Mission

The mission of the Division of Gastroenterology, Hepatology, and Nutrition is:

- To provide up-to-date and compassionate care to children with gastrointestinal (GI) and liver disorders
- To educate the next generation of gastroenterologists and pediatricians
- To advance knowledge of pediatric gastroenterology through research
FACULTY

David Keljo, MD, PhD
Interim Chief, Division of Gastroenterology, Hepatology, and Nutrition
(April 1, 2017, to the present)
Professor of Pediatrics
Codirector, Inflammatory Bowel Disease (IBD) Program

Mark E. Lowe, MD, PhD
Chief, Division of Gastroenterology, Hepatology, and Nutrition
(until March 31, 2017)
Professor of Pediatrics
Vice Chair of Graduate Medical Education

Feras Alissa, MD
Assistant Professor of Pediatrics
Director, Endoscopy Center

Riha Bhatt, MD
Assistant Professor of Pediatrics
Codirector, Pediatric Gastroenterology Fellowship Program

Kristy Boggs, PhD
Research Assistant Professor

Maria I. Clavell, MD
Associate Professor of Pediatrics

John F. Eisses, MD, PhD
Assistant Professor of Pediatrics

Tamara Feliciano Alvarado, MD
Assistant Professor of Pediatrics

Arjumand Ghazi, PhD
Assistant Professor of Pediatrics, Developmental Biology, and Cell Biology and Physiology

Sohail Z. Husain, MD
Associate Professor of Pediatrics
Director, Exocrine Pancreas Center (EPC)

Zahida Khan, MD, PhD
Assistant Professor of Pediatrics and Pathology

Sandra C. Kim, MD
Associate Professor of Pediatrics
Codirector, IBD Center

Dale King, MD
Assistant Professor of Pediatrics

Douglas Lindblad, MD
Assistant Professor of Pediatrics

Patrick J. McKiernan, MD
Professor of Pediatrics
Director, Pediatric Hepatology Program

Amitava Mukherjee, PhD
Research Instructor

Jeffrey A. Rudolph, MD
Associate Professor of Pediatrics

Wednesday Marie A. Sevilla, MD, MPH, CNSC
Assistant Professor of Pediatrics

Sapana Shah, MD
Assistant Professor of Pediatrics

Leah Siebold, MD
Assistant Professor of Pediatrics
Clinical Director of Gastroenterology

Amina Smajlovic, MD
Clinical Assistant Professor of Pediatrics

James E. Squires, MD, MS
Assistant Professor of Pediatrics
Director, Pediatric Transplant Hepatology Fellowship Program

Robert H. Squires Jr., MD
Professor of Pediatrics
Medical Director, Liver Transplant Program

Arvind Srinath, MD
Assistant Professor of Pediatrics
Codirector, Pediatric Gastroenterology Fellowship Program

Veena Venkat, MD
Associate Professor of Pediatrics

Xunjun Xiao, PhD
Research Assistant Professor
(until March 31, 2017)
OVERVIEW OF DIVISION

Over the past year, the division has experienced changes and improvements.

PERSONNEL CHANGES

• Divisional leadership changed at the end of March 2017, when Mark Lowe moved to St. Louis, Mo., and David Keljo took over as interim chief.

• New physician arrivals included the following.
  o Wednesday Sevilla moved from Memphis, Tenn., and is participating in the care of children with intestinal failure.
  o Sandra Kim moved from Nationwide Children’s Hospital in Columbus, Ohio, to become the codirector of the IBD Center.

PROGRAM DEVELOPMENT

• Under the leadership of Jeffrey Rudolph and in its seventh year, the Intestinal Care Service continued to increase its patient care activities.

• The EPC, led by Mark Lowe and Sohail Husain, increased its patient numbers and participated in the evaluation and care of children undergoing total pancreatectomy and islet cell auto-transplantation for chronic pancreatitis.

• Under the leadership of Patrick McKiernan and Robert Squires, the inpatient hepatology service now includes joint rounds with Transplant Surgery on patients with liver or small-bowel transplants.

• The IBD Program, codirected by David Keljo and Sandra Kim, cares for almost 1,000 children with Crohn’s disease or ulcerative colitis. The center is joining the Improve Care Now initiative and developing a Transition to Adulthood Program in collaboration with the IBD Center at Presbyterian Hospital of UPMC.

• Under the leadership of Arvind Srinath and Riha Bhatt, the fellowship program remains strong and continues to attract applicants who are competitive for the major training programs. Two of the fellows were supported on National Institutes of Health (NIH) T32 training grants.

CLINICAL ACTIVITIES

The following table shows data for the clinical activities of the division. Inpatient visits increased by more than 40%, driven by the hepatology consult service. The outpatient patient volume and procedure volume have been relatively constant, with variations attributable to the number of clinicians. The division staff sees outpatients in nine locations. The total number of outpatient visits was second among all the subspecialty divisions (excluding Emergency Medicine) of the Department of Pediatrics. The division staffs three inpatient services: the general GI service, the intestinal failure service, and the newly launched hepatology consult service.

<table>
<thead>
<tr>
<th>Activity</th>
<th>Fiscal Year (FY)12</th>
<th>FY13</th>
<th>FY14</th>
<th>FY15</th>
<th>FY16</th>
<th>FY17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outpatients</td>
<td>17,046</td>
<td>18,535</td>
<td>15,478</td>
<td>16,830</td>
<td>17,622</td>
<td>16,023</td>
</tr>
<tr>
<td>Inpatients</td>
<td>5,508</td>
<td>6,699</td>
<td>5,865</td>
<td>6,572</td>
<td>6,899</td>
<td>9,313</td>
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<tr>
<td>Procedures</td>
<td>4,279</td>
<td>4,381</td>
<td>4,045</td>
<td>4,264</td>
<td>4,439</td>
<td>4,337</td>
</tr>
</tbody>
</table>

Because of outstanding clinical and research activities, the division was ranked #5 in pediatric gastroenterology and surgery in the recent U.S. News & World Report ratings.

RESEARCH OVERVIEW

Research remains an important facet of the division; four faculty members have NIH funding, and the division continues to attract new research funding from the NIH and other organizations. It participates in multiple national studies for liver disease, pancreatic disease, and IBD.
LABORATORY-BASED RESEARCH

The research laboratories made major advances in the most recent academic year, and they have an even brighter future ahead with an influx of talented researchers.

- Sohail Z. Husain, MD, founded and directs the EPC. Members of the EPC include John F. Eisses, MD, PhD; Amitava Mukherjee, PhD; Kristy Boggs, PhD; and postdoctoral students Li Wen, MD, PhD, and Nayyar Ahmed, PhD. The EPC laboratory manager is Tanveer Javed. This year, the team welcomed a visiting scholar from Chengdu, China: Lihui Deng, MD. The EPC hosted three summer students in 2017. Under Husain's mentorship, five members wrote grants. Last year, EPC members were awarded an R01 competitive renewal (to Husain), a startup grant from the Children's Hospital of Pittsburgh Foundation (to Boggs), and a mid-sized pharmaceutical grant (to Husain).

- Arjumand Ghazi, PhD, and her laboratory joined the division. The Ghazi Laboratory studies the genetics of aging, reproduction, and lipid metabolism using the model system Caenorhabditis elegans. The following projects are the focus of the laboratory's research: balancing lipogenesis and lipolysis in health and aging, the role of TCER-1/TCERG1 in immunity and reproductive health, and the role of germline-intrinsic meiotic genes in somatic aging. The Ghazi Laboratory includes postdoctoral students Francis RG Armit, PhD, and Hyeljin Hwang, PhD; graduate students Julia Loose and Nikki Naim; and undergraduate student Thayjas Patil.

CLINICAL AND TRANSLATIONAL RESEARCH

Twenty clinical and clinical/translational research activities are under way in hepatology, IBD, and pancreatic diseases. Eleven pharmaceutical trials are going on within the division.

CHALLENGES

Clinical: The clinical productivity of the division is at capacity and is not adequate to meet the health system mandate of same-day scheduling. The division is addressing this by hiring more advanced practice providers (APPs), so that physicians can focus most of their energies on the most medically advanced aspects of their subspecialty training. To facilitate recruitment and optimize performance and retention of APPs, Srinath and nurse practitioner Leslie Coda are developing a curriculum for a gastroenterology APP fellowship program.

Research: Research is the future of medicine. Research funding is increasingly difficult to obtain. Eisses and Khan have promising K award applications submitted. Transitioning fellows to K awards has not been successful for a few years. One MD/PhD fellowship candidate has been accepted to the fellowship program, and another has been recruited for the combined pediatric residency/GI physician-scientist training program. Two NIH-funded researchers have been recruited for next year. Two fellows are developing new clinical research programs in IBD. Efforts are being made to participate in a larger number of pharmaceutical studies, particularly in IBD.
DEPARTMENT OF PEDIATRICS 2017 ANNUAL REPORT

DIVISION OF GASTROENTEROLOGY, HEPATOLOGY, AND NUTRITION

RESEARCH AND OTHER SCHOLARLY ACTIVITIES

David Keljo, MD, PhD

David Keljo began serving as interim division chief on April 1, 2017.

RESEARCH

David Keljo’s research focuses on clinical aspects of pediatric IBD and involves collaborative arrangements with multiple centers.

Sex Differences in Statural Growth Impairment in Pediatric Crohn’s Disease. Growth impairment is common in pediatric Crohn’s disease and appears to be more marked in males than in females. This study aims to identify the causes of that discrepancy.

Risk Stratification and Identification of Immunogenetic and Microbial Markers of Rapid Disease Progression in Children With Crohn’s Disease. An inception cohort study is gathering clinical, genetic, serologic, tissue, and microbiologic samples to try to predict which patients will have rapid progression to stricture or perforation. Enrollment is complete, and 36-month follow-up has been completed. The primary outcome paper has been published. Follow-up continues.

Predicting Response to Standardized Pediatric Colitis Therapy: The PROTECT Study. This multicenter (25 centers), open-label study funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) is designed to evaluate the safety and efficacy of standardized initial therapy using either mesalamine or corticosteroids then mesalamine for the treatment of children and adolescents newly diagnosed with ulcerative colitis. The study investigates whether response to the initial four weeks of therapy combined with clinical, genetic, and immune parameters determined during the initial course of therapy will predict severe disease as reflected by need for escalation of medical therapy or surgery. Enrollment and follow-up are complete for this study, and Pittsburgh is one of the top six enrolling centers. The primary outcome paper has been accepted for publication.

A Multidisciplinary Human Study on the Genetic, Environmental, and Microbial Interactions That Cause IBD: The GEM Study. This multicenter study sponsored by the Crohn’s and Colitis Foundation of Canada aims to recruit unaffected siblings and offspring of patients with Crohn’s disease. Siblings and offspring are 100-fold more likely to develop Crohn’s disease than the rest of the population. The study will prospectively measure environmental exposures, changes in enteric microbial flora, and changes in immune responses in relation to the barrier function of the intestine and genetic makeup of these individuals to identify the changes that determine who develops Crohn’s disease. Enrollment is ongoing.

ADVISORY COMMITTEE MEMBERSHIPS

• Information Systems Physician Advisory Committee, Children’s Hospital of Pittsburgh of UPMC

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS

• American Gastroenterological Association (AGA)
• North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN)
• Crohn’s and Colitis Foundation of America (CCFA)
• Alpha Omega Alpha

HONORS

• Best Doctors in America, Woodward/White, Inc.
• Best Doctors, Pittsburgh Magazine
Mark Lowe, MD, PhD

Mark Lowe vacated his position as division chief on March 30, 2017.

RESEARCH

Molecular Mechanisms of Dietary Fat Digestion by Pancreatic Lipases. The long-term goal of Lowe’s research is to elucidate the molecular mechanisms of dietary fat digestion by pancreatic lipases. This project focuses on dietary fat digestion by lipases in human newborns. The results will advance knowledge of dietary fat digestion by pancreatic lipases and facilitate bench-to-bedside development of novel nutritional therapies, such as more effective formulas or enzyme replacement that will transform care and improve outcomes of premature infants and critically ill newborns.

Proteotoxicity in the Pathophysiology of Chronic Pancreatitis. This project focuses on a novel mechanism for pancreatitis. Herein, the researchers address the hypothesis that carboxyl ester lipase (CEL) mutants associated with chronic pancreatitis activate adaptive cell signaling pathways and increase susceptibility of cells to injury by metabolic stress. The knowledge gained by the proposed studies will improve the overall understanding of pancreatic injury and provide insight into potential pharmacological interventions directed at a new therapeutic target, protein homeostasis.

International Study Group of Pediatric Pancreatitis: In Search for a Cure 2 (INSPIRE2) to Study Chronic Pancreatitis. The objective of this application is to determine the natural history of pediatric chronic pancreatitis, identify risk factors and genetic modifiers for its onset and sequelae, and develop approaches to improve clinical outcomes. The long-term goal is to develop diagnostic modalities, prognostic factors, and better treatment approaches for pediatric chronic pancreatitis.

STUDY SECTIONS

• Special Emphasis Panel for the Extramural Loan Repayment Program, NIDDK, NIH
• NIH Special Emphasis Panel for Silvio O. Conte Digestive Diseases Research Core Centers, NIDDK, NIH

ADVISORY COMMITTEE MEMBERSHIPS

• Board of Directors, Western Pennsylvania Chapter of the National Pancreas Foundation
• Board of Directors, National Pancreas Foundation
• Fellow and Resident Leadership Initiative, Department of Pediatrics, University of Pittsburgh
• Ambulatory Care Steering Committee, Children’s Hospital of Pittsburgh of UPMC
• Executive Committee, Department of Pediatrics, University of Pittsburgh
• Perioperative Committee, Children’s Hospital of Pittsburgh of UPMC
• Resident Performance and Evaluation Committee, Department of Pediatrics, University of Pittsburgh
• Research Task Force, Department of Pediatrics, University of Pittsburgh
• Graduate Medical Education Full Committee, University of Pittsburgh School of Medicine
• Planning Committee, PancreasFest
• Promotions Committee, Department of Pediatrics, University of Pittsburgh
• Visit Coordination Program, Children’s Hospital of Pittsburgh of UPMC
• Finance Committee, NASPGHAN
• Strategic Planning Committee, Children’s Hospital of Pittsburgh of UPMC
• Pediatric Intern Selection Committee, Department of Pediatrics, University of Pittsburgh
• Center for Rare Disease Therapy, Children’s Hospital of Pittsburgh of UPMC

EDITORSHIPS

• Associate editor, Journal of Pediatric Gastroenterology and Nutrition

HONORS

• Best Doctors in America, Woodward/White, Inc.
• Best Doctors, Pittsburgh Magazine
• Carol Ann Kraumer Endowed Chair for Pediatric Research

MAJOR LECTURESHIPS AND SEMINARS

• “Steatorrhea: What If It’s Not Cystic Fibrosis?” World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition, Montreal, Canada, 2016
• “Pancreatitis,” learning lunch, World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition, Montreal, Canada, 2016
• “Pancreatitis,” learning lunch, World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition, Montreal, Canada, 2016
• “Recent Advances in Pediatric Acute Pancreatitis,” Lviv Children’s Hospital Conference, Lviv, Ukraine, 2017
• “Nutrition and Pancreatitis: What To Do When?” fellows symposium, National Pancreas Foundation, Grapevine, Texas, 2017
• “Mechanisms of Lipase Mutation in Chronic Pancreatitis,” European Pancreas Club, Budapest, Hungary, 2017
Feras Alissa, MD

Feras Alissa’s research includes examining the dose-effect relationship of methotrexate and hepatic fibrosis in patients with IBD.

Kristy Boggs, PhD

RESEARCH

Kristy Boggs’ research focuses on defining the genomic landscape of pancreatic recovery and regeneration after injury. Through the utilization of next-generation sequencing protocols and molecular biology techniques, her aim is to characterize the transcriptome, genome, and epigenome of the pancreas following pancreatic injury. The exploitation of pancreatic recovery mechanisms may offer therapeutic targets for the treatment of pancreatitis.

Utilizing the murine caerulein hyperstimulation model of mild acute pancreatitis and recovery, she has sequenced the transcriptome of the non-injured and the histologically recovered pancreas by RNA-sequencing (RNA-seq). The RNA-seq data clearly demonstrate differentially expressed genes (DEGs) between the non-injured and the recovered pancreas, although histologically, the pancreas resembles that of the non-injured pancreas. This work has resulted in the preparation and submission to Scientific Reports of a manuscript titled “Pancreatic Gene Expression During Recovery After Pancreatitis Reveals Unique Transcriptome Profiles.” The manuscript received favorable reviews and following revisions has been re-submitted to Scientific Reports (September 2017).

Whether the DEGs identified in the recovered pancreas allow the pancreas to thwart repeated events of stress or injury is currently under investigation. Boggs is assessing whether subsequent attacks of acute pancreatitis in mice are less severe than the initial attack, utilizing the caerulein hyperstimulation model of mild acute pancreatitis and recovery. The severity of recurrent acute pancreatitis is being determined both biochemically and histologically.

In addition to the identification of DEGs in the recovered pancreas, there is the possibility of poised chromatin states in the recovered pancreas. In this case, the gene is not expressed in the recovered pancreas, as determined by RNA-seq, but the chromatin structure is in a transcriptionally permissive state that is primed for rapid gene expression. An altered chromatin state in the recovered pancreas may confer a molecular memory that regulates severity of future organ injury. In future studies, Boggs will assess chromatin accessibility in the recovered pancreas by ATAC-seq (assay for transposase-accessible chromatin sequencing), with a specific focus on identifying poised regions in the chromatin of a recovered pancreas.

Also, in future work, she will determine the epigenetic mechanism(s), focusing on histone modifications, that induce a differential chromatin signature in the recovered pancreas.
pancreas. Differentially modified histones between the non-injured and recovered pancreas will be assessed by ChIP-seq (chromatin immunoprecipitation and DNA sequencing) to identify specific post-transcriptional modifications of histone tails and the region of DNA associated with these transcriptionally active or repressive modifications. The identification of epigenetic modifications in the recovered pancreas will provided insight into the identified altered gene expression and chromatin structure in the recovered pancreas.

Boggs is affiliated with the Health Sciences Sequencing Core at Children’s Hospital of Pittsburgh. She contributes to investigations of the Husain Laboratory and the larger scientific community by developing and optimizing next-generation sequencing technologies.

HONORS AND AWARDS
- Children’s Hospital of Pittsburgh of UPMC Research Advisory Committee Grant, “Pancreatic Injury Induces a Unique Chromatin Footprint That Protects the Recovering Pancreas Against Repetitive Injury,” 100% effort, $80,000 direct funds over two years, 2017–2019

Maria I. Clavell, MD

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
- American Society for Parenteral and Enteral Nutrition
- NASPGHAN

John F. Eisses, MD, PhD

RESEARCH
John Eisses’ research focuses on understanding the role of epigenetic modifiers in regulating injury and recovery of the pancreas as it relates to pancreatic disease. He studies epigenetic regulation of pancreatitis in distinct cell types within the pancreas. Pancreatitis is a life-threatening inflammatory disorder that lacks targeted therapies. Injury and inflammation activate pancreatic stellate cells (PSCs), resulting in the remodeling of the pancreatic microenvironment, which allows pancreatic recovery to occur. Prolonged injury or aberrant regulation of PSCs has been implicated in the development or promotion of several pancreatic diseases, including chronic pancreatitis and pancreatic cancer. The overall goal of the current proposal is to examine novel epigenetic mechanisms by which pancreatic recovery is regulated in response to injury, particularly in the context of PSCs. The hypothesis is that the epigenetic regulation of gene expression in PSCs is crucial for activation and repression of gene expression necessary to promote a microenvironment suitable for pancreatic regeneration. The research is significant because it elucidates for the first time an epigenetic mechanism for regenerative signals important in regulating the pancreatic microenvironment to allow pancreatic recovery. On a much broader level, it opens a new paradigm of possible therapeutic strategies that may enhance the ability of the pancreas to recover, particularly in the context of remodeling the extracellular matrix and the pancreatic microenvironment by PSCs.

ADVISORY COMMITTEE MEMBERSHIPS
- Member, Pancreas Committee, NASPGHAN
- Member, Pediatric Pancreatology Consortium, INSPIRE

EDITORSHIPS
- Associate editor, GI Scholarly Newsletter, Children’s Hospital of Pittsburgh

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
- NASPGHAN
- European Pancreas Club
- AGA
- American Pancreatic Association
- Pediatric Pancreatology Consortium, INSPIRE
- Collaborative Alliance for Pancreatic Education and Research

Tamara Feliciano Alvarado, MD

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
- NASPGHAN

Arjumand Ghazi, PhD

RESEARCH
The Ghazi Laboratory studies the genetics of aging, reproduction, and lipid metabolism using the model system Caenorhabditis elegans. The following projects were undertaken in the past year and are currently the focus of the laboratory’s research.

Balancing Lipogenesis and Lipolysis in Health and Aging. Lipid imbalances are characteristic of obesity and a feature of many age-related ailments and reproductive pathologies in humans. Yet the relationship among lipid metabolism, aging, and reproduction remains poorly studied. This project investigates how the balance between lipid synthesis and breakdown influences an organism’s rate of aging and health. In C. elegans, eliminating the germline extends lifespan, removes fertility, and is a major challenge to lipid metabolism because the animal needs to stop fat deposition into eggs and reorganize its lipid profile. Thus, germline-less worms provide a unique platform to understand how lipid balance is established in the cells and tissues of complex multicellular animals in the
face of major physiological changes. We discovered that fat production and degradation increase simultaneously in response to germline loss. In germline-less adults, a conserved transcription factor, NHR-49, upregulates fatty-acid β-oxidation and desaturation—processes that contribute to lipid breakdown and build-up, respectively. These two, and many other processes involved in lipid synthesis and degradation, are elevated in response to germline removal by the conserved transcription factors DAF-16 and TCER-1. These data suggest that the coordinated enhancement of lipid synthesis and breakdown facilitate adaptation to germline loss by mediating lipid homeostasis. The knowledge obtained from these studies is likely to reveal fundamental insights into obesity and the relationships among lipid metabolism, reproduction, and aging.

Role of TCER-1/TCERG1 in Immunity and Reproductive Health. Reproduction and stress resistance in metazoans are poorly described. We discovered a role for TCER-1, the worm homolog of human transcription elongation, and splicing factor TCERG1 in enhancing reproductive capacity in the face of pathogen attack. In C. elegans, eliminating germline stem cells increases lifespan and elevates stress resistance. Previously, we demonstrated that TCER-1/TCERG1 specifically promotes the longevity of germline-less C. elegans but is critical for reproductive health in normal, fertile animals. Surprisingly, we have discovered that TCER-1/TCERG1 inhibited stress tolerance in adult worms. tcer-1 mutants exhibited elevated resistance against multiple biotic and abiotic stressors. TCER-1/TCERG1 impairs stress resistance by inhibiting PMK-1, a conserved innate immunity-promoting kinase. PMK-1-target genes are upregulated in tcer-1 mutants, and the immunoresistance of tcer-1 mutants is dependent upon PMK-1. The data suggest that TCER-1/TCERG1 promotes reproductive fitness and represses stress resilience under normal conditions. Under stressful conditions, TCER-1/TCERG1 is repressed, resulting in enhanced stress resilience and reduced reproductive capacity. Unlike most pro-longevity genes, TCER-1/TCERG1 appears to have distinct regulatory effects on lifespan, stress resistance, and fertility, suggesting that the protein may function as a molecular rheostat for coordinating major life-history traits. The phenotypic uncoupling observed in tcer-1 mutants provides a unique platform to dissect the pathway that governs resource allocation among procreation, stress response, and somatic maintenance in metazoans.

Role of Germline-Intrinsic Meiotic Genes in Somatic Aging. Meiotic chromosomal defects increase dramatically with age and are a major cause of miscarriages, birth defects, and age-related fertility loss in women. Correlative evidence from human studies has indicated that germline fidelity has a role in overall health. This research used the nematode C. elegans to address the mechanisms of and cause-effect relationships between germline health and somatic aging. Specifically, the researchers have focused on genes involved in C. elegans meiosis, an intrinsically germline-restricted phenomenon that is fundamental to genetic diversity. They have found that mutations in multiple genes that act at different stages of worm meiosis cause lifespan reduction and demonstrate signs of premature aging. Besides lifespan, the researchers have examined the effects of these mutations directly on the rate of organismal aging by testing various measures of healthspan. Preliminary results suggest that meiotic mutants not only exhibit reduced lifespans but also show physiological and molecular signs of accelerated aging. The data suggest that genes that govern meiotic fidelity in germ cells of C. elegans impact the rate of aging of the whole animal.
• “Lipid Metabolism and Aging,” Division of Endocrinology, Department of Pediatrics, University of Pittsburgh, Pittsburgh, Pa., April 2017
• “Concomitant Modulation of Somatic Lipid Production and Breakdown in Response to Germline Signals,” second Interventions in Aging meeting, Cancun, Mexico, March 2017
• “Fat, Fertility, and Aging in C. elegans,” featured speaker for conference held once every four years, 18th International Society for Developmental Biology meeting, National University, Singapore, June 2017

Sohail Z. Husain, MD

RESEARCH
The overarching goal of Sohail Husain’s research is to determine the mechanisms that initiate and propagate pancreatitis, a painful inflammatory disease that accounts for more than 300,000 hospitalizations and 3,200 deaths in the United States annually. Specifically, current advances in the Husain Laboratory are focused on: (1) examining the aberrant calcium signals and calcium targets within the main pancreatic cell, the acinar cell, which are critical to both the initiation and propagation of pancreatitis; (2) determining the role of epigenetic factors in pancreatic recovery and regeneration after injury; and (3) deciphering the mechanisms underlying drug-induced pancreatitis. Husain’s work is anticipated to lead to effective treatment or preventive strategies for pancreatitis that target aberrant calcium signaling, enhance pancreatic recovery, or compensate for toxic drug exposures.

STUDY SECTIONS
• Standing member, Clinical, Integrative, and Molecular Gastroenterology Study Section, NIH
• Section member, Peer-Reviewed Medical Research Program, U.S. Department of Defense
• Standing member, Research Advisory Committee, Children’s Hospital of Pittsburgh of UPMC

ADVISORY COMMITTEE MEMBERSHIPS
• Chair, Pancreatitis: Inflammation, Fibrogenesis, and Immunology Review Section, AGA
• Chair, AGA Abstract Review for Pancreatitis: Inflammation, Fibrogenesis, and Immunology
• Chair, Pancreas Committee, NASPGHAN
• Councilor, Pancreatic Disorders Section, AGA Institute Council
• Organizing member, National Pancreas Foundation, Western Pennsylvania Chapter
• Site principal investigator, INSPIRRE2: Pediatric Acute and Chronic Pancreatitis Multi-Center, NIH-funded, R01 Consortium

EDITORSHIPS
• Editorial Board, Pancreapedia
• Editorial Board, Journal of Biological Chemistry
• Editor-in-chief, GI Scholarly Newsletter, Children’s Hospital of Pittsburgh

MAJOR LECTURESHIPS AND SEMINARS
National/International:
• “Targeting the Calcium Effector Calcineurin in Pancreatitis,” invited lecture, APA annual meeting, San Diego, Calif., 2017
• “Turning Investigational Therapies into Clinical Reality: Pancreatitis in the Spotlight,” visiting professor, pediatrics seminar (host: Teresa Quattrin), University at Buffalo, Buffalo, N.Y., 2017
• “Epithelial Cell Calcineurin Signaling in Pancreatitis,” visiting professor, Mayo Clinic Cancer Seminar Series (host: Baoan Ji), Mayo Clinic, Jacksonville, Fla., 2017
• “Pancreatitis,” “Pancreatic Anatomy and Anomalies,” and “Hereditary Disorders of the Pancreas,” invited lectures, NASPGHAN Essentials Pediatric GI Review (course director: Chris Liacouras), Scottsdale, Ariz., 2017
Zahida Khan, MD, PhD

RESEARCH
Zahida Khan took a sabbatical absence the academic year of 2016–2017 to complete fellowship training in advanced pediatric transplant hepatology at Texas Children's Hospital through Baylor University. Khan completed her advanced pediatric transplant hepatology fellowship in August of 2017. She then returned to Children's Hospital of Pittsburgh of UPMC and the University of Pittsburgh School of Medicine, where she continues to provide her services clinically and research liver diseases, focusing on cellular approaches to liver regeneration and transplantation.

More than 15,000 patients are awaiting liver transplantation, but only 6,729 liver transplants were performed last year. Alpha-1 antitrypsin deficiency (ATD) is the most common hereditary liver disease in children, and it is the most frequent genetic reason for liver transplantation. In classical ATD, the PiZ mutation results in misfolded ATZ protein monomers, which cause proteotoxicity, often leading to chronic liver injury, cirrhosis, and cancer. Not all patients develop severe liver disease, and it is unclear why only some patients need a liver transplant. Khan’s research investigates the basic cell biology behind this question, using the PiZ transgenic mouse model. To understand how liver regeneration is impaired in ATD, she is studying intracellular mechanisms of protein processing and cell proliferation in PiZ hepatocytes. She is also studying how bile acid signaling can be utilized as a therapeutic target for ATD-related liver disease. Her research investigates largely unexplored pharmacologic pathways in ATD.

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
• NASPGHAN
• American Pancreatic Association
• AGA
• INSPIRE
• National Pancreas Foundation

HONORS
• Best Doctors in America, Woodward/White, Inc.
• Best Doctors, Pittsburgh Magazine

Sandra C. Kim, MD

RESEARCH
Sandra Kim focuses on clinical care of children with IBD. She has research expertise in basic, translational, and clinical/quality-improvement initiatives in pediatric and adolescent IBD. She is involved in clinical research and quality-improvement initiatives on regional and national levels for children and adolescents with IBD and has authored numerous studies on pediatric and adolescent IBD. She is a member of the Children’s Hospital of Pittsburgh’s Fellowship Clinical Competency Committee for the Pediatric Gastroenterology Program.

ADVISORY COMMITTEE MEMBERSHIPS
• Crohn’s and Colitis Foundation
  o Co-chair, Government/Industry Affairs and Advocacy, National Scientific Advisory Committee
  o Member and past chair, Pediatric Affairs Committee, National Scientific Advisory Committee
  o ImproveCareNow (ICN) Pediatric IBD Quality-Improvement Collaborative
  o Chair, Clinical Practice Committee
  o Co-chair, Transition of Care Innovation Community
  o Member, Physician Leadership Group
  o Member, Strategy Council
  o Member, Collaborative Steering Committee, ICN/Crohn’s and Colitis Foundation
Douglas Lindblad, MD

RESEARCH
Douglas Lindblad is involved with a research proposal (Cystic Fibrosis Foundation) to study the relationship between cystic fibrosis–associated liver disease and cystic fibrosis–related diabetes.

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
- AGA
- Crohn’s and Colitis Foundation
- NASPGHAN
- Alpha Omega Alpha
- Gold Humanism Society

Patrick J. McKiernan

RESEARCH
Patrick McKiernan’s research interests cover the spectrum of pediatric liver disease but have fallen into three main areas.
- Liver transplantation: His published contributions span clinical outcomes, pharmacokinetics of immunosuppressants, long-term histological outcomes, and guidelines for transition to adult care.
- Portal hypertension: He has published on the use of endoscopic techniques, including variceal band ligation and endoscopic ultrasound, and he has contributed to the development of international guidelines.
- Metabolic liver disease: He has published on the clinical management of metabolic disease, especially tyrosinemia type I, and the evolving role of liver transplantation in metabolic liver disease. He has been involved in clinical trials of stem cell treatment for metabolic disease.

In addition, McKiernan is the local principal investigator for the following first-in-humans multicenter trial: a phase I/II, randomized, open-label, ascending-dose, delayed-treatment concurrent control clinical study to evaluate the safety and preliminary efficacy of AT342, an AAV8-delivered gene transfer therapy in Crigler-Najjar syndrome subjects aged 1 year and older.

Furthermore, he is the local principal investigator for a five-year, multicenter, longitudinal observational study of patients with nonalcoholic fatty liver or nonalcoholic steatohepatitis.

ADVISORY COMMITTEE MEMBERSHIPS
- Center for Rare Disease Therapy, Children’s Hospital of Pittsburgh of UPMC

MAJOR LECTURESHIPS AND SEMINARS
- “Liver Transplantation for Metabolic Disease,” Society for the Study of Inborn Errors of Metabolism annual scientific meeting, Rome, Italy, September 2016
Amitava Mukherjee, PhD

RESEARCH
Amitava Mukherjee’s overarching goal is to uncover key molecular signaling pathways for exocrine pancreatic disorders, particularly drug-induced pancreatitis. Currently, his research focuses on deciphering the mechanisms underlying asparaginase-associated pancreatitis. The research suggests that pancreatic asparaginase synthetase (ASNS) maintains acinar cell homeostasis and that its upregulation is required to mitigate asparaginase-induced pancreatic cell injury. Therefore, therapies that selectively augment pancreatic ASNS could be used to alleviate asparaginase-associated pancreatitis. He has generated sufficient preliminary data for grant submissions. Mukherjee has published work in collaboration with the Mark Lowe Laboratory on a mutant lipase that is responsible for chronic pancreatitis in the Journal of Biological Chemistry. He has written a chapter for Liver Disease in α1-Antitrypsin Deficiency.

Mukherjee has been assisted by his research team, consisting of a postdoctoral fellow, Nayyar Ahmed, PhD; a medical fellow, Fateema Rose, MD; and a visiting researcher, Li-Hui Deng. Mukherjee has participated in training two summer students, Chaitanya Srinivasan and Mahedah Rehman.

HONORS
• PancreasFest Travel Scholarship Award: Collaborative Alliance for Pancreatic Education and Research, University of Pittsburgh, June 2017

Jeffrey Rudolph, MD

RESEARCH
Intestinal Care and Rehabilitation Center Database. This retrospective database is designed to collect data that describe the natural history and management practices of intestinal failure and rehabilitation at Children’s Hospital.

Compassionate Use of Omegaven in the Treatment of Parenteral Nutrition–Associated Liver Disease. This is a compassionate-use protocol for the use of omega-3 fatty acids as an alternative lipid source in children with total parenteral nutrition–associated liver disease.

A Prospective, Randomized, Controlled, Double-Blind, Parallel-Group, Phase III Study to Compare the Safety and Efficacy of Smoflipid 20% to Intralipid 20% in Hospitalized Neonates and Infants Requiring 28 Days of Parenteral Nutrition. Jeffrey Rudolph is site investigator for a multicenter study comparing the effects of standard parenteral lipid therapy to a novel lipid emulsion.

Biomarkers in Transplant Recipients. This entails obtaining biological samples from intestinal transplant patients during routine endoscopy for assessment of markers that predict the immunological state or organ rejection.

ADVISORY COMMITTEE MEMBERSHIPS
• Codirector, Pediatric Intestinal Failure, Rehabilitation, and Transplant Symposium, Pittsburgh, Pa., 2018
• Nutrition Committee, NASPHAN

MAJOR LECTURESHIPS AND SEMINARS
• “Trace Elements in TPN,” invited speaker, Sydra Medical Corporation, Doha, Qatar, April 2017

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
• NASPGHAN
• American Society for Parenteral and Enteral Nutrition

HONORS
• Best Doctors, Pittsburgh Magazine
Wednesday Marie A. Sevilla, MD, MPH, CNSC

RESEARCH

American Society for Parenteral and Enteral Nutrition New Opportunities for Verification of Enteral Tube Location Project. This project addresses the safety of feeding tube placement. Wednesday Marie A. Sevilla collaborates with the task force on a variety of projects, including development of a position paper on best practices for nasogastric tube placement.

Soluble Fiber Utilization in Pediatric Short Bowel Syndrome: A Survey of Current Practice Trends. This project is a collaboration with a team at Le Bonheur Children's Hospital. The data from the survey will provide an overview of the clinical practice of administering supplemental enteral fiber in pediatric patients with short bowel syndrome. Data have been collected and analyzed. A manuscript is being prepared for submission for publication. Sevilla participated in developing the survey tool, monitoring data collection and analysis, and authoring the manuscript.

ADVISORY COMMITTEE MEMBERSHIPS

• Member, Nutrition Advisory Group, Children’s Hospital of Pittsburgh

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS

• Nutrition Committee, NASPGHAN
• AGA
• Pediatrics Section and Pediatric Intestinal Failure Section, American Society for Parenteral and Enteral Nutrition
• Intestinal Transplant and Rehabilitation Association

Sapana Shah, MD

RESEARCH

Predicting Response to Standardized Pediatric Colitis Therapy: The PROTECT Study. This multicenter (25 centers), NIDDK-funded, open-label study is designed to evaluate the safety and efficacy of standardized initial therapy using either mesalamine or corticosteroids then mesalamine for the treatment of children and adolescents newly diagnosed with ulcerative colitis. The study will investigate the hypothesis that response to the initial four weeks of therapy as well as specific clinical, genetic, and immune parameters determined during the initial course of therapy will predict severe disease as reflected by need for escalation of medical therapy or surgery. Enrollment and follow-up are complete, and the Pittsburgh location is one of the top six enrolling centers. The study is in the data-analysis phase.

An Efficacy and Safety Study of Infliximab in Pediatric Participants With IBD. This multicenter study sponsored by Janssen Scientific Affairs, LLC, is designed to evaluate whether trough serum infliximab concentrations at the time of loss of clinical response will identify pediatric participants with IBD who would benefit from dose escalation above the currently approved dose of 5 mg/kg.

Improve Care Now. Improve Care Now is a multicenter, quality-improvement collaborative for patients with pediatric IBD that enables patients, families, clinicians, and researchers to improve knowledge and outcomes related to Crohn’s disease and ulcerative colitis. It engages all stakeholders in a learning health network that provides real-time quality improvement, research, and community-building for children with these conditions.

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS

• NASPGHAN

Leah Siebold, MD

RESEARCH

Leah Siebold is principal investigator for the following.

• PRO-KIIDS and NEOPICS Retrospective Cohort Study of Very Early Onset IBD
• The international Early Onset Paediatric IBD Cohort Study
• A Study of Fecal Microbiota Transplantation in Pediatric Patients With Relapsed IBD

ADVISORY COMMITTEE MEMBERSHIPS

• Clinical Care and Quality Committee, NASPGHAN
• Physical Leadership Team, Children’s Hospital of Pittsburgh
• Physician Compensation Committee, Children’s Hospital of Pittsburgh
• 8B GI liaison, Children’s Hospital of Pittsburgh
• Improve Care Now
• Taskforce for Home Infusions, NASPGHAN

Amina Smajlovic, MD

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS

• American Academy of Pediatrics

James E. Squires, MD, MS

RESEARCH AND OTHER SCHOLARLY ACTIVITIES

Potential of Human Induced Pluripotent Stem Cells (iPSCs) in Studies of Progressive Intrahepatic Cholestasis. The hepatocyte canalicular membrane serves as the gateway through which hepatocyte metabolic products pass to form bile.
Disruption of canalicular function, therefore, is expected to have detrimental effects on liver and human health. Autosomal recessive disorders are known to disrupt hepatocyte canalicular function and bile secretion. Progressive familial intrahepatic cholestasis (PFIC) is a group of rare diseases clinically manifested by intrahepatic cholestasis in children and progresses to end-stage liver disease and death or liver transplantation.

The ability to derive patient-specific iPSCs allows opportunities to model hepatic disorders, gain mechanistic insights, and explore cell-based therapies. Briefly, human fibroblasts or lymphocytes are isolated and reprogrammed into hepatocyte-like cells, which bear significant similarities to primary hepatocytes in terms of transcriptional profile and functional properties but retain the unique, patient-specific genetic defects. These patient-derived iPSC cell lines enable the study of individual phenotypes under highly controlled conditions and allow linking the observed defects directly to disease-causing genetic alterations. Liver-specific disease models include ATD, familial transthyretin amyloidosis, glycogen storage disease, Wilson’s disease, familial hypercholesterolemia, and Niemann-Pick disease. The present study hypothesizes that patient-specific human iPSCs can be generated and accurately recapitulate the main characteristics of PFIC. Squires is principal investigator.

**Graft Injury Group Observing Late-Term Outcomes.** This is a multicenter, international collaboration of pathologists, hepatologists, and transplant surgeons looking to better understand and characterize late graft injury in children who receive liver transplants. Squires is site investigator.

**Biomarkers of Acute Kidney Injury in Pediatric Liver Transplant Recipients.** Acute kidney injury (AKI) is a rapid loss of kidney function, and AKI following liver transplant adversely affects outcomes. Improved detection and management of AKI in the perioperative period would have long-term benefits in reducing the development of chronic kidney disease. Serum creatinine, the current gold-standard marker for kidney injury, is a late and insensitive marker of AKI. Newer biomarkers such as urine IGFBP7, TIMP-2, and NGAL have proven to be superior in the timely detection of renal injury and impairment in critically ill adults, and the ability to sample urine is advantageous. This research will study novel biomarkers of AKI in the pediatric liver transplant population to determine their diagnostic and predictive capabilities relating to the development of AKI in pediatric populations. Squires is principal investigator.

**Clinical Trials in Organ Transplantation in Children (CTOTC): Biomarkers for Post-Transplant Lymphoproliferative Disorders (PTLDs) in Children.** This is a clinical trial investigating biomarkers associated with the development of Epstein-Barr virus (EBV)-related PTLDs in pediatric liver, heart, heart with liver, small intestine, and liver with small intestine transplant candidates and recipients. Squires is co-investigator.

**ADVISORY COMMITTEE MEMBERSHIPS**
- Idiopathic Neonatal Cholestasis Subcommittee, Childhood Liver Disease Research Network (ChiLDReN) Alpha-1-Antitrypsin Deficiency Subcommittee, ChiLDReN
- Mitochondrial Hepatopathy Subcommittee, ChiLDReN
- Education Committee, SPLIT Hepatology Committee, NASPGHAN
- American Board of Pediatric Intensive Care Unit Liver Board Review

**EDITORSHIPS**
- Associate editor, *GI Scholarly Newsletter*, Children’s Hospital of Pittsburgh

**HONORS**
- Co-author, “Neurocognitive Status in Alagille Syndrome: Results of a Multicenter Prospective Observational Study,” AASLD Presidential Poster of Distinction
- AASLD Young Investigators Travel Award for “Liver Transplantation in Pediatric Acute Liver Failure: Practices and Patient Characteristics”

**MAJOR LECTURESHIPS AND SEMINARS**
- “Liver Dysfunction in Patients With IBD,” invited lecture, Cincinnati Children’s Hospital Medical Center Pediatric Autoimmune Liver Disease Symposium, Cincinnati, Ohio, October 2017
Robert H. Squires Jr., MD

RESEARCH

A Multicenter Group to Study Acute Liver Failure in Children (NIH/NIDDK). Acute liver failure is a rare condition in which loss of liver cell function occurs rapidly (often less than two weeks), with devastating results. Members of this consortium continue to publish, and important clinical advances have also been made. Ongoing projects utilizing stored biomedical samples coupled with detailed clinical data include: characterizing the role of CD8+ T-cell infiltration and indeterminate pediatric acute liver failure, identifying HMGB1 as an important cytokine mediator and acetaminophen toxicity, characterizing markers of immune activation, identifying genetic causes of indeterminate pediatric acute liver failure, and utilizing biomedical samples for viral discovery. A few recent achievements include: characterization of neurodevelopmental deficits in children following acute liver failure, exploration of liver transplant decisions in the setting of acute liver failure, and identification of a dynamic model using clinical and biochemical markers associated with clinical outcomes. The study is currently in its final no-cost extension phase. Squires is principal investigator.

The Pittsburgh Cholestatic Liver Disease Consortium (NIH/NIDDK). This is a renewal application that is a continuation, expansion, and merging of the Biliary Atresia Research Consortium and the Cholestatic Liver Consortium to form the Childhood Liver Disease Research and Education Network (ChiLDREN). Following enrollment, detailed longitudinal clinical data are collected as well as biomedical samples. The research team is currently enrolling participants with chronic cholestatic conditions and analyzing patient populations. There are two associated clinical trials to assess the efficacy of an apical sodium–dependent bile acid transporter inhibitor in the treatment of cholestatic liver disease in children with progressive familial intrahepatic cholestasis (sponsor: Lumena Pharmaceuticals Inc.) and Alagille syndrome (sponsor: NIH/NIDDK). Squires is principal investigator.

Hepatitis B Clinical Research Network—Data Coordinating Center (NIH/NIDDK). This application proposes a multicenter group to study chronic hepatitis B infection to examine natural history and immunopathogenesis. Squires serves as a funded pediatric advisor at the data coordinating center.

ATD Treated by Carbamazepine (CBZ). CBZ decreased the hepatic load of AT granules and hepatic fibrosis in the PiZ mouse model of ATD-associated liver disease. Squires is investigating the effect of CBZ on severe liver disease due to ATD in adolescents and adults. Sponsor: Perlmutter Laboratory. Squires is co-investigator.

Creating Models of Rare Childhood Liver Diseases Using the Human Liver-on-a-Chip. Researchers are focusing initially on POLG mutations that cause Alpers Huttenlocher syndrome, one of many rare childhood diseases that involve the liver. This study will expand to include mutations involving the canalicular membrane. Sponsor: NIH. Squires is co-investigator.

Hepatitis C Clinical Trial. The trial has enrollment and is currently monitoring three patients in an open-label, multicenter study to evaluate the pharmacokinetics, safety, and efficacy of glecaprevir/pibrentasvir in pediatric subjects with genotype 1–6 chronic hepatitis C virus infection. Sponsor: AbbVie Inc. Squires is site principal investigator.

Pediatric Intestinal Failure Consortium. Although funding for this project has ended, ongoing sub-analysis of the data continues. A recent publication by Javid et.al. highlighted that the extent of intestinal failure–related liver disease is associated with increased mortality. Sponsor: NIH/NIDDK. Squires is principal investigator.

ADVISORY COMMITTEE MEMBERSHIPS

• 2011-16 International Classification of Disease (ICD)-11 revision process, Pediatric Topic Advisory Group, Gastroenterology Working Group, World Health Organization
• American Academy of Pediatrics
  o Pediatrics Review and Education Program
  GI Editorial Board
Arvind Srinath, MD

RESEARCH
Arvind Srinath’s research focuses on subspecialty medical education, pediatric gastroenterology curriculum development, and functional GI disorders.

- A multicenter, randomized, double-blind, placebo-controlled, parallel-group, safety and efficacy study of a range of linaclotide doses administered orally to children ages 7 to 17 years who have IBS with constipation (i.e., Fulfill Rome III Criteria for Child/Adolescent IBS and Fulfill Modified Rome III Criteria for Child/Adolescent Functional Constipation)
- A phase III, multicenter, long-term, safety, efficacy, and pharmacokinetics study of lubiprostone in pediatric subjects aged ≥ 6 years to < 18 years who have functional constipation
- Impact of a nurse practitioner–led teaching program on patient and caregiver knowledge of pediatric IBD, NASPGHAN/Association for Pediatric Gastroenterology and Nutrition Nurses, Susan Moyer 2017 Nursing Research Grant (co-principal investigator)

ADVISORY COMMITTEE MEMBERSHIPS
- NASPGHAN
- Training Committee, NASPGHAN, September 2015 to the present
- Resident Selection Committee, Children’s Hospital of Pittsburgh
- Residency Program Leadership, Children’s Hospital of Pittsburgh
- Pediatric Gastroenterology Fellow Clinical Competency Committee, Children’s Hospital of Pittsburgh
- Pediatric Gastroenterology Fellow Selection Committee, Children’s Hospital of Pittsburgh

PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
- NASPGHAN
- AGA
- CCFA
- American Academy of Pediatrics

HONORS
- Best Doctors in America, Woodward/White, Inc.
MAJOR LECTURESHIPS AND SEMINARS

• “Pediatric Gastroesophageal Reflux,” general pediatric podcast with Candace Jones, 2017
• “Good Teaching: What Works and What We Can Do,” invited presentation, Children’s Mercy Hospital, Kansas City, Mo., April 2017

Veena Venkat, MD

RESEARCH

The Pittsburgh Cholestatic Liver Disease Consortium (ChiLDReN). This NIH-funded network conducts detailed clinical and translational investigations of cholestatic liver diseases in children. Veena Venkat is a co-investigator.

A Phase I/IIa Trial of Intravenous Immunoglobulin Therapy Following Portoenterostomy in Infants With Biliary Atresia. This study aims to determine the feasibility, acceptability, tolerability, and safety profile of intravenous immunoglobulin treatment after hepatic portoenterostomy for biliary atresia. Venkat is site principal investigator.

Immunosuppression Withdrawal for Stable Pediatric Transplant Recipients. The long-term objective of this NIH-funded network is to improve outcomes for pediatric liver transplant recipients through discoveries that will guide clinical decision-making related to immunosuppression withdrawal and simultaneously ensure excellent allograft function while minimizing complications of immunosuppression. Venkat is a co-investigator.

Improving Medication Adherence in Children Who Had a Liver Transplant (U34). This is the next phase of a now-completed R01 grant (MALT: Medication Adherence in Children Who Had a Liver Transplant) that validated the use of a marker of medication nonadherence, the Medication Level Variability Index (MLVI), in predicting rejection in children who have had a liver transplant. The researchers are developing a multisite trial in which pediatric liver transplant centers will use the MLVI to identify nonadherent recipients and a telemetric intervention to improve adherence.

Pediatric Primary Sclerosing Cholangitis Consortium. This is a multicenter study with the objective of describing the natural history of primary sclerosing cholangitis in children. Venkat is the site principal investigator.

A Multicenter Collaboration to Study Primary Sclerosing Cholangitis in Children: Primary Sclerosing Cholangitis Partners Seeking a Cure. The objective of this multicenter study is to collect retrospective data on children with primary sclerosing cholangitis that can be used to build a clinical trial and ultimately find an effective therapy. Venkat is the site principal investigator.

CTOTC: Biomarkers for PTLDs in Children. This is a clinical trial investigating biomarkers associated with the development of EBV-related PTLDs in pediatric liver, heart, heart with liver, small intestine, and liver with small intestine transplant candidates and recipients. Venkat is a co-investigator.

ADVISORY COMMITTEE MEMBERSHIPS

• Member, Steering Committee, Pediatric Special Interest Group, AASLD
• Co-chair, Biliary Atresia Natural History and Therapeutics Working Group, ChiLDReN Research Network
• Protocol Committee: A Prospective Database of Older Children with Biliary Atresia, ChiLDReN
• Member, Education Committee, SPLIT, November 2014 to the present

Xunjun Xiao, PhD

Xunjun Xiao served as research assistant professor until March 31, 2017.

RESEARCH

Xiao has been extensively involved in ongoing efforts to better understand how newborns digest dietary fats. His work aims to understand how PLRP2 functions in human newborns. First, he is characterizing the properties of purified PLRP2 in the laboratory. Second, he is translating his findings in newborn mice, demonstrating that PLRP2 is critical for fat digestion. The investigation may assist in finding nutritional therapies to treat the 10% of newborns who have slow weight gain at birth.

Xiao also works to elucidate the mechanism behind chronic pancreatitis. Most children with chronic pancreatitis have genetic mutations that increase their risk, but the contributing mechanisms are not well known. The researchers are using model systems to test the novel hypothesis that expression of the mutant proteins in the pancreas leads to a stress response and cell death. The findings stand to increase understanding of pancreatic injury and provide guidance for developing new pharmacological interventions to prevent the ongoing damage from progressing to chronic changes in the pancreas.
PROFESSIONAL AFFILIATIONS/SOCIETY MEMBERSHIPS
• American Society of Nutrition Sciences
• American Society of Biochemistry and Molecular Biology

HONORS
• Western Pennsylvania National Pancreas Foundation Research
• Grant Award: “Carboxyl Ester Lipase Hybrid Confers Susceptibility to Chronic Pancreatitis Through Proteotoxicity”

TEACHING ACTIVITIES

NEW TEACHING PROGRAMS AND COURSES (AND OTHER EDUCATIONAL INNOVATIONS)
During the 2016–2017 academic year, the Division of Gastroenterology, Hepatology, and Nutrition has been implementing new educational programs to enhance its faculty and fellows. Under the fellowship direction of Arvind Srinath and Riha Bhatt, as well as the division chiefs, David Keljo (interim) and Mark Lowe (past), the division has augmented and enhanced the curriculum for its fellows, as well as provided more educational opportunities for faculty to increase their knowledge in the many subspecialties that make up the division. Mentoring activities occur in the division’s research laboratories and across clinical research teams.

PEDIATRIC EXOCRINE PANCREATIC SEMINAR SERIES
Husain was awarded an unrestricted educational grant from Abbvie to launch a new educational series for fellows and faculty, titled “The Pediatric Exocrine Pancreatic Disorders Seminar Series.” The seminar series hosted authorities in the field of clinical and research pancreatology. It included the following visiting professors.

<table>
<thead>
<tr>
<th>NAME</th>
<th>INSTITUTION</th>
<th>PRESENTATION</th>
<th>DATE OF VISIT</th>
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<tbody>
<tr>
<td>Miklos Sahin-Toth, MD, PhD</td>
<td>Boston University</td>
<td>“A Spotlight on the Genetic Basis for Hereditary Pancreatitis”</td>
<td>November 18, 2016</td>
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<td>Bradley Barth, MD, MPH</td>
<td>University of Texas Southwestern</td>
<td>“Pediatric Pancreatic Interventions”</td>
<td>January 13, 2016</td>
</tr>
<tr>
<td>Tanja Gonksa, MD</td>
<td>Hospital for Sick Children and University of Toronto</td>
<td>“CFTR and Pancreatitis”</td>
<td>February 17, 2017</td>
</tr>
<tr>
<td>Vikesh Singh, MD, MS</td>
<td>Johns Hopkins University</td>
<td>“Fluids, Pancreatitis Severity, and What’s in the Pipeline for Pancreatitis Treatments”</td>
<td>March 17, 2017</td>
</tr>
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The series received overwhelmingly positive feedback, and Husain looks forward to renewed funding.

PEDIATRIC GASTROENTEROLOGY FELLOWSHIP PROGRAM
Srinath and Bhatt, directors of the Pediatric Gastroenterology Fellowship Program, through requested feedback from fellows and faculty, enhanced the program as follows. The directors, along with the division’s hepatologists, developed an inpatient rotation specifically to enhance the care of hepatology and transplant hepatology patients. The curriculum was augmented with targeted didactic objectives to be covered in monthly case-based conferences and weekly service patient conferences.

• Sevilla joined the faculty in 2016 and has since codeveloped and implemented (with the fellowship program directors) an advanced nutrition curriculum for the pediatric gastroenterology fellows. Presentations for fellows and faculty occur quarterly.
• A chief pediatric gastroenterology fellow program was piloted. The goal of the program is to offer leadership and mentoring opportunities to the two senior fellows. Feedback from the fellows has indicated success, which has led to its continuation next year.

PEDIATRIC TRANSPLANT HEPATOLOGY FELLOWSHIP PROGRAM
In November 2016, James Squires began the application process to restart the Pediatric Transplant Hepatology Fellowship Program. He received accreditation from the Accreditation Council for Graduate Medical Education (ACGME) for its establishment. He will lead the transplant hepatology team of McKiernan, Robert Squires, Khan, and Venkat and work directly with the pediatric transplant surgeon team to build the program.
RESEARCH LABORATORY TEACHING ACTIVITIES

Ghazi has been very active teaching courses and giving lectures for PhD students, fellows, residents, and medical students in a variety of courses.

TEACHING HONORS AND AWARDS

Hilary Michel was awarded First-Year Fellow of the Year by the UPMC Residency Program. This is the second year in a row that a pediatric gastroenterology fellow has received the award.

QUALITY MEASURES FOR TEACHING ACTIVITIES

In addition to continuous bidirectional feedback from faculty, fellows, and staff, the division conducts the following quality measures for teaching activities: fellow evaluations (quarterly), which have been aligned with the ACGME milestones; Clinical Competency Committee evaluations, which include evaluations of fellow teaching activities; resident evaluations (continuous throughout the year for fellows and faculty); and yearly fellow training exam scores.

THREE-YEAR BIBLIOGRAPHY

2015


2016


2017


