

## Digestive Health Center: Celebrating 15 Years



What started as a NIDDK funded “mini-center” 15 years ago has grown into a thriving digestive disease research center giving our investigators and institution national recognition. The vision of Dr. Mitchell Cohen (founding Director) and Dr. Jorge Bezerra (founding Associate Director and current Director) was to use the [Digestive Health Center](#) (DHC) as a springboard to grow and enhance digestive disease research in Cincinnati. In 2003, there were 34 members who had \$12.5 million in digestive disease funding. Fast forward 15 years, there are 84 members who have \$32.5 million in digestive disease funding. The DHC leaders look forward to continuing to work with Center members to advance their digestive disease research in the next 15 years.

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## 2018 Pilot and Feasibility Recipients

The DHC is pleased to announce the recipients of its 2018 Pilot & Feasibility grants.



**Akihiro Asai, MD, PhD; Dept Pediatrics; Division Gastroenterology, Hepatology & Nutrition**  
Project Title: “Modeling Patient-specific Genetic Cholestasis with Induced Human Hepatocytes”

Dr. Asai will study the mechanisms of bile acid metabolism in liver injury by using induced Pluripotent Stem Cells (iPSCs) to search for new therapies for cholestatic liver diseases.



**Pooja Khandelwal, MBBS Dept Pediatrics; Division Bone Marrow Transplantation & Immune Deficiency**

Project Title: Gene Expression Profiles in Acute GI GVHD

Dr. Khandelwal will identify the distinct gene expression signature of the intestinal epithelium in patients with acute gastrointestinal graft versus host disease (GVHD) after a bone marrow transplant (BMT).



**Rajat Madan, MBBS, PhD; Dept Internal Medicine; Division Infectious Diseases**

Project Title: “Impact of Obesity-associated Microbiome & Bile Acid Metabolites in Regulating *C. difficile* Lifecycle”

Dr. Madan will use a novel mouse model to study the impact of obesity associated gut microbiota and bile acid metabolites on *Clostridium difficile* lifecycle.



**Michael Rosen, MD, MSCI; Dept Pediatrics; Division Gastroenterology, Hepatology & Nutrition**  
Project Title: “Cell-specific Transcriptome Dysregulation across the Inflammatory Demarcation Line in Pediatric Ulcerative Colitis”

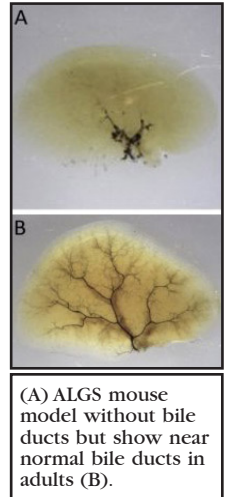
Dr. Rosen will study the differences in the cell types that compose diseased and healthy colon in pediatric patients with ulcerative colitis to identify new treatment strategies to promote bowel healing.

## Member's Research Published in *Nature*

The research work of DHC member Dr. Stacey Huppert was published in the May 10 issue of *Nature*. Using a mouse model that mimics the liver disease of human Alagille Syndrome (ALGS) the research team showed that in the absence of Notch signaling, TGF $\beta$  (transforming growth factor beta) pathway converted hepatocytes into mature cholangiocytes and formed functional bile ducts. ALGS is a rare, inherited genetic disorder resulting in the formation of too few bile ducts within the liver. These findings will be used to develop a therapy for ALGS as well as other liver diseases

that affect the biliary system.

The co-corresponding author of the study is Dr. Holger Willenbring, who is the Associate Director of Silvio O. Conte Digestive Diseases Research Core Center (DDRCC) at the University of California, San Francisco. This is an excellent example of how the NIDDK funded DDRCCs are collaborating to advance digestive disease research.



(A) ALGS mouse model without bile ducts but show near normal bile ducts in adults (B).

## Welcome DHC Integrative Morphology Core Director



Dr. Kathryn Wikenheiser-Brokamp is the new Director of the DHC Integrative Morphology Core. She is Dr. David Witte's successor who will be retiring from Cincinnati Children's this summer. Dr. Witte recruited Dr. Wikenheiser-Brokamp in 2007 to expand the pathology research program and enhance access to human tissues along with providing technical support and pathologic interpretation. She has established collaborations with the DHC Core Staff (e.g. created

a tissue processing pipeline with Dr. Matt Kofron of the confocal imaging core) and has published with Drs. Bruce Aronow, Jim Wells and Chris Mayhew. These well-established collaborations will allow for a seamless transition for her to assume her new role as the DHC Integrative Morphology Core Director. Her appointment was approved by both the DHC Internal and External Advisory Boards.

For assistance with Pathology interpretation please contact Dr. Wikenheiser-Brokamp:

[kathryn.wikenheiser-brokamp@cchmc.org](mailto:kathryn.wikenheiser-brokamp@cchmc.org)  
513-803-0239; CCHMC R4.455.

## Pluripotent Stem Cell Facility New Service and Location- R3.005

In continuing the partnership with the [Center for Stem Cell and Organoid Medicine](#) (CuSTOM), the [Pluripotent Stem Cell Facility](#) (PSCF) will help advance the research of DHC members. As part of Cincinnati Children's \$8 million investment to create CuSTOM the PSCF directed by Dr. Christopher Mayhew has expanded its services and physical space.

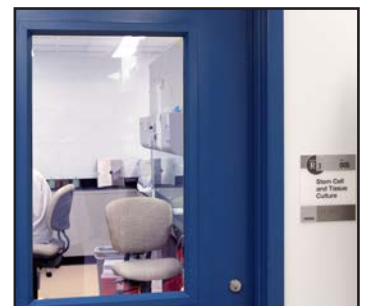
The PSCF now provides enhanced streamline services for generating patient-specific induced pluripotent stem cells (iPSCs). Additionally, in collaboration with the [Transgenic Animal and Genome Editing Core](#) at Cincinnati Children's, the PSCF offers CRISPR/Cas9 genome editing of human pluripotent stem cells (hPSCs) thereby facilitating a range of applications in basic and translational research.

The PSCF has relocated to R3.005 within Cin-

cinnati Children's and has nearly tripled its laboratory space going from 136 sq ft to 374 sq ft. This expansion will allow for the anticipated hiring of several new staff in the coming months to meet the

continued high demand for state-of-the-art human pluripotent stem cell and organoid services and will allow for future growth. In addition to more physical space, the PSCF now has two 2x6 ft and two 2x4 ft biosafety cabinets for tissue culture work.

For more information contact the core at [PSCF@cchmc.org](mailto:PSCF@cchmc.org) (513-636-3744) or visit the [PSCF core website](#).



## Biostatistical Consulting Unit and Data Management Center Merging



Beginning July 1, 2018, the Data Management Center (DMC) and the Biostatistical Consulting Unit (BCU) will merge as one Shared Facility: the Data Management and Statistics Center (DMASC). The new core remains part of the Department of Pediatrics, Division of Biostatistics and Epidemiology (DBE). Dr. Mekibib Altaye will be the Academic Director for DMASC. Rachel Akers, Cyndie Baker and Matthew Fenchel will continue in their roles, managing operations for the combined unit.

While the DMC and BCU have always worked closely together, being under “one roof” further promotes the idea that researchers are best served when study design, data management, programming and analysis are well-coordinated – from the beginning of a study to the end. This integrated process allows for higher quality data, at a lower overall cost.

### Scientific Rigor and Reproducibility

NIH requires applicants to address scientific rigor and transparency in their grant and annual progress report submissions. The expertise of the DMASC personnel (as well as faculty in DBE) can greatly assist researchers with meeting these NIH requirements. This includes, but is not limited to,

the following areas:

- Formulating clear, testable hypotheses, for which data are available
- Robust study design, minimizing various forms of bias
- Identifying which data should be collected and how it should be collected
- Case report form (CRF) development to minimize errors and maximize efficiency
- Database design, quality checks and query management
- Programming for clear and accurate regulatory and analysis reports
- Careful selection of analysis methodology, to accurately detect “signals” in the data, accounting for other variables of importance.

Researchers are strongly encouraged to contact the DMASC staff very early in the development of research proposals. Initial consultations are FREE of charge.

### Benefits for DHC Members

The DHC will provide 25% of the total charge for services provided at the DMASC with a subsidy limit of \$1,200 per member per year.

For more information contact:

[Biostatistical Consulting Unit \(BCU\) website](#)

Matt Fenchel at [bcu@cchmc.org](mailto:bcu@cchmc.org)

(513-803-0086)

[Data Management Center website](#)

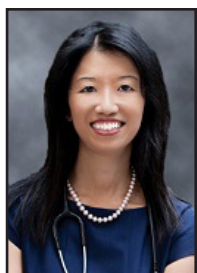
Rachel Akers at [dmc@cchmc.org](mailto:dmc@cchmc.org)

(513-636-7572)

Cyndie Baker [cynthia.baker@cchmc.org](mailto:cynthia.baker@cchmc.org)

(513- 803-4702)

## DHC Seminar Series- Summer Break



There will be no DHC seminars during the summer. Our fall seminar series will begin on Tuesday September 11 with Vicky Ng, MD from The Hospital for Sick Children. Dr. Ng completed her Pediatric Gastroenterology and Hepatology Fellowship at Cincin-

nati Children's. Her research focuses on outcomes after pediatric liver transplantation.

Seminars are held on Tuesdays at noon in CCHMC Location S Room 6.125. Light refreshments are provided. The enrichment series includes distinguished speakers from outside the Academic Medical Center as well as conferences by investigators from Cincinnati.



## Transition to Full Membership - Drs. Alenghat and Flick



Dr. Theresa Alenghat, Department of Pediatrics, Division of Immunobiology, at Cincinnati Children's, received her first NIH R01 from the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK). The title of her grant is "Epigenomic Control of Antimicrobial Immunity in the Intestine".

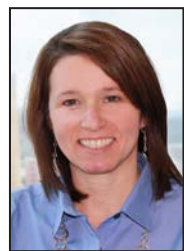
Dr. Matthew Flick, Department of Pediatrics, Division of Experimental Hematology and Cancer



Biology, at Cincinnati Children's received an NIH R01 award from the National Cancer Institute (NCI). The title of his grant is "Thrombin-Dependent Mechanisms of Pancreatic Ductal Adenocarcinoma Disease".

Drs. Alenghat and Flick used preliminary data that was generated from their DHC Pilot and Feasibility Award for their R01 grant applications. Congratulations to both of them!

## DHC Welcomes Two New Members



Jennifer Kaplan, MD, MS is an Associate Professor in the Department of Pediatrics, Division of Critical Care Medicine at Cincinnati Children's. Dr. Kaplan is working to identifying the mechanisms in which obesity contributes to the altered immune response in sepsis-induced critical illness.



Pooja Khandelwal, MBBS is an Assistant Professor in the Department of Pediatrics, Division of Bone Marrow Transplant and Immune Deficiency at Cincinnati Children's. Her research focuses on identifying the unique intestinal gene expression signature of acute gastrointestinal graft versus host disease after a bone marrow transplant.

## Interested in Becoming a Member?

By becoming a DHC member, you will receive subsidies for many core services and resources. Your orders will receive priority at the research cores. Membership is open to all Cincinnati Chil-

dren's and University of Cincinnati faculty members involved in digestive disease research. If you are interested in joining the DHC, visit [our website](#) for further instructions.

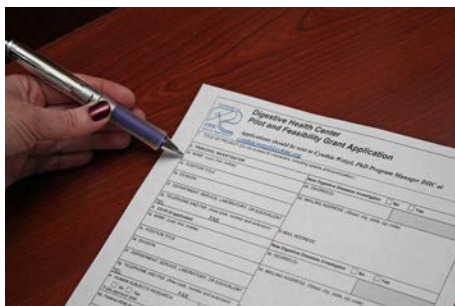
For all publications, please acknowledge the DHC as follows:

**"This project was supported in part by NIH P30 DK078392 (*insert name of core that you used*) of the Digestive Diseases Research Core Center in Cincinnati."**

For more information regarding the DHC visit our [website](#) or contact one of the following:

|                      |                         |                          |
|----------------------|-------------------------|--------------------------|
| Director:            | Jorge Bezerra, MD       | jorge.bezerra@cchmc.org  |
| Associate Directors: | Ted Denson, MD          | lee.denson@cchmc.org     |
|                      | Heidi Kalkwarf, PhD, RD | heidi.kalkwarf@cchmc.org |
|                      | Aaron Zorn, PhD         | aaron.zorn@cchmc.org     |
| Center Manager:      | Cynthia Wetzel, PhD     | cynthia.wetzel@cchmc.org |

## Request for Pilot and Feasibility Applications



The Digestive Health Center (DHC) is accepting applications for pilot projects to conduct basic, translational, patient based, or outcomes research broadly relating to pediatric digestive disease. Applications will be considered in all areas of digestive disease research with

particular emphasis on the following DHC research themes:

1. Liver Disease and Modeling
2. Digestive Disease and Immunity
3. Digestive Disease and Obesity
4. Translational Embryology (as it relates to digestive disease)

Funds are intended to allow investigators to collect preliminary data sufficient to support an application for independent research through traditional NIH mechanisms. Funding for projects will range from \$40,000 to \$50,000 depending on budgetary needs and number of selected applications. Eligible applicants must have a faculty appointment. DHC membership is not required.

Applications are due Monday December 3, 2018 at 5:00 pm. The application forms and submission guidelines are available on the [website](#).

For further information contact: Aaron Zorn, PhD, Pilot and Feasibility Program Director at [aaron.zorn@cchmc.org](mailto:aaron.zorn@cchmc.org) or Cindy Wetzel, PhD, DHC Program Manager at [cynthia.wetzel@cchmc.org](mailto:cynthia.wetzel@cchmc.org).

## IN THIS ISSUE:

- Request for Pilot and Feasibility Applications
- Annual Scientific Symposium
- 2018 Balistreri Lecture
- New Subsidy Gene Editing of Pluripotent Stem Cells
- Summary of DHC Subsidies
- Transition to Full Membership
- Symposium Announcements
- Upcoming Seminars

## Save the Date - Annual Scientific Symposium

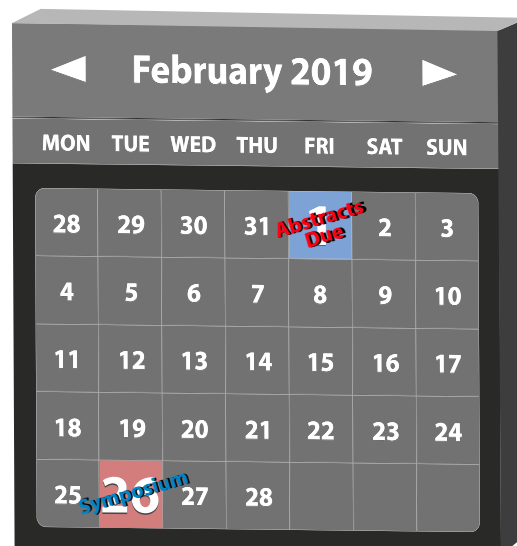
The DHC will host its Annual Scientific Symposium and External Advisory Board Meeting on **Tuesday February 26, 2019**. This is a great opportunity to learn about the digestive disease cutting edge research being performed in Cincinnati and to establish new collaborations.

The day will include a poster session and keynote address by Dr. Rebecca Wells from the University of Pennsylvania. Dr. Wells' research focuses on liver fibrosis.

We encourage you to present your digestive disease research by submitting an abstract for the poster session. You do not have to be a DHC member to present a poster.

Abstracts are due **Friday February 1, 2019**. Prizes will be given to students and trainees for the best poster presented at the symposium.

Stay tuned for more details.





## Transition to Full Membership - Dr. Michael Rosen



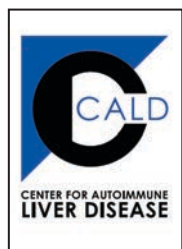
Dr. Michael Rosen, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition at Cincinnati Children's, received his first NIH R01 from the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK). The

title of his grant is "Type 2 Cytokines and Innate Lymphoid Cells in Pediatric Ulcerative Colitis".

Dr. Rosen used preliminary data that was generated from his DHC Pilot and Feasibility Award for his R01 grant application.

Congratulations to Dr. Rosen for transitioning to Full Membership status in the DHC!

## Annual Pediatric Autoimmune Liver Disease Symposium & Family Day



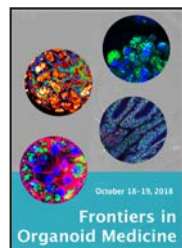
The 2nd Annual Pediatric Autoimmune Liver Disease Symposium and Family Day hosted by the Center for Autoimmune Liver Disease (CALD) will be held September 29 and 30 at Cincinnati Children's.

The focus of the symposium this year is the interaction between the gut and

liver and how this affects autoimmune liver disease. The two day event will include presentations by leaders in the field, a poster session, and educational sessions for patients with autoimmune liver disease.

To register visit the [Symposium Website](#). For more information send an email to [CALD@cchmc.org](mailto:CALD@cchmc.org)

## Frontiers in Organoid Medicine Symposium



The [Center for Stem Cell and Organoid Medicine](#) (CuSTOM) will host Frontiers in Organoid Medicine on October 18-19 at Cincinnati Children's. This international symposium is being cosponsored by CuSTOM and a number of biotechnology companies with the goal of accelerating

collaborations among those in academia and industry.

Presentations will focus on basic research to clinical and commercialization of stem cells and organoid technology. Workshops will focus on hurdles and opportunities in Organoid Medicine.

To register visit the [Symposium Website](#). For more information contact Samantha Westenberg at [Samantha.Westenberg@cchmc.org](mailto:Samantha.Westenberg@cchmc.org).

## Medical Student Summer Research Program- Fall Symposium



The NIDDK funded T35 Medical Student Summer Research Program directed by Dr. James Heubi, a current DHC member, will host its fall symposium on Friday October 19. The keynote speaker will be Dr. Mitchell Cohen the DHC founding director. Dr. Cohen is currently Chair of the De-

partment of Pediatrics at the School of Medicine at the University of Alabama at Birmingham and Physician in Chief at the Children's Hospital of Alabama. He will present "On Being a Physician Scientist: My On Again Off Again 32 Year Affair with NIDDK- Love Returned or Unrequited".

For more information contact Sandy Geideman at [Sandra.Geideman@cchmc.org](mailto:Sandra.Geideman@cchmc.org).

For all publications, please acknowledge the DHC as follows:

**"This project was supported in part by NIH P30 DK078392 (*insert name of core that you used*) of the Digestive Diseases Research Core Center in Cincinnati."**



## Seminar Series- Tuesdays at Noon, Room S6.125

| Date                                                 | Presenter                                                                                     | Title                                                                                                             |
|------------------------------------------------------|-----------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|
| 9/11/18                                              | Vicky Ng, MD, FRCP(C)<br>The Hospital for Sick Children                                       | "Pediatric Liver Transplantation in 2018: Something for Everyone to Care About"                                   |
| 9/18/18                                              | Akihiro Asai, MD, PhD<br>CCHMC: Gastroenterology                                              | "iPSC-based Disease Modeling Reveals Molecular Mechanisms of Cholestasis in the Human Hepatocytes"                |
| 9/25/18                                              | No Seminar due to Annual Digestive Diseases Research Core Centers Directors Meeting           |                                                                                                                   |
| 10/2/18<br><i>*Distinct location Res. Auditorium</i> | Rohit Loomba, MD, MHSc<br>University of California, San Diego                                 | "Novel Advances in Non-invasive Imaging Assessment in NASH Trials"                                                |
| 10/9/18                                              | Rajat Madan, MD, PhD<br>UC: Department of Internal Medicine<br>Division of Infectious Disease | "Obesity-associated Gut Microbiota Worsens <i>C. difficile</i> Infection and Induces Distinct Neutrophil Subsets" |
| 10/16/18                                             | Pooja Khandelwal, MBBS<br>CCHMC: Bone Marrow Transplant and Immune Deficiency                 | "Gene Expression Profiles in Acute Graft Versus Host Disease"                                                     |
| 10/23/18                                             | Matthew Kofron, PhD<br>CCHMC: Confocal Imaging Facility                                       | "Imaging Methods for Digestive Disease Studies Available at CCHMC Confocal Imaging Core"                          |
| 10/30/18                                             | Peter Hegyi, MD, PhD, DSc<br>University of Pécs                                               | "New Insights into the Pathomechanism and Management of Pancreatitis"                                             |
| 11/6/18                                              | Jessica Woo, MHSA, PhD<br>CCHMC: Biostatistics & Epidemiology                                 | "Identifying Microbiome Signatures in Infants at Risk of Developing Severe Childhood Obesity"                     |
| 11/13/18                                             | No Seminar due to American Association for the Study of Liver Diseases Meeting                |                                                                                                                   |
| 11/20/18                                             | No Seminar Due to the Thanksgiving Holiday                                                    |                                                                                                                   |
| 11/27/18                                             | Bruce Aronow, PhD<br>Rebecca Karns, PhD<br>CCHMC: DHC Bioinformatics Core                     | "Introducing ToppCell: A Single Cell Expression Database and Workbench to Analyze Lineages and Tissues"           |
| 12/4/18                                              | Pranavkumar Shivakumar, PhD<br>CCHMC: Gastroenterology                                        | "Understanding the Pathogenesis of Biliary Atresia: Recent Advances"                                              |
| 12/11/18                                             | Michael Rosen, MD, MSCI<br>CCHMC: Gastroenterology                                            | "Cell-specific Transcriptome Dysregulation across the Inflammatory Front Line in Ulcerative Colitis"              |

For more information regarding the DHC visit our [website](#) or contact one of the following:

|                      |                         |                          |
|----------------------|-------------------------|--------------------------|
| Director:            | Jorge Bezerra, MD       | jorge.bezerra@cchmc.org  |
| Associate Directors: | Lee Denson, MD          | lee.denson@cchmc.org     |
|                      | Heidi Kalkwarf, PhD, RD | heidi.kalkwarf@cchmc.org |
|                      | Aaron Zorn, PhD         | aaron.zorn@cchmc.org     |
| Center Manager:      | Cynthia Wetzel, PhD     | cynthia.wetzel@cchmc.org |



## Annual Scientific Symposium Tuesday February 26, 2019

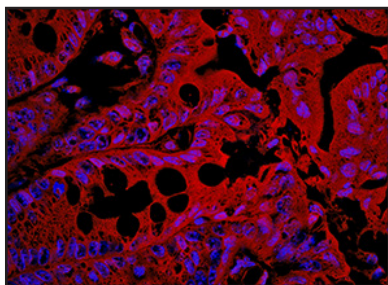
Poster Session: 9:30 to 11:45 am  
Location S Room 1.203 and 1.204  
Keynote Address: Rebecca Wells, MD  
Location R Room 3381 (Research Auditorium) 12:00 pm

The Digestive Health Center (DHC) will host its Annual Scientific Symposium and External Advisory Board Meeting on February 26, 2019. The day will include a poster session and keynote address by Dr. Rebecca Wells from the University of Pennsylvania. Building upon the success of previous years, the poster session will feature work related to any area of digestive disease, including the four DHC themes:

- 1) Liver Disease and Modeling
- 2) Digestive Disease and Immunity
- 3) Digestive Disease and Obesity
- 4) Translational Embryology (of the Digestive System)

To present a poster, visit the [DHC website](#) for the abstract submission form. Abstracts must be submitted electronically by Friday, February 1, 2019 to [cynthia.wetzel@cchmc.org](mailto:cynthia.wetzel@cchmc.org). Prizes will be given to students and trainees for the best poster presented.

## ScienceDaily Featured Members' Research



Confocal image of epithelial cells lining a mouse intestine.

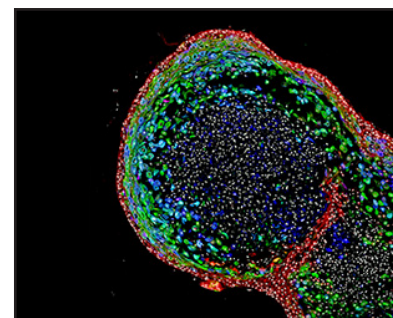
*ScienceDaily*, a popular science news website, featured two articles published by our DHC Members. The research work of DHC members Drs. Theresa Alenghat (previous Pilot and Feasibility Recipient), Ted Denson, Bruce Aronow, Artem Barski, Yael Haberman, Michael Helmrath and Michael Rosen (previous Pilot and Feasibility Recipient) was published in the September 20 issue of *JCI Insight*. They identified an epigenetic signature in patient cells that appears to predict the inflammation risk in patients with Crohn's disease. Epigenetics is the study of DNA and protein modifications that determine if a gene is turned on or off. This study suggests that the intestinal microbiome could cause epigenetic changes that would make

some patients more prone to intestinal inflammation.

The research work of DHC members Drs. Jim Wells, Marc Rothenberg, Susa Wells, and Aaron Zorn was published in the October 4 issue of *Cell Stem Cell*. They, along with first author Dr. Stephen Trisno, used direct differentiation of human pluripotent stem cells (PSCs) to generate esophageal organoids. The research team used this in vitro system, as well as mouse models, to study esophageal development and discovered that Sox2 inhibits the Wnt signaling pathway, is required for the formation of esophageal tissues and prevents the formation of respiratory tissue. The esophageal organoids will be a new model to study birth defects such as esophageal atresia and diseases such as eosinophilic esophagitis. DHC investigators have now used PSCs to grow human intestine, stomach, colon, and liver organoids.

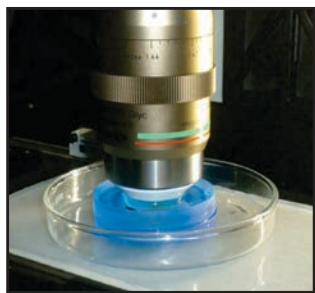
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- Annual Scientific Symposium
- *ScienceDaily* Featured Members' Research
- New Equipment at Confocal Core
- New Service at DNA Sequencing Core
- New External Advisory Board Member
- Transition to Full Membership
- New DHC Member
- Upcoming Seminars



In about 2 months, the esophageal organoids reached a length of 300-800 micrometers.

## New Equipment at Confocal Imaging Core



The Confocal Imaging Core at Cincinnati Children's has upgraded three systems (3021 LUNV A1R, 3022 A1R, 3023 A1R MP) to Nikon's recently released HD scanners. The HD resonant scanner pro-

vides improved signal-to-noise ratio, greater sensitivity and higher speed for resonant scanning applications. A 5 to 10-fold increase in scanning speed can be accomplished with these upgraded systems. The Core has also added a 20X NA 1.0 LWD multi-immersion WD 8.5mm for cleared tissue imaging and a 100X silicone immersion objective for live cell/tissue use.

A ThermoFisher CX7-LZR high-content imaging system has been purchased by research administration and will be housed in and maintained by the Confocal Imaging Core. The microscope is scheduled to be installed in December. This sys-

tem will offer fully automated laser-based spinning disk optical sectioning, multi-spectral fluorescence wide-field imaging and transmitted light imaging. It will be equipped with robotics and scheduling software to allow multiple users to perform parallel assays with up to 42 plates in a robotic incubator. The system will also be equipped with a stacker for fixed samples in plates, slides or custom chambers. The software will also perform real-time analysis of images concurrent with data acquisition. The CX7-LZR will be housed in room R-3524 and be certified for BL2 use.

**Benefits for DHC Members:** The DHC will provide 25% of the total charge with a subsidy limit of \$1,200 per member per year.

The Confocal Imaging Facility is located in Location R Room 3007A and 3020-3024.

For more information visit:

Visit the [Confocal Imaging Core website](#) or contact Dr. Matt Kofron at 513-803-9055; [matthew.kofron@cchmc.org](mailto:matthew.kofron@cchmc.org).

## New Service at DNA Sequencing- Bisulfite Sequencing

Epigenomics is the study of the physical modifications, associations and conformations of genomic DNA sequences that will affect if the gene is turned "on" or "off". While current techniques in the field characterize the average epigenomic features across large cell populations, an increasing interest in the epigenetics of complex and heterogeneous tissues is driving the development of single-cell epigenomics.

Bisulfite sequencing has enabled high quality DNA methylation profiling in diverse epigenomic settings over the past decades. This technique became particularly powerful when combined with high-throughput sequencing.

The DNA Sequencing Core at Cincinnati Children's recently developed a single cell methylome assay based on reduced representation bisulfite sequencing. Compared with other published methods, the workflow has been further optimized with the entire process being finished within four

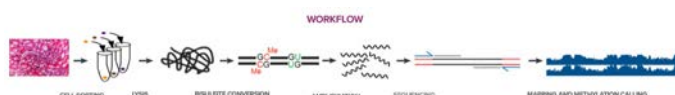
hours from the lysed cell. All of the gel purification and size selection steps have been omitted, which significantly reduces sample loss and improves the library recovery. More importantly, it only requires one 25 cycle PCR amplification round verses two rounds which decreases the duplication rate and improves data quality.

**Benefits for DHC Members:**

The DHC will provide 25% of the total charge for services provided at the DNA Sequencing and Genotyping Core with a subsidy limit of \$2,400 per member per year.

For more information:

Visit the [DNA Sequencing and Genotyping Core website](#) or contact Dr. Xueguang Sun at [xueguang.sun@cchmc.org](mailto:xueguang.sun@cchmc.org); 513-636-0122.



## New External Advisory Board Member



Dr. Noah Shroyer has joined the DHC External Advisory Board. He is a former DHC member and Pilot and Feasibility Recipient. He is currently an Associate Professor at Baylor College of Medicine and Director of the Gastrointestinal Experimental Model Systems Core of the NIDDK funded Texas Medical Center Digestive Diseases

Research Core Center. His research focuses on understanding the mechanisms that control intestinal development and homeostasis.

Dr. Shroyer will join current External Advisory Board Members: Drs. Stephen Duncan (Medical University of South Carolina), Scott Snapper (Boston Children's Hospital), and Rebecca Wells (University of Pennsylvania). Dr. Phillip Tarr (Washington University in St. Louis) has rotated off.

## Transition to Full Membership - Dr. Chunyue Yin



Dr. Chunyue Yin, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition at Cincinnati Children's, received her first NIH R01 from the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK). The ti-

tle of her grant is "Molecular Targets in Cholestasis Caused by Bile Salt Export Pump Deficiency".

Dr. Yin used preliminary data that was generated from her DHC Pilot and Feasibility Award for her R01 grant application.

Congratulations to Dr. Yin for transitioning to Full Membership status in the DHC!

## New DHC Members



The DHC is pleased to welcome two new members.

Anna Peters, MD, PhD is an Instructor and a new faculty member in the Division of Gastroenterology, Hepatology, and Nutrition at Cincinnati Children's. Her research focuses on investigating the cellular and molecular mechanisms of pediatric liver transplant rejections.

Kelli VanDussen, PhD is an Assistant Professor and a new faculty member in the Division of

Gastroenterology, Hepatology, and Nutrition at Cincinnati Children's. Her research focuses on studying the function of intestinal epithelial cells during homeostasis, injury, wound repair, and in inflammatory bowel disease.



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For all publications, please acknowledge the DHC as follows:

**"This project was supported in part by NIH P30 DK078392 (*insert name of core that you used*) of the Digestive Diseases Research Core Center in Cincinnati."**

For more information regarding the DHC visit our [website](#) or contact one of the following:

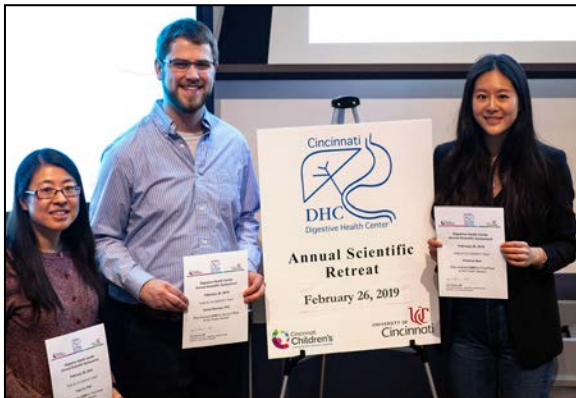
|                      |                         |                          |
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| Director:            | Jorge Bezerra, MD       | jorge.bezerra@cchmc.org  |
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|                      | Heidi Kalkwarf, PhD, RD | heidi.kalkwarf@cchmc.org |
|                      | Aaron Zorn, PhD         | aaron.zorn@cchmc.org     |
| Center Manager:      | Cynthia Wetzel, PhD     | cynthia.wetzel@cchmc.org |

## Seminar Series- Tuesdays at Noon, Room S6.125

| Date    | Presenter                                                                                                                                                                                       | Title                                                                                                      |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------|
| 1/8/19  | William Faubion, MD<br>Mayo Clinic                                                                                                                                                              | "The Epigenetics of T cell Fate Decisions: If It Were Always This EZ(h2)"                                  |
| 1/15/19 | Todd Jenkins, PhD, MPH<br>CCHMC: Ped General & Thoracic Surgery                                                                                                                                 | "Adolescent Bariatric Surgery: 5 Year Findings from the Teen-LABS Study"                                   |
| 1/22/19 | Alexander Miethke, MD<br>CCHMC: Gastroenterology                                                                                                                                                | "Bile Acids and its Receptor FXR as Targets for Anti-Inflammatory Therapies in Cholestatic Liver Diseases" |
| 1/29/19 | Yvonne Ulrich-Lai, PhD<br>UC: Department of Pharmacology and Systems Physiology                                                                                                                 | "What Puts the Comfort in "Comfort" Foods?"                                                                |
| 2/5/19  | Miklos Sahin-Toth, MD, PhD<br>Boston University                                                                                                                                                 | "Modeling Human Hereditary Pancreatitis in Mice"                                                           |
| 2/12/19 | M. Tarek Shata, MD, MSc, PhD<br>UC: Department of Internal Medicine Division Digestive Diseases                                                                                                 | "Characterization of Non-Responder Phenotypes after HCV Treatment in Genotype 4 Infection in Egypt"        |
| 2/19/19 | Sing Sing Way MD, PhD<br>CCHMC: Infectious Diseases                                                                                                                                             | "Systemic Immunological Changes with Candida Albicans Intestinal Colonization"                             |
| 2/26/19 | DHC Annual Scientific Symposium<br>Keynote Address by: Rebecca Wells, MD<br>University of Pennsylvania<br>"Injury and the Neonatal Bile Duct"<br><b>*Distinct Location: Research Auditorium</b> |                                                                                                            |
| 3/5/19  | Susanne Wells, PhD<br>CCHMC: Oncology                                                                                                                                                           | "From Human Pluripotent Stem Cells to 3D Epidermis - Phenotype Discovery in Fanconi Anemia"                |
| 3/12/19 | Ting Wen, PhD<br>CCHMC: Allergy and Immunology                                                                                                                                                  | "Compositional and Functional Dynamics of Tissue T-cells in Human Allergic Inflammation"                   |
| 3/19/19 | Michael Pauciulo, MBA<br>CCHMC: Discover Together Biobank                                                                                                                                       | "Discover Together Biobank: Future Directions for Biobanking at CCHMC"                                     |
| 3/26/19 | Alexander Bondoc, MD<br>CCHMC: Ped General & Thoracic Surgery                                                                                                                                   | "Modelling Human Hepatoblastoma to Develop Novel Therapeutic Strategies"                                   |
| 4/2/19  | David Kleiner, MD, PhD<br>National Cancer Institute                                                                                                                                             | "The Histopathology of Fatty Liver Disease in Children and Adults"                                         |
| 4/9/19  | Michael Helmrath, MD, MS<br>CCHMC: Ped General & Thoracic Surgery                                                                                                                               | "Organoid Modeling of Human Intestine"                                                                     |



## Highlights from the 2019 Annual Scientific Symposium



Poster Winners from Left to Right: Yuqi Cai, PhD  
Daniel Kechele, PhD and  
Vivienne Woo.

### IN THIS ISSUE:

- Annual Scientific Symposium
- Annual NIH Progress Report Submission
- Transition to Full Membership
- New DHC Member
- Member Highlights
- Alagille Symposium Announcement
- Upcoming Seminars

The Digestive Health Center (DHC) held its Annual Scientific Symposium on Tuesday, February 26. Dr. Rebecca Wells presented the keynote address "Injury and the Neonatal Bile Duct". Posters were displayed by 43 researchers representing 7 Divisions in the Department of Pediatrics and 5 Departments within the University of Cincinnati, College of Medicine. Additionally, there were 10 posters displayed highlighting Research Core Services. Prizes were awarded for the best presented posters:

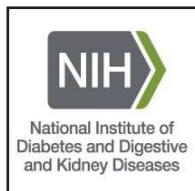
**First Place:** Vivienne Woo (Graduate Student, Cincinnati Children's, Division of Immunobiology member of Dr. Theresa Alenghat's lab) for "Commensal Bacteria Calibrate Host Defense by Enhancing Retinoic Acid Signaling".

**Second Place:** Daniel Kechele PhD (Research Fellow, Cincinnati Children's, Division of Developmental Biology, member of Dr. Jim Wells' lab) for "SOX21 Represses CDX2 and the Intestinal Program During Developmental Patterning and Metaplasia in Humans".

**Third Place:** Yuqi Cai, PhD (Research Associate, Cincinnati Children's, Division of Gastroenterology, Hepatology, and Nutrition, member of Dr. Takanori Takebe's lab) for "Scalable and High-Fidelity Drug Induced Liver Injury Screen Using Human iPSC-Liver Organoids".

See Page 2 for more highlights from the Annual Scientific Symposium.

## Annual Progress Report Will be Submitted to NIH- April 1



The annual DHC Progress Report will be submitted to NIH by April 1. We thank all the DHC members for their prompt response in providing us with their current grant funding and their 2018 publications. This information along with Core usage, was presented to the External Advisory Board during their visit to evaluate our center as required by NIDDK.

Below summarizes some of the 2018 DHC accomplishments.

- Our 80 members generated 129 digestive disease related publications that contained results

from a DHC supported research core. 57 (44%) of these publications had 2 or more members as co-authors.

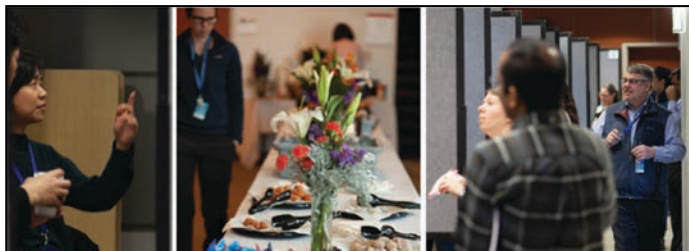
- Members received \$32.4 million in extramural funds for digestive disease research of which \$11.9 million was from NIDDK.
- In the past 10 years, 14 Pilot and Feasibility Recipients have transitioned to NIH R01 funded investigators. \$1.7 million has been distributed to 34 awardees who have \$34.9 million in extramural funding, a 21 fold return on investment.

## Photos and Highlights from Annual Scientific Symposium Continued

We would like to thank Jill Soldano for her amazing job hosting the visit of the External Advisory Board Members and her superb organization of the Annual Scientific Symposium. We would also like to thank Ruth Castle, GiGi DiPuccio, Deanna Louis, and Angie Vickers for their outstanding assistance with hosting the Symposium.



Left to Right: Deanna Louis, Jill Soldano, Angie Vickers, GiGi DiPuccio, and Ruth Castle.



### Thanks to the poster judges and amazing organizers!

We also thank those who reviewed posters:

Drs. Alenghat, Asai, Barski, Divanovic, Fulkerson, Gandhi, Haslam, Heubi, Hommel, Huppert, Khandelwal, Madan, Miethke, Minar, Mohanty, Montrose, Nakamura, Naren, Nommsen-Rivers, Patel, Shata, Sherman, Shin, Shivakumar, Takebe, Tso, VanDussen, Wells, Yacyshyn, Yin, and Zingarelli.

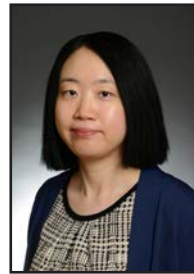


## Transition to Full Membership - Drs. Christian Hong and Soona Shin



Dr. Christian Hong, Department of Pharmacology and Systems Physiology at the University of Cincinnati, College of Medicine, received his first NIH R01 from the National Institute of Diabetes and Digestive Kidney Diseases (NIDDK). The title of his grant is "Roles of Circadian Rhythms in Gastrointestinal Systems".

Dr. Soona Shin, Department of Surgery, Division of Pediatric General and Thoracic Surgery, at Cincinnati Children's received her first NIH R01 which was converted to an R37 award due to her



meritorious score from the National Cancer Institute (NCI). Dr. Shin has the opportunity to receive an additional 2 years of funding based on the accomplishments during the first 5 years of her project. The title of her grant is "Pathogenic Role of Foxl1+ Hepatic Progenitor Cells in Fibrotic Liver Disease". Dr. Shin used preliminary data that was generated from her DHC Pilot and Feasibility Award for her NIH grant application.

Congratulations to both of them!



## New DHC Member



The DHC is pleased to welcome one new member.

Laurie Nommsen-Rivers, PhD, RD, IBCL is an Associate Professor in the Department of Rehabilitation, Exercise and Nutrition Sciences at University of Cincinnati, College of

Allied Health. Her research focuses on identifying and correcting the underlying drivers of insufficient milk production in obese mothers.

If you are interested in joining the DHC, visit [our website](#) for further instructions. Membership is open to all faculty members involved in digestive disease research.

## DHC Member Highlights

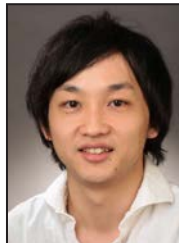


### Rosen's New Role at CCF

Michael Rosen, MD, MSCI has been elected as the Chair of the Crohn's & Colitis Foundation PROKIDS (Pediatric Resource Organization for Kids with Inflammatory Intestinal Diseases) Research Network. In this role, Dr. Rosen will work with the foundation to guide the direction of new research initiatives over the next 3 years. He is a faculty member in the Gastroenterology Division at Cincinnati Children's.

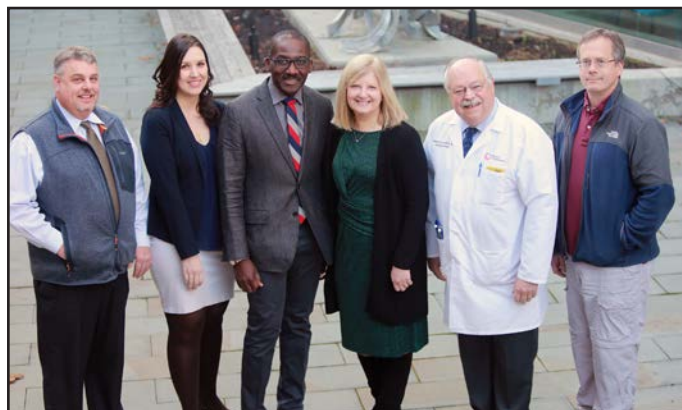
### Takebe Receives Awards

Takanori Takebe, MD was one of 25 recipients of the Japan Society for the Promotion of Science Prize and was selected as one of 6 recipients of the Japan Academy Medal. These awards are given to young researchers who have made significant scientific contributions. He is a faculty member in the Divisions of Gastroenterology and Developmental Biology at Cincinnati Children's.



### Intestinal Rehabilitation Center Receives Award

DHC members Michael Helmrath, MD and James Wells, PhD along with Conrad Cole, MD; Samuel Kocoshis, MD; Stephanie Oliveira, MD; and Brenda Poindexter, MD received the Cincinnati Children's Clinical Team Faculty Award for the Intestinal Rehabilitation Center. The Center is comprised of a cohesive team spanning multiple divisions who have improved the quality of care to change the outcomes in children with intestinal failure.



From Left to Right: Drs. Helmrath, Oliveira, Cole, Poindexter, Kocoshis, and Wells.

## International Symposium and Scientific Meeting on Alagille Syndrome



The Scientific Meeting will consist of world renown experts speaking and/or moderating sessions covering:

1. Current knowledge gaps in Alagille Syndrome

2. Jagged1-Notch mediated signaling
3. Vascular biology
4. Organogenesis
5. Pre-clinical models and emerging therapies

To attend the symposium visit the [Registration Website](#).

For more information regarding the schedule visit the [Symposium Website](#) or send questions to Dr. Stacey Huppert, who is a symposium organizer, at [Stacey.Huppert@cchmc.org](mailto:Stacey.Huppert@cchmc.org).

## Seminar Series- Tuesdays at Noon, Room S6.125

| Date    | Presenter                                                         | Title                                                                                              |
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| 4/9/19  | Michael Helmrath, PhD<br>CCHMC: Ped General & Thoracic Surgery    | "Organoid Modeling of Human Intestine"                                                             |
| 4/16/19 | Sharad Wadhwani, MD, MPH<br>CCHMC: Gastroenterology               | "Precision Public Health: A Model to Improve Care for Pediatric LT Recipients"                     |
| 4/23/19 | Nicholas Ollberding, PhD<br>CCHMC: Biostatistics and Epidemiology | "Recent Advancements in Statistical Analysis of Microbial Metagenomic Sequence Data"               |
| 4/30/19 | Anna Henderson, MD<br>CCHMC: Gastroenterology                     | "Monitoring Eosinophilic Esophagitis Disease Activity with Blood Eosinophil Progenitor Levels"     |
| 5/7/19  | Soofia Khan, MD<br>CCHMC: Gastroenterology                        | "Healthy Bones in Gastroenterology and Hepatology: An Example of Nonalcoholic Fatty Liver Disease" |
| 5/14/19 | Gavin Arteel, PhD<br>University of Pittsburgh                     | "Role of the ECM in Inflammatory Liver Injury"                                                     |
| 5/21/19 | No Seminar Due to Digestive Disease Week Annual Meeting           |                                                                                                    |
| 5/28/19 | Kaitlin Gibler Whaley, MD<br>CCHMC: Gastroenterology              | "Anti-TNF Therapy for Refractory Colitis in Hospitalized Children: The ARCH Study"                 |

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|                      | Aaron Zorn, PhD         | aaron.zorn@cchmc.org     |
| Center Manager:      | Cynthia Wetzel, PhD     | cynthia.wetzel@cchmc.org |