $47,983
Minar, P  Pilot & Feasibility Grant  $7,984

*Immunologic Dysfunction in Biliary Atresia*
National Institutes of Health
R01 DK 064008  02/01/13-01/31/17  $266,617

*JAUNDICE NEXT: A Diagnostic Tool for Cholestatic Liver Disease*
National Institutes of Health (P2D, Inc)
R43 DK 093214  07/01/12-06/30/13  $46,362

**BUCUVALAS, J**

*Immunosuppression Withdrawal for Stable Pediatric Liver Transplant Recipients*
National Institutes of Health (University of California, San Francisco)
U01 AI 100807  07/27/12-06/30/17  $104,452

*Medication Adherence in Children Who Had Liver Transplant*
National Institutes of Health (Mount Sinai School of Medicine)
R01 DK 080740  12/22/09-06/30/14  $46,106

**COHEN, M / DENSON, L (MPI)**

*Pediatric Gastroenterology and Nutrition Training Grant*
National Institutes of Health
T32 DK 007727  07/01/10-06/30/15  $426,734

**COLE, C**

*Efficacy of Enteral Glutamine in Reducing Bloodstream Infections in SBS Infants*
National Institutes of Health
R21 DK 088027  09/01/11-08/31/14  $166,001

**DENSON, L**

*Human IgG-Mediated Anaphylaxis*
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<td>Innate Dysregulation and Growth Failure in Pediatric Crohn’s Disease</td>
<td>Crohn’s &amp; Colitis Foundation of America</td>
<td>07/01/11-06/30/14</td>
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<td>Predicting Response to Standard Pediatric Colitis Therapy: The PROTECT Study</td>
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<td>05/01/12-06/30/17</td>
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<td>Risk Stratification and Identification of Immunogenetic and Microbial Markers of Complicated Disease Course</td>
<td>Crohn’s &amp; Colitis Foundation of America (Emory University)</td>
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<td>Defective 5-ASA Metabolism in Inflammatory Bowel Disease</td>
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<td>A Multidisciplinary Human Study on the Genetic, Environmental and Microbial Interactions that Cause IBD</td>
<td>Crohn’s and Colitis Foundation of Canada (Mount Sinai Medical Center - Toronto)</td>
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<td>AASLD Advanced Transplant Hepatology Fellowship Program</td>
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<td>Regulation of Adult Stem Cell Homeostatic Response to Inflammatory Injury</td>
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<td>Molecular Requirements for Proliferation of Fetal and Adult Liver Progenitors</td>
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<td>Benefits of Exercise: CNS and Hepatic Mechanisms</td>
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<td>The Role of Regulatory T Cells in Biliary Atresia</td>
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<td>Ursodeoxycholic Acid Therapy in Pediatric Primary Sclerosing Cholangitis: A Pilot Withdrawl/Reinstitution Trial</td>
<td>Food and Drug Administration (University of Tennessee)</td>
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<td>Generate a Mouse Model of Environmental Enteropathy</td>
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<td>Novel Metabonomic Biomarkers of Gut Function and Health: Modeling Enteropathy (EE) and Field Validation</td>
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<td>Clinical Research Network in Non-Alcoholic Steatohepatitis (NASH)</td>
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**Current Year Direct Receipts** $301,624

**Total** $5,812,261