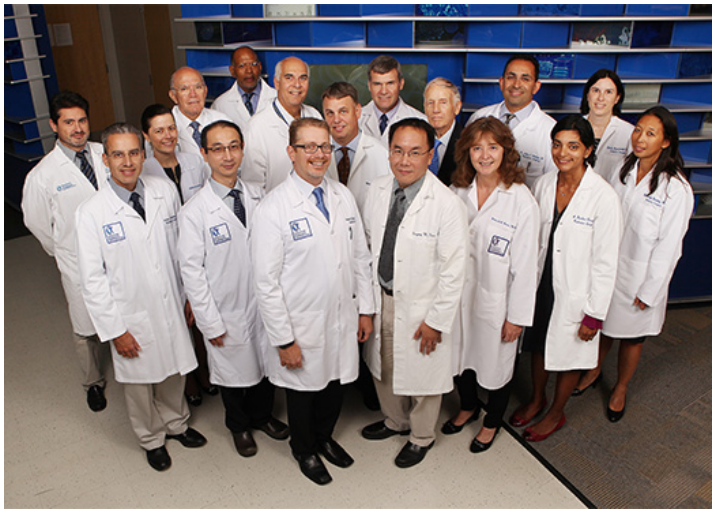
Cincinnati Children's

2015 Research Annual Report

Pediatric General and Thoracic Surgery

RESEARCH AND TRAINING DETAILS



Click to view members

Faculty	**26**
Research Fellows	**9**
Research Students	**23**
Support Personnel	**29**
Direct Annual Grant Support	**$2,800,033**
Direct Annual Industry Support	**$64,173**
Peer Reviewed Publications	**84**

CLINICAL ACTIVITIES AND TRAINING

Clinical Staff	**22**
Clinical Fellows	**8**
Inpatient Encounters	**6,542**
Outpatient Encounters	**11,665**

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Research Highlights

Pediatric General and Thoracic Surgery Innovations

The Division of Pediatric General and Thoracic Surgery has a strong focus on innovation ranging from novel therapeutic techniques to device development and sophisticated discovery based research models.

Therapeutic Interventions

An example of the cutting edge therapeutic interventions being developed in the Division comes from the fetal therapy section. Fetal interventions offer the opportunity to mitigate or reverse the complications associated with numerous prenatally diagnosed congenital malformations. Open fetal repair of myelomeningocele is one intervention that has proved beneficial. Unfortunately, these interventions are often complicated by preterm labor which constitutes the most common serious complication of fetal surgery. Reducing the invasiveness for the intervention would likely significantly improve the outcomes. Dr. Jose Peiro has developed a minimally invasive (fetoscopic) technique for the repair of spinal cord defects in fetuses. The procedure was developed in the animal model and is now undergoing trials in humans with more than 20 international cases done to date. The preliminary results are excellent and a broader, more comprehensive, trial to establish the safety and efficacy of the technique has been designed and will begin to enroll patients at Cincinnati Children'sin the near future.

This major therapeutic project is the most dramatic example of a clinical treatment innovation. The faculty constantly seeks improvements in the technical aspects of surgery, including minimally invasive and robotic procedures along with improvements in treatment protocols and algorithms.

Device Development

Members of the division have been very active in device development. The hospital enjoys a formal relationship with the engineering program at Ben Gurion University in Israel, and sponsors a joint grant program to fund innovative device ideas. The Division of General and Thoracic Surgery has been successful in obtaining three of the four grants awarded to date. A new surgical clamp to be used in bariatric surgery has already been licensed; an image guided robotic device has advanced to the marketing and business planning stage; and a project exploring technology for developing “smart catheters” continues to evolve. The broader vision of bringing advanced technology to surgery is driving an exciting collaboration between Phillips Medical and Cincinnati Children's to develop the operating room of the future incorporating advanced image guided surgery into everyday procedures.

Richard Falcone, MD

Trauma research continues to focus on the triage of pediatric trauma patients within the trauma system, and at the level of the pediatric trauma hospital. The trauma group is currently working on a project in collaboration with researchers from Children’s Hospital of Los Angeles and the Medical College of Wisconsin on work to better understand how pediatric trauma teams are activated to minimize under-triage to improve care. Understanding the statewide triage of pediatric trauma patients in also a current project. In addition, work has continued on expanding our trauma simulation program to educate rural emergency department providers, and studying the impact of this training on quality of care for pediatric trauma. Finally, the group continues to expand work on reducing unintentional injuries to children under five in Hamilton County with support from Kohl’s Cares for Kids and Messer Construction Co. Foundation funding.

Michael Helmrath, MD

Dr. Michael Helmrath is the surgical director of the Intestinal Rehabilitation Center. Basic and clinical studies evaluating the adaptive response of the bowel to injury and loss are the overarching themes in the lab. Specifically, the laboratory focuses on the role of intestinal stem cells in small intestinal physiology. Using a comprehensive approach of intestine development, the labs of both Helmrath and Wells developed an innovative *in vivo* model to study the human intestine: Read this study here. This advancement has led to numerous collaborative projects with investigators at Cincinnati Children's and other institutions, as well. Human translational studies involving shiga-toxin, cystic fibrosis, norovirus, aging

and circadian rhythm highlight the innovative advancement of this model. Additionally, Max Mahe, PhD, was awarded a grant from the Digestive Health Center at Cincinnati Children's to further develop a more robust human intestinal model incorporating the enteric nervous system.

Thomas Inge, MD, PhD

Dr. Thomas Inge is a full-time attending physician in the Division of Pediatric General and Thoracic Surgery, is the director of The Surgical Weight Loss Program for Teens, and is also the co-director of the Center for Bariatric Research and Innovation (CBRI). He has extensive clinical expertise in medical and surgical management of patients with severe obesity. The main focus of his research is the outcomes of bariatric surgery, for which he has been funded from the National Health Institutes (NIH) continuously since 2005. He is the principal investigator of the multicenter Teen LABS study which is in its ninth year of funding by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). The CBRI is currently partnering with multiple Cincinnati Children's divisions and other institutions to study the changes in patients after bariatric surgery. In 2015, Dr. Inge and coinvestigators were given an Academic and Research Committee award from the Children's Cancer Research Fund (CCRF) to collaborate with other leading Cincinnati Children's physicians and investigators to create the Pediatric Diabetes and Obesity Center (PDOC).

Helen Jones, PhD

Helen Jones, PhD and her lab members investigate placental anomalies and malfunction in a broad range of pathologies and are developing targeted gene therapy protocols that can be used during pregnancy to improve placental function and fetal growth. With collaborators from the University of Cincinnati, they have developed and demonstrated successful, cell-specific gene delivery both in primary human trophoblast cultures and a mouse model of placental insufficiency, along with maintenance of normal fetal growth in the mouse model upon.

In collaboration with James Cnota, MD and the Heart Institute, the Jones lab have demonstrated significant alteration of placental vascular and villous development in cases of Hypoplastic Left Heart Syndrome (HLHS) in humans and are utilizing a new mouse model of HLHS to assess placental development throughout gestation.

Dr. Jones and her team have also established collaborations with Drs. Louis Muglia, MD, PhD, and Michaela Pavlicev PhD, Center for Prevention of Preterm Birth, to investigate placental involvement in preterm birth with studies involving single cell sequencing of human placentas.

Jaimie Nathan, MD

Studying the Role of Intestinal Microbiota in Human Diseases

Jaimie Nathan, MD, Surgical Director of the Intestinal Transplant Program, and his team are investigating the role of intestinal microbiota in intestinal transplantation and in progression of chronic liver diseases. With grant funding from the American Society of Transplant Surgeons, the team is studying the role of intestinal microbiota in acute rejection after intestinal transplantation with the goal of identifying novel non-invasive biomarkers to predict the development of rejection. Investigating the role that changes in intestinal microbiota play in the progression of chronic liver disease and its complications, and in the development of post-liver transplantation complications in children is the focus of another study funded by the Markham Family Award on Liver Diseases/Liver Transplantation. Using a mouse model of small bowel bacterial overgrowth, the Nathan lab is studying the gut-liver axis as it relates to the pathogenesis of a number of cholangiopathies which can progress to end-stage liver disease.

Jose L Peiro MD, PhD

A research team led by Jose L. Peiro, MD, PhD, Director of Endoscopic Fetal Surgery at the Cincinnati Fetal Center, is continuing investigating the basic mechanisms of pediatric and fetal surgical congenital malformations, focusing especially upon fetal myelomeningocele (MMC), congenital diaphragmatic hernia (CDH) and gastroschisis.

New Trends in Spina Bifida

Improving the fetoscopic approach for intrauterine repair by evaluating different patches and sealants in animal models (in a collaborative work with biomedical engineers at the University of Cincinnati, Professor Chia-Ying Lin's Laboratory), and then translating these techniques for use in the human fetus is the focus in MMC. A new clinical trial will compare fetoscopic MMC repair in humans against the standardized open fetal surgery approach.

The team is also are studying ways to use neural progenitor cells collected from the amniotic fluid of MMC patients as a potential form of neural regeneration (cell therapy).

They are using a mouse model of neural tube defects to investigate how maternal immune status can influence incidence of congenital malformations.

Evaluating Fetal Surgery to Support Lung Development

In CDH, they will continue studies in animal models that indicate that early fetal tracheal occlusion may induce faster and better fetal lung growth. A new animal model of CHAOS ligation of the fetal trachea early in gestation perfectly resembles the human histology of this condition. To continue this work, the team has begun studies to evaluate the metabolomics and proteomics of these tissues and fluids. They are analyzing the Echocardiographic effects of CDH and tracheal occlusion in the fetal rabbit model.

They expect to start this year with fetoscopic tracheal occlusion in human fetuses with severe CDH by detachable balloon insertion. This work will contribute to the ongoing multicenter TOTAL trial.

Can Elective Preterm Delivery Prevent Gastroschisis

In gastroschisis, they lead participation in an innovative international multicenter randomized study (GUT) designed to analyze elective preterm deliveries at 34 weeks' gestation instead of later induced or spontaneous delivery, as an approach to prevent intestinal inflammation, preserve intestinal motility and obtain better neonatal outcomes. Fetal animal models are now under study to support that therapeutic strategy by histologic preservation.

Aimen Shaaban, MD

Immunologic Tolerance to In Utero Hematopoietic Cell transplantation

Aimen F Shaaban, MD is the director for the Center for Fetal Cellular and Molecular Therapy. Research focuses on in utero hematopoietic cell transplantation (IUHCT) for the treatment of congenital diseases such as sickle cell disease and thalassemia with the goal of understanding the steps necessary for successful engraftment and long-term tolerance induction. In a small-animal model, the team is defining the manner in which the fetal immune system first learns to differentiate self from foreign cells. Over the past year, these studies have resulted in publications in the *Journal of Immunology* and *Frontiers in Pharmacology,* and research presentations at the Academic Surgical Congress. Our research program is funded by support from the National Institutes of Health (NIH) and the Children's Hospital Research Foundation.

Additionally, maintained productive collaborations with: 1) Dr. Sing Sing Way from the Infectious Diseases Division in probing how fetal exposure to mother's cells affects future reproductive fitness; 2) Dr. Helen Jones in exploring how the cross-talk between the maternal and fetal immune system affects placental development; 3) Drs. Foong-Yen Lim from the Cincinnati Fetal Center; Jose Luis Peiro from the Division of Pediatric General and Thoracic Surgery; and Beth Kline-Fath from the Department of Radiology in the study of how the human fetal lung grows in cases of congenital diaphragmatic hernia; 4) Dr. Kasper Hoebe from the Division of Immunobiology in exploring the mechanisms underlying fetal NK cell development; and 5) Dr. Damien Reynaud from the Division of Experimental Hematology and Cancer Biology in exploring the mechanisms controlling cell-fate decisions in the hematopoietic system. These collaborative works were published

in *Cell*, *Prenatal Diagnosis* and the *Journal of Pediatric Surgery*.

Gregory Tiao, MD

Dr. Tiao's lab continues to work on the pathogenesis of biliary atresia through an ongoing R01 project funded by the National Institutes of Health (NIH) with the assistance of his research team including Dr. Sujit Mohanty, research assistant Bryan Donnelly, and research fellows Inna Lobeck and Phylicia Dupree. Recently published data from his lab illustrated the role of Rhesus rotavirus (RRV) VP4 gene/protein in the activation of natural killer (NK) cells. The mechanism reported in this study demonstrated that those rotavirus strains which were capable of infecting murine bile ducts *in vivo* had a higher homology to RRV VP4. It was found that the infection alone was not enough to develop murine biliary atresia but it is VP4 dependent as RRV's VP4 was required for the activation of NK cells, which in turn were capable of killing naïve cholangiocytes leading to an obstructive cholangiopathy. In an additional study, our lab has identified a novel cell binding site on rotavirus's VP4 protein. The amino acid sequence "SRL" (445-447) binds to the extracellular form of heat shock cognate protein 70 (Hsc70) expressed on biliary epithelial cells (cholangiocytes). This binding site was found on only those strains that induce murine biliary atresia.

Nikolai Timchenko, PhD

Nikolai Timchenko, PhD, professor within the UC Department of Surgery and a leader of the Liver Tumor Program, and his lab, investigate mechanisms of hepatoblastoma (HBL) and hepatocellular carcinoma (HCC). The main hypothesis of these studies is that HBL is caused by a failure of hepatic stem cells to differentiate into mature hepatocytes; while development of HCC is associated with de-differentiation of hepatocytes into cancer stem cells. Dr. Timchenko's lab has generated five unique animal models with accelerated or inhibited liver cancer after treatments with certain carcinogens. Investigations of molecular pathways in these animal models revealed that the key event in development of HCC is the proteasome-mediated elimination of tumor suppressor proteins and proteins that support differentiation status of hepatocytes. In collaborations with Dr. Gregory Tiao, MD and Dr. James Geller, MD from the Division of Oncology, along with other members of Liver Tumor Program, Dr. Timchenko is analyzing liver samples from patients with HBL. These studies help to translate the knowledge of the molecular mechanisms of liver cancer, generated in animal models, to clinical application in human patients.

Significant Publications

Bout-Tabaku S, Michalsky MP, Jenkins TM, Baughcum A, Zeller MH, Brandt ML, Courcoulas A, Buncher R, **Helmrath M**, Harmon CM, Chen MK, **Inge TH**. Musculoskeletal Pain, Self-Reported Physical Function, and Quality of Life in the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-Labs) Cohort. *JAMA Pediatr.* 2015 Jun;169(6):552-9.

Obesity is associated with chronic musculoskeletal pain and is a risk factor for disability and osteoarthritis. This report describes the prevalence, sites, and intensity of musculoskeletal pain in adolescents with severe obesity. Among 233 adolescents undergoing bariatric surgery, 49% had poor functional status and 76% had musculoskeletal pain. Lower back pain was prevalent (63%), followed by ankle/foot (53%), knee (49%), and hip (31%) pain; 26% had pain at all 4 sites. In adjusted analyses, compared with pain-free participants, those reporting lower extremity pain had greater odds of having poor physical function according to scores on the Health Assessment Questionnaire Disability Index (odds ratio = 2.82; 95% CI, 1.35 to 5.88; P < .01). Compared with pain-free participants, those reporting lower extremity pain had significantly lower Impact of Weight on Quality of Life–Kids total scores (β = −9.42; 95% CI, −14.15 to −4.69; P < .01) and physical comfort scores (β = −17.29; 95% CI, −23.32 to −11.25; P < .01).

Chaturvedi V, Ertelt JM, Jiang TT, Kinder JM, Xin L, Owens KJ, **Jones HN**, Way SS. Cxcr3 Blockade Protects against Listeria Monocytogenes Infection-Induced Fetal Wastage. *J Clin Invest.* 2015 Apr;125(4):1713-25.

This collaborative study with the Way lab evaluated the contribution of fetal antigen-specific CD8 T cells in fetal

wastage cause by listeriosis and potential therapeutic mechanisms preventing fetal loss. The Jones lab assisted in identifying infiltrating lymphocytes in the placenta.

Inge TH, Siegel RM, Xanthakos SA. Weight Loss Maintenance: A Hard Nut to Crack. *JAMA Pediatr.* 2014 Sep;168(9):796-7.

This editorial was written in response to a clinical trial that showed if children who are obese are institutionalized in an effort to treat their weight gain, they can lose weight over six months. However by two years all the weight they lost had been regained. While losing weight is possible, it is apparent weight loss maintenance is an almost impossible task, thus supporting the need for bariatric surgery in certain cases.

Jones K, Wei C, Schoser B, Meola G, **Timchenko N**, Timchenko L. Reduction of Toxic Rnas in Myotonic Dystrophies Type 1 and Type 2 by the Rna Helicase P68/Ddx5. *Proc Natl Acad Sci U S A.* 2015 Jun 30;112(26):8041-45.

In collaboration with Andrew Hershey, MD and Lubov Timchenko, PhD in the Division of Neurology, Dr. Nikolai Timchenko and team have identified a protein (RNA helicase p68), which can destroy toxic RNAs associated with Myotonic Dystrophy type 1 and 2 (DM1 and DM2). The team has shown the correction of p68 levels in animal models of the diseases reduces toxic RNAs and improves muscle functions and biology. This finding is a discovery which might be used for development of therapeutic approaches for DM1 and DM2. Dr. Timchenko's lab was responsible for providing the key reagents generated in his lab, p68 purification by HPLC techniques and intellectual contribution on the steps of generation of design, interpretations and paper preparation.

Watson CL, Mahe MM, Munera J, Howell JC, Sundaram N, Poling HM, Schweitzer JI, Vallance JE, Mayhew CN, Sun Y, Grabowski G, Finkbeiner SR, Spence JR, Shroyer NF, Wells JM, **Helmrath MA**. An in Vivo Model of Human Small Intestine Using Pluripotent Stem Cells. *Nat Med.* 2014 Nov;20(11):1310-4.

Using step-wise differentiation of human pluripotent stem cells (hPSCs), we generated human intestinal organoids (HIOs) produced in vitro and transplanted them into immunodeficient mice. After transplantation, these HIOs form mature human intestinal epithelium with a marked expansion and maturation of the epithelium and mesenchyme. Transplanted intestinal tissues demonstrated digestive functions as shown by permeability and peptide uptake studies.

Division Publications

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2. Alhajjat AM, Lee AE, Strong BS, Shaaban AF. **NK cell tolerance as the final endorsement of prenatal tolerance after in utero hematopoietic cellular transplantation**. *Front Pharmacol*. 2015; 6:51.
3. Azarow KS, Cusick R, Wynn J, Chung W, Mychaliska GB, Crombleholme TM, Chung DH, Lim FY, Potoka D, Warner BW, Aspelund G, Arkovitz MS. **The association between congenital diaphragmatic hernia and undescended testes**. *J Pediatr Surg*. 2015; 50:744-5.
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5. Balaji S, LeSaint M, Bhattacharya SS, Moles C, Dhamija Y, Kidd M, Le LD, King A, Shaaban A, Crombleholme TM, Bollyky P, Keswani SG. **Adenoviral-mediated gene transfer of insulin-like growth factor 1 enhances wound**

healing and induces angiogenesis. *J Surg Res*. 2014; 190:367-77.

6. Balaji S, Moles CM, Bhattacharya SS, LeSaint M, Dhamija Y, Le LD, King A, Kidd M, Bouso MF, Shaaban A, Crombleholme TM, Bollyky P, Keswani SG. **Comparison of interleukin 10 homologs on dermal wound healing using a novel human skin ex vivo organ culture model**. *J Surg Res*. 2014; 190:358-66.

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9. Bischoff A, Frischer J, Dickie BH, Pena A. **Anorectal malformation without fistula: a defect with unique characteristics**. *Pediatr Surg Int*. 2014; 30:763-6.

10. Bischoff A, Martinez-Leo B, Pena A. **Laparoscopic approach in the management of anorectal malformations**. *Pediatr Surg Int*. 2015; 31:431-7.

11. Bout-Tabaku S, Michalsky MP, Jenkins TM, Baughcum A, Zeller MH, Brandt ML, Courcoulas A, Buncher R, Helmrath M, Harmon CM, Chen MK, Inge TH. **Musculoskeletal Pain, Self-reported Physical Function, and Quality of Life in the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) Cohort**. *JAMA Pediatr*. 2015; 169:552-9.

12. Chaturvedi V, Ertelt JM, Jiang TT, Kinder JM, Xin L, Owens KJ, Jones HN, Way SS. **CXCR3 blockade protects against Listeria monocytogenes infection-induced fetal wastage**. *J Clin Invest*. 2015; 125:1713-25.

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Faculty, Staff, and Trainees

Faculty Members

Daniel von Allmen, MD, Professor

Leadership Director, Division of General and Thoracic Surgery; Program Director of Pediatric Surgery Fellowship ; Professor, UC Department of Surgery

Research Interests Oncology; innovation; surgical workforce

Richard Azizkhan, MD, Professor

Leadership Surgeon-in-Chief; Lester W. Martin Chair of Pediatric Surgery; Surgical Director Emeritus, Hemangioma and Vascular Malformation Program; Professor, UC Department of Surgery

Research Interests Trauma systems; injury prevention; fetal lung development; vascular malformations; solid tumors in childhood

Maria Alonso, MD, Associate Professor

Leadership Co-Surgical Director, Intestinal Transplant Surgery; Associate Professor, UC Department of Surgery

Andrea Bischoff, MD, Assistant Professor

Leadership Pediatric Surgeon, Peña Colorectal Center; Assistant Professor, UC Department of Surgery

Rebeccah Brown, MD, Associate Professor

Leadership Director, Buckle Up For Life; Associate Director, Trauma Services; Associate Professor, UC Department of Surgery

Research Interests Pediatric trauma; injury prevention

A. Roshni Dasgupta, MD, MPH, Associate Professor

Leadership Pediatric Surgeon, Division of Pediatric General and Thoracic Surgery; Associate Professor, UC Department of Surgery

Research Interests Oncology and vascular malformations

Belinda Dickie, MD, PhD, Assistant Professor

Leadership Pediatric Surgeon, Peña Colorectal Center; Surgical Director, Hemangioma and Vascular Malformation Program; Assistant Professor, UC Department of Pediatrics

Peter Dickie, PhD, Assistant Professor

Richard Falcone, MD, MPH, Associate Professor

Leadership Director, Trauma Services; Associate Professor, UC Department of Surgery

Research Interests Injury prevention; health disparities; pediatric colorectal disorders; use of simulation to improve teamwork and safety

Jason Frischer, MD, Assistant Professor

Leadership Director, Peña Colorectal Center; Director, Extracorporeal Membrane Oxygenation (ECMO) Program; Division of Pediatric General and Thoracic Surgery; Assistant Professor, UC Department of Surgery

Victor Garcia, MD, FACS, FAAP, Professor

Leadership Founding Director, Trauma Services; Professor, UC Department of Surgery

Mounira Habli, MD, Assistant Professor

Leadership Maternal Fetal Medicine Specialist, Cincinnati Fetal Center; Assistant Professor, UC Department of Surgery

Michael Helmrath, MD, MS, Professor

Leadership Surgical Director, Intestinal Rehabilitation Program; Director of Surgical Research; Pediatric Surgeon, Peña Colorectal Center; Professor, UC Department of Surgery

Thomas Inge, MD, PhD, FACS, FAAP, Professor

Leadership Surgical Director, Surgical Weight Loss Program for Teens ; Director, Center for Bariatric Research and Innovation; Attending Surgeon, Cincinnati Children's Hospital Medical Center; Professor, UC Department of Surgery

Todd Jenkins, PhD, MPh, Assistant Professor

Leadership Director, Data Coordinating Center

Helen Jones, PhD, Assistant Professor

Leadership Assistant Professor, UC Department of Surgery

Research Interests Regulation of placental growth and function; regulation of mechanisms of placental nutrient transfer and consequences for fetal growth

Foong-Yen Lim, MD, Associate Professor

Leadership Surgical Director, Cincinnati Fetal Center; Associate Professor, UC Department of Surgery

Sujit Mohanty, PhD, Instructor

Jaimie Nathan, MD, Assistant Professor

Leadership Surgical Director, Intestinal Transplant Program; Surgical Director, Pancreas Care Center; Assistant Professor, UC Department of Surgery; UC Department of Pediatrics

Jose Peiro, MD, Associate Professor

Leadership Endoscopic Fetal Surgery Director, Cincinnati Fetal Center; Pediatric Surgeon, Division of General and Thoracic Surgery; Associate Professor, UC Department of Surgery

Research Interests Myelomeningocele intrauterine repair; fetal tracheal occlusion for CDH

Alberto Peña , MD, Professor

Leadership Founding Director, Peña Colorectal Center; Professor, UC Department of Surgery

Frederick Ryckman, MD, Professor

Leadership Sr. Vice President, Medical Operations; Professor, UC Department of Pediatrics; UC Department of Surgery

Beth Rymeski, DO, Assistant Professor

Leadership Pediatric Surgeon, Peña Colorectal Center; Assistant Professor, UC Department of Surgery

Aimen F. Shaaban, MD, Professor

Leadership Director, Center for Fetal Cellular and Molecular Therapy; Professor, UC Department of Surgery

Gregory Tiao, MD, Professor

Leadership Surgical Director, Liver Transplantation; Associate Director, Pediatric Surgery Fellowship; Richard and Geralyn Azizkhan Chair in Pediatric Surgery; Professor, UC Department of Surgery; UC Department of Pediatrics

Nikolai Timchenko, PhD, Professor

Leadership Head of Liver Tumor Biology, Liver Tumor Program; Professor, UC Department of Surgery

Clinical Staff Members

- **Jennifer Bailey, MSN, APRN, CNP**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Christina Bates, MSN, APRN, CPNP**, Nurse Practitioner, Division of General and Thoracic Surgery

- **Erin Butt, MSN, APRN, CNP**, Nurse Practitioner, Trauma Services
- **Kimberly Cain, MSN, APRN, CFNP, CWOCN**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Becky Cook, DNP, APRN, CPNP**, Nurse Practitioner, Trauma Services
- **Viki Dittrich, RNII, MSN**, Registered Nurse, Division of General and Thoracic Surgery
- **Kevin Fischer, MSN, APRN, CNP**, Nurse Practitioner, Division of Pediatric General and Thoracic Surgery
- **Betsy Gerrein, DNP, APRN**, APRN Program Lead, Division of Pediatric General and Thoracic Surgery
- **Jenny Hogan-Scott, APRN, CNP**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Emily McKenna, MSN, APRN, FNP**, Nurse Practitioner, Division of Pediatric General and Thoracic Surgery
- **Ebony Moorefield, MSN, APRN, PNP**, Pediatric Nurse Practitioner, Peña Colorectal Center
- **Linda Kollar, MSN, APRN, CNP**, Bariatric Clinical Director, Surgical Weight Loss Program for Teens;Nurse Practitioner, Division of Pediatric and Thoracic Surgery
- **Stephen M. Ogg, MSN, APRN, FNP-C**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Jennifer Sauser, MSN, APRN, CPNP**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Kaaren Shebesta, MSN, APRN, CPNP**, Nurse Practitioner, Trauma Services
- **Stacey Simmons, MSN, APRN**, Nurse Practitioner, Division of General and Thoracic Surgery
- **Joyce Slusher, BSN, APRN, CNP, CCTC**, Transplant Coordinator, Division of General and Thoracic Surgery
- **Marilyn Stoops, MSN, APRN, CPNP**, Nurse Practitioner, Division of General and Thoracic Surgery

Trainees

- **Myron Allukian, MD**, PL-9, Brown University, Providence, RI
- **Beth Rymeski, DO**, PL-9, University of New England College of Osteopathic Medicine, Biddeford, ME
- **Carlos Albarez-Allende, MD**, PL-6, University of Puerto Rico School of Medicine
- **Nadja Apelt, MD**, PI-6, Dr. von Haunersches Children's Hospital, Munich University, Munich, Germany
- **Young Chun, MD**, PL-4, Morris Town Medical Center, New Jersey
- **Louis Le, MD**, PL-6, Cincinnati Children's Hospital Medical Center
- **Anthony Munaco, MD**, PL-7, Henry Ford Hospital, Detroit, Michigan
- **Miho Watanabe, MD, PhD**, PL-6, Children's Hospital of Philadelphia

Grants, Contracts, and Industry Agreements

Grant and Contract Awards **Annual Direct**

Falcone, R

Multi-Center Evaluation of Defined Pediatric Trauma Activation Criteria

Laerdal Foundation(Children's Hospital Los Angeles)

	1/1/2015-12/31/15	$7,684

Helmrath, M

Investigation of Regional Identity in Human Intestinal Stem Cells

National Institutes of Health

U01 DK103117	9/1/2014-8/31/2019	$256,611

Inge, T

Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS)

National Institutes of Health

UM1 DK072493	9/23/2011-8/31/2016	$538,455

Jenkins, T

Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS)

National Institutes of Health(University of Cincinnati)

UM1 DK095710	9/23/2011-8/31/2016	$597,182

Jones, H

Insulin-like Growth Factor 1 Gene Therapy: Correction of Placental Insufficiency

National Institutes of Health

R00 HD068504	4/1/2014-3/31/2017	$152,176

Keswani, S

Novel Mechanisms of Regenerative Wound Healing

National Institutes of Health

R01 GM111808	9/1/2014-8/31/2019	$200,000

Laake, D

Youth Occupant Protection Regional Coordinator Program

Ohio Department of Health

	4/22/2014-9/30/2015	$38,000

Lim, F

Identification of Novel Genes for Congenital Diaphragmatic Hernia

National Institutes of Health(The Trustees of Columbia University)

R01 HD 057036	7/1/2008-6/30/16	$10,857

Shaaban, A

The NK Cell Response to Prenatal Allotransplantation

National Institutes of Health

R01 HL103745	3/5/2013-6/30/2016	$245,000

Tiao, G

The Molecular Determinants of Virus Induced Biliary Atresia

National Institutes of Health

R01 DK091566	4/1/2011-3/31/2016	$230,584

Timchenko, N

Role of Age in Liver Cancer

National Institutes of Health

R01 CA159942	6/1/2014-5/31/2016	$207,500

NAFLD: Mechanisms and Treatments

National Institutes of Health

R01 DK102597	1/1/2015-12/31/2018	$225,000

Molecular Mechanisms of C/EBP Alpha Mediated Growth Arrest

National Institutes of Health

R01 GM055188	7/1/2014-11/30/2014	$90,984

Current Year Direct	**$2,800,033**

Industry Contracts

Inge, T

Ethicon Endo-Surgery, Inc.	$64,173

Current Year Direct Receipts	**$64,173**

Total	**$2,864,206**

Intestinal Organoids Grown from Stem Cells Open Doors for Bioengineered Tissue, Personalized Medicine

Michael Helmrath, MD, MS

RESEARCH AND TRAINING DETAILS

Faculty	26
Research Fellows	9
Research Students	23
Support Personnel	29
Direct Annual Grant Support	$2.8M
Direct Annual Industry Support	$64,173
Peer Reviewed Publications	84

Watson CL, Mahe MM, Munera J, Howell JC, Sundaram N, Poling HM, Schweitzer JI, Vallance JE, Mayhew CN, Sun Y, Grabowski G, Finkbeiner SR, Spence JR, Shroyer NF, Wells JM, Helmrath MA. An *in vivo* model of human small intestine using pluripotent stem cells. *Nat Med.* 2014;20(11):1310-1314.

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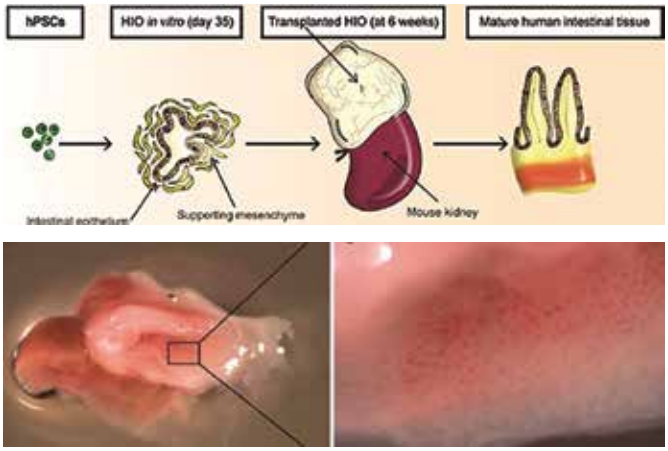
Nature Medicine

Doctors in the Division of Pediatric General and Thoracic Surgery are exploring unprecedented areas of tissue bioengineering and personalized medicine through their documented ability to grow human intestinal tissue from stem cells, transplant the tissues into mice and watch them perform as fully functioning human intestines.

In an Oct. 19, 2014, study in *Nature Medicine*, Michael Helmrath, MD, MS, Division of Pediatric General and Thoracic Surgery, reported his team had generated human intestinal organoids (HIOs) by manipulating either human embryonic stem cells (ESCs) or induced pluripotent stem cells (IPSCs). Implanted into mice and connected to the kidney for blood flow, the HIOs developed specialized intestinal epithelial and stem cells, enzymes, and vascular structures of the intestines. They also demonstrated basic digestive functions.

"The ability to regrow an organ is now possible, and it's so impressive how the cells themselves know how to do this," says Helmrath. "These studies support the concept that patient-specific cells can be used to grow intestine, and they provide a new way to study the many diseases and conditions that can cause intestinal failure, from genetic disorders appearing at birth to conditions that strike later in life, such as cancer and Crohn's disease. These studies also advance the longer-term goal of growing tissues that can replace damaged human intestine."

The ability to grow intestines from a patient's own cells also has broad implications for organ transplantation, post-surgical responses, accelerated drug development (by bypassing animal tests), and developing personalized medicine protocols for patients, depending on how their tissues respond to certain drugs or treatments.



This confocal microscopic image shows human intestinal cells that were successfully grown in a mouse model. The finger-like villi that support digestion appear in purple while muscle tissue appears in green.

"The ability to regrow an organ is now possible, and it's so impressive how the cells themselves know how to do this."