

Division of Gastroenterology, Hepatology & Nutrition

DIVISION PROFILE	
Number of Faculty	21
Number of Fellows	
Clinical Fellows	11
Research Fellows	5
Number of Graduate Students	1
Number of Other Students (full and part-time)	0
Number of Support Personnel	66
Annual Total Grant Support (direct)	\$3,120,767
Annual Total Industry Contracts (direct)	\$124,731
Number of Peer Reviewed Publications	40
Patient Encounters	
Outpatient	10,448
Inpatient	8,408

FACULTY LISTING

Mitchell B. Cohen, MD, CCHMC Endowed Chair, Professor of Pediatrics, Director, Division of Gastroenterology, Hepatology and Nutrition; Director, Cincinnati Digestive Disease Research Development Center

William F. Balistreri, MD, Dorothy M.M. Kersten, Professor of Pediatrics, Medical Director, Pediatric Liver Care Center; Associate Chair for Subspecialty Training, Department of Pediatrics; Editor, Journal of Pediatrics

Michael D. Bates, MD, PhD, Assistant Professor of Pediatrics, Associate Fellowship Director, Training Program in Pediatric Gastroenterology, Hepatology and Nutrition

Jorge A. Bezerra, MD, Professor of Pediatrics, Director of Research, Division of Gastroenterology, Hepatology and Nutrition; Director, Biliary Atresia Center; Associate Director, Cincinnati Digestive Disease Research Development Center

John C. Bucuvalas, MD, Professor of Pediatrics, Associate Medical Director, Pediatric Liver Care Center; Director of Clinical Operations, Division of Gastroenterology, Hepatology and Nutrition

Kathleen M. Campbell, MD, Assistant Professor of Pediatrics, Associate Fellowship Director, Training Program in Pediatric Gastroenterology, Hepatology and Nutrition

Lee A. Denson, MD, Assistant Professor of Pediatrics, Director, Training Program in Pediatric Gastroenterology, Hepatology and Nutrition

Michael K. Farrell, MD, Professor of Pediatrics, Chief of Staff

Xiaonan Han, PhD, Research Instructor

James E. Heubi, MD, Professor of Pediatrics, Director, General Clinical Research Center; Assistant Dean for Clinical Research, University of Cincinnati College of Medicine

Ajay Kaul, MD, Assistant Professor of Pediatrics, Director, GI Motility Disorders Center

Samuel A. Kocoshis, MD, Professor of Pediatrics, Director, Nutrition and Intestinal Care Center

Mike A. Leonis, MD, PhD, Instructor

M. Susan Moyer, MD, Professor of Pediatrics, Director, Schubert-Martin Inflammatory Bowel Disease Center

Philip E. Putnam, MD, Associate Professor of Pediatrics, Director, Endoscopy Services; Medical Director, Cincinnati Center for Eosinophilic Disorders

Jeffrey A. Rudolph, MD, Assistant Professor of Pediatrics

Noah Shroyer, PhD, Assistant Professor of Pediatrics, Associate Fellowship Director, Training Program in Pediatric Gastroenterology, Hepatology and Nutrition

Kris Steinbrecher, PhD, Assistant Professor of Pediatrics

Gitit Tomer, MD, Assistant Professor of Pediatrics

Stavra Xanthakos, MD, Assistant Professor of Pediatrics

Nada A. Yazigi, MD, Assistant Professor of Pediatrics, Associate Fellowship Director, Training Program in Pediatric Gastroenterology, Hepatology and Nutrition

OVERVIEW



Left to Right: (1st row) L. Denson, J. Bezerra, N. Yazigi, W. Balistreri, W. Schubert, M. Cohen, G. Tomer (2nd row) X. Han, K. Steinbrecher, N. Shroyer, K. Campbell, S. Xanthakos, M. Bates, A. Kaul, P. Putnam, M.S. Moyer, J. Rudolph, M. Leonis

The overall goals of the division are 1) to be a leader in the care of children with gastrointestinal and liver disease by providing safe, effective, efficient, equitable and family centered care, and 2) to advance research that will lead to novel and improved therapeutic strategies for children with digestive diseases and to incorporate research opportunities into our clinical care. The division is organized to advance our strategic goals and to match scientific priorities with specific clinical disorders, i.e., disease based research, so that we might have the greatest impact on “Changing the Outcome” for pediatric digestive diseases. Specifically, our goals are to improve digestive health for children through better treatments and outcomes for key pediatric digestive diseases including biliary atresia, inflammatory bowel disease (IBD), eosinophilic gastrointestinal disorders (EGIDs), liver and intestinal failure and liver and intestinal transplantation, obesity and developmental and motility disorders of the gastrointestinal tract. The division supports and participates in a number of multidisciplinary centers of clinical excellence including the Schubert Martin IBD Center, the Cincinnati Center for Eosinophilic Disorders and the Colorectal Center. We also are home to or participate in a number of NIH funded translational research centers including the Biliary Atresia Research Consortium, Cholestatic Liver Disease Consortium, Studies in Pediatric Liver Disease (SPLIT), the Acute Liver Failure Network (ALF), Adolescent Bariatrics: Assessing Benefits and Risks, the Enteric Vaccine and Treatment Evaluation Unit (VTEU) and the Cincinnati Digestive Disease Research Development Center. We have a strong commitment to professional education including an outstanding NIH funded Fellowship Training Program. The division also has active health services research programs to enable us to be the leader in improvement of outcomes and family centered care. Although progress is not always linear, often basic research informs translational research opportunities that lead to more definitive patient oriented research studies such as clinical trials. Once new treatments are in place, outcomes and health care delivery research allow maximization of the benefits of the translated basic science work to children with digestive diseases.

HIGHLIGHTS

Clinical Care

Our clinical care efforts are centered on important diseases that will allow us to improve digestive health through better treatments and outcomes. These target diseases include biliary atresia (BA), inflammatory bowel disease (IBD), eosinophilic gastrointestinal disorders (EGIDs), liver and intestinal failure and transplantation, motility disorders, anorectal malformations and obesity. In each case we are further strengthening the integration of disease based research into our clinical care models. These efforts are facilitated by interdisciplinary clinical and research centers and their program leaders including the: Schubert-Martin IBD Center (M. Susan Moyer), Cincinnati Center for Eosinophilic Disorders (CCED) (P. Putnam),

Aerodigestive and Sleep Center (ADSC) (P. Putnam, A. Kaul), Interdisciplinary Feeding Team (A. Kaul), Pediatric Liver Care Center (PLCC) (W. Balistreri, J. Bucuvalas), BA Research Consortium (BARC) (J. Bezerra), Cholestatic Liver Disease Consortium (CLiC) (J. Heubi), Acute Liver Failure (ALF) Consortium (N. Yazigi), Studies in Pediatric Liver Transplantation (SPLIT) (J. Bucuvalas), and Nutrition and Intestinal Care Center (NICC) (S. Kocoshis).

The division has ongoing major quality improvement efforts relating to: A) IBD, and participates in the Pediatric IBD Network, the North American collaborative improvement project and has developed CCHMC Evidence Based Guidelines for use of mecaptopurine and infliximab. The IBD Center has approximately 550 patients in its newly revitalized registry. B) NICC, and is developing a clinical registry to improve care for the approximately 80 patients followed with intestinal failure. Improvement efforts involve standardization of care with the goals of prevention and improved treatment for central venous catheter associated bacteremia, a major cause of morbidity and mortality in these patients. C) Access, and has significantly decreased the waiting time for new patient visits to <14 days with referral letters sent back to primary care providers in an average of <3 days.

Family centered rounds and safety were further emphasized this year. This is exemplified by the nearly universal daily discussion of progress towards discharge goals with the family and medical team and the read back of newly prescribed medications on rounds to enhance patient safety.

Research

Drs. Xiaonan Han and Noah Shroyer joined the research faculty this year.

The research endeavors of the division are highly aligned with the clinical care programs. Prominent is cutting edge research focused on BA and related disorders (J. Bezerra, J. Heubi). This includes investigation of molecular mechanisms of BA/cholestasis, development of new diagnostic tools, e.g., the Jaundice chip, studies on nutritional and steroid treatment after BA surgery and inborn errors of bile acid metabolism. Research programs related to liver transplantation (J. Bucuvalas, K. Campbell, M. Leonis, N. Yazigi) include investigation of patient and allograft survival, gene polymorphisms that increase risk for renal dysfunction after transplantation and mechanisms leading to the development of hepatoblastoma. Programs related to IBD and EGIDs (M. Cohen, T. Denson, X. Han, P. Putnam, N. Shroyer, K. Steinbrecher, G. Tomer) include studies on inflammatory mechanisms of IBD, growth hormone treatment to decrease mucosal inflammation, genotype-phenotype correlations in IBD, molecular control of eosinophils in EGIDs, biomarkers of EGIDs and targeted anti-inflammatory treatment. Research programs related to intestinal failure and anorectal malformations (M. Bates, M. Cohen, J. Heubi, S. Kocoshis, J. Rudolph, N. Shroyer) include molecular control of intestinal proliferation and development, molecular control of intestinal apoptosis in animal models and transplant recipients, treatment/prevention of small bowel bacterial overgrowth, outcomes of intestinal transplantation, and diagnostic tests for fat malabsorption.

In addition, the division is the home to the NIH supported Digestive Disease Research Development Center (DDRDC) (M. Cohen, J. Bezerra) which fosters translational research in pediatric digestive disease through support for research cores.

Education

Dr. Lee (Ted) Denson became the Fellowship Director on July 1, 2006.

The NIH supported Fellowship Training Program continues to produce outstanding graduates who predominantly enter academic medicine (>80% over the past 10 years). This year our graduates took positions at the University of Wisconsin (N. Erickson), Eastern Virginia Medical School (M. Konikoff) and Cook Children's Hospital, Dallas, (B. Osuntokun). The fellowship program has now expanded to 4 fellows per year.

This year also marked the beginning of the combined GI-Liver service with a single resident team caring for all GI inpatients. Teaching was highly rated on this new team designed to improve patient care and enhance the teaching experience.

TRAINING

Jill Dorsey, MD	PL-4	Medical University of South Carolina
Alexander Miethke, MD	PL-4	Cincinnati Children's Hospital Medical Center
Brad Pasternak, MD	PL-4	S.U.N.Y. Downstate Medical Center
Scott Pentiuik, MD	PL-4	Cincinnati Children's Hospital Medical Center
Lynelle Boamah, MD	PL-5	Naval Medical Center - Portsmouth, Virginia
Rebecca Carey, MD	PL-5	University of Utah
Monica Garin-Laflam, MD	PL-5	Jackson Memorial Hospital
Veena Venkat, MD	PL-5	Cincinnati Children's Hospital Medical Center
Nissa Erickson, MD	PL-6	University of Wisconsin Hospital and Clinics
Michael Konikoff, MD	PL-6	Cincinnati Children's Hospital Medical Center
Bankole Osuntokun, MD	PL-6	Monmouth Medical Center
Cong Liu, PhD		University of Cincinnati
Ursula Matte, PhD		Universidade Federal do Rio Grande do Sul, Brazil
Sujit Mohanty, PhD		All Indian Medical Institute, New Delhi, India
Kumar Shanmukhappa, PhD		Kansas University, Missouri
Pranav Shivakumar, PhD		New Delhi University, India

GRANTS, CONTRACTS AND INDUSTRY AGREEMENTS

Grant and Contract Awards Annual Direct/Project Period Direct

Balistreri, W

Pegylated Interferon +/- Ribavirin for Children with HCV
National Institutes of Health (Johns Hopkins University subcontract)
U01 DK 067767 09/30/03 – 08/31/06 \$25,728/\$45,600

Bezerra, J

Clinical Center for Biliary Atresia: Etiopathogenesis and Clinical Outcome
National Institutes of Health
U01 DK 062497 09/15/02 – 05/31/09 \$159,329/\$962,733

Immunologic Dysfunction in Biliary Atresia
National Institutes of Health
R01 DK 064008 08/15/03 – 06/30/07 \$193,750/\$820,003

The Jaundice Chip: A Diagnostic Tool for Cholestatic Liver
National Institutes of Health (P2D, Inc. subcontract)
R41 DK 075162 05/01/06 – 04/30/07 \$44,319

Bucvalas, J

Studies of Pediatric Liver Transplantation
National Institutes of Health (The EMMES Corporation subcontract)
U01 DK 061693 05/14/04 – 03/31/09 \$20,800/\$52,000

Functional Outcomes in Pediatric Liver Transplantation
National Institutes of Health (Children's Memorial Hospital subcontract)
R01 HD 045694 04/01/05 – 03/31/10 \$12,583/\$77,569

Functional Outcomes in Pediatric Liver Transplantation
National Institutes of Health (Children's Memorial Hospital subcontract – per patient)
R01 HD 045694 04/01/05 – 03/31/10 \$48,658/\$243,290

Campbell, K

Pharmacogenetics of Post-Transplant Renal Dysfunction
American Liver Foundation
07/01/05 – 06/30/07 \$75,000/\$150,000

Cohen, M		
Expression and Function of the Guanylin Ligand Family National Institutes of Health		
R01 DK 047318	02/01/05 – 11/30/09	\$214,830/\$1,100,000
Pediatric Gastroenterology and Nutrition Training Grant National Institutes of Health		
T32 DK 007727	07/01/05 – 06/30/10	\$358,961/\$1,771,477
Cincinnati DDRDC: Center for Growth and Development National Institutes of Health		
R24 064403	05/08/03 – 03/31/08	\$336,105/\$1,732,500
Studies on Intestine-Enriched Transcription Factor IKFL National Institutes of Health		
R01 DK 058701	07/01/02 – 06/30/06	\$170,000/ \$680,000
Evaluation of Control Measures Against Diseases Other than AIDS: Part C-Cholera National Institutes of Health		
N01 AI 025459	06/01/02 – 05/31/07	\$438,896/\$2,202,030
Denson, L		
Cytokine Regulation of Liver Growth Hormone Signaling National Institutes of Health		
R01 DK 068164	04/01/06 – 12/31/10	\$200,000/\$1,000,000
Han, X		
Characterization of STAT5b as a Novel Therapeutic Target in Crohn's Disease Crohn's & Colitis Foundation of America		
	01/01/06 – 12/31/08	\$73,676/\$229,737
Heubi, J		
Intraluminal Effects of Cholesterol Absorption/Synthesis National Institutes of Health		
R01 DK 068463	05/01/05 – 01/31/10	\$359,211/\$1,907,911
Fecal Behenic Acid: A New Marker for Fat Malabsorption Cystic Fibrosis Foundation Therapeutics, Inc.		
HEUBI05A0	01/01/06 – 12/31/06	\$139,624
Moyer, S		
Multi-Site Trial of Azathioprine Dosing in Crohn's Disease National Institutes of Health (University of Chicago subcontract)		
U01 DK 060083	05/01/06– 04/30/07	\$13,378
Pasternak, B		
First and Second Year Clinical Fellowship Cystic Fibrosis Foundation		
PASTER05B0	07/01/05 – 06/30/07	\$42,000/ \$85,750
Shroyer, N		
Intestinal Secretory Lineage Differentiation and Function AGA/FDHN Research Scholars Award		
	067/01/06 – 06/30/08	\$1,354/\$34,375
Intestinal Secretory Lineage Differentiation and Function National Institutes of Health		
K01 DK071686	06/01/06 - 08/31/09	\$10,195/\$387,425
Rudolph, J		
Cyclic-AMP Induced Crypt Cell Survival in the Intestine National Institutes of Health		
K08 DK 066297	02/01/04 – 12/31/08	\$115,751/\$578,755

Yazigi, N		
A Multi-Center Group to Study Acute Liver Failure in Children		
National Institutes of Health (Children's Hospital of Pittsburgh subcontract)		
U01 DK 072146	09/01/05 – 08/31/07	\$66,619/\$133,238
Current Year Direct		\$3,120,767
Industry Contracts		
Balistreri, W		
Digestive Care		\$1,273
Glaxo NVC		\$2,931
Gilead Sciences		\$6,808
Bucuvalas, J		
Novartis		\$2,319
Cohen, M		
Salix Pharmaceutical		\$3,003
Denson, L		
Genentech		\$100,697
Centacor		\$7,700
Current Year Direct Receipts		\$124,731
TOTAL		\$3,245,498

PUBLICATIONS

- Balistreri WF, Bezerra JA. Whatever happened to "neonatal hepatitis"? Clin Liver Dis 2006;10(1):27-53, v.
- Balistreri WF, Bezerra JA, Jansen P, Karpen SJ, Shneider BL, Suchy FJ. Intrahepatic cholestasis: summary of an American Association for the Study of Liver Diseases single-topic conference. Hepatology 2005;42(1):222-35.
- Balistreri WF, Jobe A, Boat TF. Pediatric Subspecialty Training Fellowships at Cincinnati Children's Hospital Medical Center (CCHMC). J Pediatr 2005;147(3):277-8.
- Wieman RA, Balistreri WF. Nutritional support in children with liver disease. In: Baker RD, Baker SS, Davis AM, editors. Pediatric nutrition support handbook. Sudbury, MA: Jones and Bartlett Publishers; 2006. p. 445-461.
- Erwin CR, Jarboe MD, Sartor MA, Medvedovic M, Stringer KF, Warner BW, Bates MD. Developmental characteristics of adapting mouse small intestine crypt cells. Gastroenterology 2006;130(4):1324-32.
- Mikhailkevich N, Becknell B, Caligiuri MA, Bates MD, Harvey R, Zheng WP. Responsiveness of naive CD4 T cells to polarizing cytokine determines the ratio of Th1 and Th2 cell differentiation. J Immunol 2006;176(3):1553-60.
- Bezerra J. Biliary atresia: translational research on key molecular processes regulating biliary injury and obstruction. Chang Gung Med J 2006;29:222-230.
- Bezerra J, Shneider BL. Genetic modifiers of cholestatic liver disease: an evolving field. J Pediatr Gastroenterol Nutr 2006;42(1):7-8.
- Carvalho E, Liu C, Shivakumar P, Sabla G, Aronow B, Bezerra JA. Analysis of the biliary transcriptome in experimental biliary atresia. Gastroenterology 2005;129(2):713-7.
- Mohanty SK, Shivakumar P, Sabla G, Bezerra JA. Loss of interleukin-12 modifies the pro-inflammatory response but does not prevent duct obstruction in experimental biliary atresia. BMC Gastroenterol 2006;6:14.

11. Shanmukhappa K, Mourya R, Sabla GE, Degen JL, Bezerra JA. Hepatic to pancreatic switch defines a role for hemostatic factors in cellular plasticity in mice. *Proc Natl Acad Sci U S A* 2005;102(29):10182-7.
12. Shneider BL, Brown MB, Haber B, Whittington PF, Schwarz K, Squires R, Bezerra J, Shepherd R, Rosenthal P, Hoofnagle JH, Sokol RJ. A multicenter study of the outcome of biliary atresia in the United States, 1997 to 2000. *J Pediatr* 2006;148(4):467-474.
13. Bucuvalas J, Yazigi N, Squires RH, Jr. Acute liver failure in children. *Clin Liver Dis* 2006;10(1):149-68, vii.
14. Bucuvalas JC. Critical analysis of the pediatric end-stage liver disease scoring system: a single center experience. *J Pediatr Gastroenterol Nutr* 2005;41(4):487-8.
15. Gross TG, Bucuvalas JC, Park JR, Greiner TC, Hinrich SH, Kaufman SS, Langnas AN, McDonald RA, Ryckman FC, Shaw BW, Sudan DL, Lynch JC. Low-dose chemotherapy for Epstein-Barr virus-positive post-transplantation lymphoproliferative disease in children after solid organ transplantation. *J Clin Oncol* 2005;23(27):6481-8.
16. Squires RH, Jr., Shneider BL, Bucuvalas J, Alonso E, Sokol RJ, Narkewicz MR, Dhawan A, Rosenthal P, Rodriguez-Baez N, Murray KF, Horslen S, Martin MG, Lopez MJ, Soriano H, McGuire BM, Jonas MM, Yazigi N, Shepherd RW, Schwarz K, Lobritto S, Thomas DW, Lavine JE, Karpen S, Ng V, Kelly D, Simonds N, Hynan LS. Acute liver failure in children: the first 348 patients in the pediatric acute liver failure study group. *J Pediatr* 2006;148(5):652-658.
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19. Campbell KM, Yazigi N, Ryckman FC, Alonso M, Tiao G, Balistreri WF, Atherton H, Bucuvalas JC. High prevalence of renal dysfunction in long-term survivors after pediatric liver transplantation. *J Pediatr* 2006;148(4):475-80.
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29. Boesch RP, Daines M, Kaul A, Cotton R, Amin R. Lymphoproliferative disorder of the airway of an adolescent without immunodeficiency. *Int J Pediatr Otorhinolaryngol* 2005;69(11):1591-4.
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31. Focht DR, Kaul A. Food impaction and eosinophilic esophagitis. *J Pediatr* 2005;147(4):540.
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39. Xanthakos S, Miles L, Bucuvalas J, Daniels S, Garcia V, Inge T. Histologic spectrum of nonalcoholic fatty liver disease in morbidly obese adolescents. *Clin Gastroenterol Hepatol* 2006;4(2):226-32.
40. Xanthakos SA, Schwimmer JB, Melin-Aldana H, Rothenberg ME, Witte DP, Cohen MB. Prevalence and outcome of allergic colitis in healthy infants with rectal bleeding: a prospective cohort study. *J Pediatr Gastroenterol Nutr* 2005;41(1):16-22.