Pediatric Gastroenterology Hepatology & Nutrition
M.D. and Ph.D. Fellowship Training Program

Benjamin L. Shneider, M.D.
Section Head

Kristin Van Buren, M.D.
Fellowship Director

Douglas G. Burrin, Ph.D.
Director of Research Training

Seema Mehta Walsh, M.D.
Associate Fellowship Director

Robert J. Shulman, M.D.
Associate Director of Research Training

Texas Children’s Hospital

Baylor College of Medicine
# TABLE OF CONTENTS

Message from the Section Head and Physician-in-Chief ................................................................. 2  
Background of the Program ............................................................................................................. 3  
Clinical & Research Faculty ......................................................................................................... 4  
M.D. RESEARCH TRAINING / COURSEWORK ....................................................................... 5  
M.D. CLINICAL TRAINING ........................................................................................................ 6  
M.D. and Ph.D. Research Training Overview ........................................................................... 7-9  
Conference Schedule / Visiting Faculty / Benefits ................................................................... 10  
Scientific Meetings / Job Placement .......................................................................................... 11  
Current Positions of Former Trainees ....................................................................................... 12-13  
The Educational Environment ..................................................................................................... 14-17

- Baylor College of Medicine  
- Baylor Clinical Scientist Training Program  
- Texas Medical Center Digestive Disease Center  
- Department of Pediatrics  
- Fellow’s Day  
- Children’s Nutrition Research Center  
- Texas Children’s Hospital  
- Gastrointestinal Procedures Suite  
- Motility Center  
- Camp SIA  
- Gastroenterology Nursing Staff  
- Inflammatory Bowel Disease Center  
- Peds-Cori Research Center  
- Pancreaticobiliary Program  
- Liver Center  
- Texas Children’s Hospital Microbiome Center  
- Center for Pediatric Abdominal Pain Research  
- The Houston Center for Quality of Care and Utilization Studies  
- The Inter-Departmental Translational Biology & Molecular Medicine Graduate Program  

The Texas Medical Center ............................................................................................................. 18  
The City of Houston ..................................................................................................................... 19  
Faculty Research Interests ......................................................................................................... 20  
Faculty Table of Contents ........................................................................................................ 21-24  
Faculty Descriptions ................................................................................................................ 25-55  
Eligibility Criteria ....................................................................................................................... 56-60
I am delighted that you are interested in the training programs here at Texas Children’s Hospital and the Baylor College of Medicine. Our fellowship offers a tremendous opportunity for both breadth and depth of investigation in clinical, translational and basic investigation. Teaching and investigation are key components of our mission statement, “to strive for outstanding and compassionate patient care through evidence-based and expert practice achieved through research and education.” There has been exciting growth in the programs at Texas Children’s Hospital and in our Section of Pediatric Gastroenterology, Hepatology and Nutrition. Our basic research laboratories have been completely renovated and re-equipped with state-of-the-art molecular instrumentation. Clinical research has been reinvigorated in the section with the development of a clinical research coordinator team and we now conduct over 200 IRB approved clinical research protocols. Our teams are actively involved in a number of NIH-funded clinical consortia. We will continue to push the boundaries of our knowledge and our research and clinical practice – we hope you will consider joining us.

Benjamin L. Shneider, M.D.
George Peterkin Endowed Chair
Professor of Pediatrics and Head of Section,
Pediatric Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine
Chief of Service, Pediatric Gastroenterology, Hepatology and Nutrition

Baylor College of Medicine and Texas Children’s Hospital have a long and illustrious history of excellence in patient care, research, education and service in the areas of pediatric gastroenterology, hepatology and nutrition. Our commitment is to have comprehensive programs in these areas second to none worldwide, and we feel we are well on the way to achieving that. Houston, Texas is the most diverse big city in America. It provides an amazingly rich milieu in which to live and train. Our Department of Pediatrics is the largest in North America, with more than 1250 faculty members. I often say that we are the largest aggregation of pediatric subspecialists on the planet! With more than $100 million annually in extramural research funding, the Department supports an impressive array of investigators and research activities, driving innovation to transform pediatric healthcare. Texas Children’s Hospital, with more than 600 licensed beds, is the largest children’s hospital in North America, and growing. In partnership continuously since 1954, Baylor and Texas Children’s will always expand your horizons and never limit your possibilities. We will dedicate ourselves to supporting you in every conceivable way. We welcome your interest in our training programs.

Mark W. Kline, M.D.
Physician-in-Chief
Texas Children’s Hospital
J.S. Abercrombie Professor and Chairman
Ralph D. Feigin Chair
Department of Pediatrics

Section of Pediatric Gastroenterology, Hepatology, and Nutrition
Baylor College of Medicine, Texas Children’s Hospital
6621 Fannin Street, MAWT 1010.00, Houston, TX 77030
Tel: 832-822-3131
https://www.texaschildrens.org/departments/gastroenterology-hepatology-and-nutrition
BACKGROUND

The Nutrition and Gastroenterology Fellowship Training Program was established in 1973 by Buford L. Nichols, M.D. The Section gained national prominence under the Section Chief leadership of William J. Klish, M.D., and Mark Gilger, M.D.. Benjamin Shneider M.D. is the current Section Chief and Mark W. Kline, M.D. is the Chairman of the Department of Pediatrics.

The Department of Pediatrics is one of the largest in the U.S., over 1260 Faculty members. Baylor College of Medicine is listed 19th among all U.S. medical schools for National Institutes of Health funding, and No. 2 in the nation in federal funding for research and development in the biological sciences at universities and colleges by the National Science Foundation. The Section of Pediatric Gastroenterology, Hepatology, and Nutrition currently includes 33 faculty members and a support staff of 90. The Section was ranked number 4th nationally among digestive disorders subspecialty programs in the 2018 U.S. News and World Report Survey on the Best Children's Hospitals. The clinical training program is conducted under the auspices of Texas Children's Hospital (see p. 15) and includes 31 Faculty who perform over 27,000 annual clinic visits and 2800 procedures annually (See pg 4, 15).

Clinical training is enhanced through several Texas Children’s Hospital Centers and Clinics:

Gastrointestinal Endoscopy and Therapeutic Endoscopy………Douglas S. Fishman, M.D., Director
Inflammatory Bowel Disease Center…………………………….Richard Kellermayer, M.D., Director
Liver Transplant Center ..................................................Daniel Leung, M.D., Medical Director
Neurogastroenterology and Motility Center ........................Sundararajah Thevananther, Ph.D., Research Director
PEDS-CORI Research Center..........................................Douglas Fishman, M.D., Director
Research Training is enhanced by:
NIH Institutional Training Grant (T32 DK07664) ..............Robert J. Shulman, M.D., Director
……………………………………………………Douglas G. Burrin, Ph.D., Associate Director

Sub Specialty Clinics:
Aerodigestive Disorders Clinic............................................Eric Chiou M.D., Co-Director
Eosinophilic Disorders Clinic ............................................Anthony Olive, M.D., Co-Director
GROW Clinic..............................................................Carol Redel, M.D., Director
Intestinal Rehabilitation Clinic ...........................................Lynette Van Buren, M.D., Director
Prader-Willi Clinic.........................................................Ann Scheimann, M.D., Director
Rett Syndrome Clinic ....................................................Kathleen Motil, M.D., Ph.D., Director
Viral Hepatitis Clinic ....................................................Daniel H. Leung, M.D., Director

Research training draws on faculty throughout the Texas Medical Center (p.18) and benefits from the abundant research resources of the Texas Medical Center in general and of Baylor College of Medicine in particular (p.14-17). Research opportunities range from clinical studies, including outcomes and translational research, through an array of basic science laboratories at the forefront of molecular medicine (p. 25-55).

OVERVIEW OF TRAINING

Mission Statement - To strive for outstanding and compassionate patient care through evidence-based and expert practice achieved through research and education

The goal of our Fellowship Program is to educate pediatricians to become outstanding clinicians who can also compete at the cutting edge of research in academia.

The program is designed around the guidelines developed by the North American Society for Pediatric Gastroenterology and Nutrition, and is intended to allow trainees to meet the requirements for certification by the Sub-Board for Pediatric Gastroenterology of the American Board of Pediatrics.

All entrants must have completed the equivalent of three years of ACGME accredited residency training in pediatrics.

The Fellowship Program includes clinical training and research training and is completed by all Fellows. The basic training consists of 12 months of clinical training and 24 months of research training. This 36-month program includes clinical service, teaching, and research. It provides the trainee with the state-of-the-art knowledge and skills required for an academic career. A program for Ph.D. postdoctoral GI research training is available through the NIH Institutional Training Grant (T32 DK07664). Training for up to 24 months is potentially available (see p. 7).
Clinical and Research Faculty
Pediatric Gastroenterology, Hepatology and Nutrition

Chief of Section:
Benjamin L. Shneider, M.D.
Amaka Akalonu, M.D.
Keisha Barton, M.D.
Douglas G. Burrin, Ph.D.
Eric Chiou, M.D.
Andrew Chu, M.D.
Bruno P. Chumpitazi, M.D., M.P.H.
Douglas S. Fishman, M.D.
Donna Garner, R.N., M.S.N., P.N.P.
Caroyl L. Gilbert, R.N., M.S.N, P.N.P.
Annie Goodwin, M.D.
Sanjiv Harpavat, M.D., Ph.D.
Paula M. Hertel, M.D.
John Hollier, M.D.
Amir Jazayeri, M.D.
Craig L. Jensen, M.D.
Lina B. Karam, M.D.
Richard E. Kellermayer, M.D., Ph.D.
Kristi D. King, M.P.H., R.D., L.D.
Seiji Kitagawa, M.D.
Daniel H. Leung, M.D.
Jennifer Maupin, M.S., R.N., C.P.N.P.
Carmen Mikhail, Ph.D.
Kathleen Motil, M.D., Ph.D.
Krupa Mysore, M.D.
Huyen Nguyen, D.O.
Anthony P. Olivé, M.D.
Yen Pham, M.D.'
Geoffrey A. Preidis, M.D., Ph.D.
Priya Raj, MS, M.D.
Carol A. Redel, MNS, M.D.
Tanisha Richards, MSN, APRN, FNP-
Ann O. Scheimann, M.D., MBA
Robert J. Shulman, M.D.
Mary Elizabeth Tessier, M.D.
Sundararajah Thevananther, Ph.D.
Nicole D. Triggs, MSN, APRN, CPNP,
CPN
Kristin Whitfield Van Buren, M.D.
Bryan S. Vartabedian, M.D.
Seema Mehta Walsh, M.D.
Hongtao (Alex) Wang, M.D., Ph.D.
Allyson N. Wyatt, MD

Associated Clinical Faculty
Mary L. Brandt, M.D.......................... Pediatric Surgery
Ronald T. Cotton, M.D........................ Pediatric Surgery
Danita Czyzewski, Ph.D........................ Psychiatry & Behavioral Sciences
Nhu Thao Nguyen Galvan, M.D.......... Transplant Surgery
John A. Goss, M.D............................ Transplant Surgery
Paul K. Minifee, M.D.......................... Pediatric Surgery
Christine O'Mahony, M.D................. Transplant Surgery
David E. Wesson, M.D........................ Pediatric Surgery

Associated Research Faculty
Robert A. Britton, Ph.D...................... Molecular Virology and Microbiology
Douglas Burrin, Ph.D......................... Pediatrics, Children’s Nutrition Research Center
Margaret Conner, Ph.D...................... Molecular Virology and Microbiology
Gretchen Diehl, Ph.D......................... Molecular Virology and Microbiology
Hashem B. El-Serag, M.D, M.P.H........ Medicine, Gastroenterology and Health Services
Mary K. Estes, Ph.D.......................... Medicine, Molecular Virology & Microbiology
Joseph Hyser, Ph.D.......................... Medicine, Molecular Virology & Microbiology
Hamed Jafar-Nejad, M.D..................... Molecular and Human Genetics
Brendan Lee, M.D., Ph.D.................... Pediatrics, Molecular and Human Genetics
Lenard Lichtenberger, Ph.D................ Biology and Pharmacology– University of Texas Medical School
David D. Moore, Ph.D....................... Molecular and Cellular Biology
J. Marc Rhoads, M.D......................... Pediatric Gastroenterology– University of Texas Medical School
Tor Savidge, Ph.D............................ Pathology and Immunology
Noah Shroyer, Ph.D.......................... Medicine, Gastroenterology
Betty L. Slagle, Ph.D........................ Molecular Virology and Microbiology
James Versalovic, M.D., Ph.D............. Pathology & Immunology, Genetics, Molecular Virology and Microbiology
Huda Y. Zoghbi, M.D......................... Pediatrics, Molecular and Human Genetics
SCHEDULING OF RESEARCH TRAINING

Clinical and research months may be allocated in various ways. The first year of training will always have at least three research months. These months are distributed among the clinical months so that there are never more than three consecutive clinical months. A 4th research block during the first year is optional.

<table>
<thead>
<tr>
<th></th>
<th>Clinical Training (months)</th>
<th>Research Training (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year 1</td>
<td>9</td>
<td>3</td>
</tr>
<tr>
<td>(Includes conference and vacation) *</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Year 2</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Year 3</td>
<td>3</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>Junior Faculty*</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>12</td>
<td>36</td>
</tr>
</tbody>
</table>

* Optional as part of the NIH T32 Training Grant

COURSEWORK

There are several courses required of all trainees:

- **Pediatric Gastroenterology, Hepatology and Nutrition**: This didactic course is taught by several members of the Faculty. Lectures are held each Friday. Typically a full three years is required to cover all the material. An additional component of the course is a series of lectures from Dr. Burrin and other research Faculty on issues relevant to building an academic career (e.g., scientific writing, grantsmanship, etc.).

- Baylor College of Medicine and the Dept of Pediatrics offer workshops in the following ACGME required coursework: Sleep and Safety, Fellows as Teachers, Evidence-based Medicine, and Systems-based Practice, and Quality Improvement.

- **Fundamentals of Clinical Investigation**: A course is offered each August by the Department of Pediatrics to research Fellows in all divisions and generally taken by our Fellows in their second year. This is an intensive course (2 hours per day for one month), which covers biostatistics, outcomes research, clinical trials, metabolic and molecular methods, literature skills, translational research and research ethics. Our experience in training M.D. Fellows in research indicates that this course fills a variety of critical gaps in their knowledge base.

Optional Coursework:
Fellows are encouraged to update their knowledge, if necessary, by auditing courses such as biostatistics, molecular biology, drug discovery and computational biology methods offer by Baylor College of Medicine Graduate School of Biomedical Sciences. Fellows are also able to attend Baylor College of Medicine courses offered on Career Development Center that cover grantsmanship, scientific writing, interviewing skills. Individual research committees will evaluate each trainee’s background knowledge vis a vis the proposed research and will recommend additional courses if necessary.
Dr. Lynette Van Buren is the Fellowship Director responsible for clinical training and program administration. The other members of the clinical Faculty are listed on page 4.

**Inpatient:** All Fellows receive 12 months of inpatient training at Texas Children’s Hospital. It is divided into three “teams,” Gastroenterology, Hepatology, and Nutrition; each consists of a Fellow and an attending physician. Two teams, Gastroenterology and Hepatology, have alternate call days with the on-call team being responsible for consults overnight. The third team handles daytime consults at Texas Children’s Hospital.

- Consults are done on an average of four to six new patients each day. In addition to consults, patients cared for by the Faculty also may be admitted directly to the Gastroenterology or Liver teams, in which case the Fellow and the attending physician direct the care of the patient.
- All patient care is performed by the Fellow under the supervision of the attending. For example, consults are done by the Fellow and then are presented to the attending physician for discussion and teaching.
- All procedures are performed by the Fellow under supervision of the attending physician.
- Monday through Thursday the Fellows are “on call” once to twice a week on alternating days. Weekend call usually occurs every ten weeks for each Fellow. Fellows take night call and weekend call from home. There is a second fellow on call Saturday 5pm– Sunday 7am to allow the primary weekend fellow a rest period from consults in patient issues, and parent phone calls.
- Because attending physicians rotate twice a month, the Fellow has the opportunity to work with a number of different Faculty and, as a result, is exposed to a variety of clinical perspectives.

**Outpatient:** Through all years of the Fellowship, the trainee attends Gastroenterology, Hepatology and Nutrition outpatient clinics.

- Second and third year fellows have responsibility for continuity patients through a weekly 1/2 day Fellows’ Clinic. Fellows’ clinic is staffed by selected teaching faculty. During Fellows’ Clinic there is exposure to initial evaluation and diagnostics, clinical management, and patient follow up for the duration of fellowship training. Responsibility for all patient/family communication belongs to the continuity fellow, with coverage arranged among fellows during times the fellow is unavailable.
- All Fellows rotate through the Nutrition related Clinics during their first year.
- Optional outpatient rotations include the General Gastroenterology Clinics, Eating Disorders Clinic, Feeding Disorders Clinic, Prader-Willi Clinic, Grow Clinic, and Intestinal Rehabilitation Clinic, Eosinophilic Disorder Clinic.

**Skills:** Expertise that the trainee will acquire includes:

- Diagnostic and management skills in a wide array of gastrointestinal, hepatic, pancreatic and nutritional disorders.
- State-of-the-art training in gastrointestinal procedures, including diagnostic upper and lower endoscopy, therapeutic endoscopy (e.g., stricture dilation, variceal band ligation), intestinal motility, and capsule endoscopy.

**Other Activities:** Fellows have the opportunity to participate in the activities of a number of other clinical services and teams run by the Section of Pediatric Gastroenterology, Hepatology and Nutrition. These services are provided by the following groups:

- Hepatology/Liver Transplant Medicine with available 4th year fellowship
- IBD
- Neurogastroenterology and Motility
- EGID
- Pancreatobiliary
- Advanced Procedures
- Intestinal rehabilitation
- Aerodigestive
M.D. AND PH.D. RESEARCH TRAINING OVERVIEW

RESEARCH TRAINING

Dr. Douglas Burrin oversees the research training of the Fellows. The Section has maintained a NIH T32 Institutional Training Grant since 1991, administered by Dr. Robert Shulman, Principal Investigator. This grant provides funds for selected M.D. and Ph.D. Fellows with long term interests in research. The research training program is designed to accommodate a wide range of research experience and the individual interests of each trainee. We also have developed distinct research training tracks (see details p. 8) to help clinical fellows find the most appropriate training experience to meet their career objectives.

For M.D. Fellows: during year one, 3 one-month blocks of training are dedicated to research rotations. This gives the Fellow firsthand experience and provides the basis of choosing a mentor and an area of research interest. Throughout these rotations, the Fellow continues participation in the Gastroenterology, Hepatology and Nutrition outpatient clinics. This ensures that the Fellow is never totally removed from clinical activities.

As noted previously, the training program for M.D. Fellows includes a minimum of 24 months of research training and is designed to fulfill the research requirements that must be met by a Fellow before he/she is eligible to take the sub-board examination in pediatric gastroenterology. The official position of the sub-board on the research requirements can be found on pages 60-64. These requirements emphasize the importance of research training in the education of an academic pediatric gastroenterologist.

For Ph.D. Fellows: the expectation is that 24 months of research support will be provided. During this time, work also is geared toward obtaining future research support for the Fellow (e.g., NIH F32 grants) and preparing them for an academic career and the transition to a full-time Faculty position.

THE RESEARCH PROJECT

Each M.D. and Ph.D. trainee pursues a research project under the direction of a mentor selected from the list of potential mentors (p. 20). Mentors are chosen on the basis of solid research, a good track record in training new investigators, and a strong desire to see our Fellows have a successful research career. To facilitate the choice of mentor, M.D. Fellows spend their first three research months rotating between candidate mentors. Ph.D. Fellows directly select a research mentor from among Training Grant mentors (p. 20). After selecting a research mentor and identifying a research project, each trainee forms a Scholarship Oversight Committee (SOC) including the mentor and three (or more) additional members. Dr. Burrin serves as chairman of the research committee.

Using the SOC members as consultants, the Fellow writes a research proposal, which will be the foundation for studies to be completed during the research years. This proposal is reviewed by the research committee and orally defended before this committee. M.D. and Ph.D. Trainees present an oral progress report to their SOC at least twice per year. They also are expected to give a presentation at the Pediatric GI Research Workshop once per year. Additional meetings of the research committee are called as needed.

NIH T32 TRAINING GRANT

Only selected M.D. Fellows receive support from this prestigious training award and it is viewed as an important commitment toward a research career as a physician scientist. M.D. Fellows apply for Training Grant support in the Spring of their first year of Fellowship. The Training Grant provides research support for 24 months for M.D. Fellows.

All Ph.D. Fellows are supported by the NIH T32 Training Grant. Ph.D. candidates interested in the program can submit an application any time throughout the year provided that a slot is available. Applicants selected into the program are usually supported for 24 months.

M.D. AND Ph.D. - SIDE BY SIDE TRAINING

A unique and valuable facet of our program is that M.D. and Ph.D. Fellows interact not only in the laboratory, but in joint training activities (see p. 9). By bringing their specific knowledge base to the table, the education of both clinical and basic Fellows is enhanced. Furthermore, when M.D. and Ph.D. Fellows (and their mentors) come together, it stimulates teamwork and the development of translational research, which is a cornerstone of modern medicine.
M.D. AND PH.D. RESEARCH TRAINING OVERVIEW

RESEARCH TRAINING TRACKS

As the field of Pediatric Gastroenterology, Hepatology and Nutrition has evolved, the breadth and depth of areas of clinical expertise and research endeavor have increased dramatically. Given the commitment of our program to the training of academic physicians, it has become clear that a single track of training is not adequate to meet the needs of the field and our trainees. Three distinct tracks of training have been developed, with a focus on research activities in the second and third year of fellowship. The tracks are designed to help identify, at an early stage/first year in fellowship, the most appropriate training experience to meet the individual’s career objectives. It should be noted at the outset that there is no intrinsic enhanced value of one track over another. They are designed to meet the distinct needs of trainees. All are rigorous in training and in expectation of academic pursuit and product. The three tracks are briefly described below and further delineated in specific detailed descriptions or timelines for each of the tracks.

INVESTIGATOR TRACK

This track is designed to permit training in a wide-range of endeavors that will permit the trainee to experience the full range of the process of scientific investigation (hypothesis development, planning and executing investigations, interpreting and presenting the newly developed data in the context of the existing literature). A key goal will be to develop the skills necessary for independent assessment of scientific evidence. Mentors and the scientific oversight committees for this track will work with the trainee to develop lines of investigation that are important, feasible and conceptualized to permit meaningful data acquisition in the first 12 to 15 months of the research training. This will allow the trainee adequate time to delve into the interpretation of the new data and yield ample opportunity for presentation/publication of the data in the context of existing information. This process will give the trainee the requisite skills for critical interpretation of new data, which could be laboratory or clinically based.

CLINICAL NICHE TRACK

This track permits simultaneous training in investigation along with a more in-depth clinical experience in a particular niche in Pediatric Gastroenterology, Hepatology and Nutrition. This track is designed for those individuals who desire a patient care focused career in a specific sub-specialty area such as inflammatory bowel disease, neurogastroenterology and motility, hepatology, advanced procedures, or aerodigestive disorders, as examples. In this track, advanced clinical training is carefully integrated with a rigorous research endeavor to lay the groundwork to develop clinical specialists who have the ability to carry out patient oriented research. The scope of investigation and/or research product is tailored to accommodate the need for additional clinical training without diminishing the academic rigor of the line of investigation and/or the product that is developed as a result of the investigation. To pursue this track, a specific clinical niche needs to be identified by the trainee within 9 months of entering fellowship. View the Clinical Niche Track details.

PHYSICIAN-SCIENTIST TRACK

This track is designed to provide clinically relevant research training with the specific goal of attaining an independently funded career as a physician-scientist in Pediatric Gastroenterology, Hepatology and Nutrition. The near term goal of the program is for the individual to obtain NIH K-award (or equivalent thereof) funding within three years of completion of the fellowship. Individuals interested in this track will follow a distinct application and interview process when applying for a fellowship position. Criteria for acceptance into this track are very rigorous; the successful applicant typically will have extensive research experience prior to starting fellowship. There is institutional commitment to individuals in this track for three years of 75% protected time as an Assistant Professor after fellowship, presuming specific benchmarks are met during the three years of fellowship. The scientific endeavor in this track can include basic, translational, clinical or educational research.
PEDIATRIC GI WORKSHOP
This biweekly meeting is held over the noon hour and hosts presentations by Faculty and Fellows. The meeting is designed for Fellows and Faculty to share their research findings and foster collaboration among researchers with an interest in pediatric gastroenterology, hepatology and nutrition within Baylor College of Medicine and other outside institutions. All Fellows are required to present their research progress in this workshop each year. Twice per year, the workshop also hosts a “Visiting Young Investigator” considered as an up and coming person in pediatric gastroenterology to present their research and meet informally with our Fellows and Junior Faculty to discuss how to launch an academic career.

PEDIATRIC GI JOURNAL CLUB
This is a monthly gathering of Fellows or Faculty involved in our research training program. The meeting is designed to have Fellows select a clinical and basic science journal article that highlights a new research concept or advance with relevance to pediatric gastroenterology, hepatology and nutrition. The journal club is organized by the 2nd year Fellows and all trainees are required to present one clinical and one basic science article per year. Each Fellow leads an informal discussion of the design, outcomes and significance of the paper. The meetings are held in the evenings, hosted in the homes of our Faculty mentors, and includes dinner. These meetings are a vital social gathering for interaction among Fellows and Faculty to discuss their research and get acquainted personally. New collaborations and ideas often emerge from these meetings.

PEDIATRIC GI SCIENTIFIC SOCIAL
This is a quarterly meeting among Faculty and Fellows involved in the NIH Training Grant. The meeting is held in the evening and is designed to be a more intimate and informal gathering that includes dinner at a site in the Texas Medical Center. The program invites two mentors and one trainee from the Training Grant to give a brief, informal overview of their research intended to foster interaction, questions, and feedback among the attendees. The goal of this program is to give Fellows an opportunity to “think on their feet” and respond to feedback from Faculty mentors on their research. It also is another effective forum that often leads to research collaborations among Faculty mentors.

DIGESTIVE DISEASE CENTER GI FORUM
This is a weekly seminar series hosted by the Texas Medical Center Digestive Disease Center (DDC) (see p. 14) where local Faculty and invited guests from around the U.S. present their research in the areas of gastroenterology and hepatology. The DDC is an integral component of the GI and liver research community in the Texas Medical Center and brings together Faculty from Baylor College of Medicine, University of Texas Health Science Center, M.D. Andersen Cancer Center, Rice University, University of Houston, and Texas A&M Institute of Biosciences and Technology. The DDC also hosts the Annual Frontiers in Digestive Disease on the Texas Medical Center campus, which is a one day thematic symposium that features oral presentations from invited speakers, local Faculty, and trainees along with a poster sessions. It is yet another forum for our trainees to interact, network and socialize with Faculty and other members of the GI research community in Houston.

CAREER DEVELOPMENT WORKSHOPS
These are informal lectures given by training grant Faculty on vital skills and knowledge needed for successful Fellowship and Junior Faculty research career. Topics include how to write a manuscript, how to get published in peer-reviewed journals, how to apply for NIH grant funding, and how to prepare oral presentations and posters for scientific meetings. Similar presentations on these and other career development topics are also given during the Baylor College of Medicine Department of Pediatrics Fellows Day held annually in the Spring.
CONFERENCE SCHEDULE
Conferences are an important part of any Fellowship training program. The Section of Gastroenterology, Hepatology and Nutrition holds conferences on a regular basis in addition to those held by the Department of Pediatrics. The following table shows the current calendar. Asterisks (*) denote required conferences for M.D. Fellows. Daggers (†) indicate required conferences for Ph.D. Fellows. Other conferences are optional, depending on the Fellow’s interests and time constraints.

<table>
<thead>
<tr>
<th>Day</th>
<th>Time</th>
<th>Conference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monday</td>
<td>12:00pm - 1:00pm</td>
<td>* † GI Research Workshop (first and third Monday)</td>
</tr>
<tr>
<td></td>
<td>12:00pm - 1:00pm</td>
<td>*GI Pathology Conference (fourth Monday)</td>
</tr>
<tr>
<td></td>
<td>12:00pm - 1:00pm</td>
<td>*Liver Pathology Conference (second Monday)</td>
</tr>
<tr>
<td></td>
<td>1:00pm - 2:00pm</td>
<td>Hepatology Team Conference</td>
</tr>
<tr>
<td>Tuesday</td>
<td>12:00pm - 12:45pm</td>
<td>*Faculty and Fellows Meeting (monthly, second Tuesday)</td>
</tr>
<tr>
<td></td>
<td>12:45pm - 1:45pm</td>
<td>*Pedi GI Grand Rounds (monthly, second Tuesday)</td>
</tr>
<tr>
<td></td>
<td>1:00pm - 2:00pm</td>
<td>*GI Case Conference (weekly/except second Tuesday of month)</td>
</tr>
<tr>
<td></td>
<td>6:00pm - 7:30pm</td>
<td>* † Journal Club (first Tuesday of month, except Jan, and July)</td>
</tr>
<tr>
<td>Wednesday</td>
<td>1:00pm - 2:00pm</td>
<td>Liver Transplant MRB Conference (weekly)</td>
</tr>
<tr>
<td>Thursday</td>
<td>8:30am - 9:30am</td>
<td>Children’s Nutrition Research Center Conference (weekly)</td>
</tr>
<tr>
<td></td>
<td>12:00pm - 1:00pm</td>
<td>IBD Conference (Monthly, 1st and 4th weeks)</td>
</tr>
<tr>
<td></td>
<td>12:00pm - 1:00pm</td>
<td>Clinical Research Conference (Monthly, 3rd week)</td>
</tr>
<tr>
<td></td>
<td>4:00pm - 5:00pm</td>
<td>Digestive Disease Center—GI Forum (weekly)</td>
</tr>
<tr>
<td>*IBD Conference, Team E Conference, and Clinical Research Conference are rotating conferences</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Friday</td>
<td>8:30am - 9:30am</td>
<td>Pediatric Grand Rounds (weekly)</td>
</tr>
<tr>
<td></td>
<td>12:00pm - 1:00pm</td>
<td>*Pediatric Gastroenterology, Hepatology and Nutrition Fellow Core Curriculum</td>
</tr>
</tbody>
</table>

VISITING FACULTY PROGRAMS
Because of its size of and the amount of activity in the Texas Medical Center, we are afforded numerous opportunities to interact with visiting clinicians and researchers. In addition, the Section of Gastroenterology, Hepatology and Nutrition has its own invited speaker program, known as the Visiting Young Investigator series which is funded by our NIH T32 Training Grant. In this series, young pediatric gastroenterologists from around the country with established research credentials are brought in as role models for our senior Fellows and Junior Faculty. Each investigator gives a formal research seminar at the GI Research Workshop (see above) and has informal discussions (including career advice) with the Fellows and Junior Faculty.

VACATION AND BENEFITS
All Residents and Fellows are provided 44 paid days off per academic year (July 1 – June 30). This time off is non-vested (meaning the house staff physician is not paid for it if he or she leaves before having utilized), does not accrue, and does not roll over from one academic year to the next. These 44 days include:
*21 vacation days
*14 sick days (to be used only for personal illness)
*9 paid time off (PTO) days
This includes personal days, holiday, and educational leave (standard leave).
Jury Duty: Paid leave will be provided for jury duty as required by law.
NATIONAL SCIENTIFIC MEETING ATTENDANCE OPPORTUNITIES

Each M.D. and Ph.D. Fellow is provided with travel funds to attend one national conference per year. Additional conference travel funds may be available if the Fellow is presenting a paper or a poster, but permission must be sought individually from the Chief of the Section. Examples of typical annual conferences attended by Fellows and Faculty are:

- North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (held in November)
- Digestive Disease Week - A combined meeting of American Gastroenterological Association, American Association for the Study of Liver Diseases, American Society for Gastrointestinal Endoscopy, Society for Surgery of the Alimentary Tract (held in May)
- American Association for the Study of Liver Diseases (held October/November)
- Pediatric Academic Societies' Annual Meeting - Sponsored by American Pediatric Society, Society for Pediatric Research, Academic Pediatric Association, and American Academy of Pediatrics (held in May)
- Experimental Biology - Federation of American Societies for Experimental Biology is a combined meeting of the following societies: The American Physiological Society, American Society for Biochemistry and Molecular Biology, American Society for Pharmacology and Experimental Therapeutics, American Society for Investigative Pathology and American Association of Immunologists (held in April)

In addition to these national meetings, M.D. Fellows have the opportunity to participate in special Fellow conferences, which are organized by the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN):

- First Year Fellows Conference (sponsored by Nestle Nutrition)
- Second Year Fellows Conference (sponsored by Ross Labs)
- Third Year Fellows Conference (sponsored by Mead-Johnson)

The sponsoring companies cover all expenses, travel, food and accommodations for these meetings. During their research time, Fellows may have the opportunity to attend small conferences in their area of research. However, total conference attendance is limited to three per year in order to protect time in the training program.

JOB PLACEMENT

Assistance in obtaining positions after Fellowship training is taken very seriously by the Faculty. In addition to opportunities that are advertised, Faculty members often are aware of unpublished openings and are dedicated to finding the best match for each Fellow. The positions of the most recent previous Fellows are listed on the following page.
<table>
<thead>
<tr>
<th>Name</th>
<th>Period Training</th>
<th>Current Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gulati, Ajay</td>
<td>2004-2007</td>
<td>Associate Professor of Pediatrics, University of North Carolina, Chapel Hill, NC</td>
</tr>
<tr>
<td>McOmber, Mark</td>
<td>2005-2008</td>
<td>Assistant Professor, Phoenix Children’s Hospital, Phoenix, AZ</td>
</tr>
<tr>
<td>Kim, Steven</td>
<td>2005-2008</td>
<td>Staff Physician, Kaiser Permanente, Sacramento, CA</td>
</tr>
<tr>
<td>Venkataraman, Priya</td>
<td>2005-2008</td>
<td>Medical Officer, FDA, Walter Reed Pediatric Gastroenterology, Silver Spring, MD</td>
</tr>
<tr>
<td>Kellermayer, Richard</td>
<td>2006-2008</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Himes, Ryan</td>
<td>2006-2009</td>
<td>Section Head, Pediatric GI, Ochsner Medical Center in New Orleans, LA</td>
</tr>
<tr>
<td>Jain, Ajay Kumar</td>
<td>2006-2009</td>
<td>Associate Professor of Pediatrics, Saint Louis University, St. Louis, MO</td>
</tr>
<tr>
<td>Hattar, Lana</td>
<td>2007-2010</td>
<td>Private Practice, Wichita, KS</td>
</tr>
<tr>
<td>Mehta, Seema</td>
<td>2007-2010</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Whitfield, Lynette</td>
<td>2007-2010</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Schaible, Tiffany</td>
<td>2008-2011</td>
<td>Assistant Professor of Pediatrics, Brenner Children’s Hospital, Winston-Salem, NC</td>
</tr>
<tr>
<td>Cantu, Samson</td>
<td>2008-2011</td>
<td>Private Practice, Fort Worth, TX</td>
</tr>
<tr>
<td>Davidovics, Zev</td>
<td>2009-2012</td>
<td>Assistant Professor, University of Connecticut School of Medicine, Hartford, CT</td>
</tr>
<tr>
<td>Harpavat, Sanjiv</td>
<td>2011-2012</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Mir, Sabina</td>
<td>2010-2013</td>
<td>Assistant Professor of Pediatrics, University of North Carolina, Chapel Hill, NC</td>
</tr>
<tr>
<td>Wong, Greg</td>
<td>2010-2013</td>
<td>Staff Physician, Children’s Hospital of Orange County, Orange, CA</td>
</tr>
<tr>
<td>Ng, Kenneth</td>
<td>2010-2013</td>
<td>Assistant Professor of Pediatrics, Johns Hopkins School of Medicine, Baltimore, MD</td>
</tr>
<tr>
<td>Chen, Leon</td>
<td>2011-2014</td>
<td>Private Practice, Children’s Gastroenterology, MCG, Long Beach, CA</td>
</tr>
<tr>
<td>Hollier, John</td>
<td>2012-2015</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Hiremath, Girish</td>
<td>2013-2016</td>
<td>Assistant Professor of Pediatrics, Vanderbilt University, Nashville, TN</td>
</tr>
<tr>
<td>Mysore, Krupa</td>
<td>2013-2016</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Ihekweazu, Faith</td>
<td>2013-2016</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Priestis, Geoff</td>
<td>2014-2018</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Wang, Alex</td>
<td>2014-2017</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Osgood, Peter</td>
<td>2015-2018</td>
<td>Assistant Professor of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL</td>
</tr>
<tr>
<td>Keisha Barton</td>
<td>2016-2019</td>
<td>Assistant Professor of Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Carla Perez</td>
<td>2016-2019</td>
<td>Private Practice, Nicklaus Children’s Hospital, Miami, FL</td>
</tr>
<tr>
<td>Ligia Alfaro-Cruz</td>
<td>2016-2019</td>
<td>Private Practice, Johnson City, TN</td>
</tr>
<tr>
<td>Annie Goodwin</td>
<td>2016-2019</td>
<td>Instructor, Pediatrics, Baylor College of Medicine, Houston, TX</td>
</tr>
<tr>
<td>Name</td>
<td>Period of Training</td>
<td>Current Position</td>
</tr>
<tr>
<td>-----------------------</td>
<td>--------------------</td>
<td>----------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Blutt, Sarah</td>
<td>1999-2001</td>
<td>Associate Professor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Robker, Rebecca</td>
<td>2000-2002</td>
<td>Research Associate, The University of Adelaide</td>
</tr>
<tr>
<td>Madden, Charles</td>
<td>2000-2001</td>
<td>Assistant Professor, George Mason University</td>
</tr>
<tr>
<td>Dekaney, Christopher</td>
<td>2001-2004</td>
<td>Assistant Professor, University North Carolina State</td>
</tr>
<tr>
<td>Shroyer, Noah</td>
<td>2002-2003</td>
<td>Associate Professor of Pediatrics, Baylor College of Medicine</td>
</tr>
<tr>
<td>Ochsner, Scott</td>
<td>2003-2005</td>
<td>Senior Staff Scientist, Baylor College of Medicine</td>
</tr>
<tr>
<td>Hutson, Anne</td>
<td>2003-2005</td>
<td>Medical Science Liaison, Lundbeck</td>
</tr>
<tr>
<td>Zhou, Yong</td>
<td>2007-2009</td>
<td>Assistant Professor, University of Texas Health Science Center</td>
</tr>
<tr>
<td>Antar, Alli</td>
<td>2007-2009</td>
<td>Assistant Professor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Hyser, Joseph</td>
<td>2008-2010</td>
<td>Assistant Professor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Wooten-Kee, Ruth</td>
<td>2008-2010</td>
<td>Instructor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Mei, Yu</td>
<td>2010-2011</td>
<td>Research Fellow, Boston Children’s Hospital</td>
</tr>
<tr>
<td>Pflughoeft, Kathryn</td>
<td>2011-2012</td>
<td>Research Assistant Professor, University of Nevada School Medicine</td>
</tr>
<tr>
<td>Cana, Ross</td>
<td>2013-2015</td>
<td>Professor, Lee College</td>
</tr>
<tr>
<td>Engevik, Mindy</td>
<td>2014-2016</td>
<td>Instructor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Greg Guthrie</td>
<td>2015-2017</td>
<td>Instructor, Baylor College of Medicine</td>
</tr>
<tr>
<td>Jeff Galley</td>
<td>2016-2018</td>
<td>Research Scientist, Nationwide Children’s Hospital, Ohio State University</td>
</tr>
</tbody>
</table>
BAYLOR COLLEGE OF MEDICINE

Baylor College of Medicine is located in the Texas Medical Center in Houston, Texas which is the world’s largest medical center. Baylor College of Medicine is dedicated to promoting health for all people through education, research and public service. The College pursues this mission by sustaining excellence in educating medical and graduate students, biomedical scientists and allied health professions, as well as advancing basic and clinical biomedical research. The College is ranked 21st overall among the nation’s top medical schools for research and 5th for primary care and 10th for pediatrics in the United States. It has more than 5421 full-time, part-time, emeritus, and voluntary Faculty and conducts independent research amounting to more than $455 million annually. The College enrolls 736 medical students in a four-year program, approximately 603 Ph.D. graduate students, more than 1534 residents and Fellows in postgraduate medicine and surgery. Baylor College of Medicine has more than 90 research and patient care centers. This thriving environment has fostered international recognition, especially in the Departments of Pediatrics, Molecular and Cellular Biology, Molecular Virology & Microbiology, Molecular and Human Genetics, the Howard Hughes Research Institute, and the Human Genome Center.  www.bcm.edu

THE DEPARTMENT OF PEDIATRICS

Under the leadership of Dr. Mark Kline, Pediatrics is one of the pre-eminent departments in the U.S. The Department has trained more than 60% of the pediatricians in Texas and nearly 5% of all pediatricians in the United States. The Department of Pediatrics receives more than $104 million per year in extramural grant support, the majority of which comes from NIH. In any given year, the members of the department publish more than 800 papers in the peer-reviewed medical literature. Today, the Department of Pediatrics has more than 1260 Faculty. Some of these Faculty members provide staffing for the Pediatric Services at Ben Taub General Hospital (a public hospital providing care to citizens of Harris County). In addition, there are also 8 research centers in specific disciplines, the most relevant to this program being the Center for Cell and Gene Therapy, the Children’s Nutrition Research Center, the Obesity Center, and the Liver Center. www.bcm.edu/departments/pediatrics

BAYLOR CLINICAL SCIENTIST TRAINING PROGRAM

In 1999, Baylor College of Medicine received a K-30 grant from the National Institutes of Health to establish a college-wide multidisciplinary didactic 1-5 year training program known as the Clinical Scientist Training Program. This program is committed to promoting the education and training of highly motivated Junior Faculty to become successful, independent clinical investigators and future leaders in academic medicine and biomedical research. The program offers M.S. and Ph.D. degrees in Clinical Investigation through the Graduate School of Biomedical Sciences. Both programs are designed for individuals with a significant commitment to clinical research.

M.D. trainees interested in clinical research can extend their period of training by pursuing either the M.S. or Ph.D. degree from the Clinical Scientist Training Program. The core courses for the program are entitled Fundamentals of Clinical Investigation, Clinical Investigation for the Career Scientist, Responsible Conduct of Research for Clinical Investigators, and electives (Intermediate Biostatistics at the UT School of Public Health). Fundamentals of Clinical Investigation is offered in August every year. Fulfilling the course requirements, students will write a K-23 research proposal that will be developed into a thesis and the students also will write a R01 proposal. www.bcm.edu/education/programs/clinical-scientist-training/

TEXAS MEDICAL CENTER DIGESTIVE DISEASE CENTER

Mentors and trainees associated with this training program derive significant benefit from the Texas Medical Center Digestive Disease Center (DDC). The DDC is only the 17th such NIDDK-funded center in America which promotes coordinated digestive disease activities, and the only one in the Southwest or Gulf States area. The mission of the DDC is to facilitate on-going research in digestive diseases, promote translational research between basic and clinical areas, develop new projects, nurture new investigators, and provide GI educational activities. The DDC supports three Basic Science Cores (Cellular and Molecular Morphology, Functional Genomics and Proteomics, Integrative Biology), and one Clinical Core (Study Design and Clinical Research). The Center draws together a multidisciplinary group of investigators, including basic scientists with proven tract records of success, and well coordinated clinical programs dealing with pediatric and adult GI patients.

In addition, Fellows supported on our NIH Training Grant are eligible, in their third year, to apply for pilot/feasibility funding (up to $35,000) from the Center in order to develop research projects suitable for external funding. www.bcm.edu/gastro/DDC
EDUCATIONAL ENVIRONMENT

PEDIATRIC RESEARCH AND FELLOWS SYMPOSIUM
The Department of Pediatrics supports research training through their sponsorship of an annual research symposium where trainees have the opportunity to present their research in either oral or poster format. The symposium also includes faculty presentations on topics relevant to the development of academic physicians. www.bcm.edu/pediatrics

CHILDREN’S NUTRITION RESEARCH CENTER
The Children’s Nutrition Research Center (CNRC) is the first federally funded human nutrition research center to investigate the nutritional needs of children room conception through adolescence. The 11-story Center has 50 full-time Faculty members dedicated to defining the nutrient needs of children from conception through adolescence, pregnant women, and nursing mothers. Since 1978, CNRC research has helped form the foundation of national nutrition policies and clinical nutrition practices that have improved the health of mothers and children of all ages. It is operated by Baylor College of Medicine in cooperation with Texas Children’s Hospital and the Agricultural Research Service of the U.S. Department of Agriculture (USDA/ARS). The CNRC houses an Energy Metabolism and Exercise Laboratory with indirect room calorimetry, an advanced Body Composition Laboratory, a Behavioral Studies Unit and Children’s Eating Laboratory. These facilities enable the Center scientists to conduct some of the world’s most advanced nutritional studies, which have earned the CNRC an international reputation for research excellence. www.kidsnutrition.org

GASTROINTESTINAL (GI) PROCEDURES SUITE
Texas Children’s Hospital houses the 7,300-sq. ft. Gastrointestinal Procedures Suite. The GI Procedures Suite is at the cutting edge of patient care and research. More than 2,660 procedures (e.g., upper endoscopy, colonoscopy and liver biopsy) are performed each year in the Suite as well as a wide array of diagnostic tests (e.g., 24-hour esophageal pH monitoring, breath testing). The Suite is nationally known for its leadership role in sedation techniques in children and is the headquarters of the PEDS-CORI project (Pediatric Endoscopy Database System—Clinical Outcomes Research Initiative). The suite is composed of three endoscopic rooms, two non-endoscopic procedure rooms, a prep room, holding area, recovery room and endoscope disinfection room. www.bcm.edu/pediatrics

TEXAS CHILDREN’S HOSPITAL
Texas Children’s Hospital (TCH) is an internationally recognized full-care pediatric hospital. It is the largest children’s hospital in the United States. TCH is dedicated to providing the finest possible pediatric patient care, education and research. TCH is nationally ranked 4th among children’s hospitals by U.S. News & World Report. The hospital has garnered widespread recognition for its expertise and breakthrough developments in the treatment of cancer, diabetes, asthma, HIV, preterm babies, and cardiologic disorders. The hospital had more than 33,000 surgeries, 228,000 patient days, 126,000 Emergency Center visits and 3.7 million patient encounters. The hospital’s Feigin Center is a 20-story facility dedicated entirely to pediatric research. Texas Children’s Hospital is Houston’s only freestanding children’s hospital and is the primary teaching hospital of Baylor College of Medicine. The hospital’s award-winning medical staff consists of more than 1,580 board-certified, primary-care physicians, pediatric subspecialists, pediatric surgical subspecialists, and dentists. In addition, TCH offers a dedicated and highly skilled nursing staff, health care professionals and support staff of more than 6,000.

Also located adjacent to the Clinical Care Center is the TCH Pavilion for Women which provides a full continuum of family-centered care to women, mothers and their babies, beginning before conception and continuing through all the years of a woman’s life. In 2018, TCH opened a new 19-floor pediatric tower with new surgical operating rooms, intensive care unit, heart center and Helipad roof.

TCH West Campus houses a 48-bed acute care hospital located 25 miles from the Texas Medical Center. It houses a pediatric emergency center, surgical suites, and an advanced diagnostic imaging center.

In 2017, TCH opened the Woodlands Campus with a 560,000-square-foot, state-of-the-art facility with 25 emergency center rooms, 72 outpatient rooms, 12 radiology rooms, four operating rooms, 28 critical care beds and 32 acute care beds with plans to add up to 200 additional beds. www.texaschildrens.org
EDUCATIONAL ENVIRONMENT

INFLAMMATORY BOWEL DISEASE CENTER
The first of its kind in Houston and the Southwest, Texas Children’s Inflammatory Bowel Disease (IBD) Center offers a comprehensive, multidisciplinary approach to the diagnosis and treatment of Crohn’s disease and ulcerative colitis in children. A team of specialists provides individualized care, education and cutting-edge research to help patients and families manage the long-term aspects of the disease. We also treat other disorders with chronic diarrhea in pediatric patients, such as recurrent Clostridium difficile infection. Our program offers state-of-the-art diagnostic and therapeutic procedures such as whole exome sequencing, a wide array of endoscopic investigations including enteroscopy and capsule endoscopy, and MRI enterography. We are a pediatric center for fecal microbiota transplantation (FMT) in the treatment of recurrent Clostridium difficile infection, which is supported by the state-of-the-art Texas Children’s Microbiome Center. [https://www.texaschildrens.org/departments/inflammatory-bowel-disease-program](https://www.texaschildrens.org/departments/inflammatory-bowel-disease-program)

TEXAS CHILDREN’S HOSPITAL MICROBIOME CENTER
The Texas Children’s Microbiome Center is a cutting-edge laboratory housed within Texas Children’s Hospital. Staffed by leading scientists in the field of metagenomic science, the Texas Children’s Microbiome Center is strategically placed to partner with pediatric gastroenterology and other specialties. Clinical research coordinators are available for recording valuable information regarding the current condition of the child as well as historical medical information of importance. The Texas Children’s Microbiome Center Sequencing Core is skilled in the extraction of nucleic acid from a variety of specimen types, and the TCMC provides metagenomic analysis of the gut microbiome by next-generation sequencing partnered with bioinformatics support. [www.texaschildrens.org](http://www.texaschildrens.org)

THE NEUROGASTROENTEROLOGY AND MOTILITY PROGRAM
The Neurogastroenterology and Motility Center at Texas Children’s Hospital's goal is to provide world-class evaluation, therapy, and research in childhood functional and motility gastrointestinal disorders. Since 2008, a full motility laboratory including state-of-the art high resolution manometry, esophageal impedance, and breath testing has been available for diagnostic evaluations. All GI Fellows will have exposure to patients seen within the Center, and are welcome to attend Center outpatient clinics, observe/perform manometry procedures, or choose a research project relating to functional or motility disorders.

CENTER FOR PEDIATRIC ABDOMINAL PAIN RESEARCH
This Center is a multidisciplinary research program focused on understanding the pathophysiology of functional abdominal pain disorders in children. Research efforts also are dedicated to the treatment and management of these conditions. The research team consists of both clinical and basic science researchers and has a multispecialty focus with the contribution of pediatric psychologists, the Texas Children’s Microbiome Center, the Alkek Center for Metagenomics and Microbiome Research at Baylor College of Medicine, the Texas Children’s Hospital Motility Center, and the Leukocyte Biology Laboratory at the Children’s Nutrition Research Center. A number of national collaborations further enhance the Center’s activities. [www.bcm.edu/cnrc/kidsabdominalpain/](http://www.bcm.edu/cnrc/kidsabdominalpain/)

CAMP SIA
Camp SIA is a free camp for our patients who have life-long conditions including liver and bowel disease. The camp is held at the Camp For All facility in Burton, Texas. Camp SIA allows our GI patients time to meet and do activities with other kids who have similar conditions. Camp is great fun, not only for our campers, but for our medical staff as well. Medical staff is on hand 24-hours a day including a doctor, nurses, medical assistants, and a dietitian. [https://www.texaschildrens.org/departments/inflammatory-bowel-disease-program](https://www.texaschildrens.org/departments/inflammatory-bowel-disease-program)
EDUCATIONAL ENVIRONMENT

PEDS-CORI RESEARCH CENTER
In early 1999, the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the Children’s Digestive Health and Nutrition Foundation approved the PEDS-CORI proposal and the first site was established at Texas Children’s Hospital and Baylor College of Medicine. The goal was to develop and maintain a national repository of pediatric endoscopic procedures. PEDS-CORI provides investigators the ability to explore the discipline of pediatric endoscopy and gain insight into the current and future practice of pediatric endoscopy.

GASTROENTEROLOGY NURSING STAFF
The GI nurses are an integral part of the management of follow up care of GI patients. Due to the complex nature of our patients, we are fortunate to have a number of specialized nurses who provide continuity of care in the clinic via their phone triage system. In this way the nursing staff aids the Fellows in day to day management of the outpatient GI patient.
https://www.texaschildrens.org/departments/digestive-disorders/our-team

LIVER CENTER
Texas Children’s Liver Center is the largest pediatric liver disease program in the South, and is among the largest in the United States. The Center’s highly skilled transplant surgeons and liver specialists provide first-level clinical care to children with all forms of pediatric liver disease. Working in a state-of-the-art facility with a focus on family-centered care, our experienced team performs 35-45 liver transplants a year in children, ranging from young infants (younger than a month) to young adults, making us one of the most experienced liver transplant programs in the United States and the world. The Liver Center has performed more than 500 pediatric liver transplants with 35-45 per year in 2000. The liver transplant team at Texas Children’s Hospital is much more than just a surgical team. Our transplant coordinators work with surgeons, cardiologists, social workers, child life specialists, dietitians, pharmacists and physical and occupational therapists.
Within the Liver Center, the Biliary Atresia Clinic provides comprehensive medical, surgical and transplant care for infants and children with biliary atresia. The Viral Hepatitis Program at Texas Children’s Hospital provides comprehensive screening, education, and treatment for children and their families affected by viral hepatitis B and C. The Intestinal Rehabilitation Clinic provides multidisciplinary services that evaluate and treat patients with short bowel syndrome (SBS) and associated medical and social issues.
The Texas Medical Center is the world’s largest medical center and it is an internationally recognized community of healing, education, and groundbreaking research. It occupies an area of more than 1000 acres, 26 miles of public and private streets and is located 5 miles south of downtown Houston. It is dedicated to medical care and research. It is Houston’s largest employer, with more than 106,000 employees. The Medical Center is the home of many of the nation’s best hospitals, physicians, researchers, educational institutions and health care providers.

Within the confines of the Medical Center are three medical schools (Baylor College of Medicine, The University of Texas Medical School at Houston, and Texas A&M College of Medicine) and twenty-one hospitals (including Texas Children’s Hospital, St. Luke’s Episcopal Hospital and its affiliate the Texas Heart Institute, Methodist Hospital, Ben Taub General Hospital, the Michael E. DeBakey Veterans’ Hospital, The University of Texas at Houston affiliated Hermann Hospital, M. D. Anderson Cancer Center, Hermann Hospital Institute for Rehabilitation and Research (TIRR), and Shriner’s Children Hospital.)

The Medical Center is situated in a largely residential area of Houston. Thus, abundant housing is within walking distance. Rice University’s tree-lined campus is adjacent to the Medical Center, as are the recreational facilities of Hermann Park.
THE CITY OF HOUSTON

FUN IN THE CITY
As the fourth largest city in the United States with more than two million inhabitants from a variety of cultures, Houston is a city of surprises. Long known for its energy industry, Houston is an international city that is a leader in the arts, education and health care. Houston is ranked #1 Metro for building wealth by Bankrate.com. Houston ranks in the top five of America’s Coolest Cities in 2014 by Forbes. It is one of only four cities in the United States with permanent companies in all performing arts: dance, symphony, opera and theater. Houston’s Midtown area features an internationally known Museum District as well as a growing nightlife. Downtown is the entertainment focal point, with world-class performing arts at the Bayou Place Center for the Performing Arts, Jones Hall, the Alley Theatre, and the Wortham Center. Discovery Green is a 12-acre, downtown park featuring arts, entertainment, and children & family events all year long. The city has so many exciting attractions for everyone.

Houston is also a sports city. Outdoor sports abound due to the year-round mild climate. The beaches of Galveston are only an hour away, featuring the Historical Galveston Island Pleasure Pier amusement park. For spectator sports fans we have the Houston Texans lead by JJ Watt and Deshaun Watson in the NRG stadium, and the Houston Rockets led by James Harden and Russell Westbrook in the Toyota Center. The Houston Astros baseball team, 2017 World Series Champs, is located in Minute Maid Park downtown. The Houston Dynamo, the champions of major league soccer in 2006 and 2007 play in BBVA Compass Stadium near downtown Houston. Houstonians can travel to downtown for the arts and sporting events with the expanding METRO light rail.

Houston also annually hosts the Houston Livestock Show and Rodeo at the NRG Stadium, attracting millions of attendees yearly. The rodeo has been referred to as Houston’s signature event. This three week event includes some of the world’s biggest recording artists, rodeo parade, trail riders, Bar-B-Que Contests, Carnival, and much more.
# FACULTY RESEARCH INTERESTS

<table>
<thead>
<tr>
<th>Name</th>
<th>Research Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Britton, Robert A.*</td>
<td>Basic and Translational Therapeutic Microbiology</td>
</tr>
<tr>
<td>Burrin, Douglas G.*</td>
<td>Nutritional Regulation of Neonatal GI and Liver Health and Disease</td>
</tr>
<tr>
<td>Chiou, Eric</td>
<td>Disorders of Esophageal Motility</td>
</tr>
<tr>
<td>Chumpitazi, Bruno P.</td>
<td>Clinical Diagnosis, Treatment, &amp; Outcomes of Pediatric Functional and Motility GI</td>
</tr>
<tr>
<td>Conner, Margaret E.*</td>
<td>Pathogenesis of Intestinal Viral Infections</td>
</tr>
<tr>
<td>Diehl, Gretchen*</td>
<td>Crosstalk Between the Intestinal Immune System and the Microbiota</td>
</tr>
<tr>
<td>El-Serag, Hashem*</td>
<td>Clinical Epidemiology and Outcomes of GI and Liver Disorders</td>
</tr>
<tr>
<td>Estes, Mary K.*</td>
<td>Gastrointestinal Virus-Cell Interactions, Pathogenesis and Immunity</td>
</tr>
<tr>
<td>Fishman, Douglas</td>
<td>Advances in Therapeutic Endoscopy and Pancreaticobiliary Disease</td>
</tr>
<tr>
<td>Harpavat, Sanjiv</td>
<td>Developmental Etiology and Clinical Studies of Biliary Atresia</td>
</tr>
<tr>
<td>Hertel, Paula M.</td>
<td>Infantile Disorders of Biliary Function: Closing Current Knowledge Gaps</td>
</tr>
<tr>
<td>Hyser, Joseph</td>
<td>Cellular Signaling Pathways in GI Health and Infectious Diarrhea</td>
</tr>
<tr>
<td>Ihekweazu, Faith</td>
<td>Shaping the Gut Microbiome to Modulate Intestinal Inflammation</td>
</tr>
<tr>
<td>Jafar-Nejad, Hamed</td>
<td>Role of O-glucose Glycans in Notch Signaling and Liver Development</td>
</tr>
<tr>
<td>Kellermayer, Richard</td>
<td>Epigenomic and Microbiomic Aspects of Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>Lee, Brendan*</td>
<td>Biochemical Genetics of the Urea Cycle and Nitric Oxide Synthesis</td>
</tr>
<tr>
<td>Leung, Daniel</td>
<td>Viral Hepatitis and Cystic Fibrosis Liver Disease</td>
</tr>
<tr>
<td>Moore, David D.*</td>
<td>Metabolic Regulation by Nuclear Receptors</td>
</tr>
<tr>
<td>Mysore, Krupa</td>
<td>Immune Regulation of Pediatric Liver Diseases</td>
</tr>
<tr>
<td>Preidis, Geoffrey</td>
<td>Malnutrition and its Effects on the Liver, Gastrointestinal Tract, and Gut Microbiome</td>
</tr>
<tr>
<td>Rhoads, J. Marc*</td>
<td>Probiotic Mechanism of Action in GI Diseases</td>
</tr>
<tr>
<td>Savidge, Tor</td>
<td>Enteric Neuroimmune Microbe Interactions and Infectious Disease</td>
</tr>
<tr>
<td>Shneider, Benjamin L.*</td>
<td>Basic and Translational Research in Bile Acid Homeostasis and Disease</td>
</tr>
<tr>
<td>Shroyer, Noah*</td>
<td>Mechanisms that control intestinal development and homeostasis</td>
</tr>
<tr>
<td>Shulman, Robert J.*</td>
<td>Functional Gastrointestinal Pain Disorders in Children</td>
</tr>
<tr>
<td>Slagle, Betty L.*</td>
<td>Hepatitis B Virus Pathogenesis</td>
</tr>
<tr>
<td>Tessier, Mary Elizabeth</td>
<td>Microbiome Regulation of Enterohepatic Bile Acid Signaling</td>
</tr>
<tr>
<td>Thevananther, Sundararajah*</td>
<td>Molecular Mechanisms of Liver Regeneration, NASH, and Hepatocellular Carcinoma</td>
</tr>
<tr>
<td>Versalovic, James*</td>
<td>Microbiome and Probiotics</td>
</tr>
<tr>
<td>Hongtao (Alex) Wang</td>
<td>Nuclear receptor signaling in Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>Zoghbi, Huda Y.*</td>
<td>Molecular Genetic Approaches to Cell Specification and Degeneration</td>
</tr>
</tbody>
</table>

* Bold font indicates a Training Grant Mentor
<table>
<thead>
<tr>
<th>*Indicates Training Grant Mentor</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Robert Britton, Ph.D.</em></td>
<td>pg. 25</td>
</tr>
<tr>
<td>Professor</td>
<td></td>
</tr>
<tr>
<td>Department of Molecular Virology and Microbiology</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>* Douglas G. Burrin, Ph.D.*</td>
<td>pg. 26</td>
</tr>
<tr>
<td>Professor</td>
<td></td>
</tr>
<tr>
<td>Children's Nutrition Research Center</td>
<td></td>
</tr>
<tr>
<td>Director, Fellowship Research Training</td>
<td></td>
</tr>
<tr>
<td>Gastroenterology, Hepatology and Nutrition</td>
<td></td>
</tr>
<tr>
<td>Department of Pediatrics</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>Eric Chiou, M.D.</td>
<td>pg. 27</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td></td>
</tr>
<tr>
<td>Departments of Pediatrics, Gastroenterology</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>Bruno P. Chumpitazi, M.D., M.P.H.</td>
<td>pg. 28</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td></td>
</tr>
<tr>
<td>Department of Pediatrics</td>
<td></td>
</tr>
<tr>
<td>Director, Neurogastroenterology and Motility Program</td>
<td></td>
</tr>
<tr>
<td>Texas Children’s Hospital</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>* Margaret E. Conner, Ph.D.*</td>
<td>pg. 29</td>
</tr>
<tr>
<td>Associate Professor</td>
<td></td>
</tr>
<tr>
<td>Department of Molecular Virology and Microbiology &amp; Immunology</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>* Gretchen Diehl, Ph.D.*</td>
<td>pg. 30</td>
</tr>
<tr>
<td>Assistant Professor</td>
<td></td>
</tr>
<tr>
<td>Molecular Virology and Microbiology</td>
<td></td>
</tr>
<tr>
<td>Co-Director, Biology of Inflammation Center</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>* Hashem B. El-Serag, M.D., M.P.H.*</td>
<td>pg. 31</td>
</tr>
<tr>
<td>Professor</td>
<td></td>
</tr>
<tr>
<td>Chair, Department of Medicine</td>
<td></td>
</tr>
<tr>
<td>Director, Texas Medical Center Digestive Disease Center</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>* Mary K. Estes, Ph.D.*</td>
<td>pg. 32</td>
</tr>
<tr>
<td>Professor</td>
<td></td>
</tr>
<tr>
<td>Cullen Endowed Chair of Molecular and Human Virology</td>
<td></td>
</tr>
<tr>
<td>Departments of Molecular Virology and Microbiology, and Medicine-GI</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
<tr>
<td>Douglas Fishman, M.D.</td>
<td>pg. 33</td>
</tr>
<tr>
<td>Associate Professor</td>
<td></td>
</tr>
<tr>
<td>Department of Pediatrics</td>
<td></td>
</tr>
<tr>
<td>Gastroenterology, Endoscopy and Pancreaticoiliary Program (PBP)</td>
<td></td>
</tr>
<tr>
<td>Texas Children’s Hospital</td>
<td></td>
</tr>
<tr>
<td>Baylor College of Medicine</td>
<td></td>
</tr>
</tbody>
</table>
FACULTY

* Indicates Training Grant Mentor

Sanjiv Harpavat, M.D., Ph.D.  pg. 34
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

Paula M. Hertel, M.D.  pg. 35
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

Joseph Hyser, Ph.D.  Pg. 36
Assistant Professor
Departments of Molecular Virology and Microbiology
Baylor College of Medicine

Faith Ihekweazu, M.D.  pg. 37
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

* Hamed Jafar-Nejad, M.D.  pg. 38
Associate Professor
Molecular and Human Genetics
Baylor College of Medicine

Richard Kellermayer, M.D., Ph.D.  pg. 39
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Children’s Nutrition Research Center
Baylor College of Medicine

* Brendan H. L. Lee, M.D., Ph.D.  pg. 40
Robert and Janice McNair Endowed Chair and Professor
Chairman, Department of Molecular and Human Genetics
Baylor College of Medicine

Daniel Leung, M.D.  pg. 41
Associate Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Department of Viral Hepatitis Clinic
Texas Children’s Hospital
Baylor College of Medicine

* David D. Moore, Ph.D.  pg. 42
Professor
Department of Molecular and Cellular Biology
Baylor College of Medicine

Krupa Mysore, M.D.  pg. 43
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine
<table>
<thead>
<tr>
<th>Name</th>
<th>Title</th>
<th>Department</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geoffrey Preidis, M.D., Ph.D.</td>
<td>Assistant Professor</td>
<td>Department of Pediatrics</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>J. Marc Rhoads, M.D.</td>
<td>Professor</td>
<td>Section Chief, Pediatric Gastroenterology</td>
<td>University of Texas Health Sciences Center at Houston</td>
</tr>
<tr>
<td>Tor Savidge, Ph.D.</td>
<td>Associate Professor</td>
<td>Texas Children's Microbiome Center</td>
<td>Department Pathology and Immunology</td>
</tr>
<tr>
<td>Benjamin Shneider, M.D.</td>
<td>Professor</td>
<td>Section Chief, Gastroenterology, Hepatology and Nutrition</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>Noah Shroyer, Ph.D.</td>
<td>Associate Professor</td>
<td>Section of Gastroenterology and Hepatology</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>Robert J. Shulman, M.D.</td>
<td>Professor</td>
<td>Director, Center for Pediatric Abdominal Pain Research</td>
<td>Children's Nutrition Research Center</td>
</tr>
<tr>
<td>Betty L. Slagle, Ph.D.</td>
<td>Associate Professor</td>
<td>Department of Molecular Virology and Microbiology</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>Elizabeth Tessier, M.D.</td>
<td>Assistant Professor</td>
<td>Department of Pediatrics</td>
<td>Baylor College of Medicine</td>
</tr>
<tr>
<td>Sundararajah Thevananther, Ph.D.</td>
<td>Associate Professor</td>
<td>Department of Pediatrics</td>
<td>Baylor College of Medicine</td>
</tr>
</tbody>
</table>
**Faculty**

* Indicates Training Grant Mentor

* James Versalovic, M.D., Ph.D.  
  Professor  
  Department of Pathology & Immunology  
  Vice Chair of Molecular Pathology and Omics  
  Head, Department of Pathology  
  Pathologist-in-Chef  
  Director, Texas Children’s Hospital Microbiome Center

Alex Wang, M.D., Ph.D.  
  Assistant Professor  
  Department of Pediatrics  
  Gastroenterology, Hepatology and Nutrition  
  Baylor College of Medicine

* Huda Y. Zoghbi, M.D.  
  Professor  
  Department of Molecular and Human Genetics, Pediatrics, Neurology, and Neuroscience  
  Director, Jan and Dan Duncan Neurological Research Institute at Texas Children’s Hospital  
  Baylor College of Medicine
### Therapeutic Microbiology Laboratory

The Britton laboratory is interested in the role of microbes in health and disease, with a focus on identifying microbes with therapeutic properties for a variety of ailments. We use bacterial genetics, genomics, microbial ecology, and physiology to investigate individual microbes and microbial community structure and function.

#### 1. The role of intestinal bacteria in health and disease

Recent work into the role of intestinal bacteria in a variety of disease states including inflammatory bowel disease, obesity, and diabetes has established a clear link between these bacteria and our health. The Britton laboratory is focused on two areas of research in this area: the role of probiotic bacteria in treating disease and the role of the intestinal microbiota in preventing pathogen invasion.

**Probiotic Lactobacillus reuteri.** Much of our work focuses on characterizing how different strains of Lactobacillus reuteri impact various aspects of the host response including inflammation, bone health, pathogen invasion and intestinal function. We use a variety of in vitro and animal models to explore how L. reuteri impacts health. Our overall goals are to identify novel probiotic strains that can be used to prevent or ameliorate disease and to develop a platform for the delivery of biotherapeutics.

**Microbiota and prevention of pathogen invasion.** We are interested in understanding how the intestinal microbiota provides a barrier to incoming pathogens and how perturbations of the microbiota result in an established infection. We have focused most of our attention on the pathogen Clostridium difficile, which is the most common cause of antibiotic associated diarrhea and is quickly becoming the most common cause of nosocomial infections. We have developed mini-bioreactors and mice colonized with a human intestinal microbiota to address which members of the community are responsible for inhibiting C. difficile invasion. Our ultimate goal is to develop a probiotic cocktail derived from the human intestinal microbiota that will suppress C. difficile invasion.

#### Regulation of gut hormone production by the microbiota

Obesity and type 2 diabetes are emerging problems in the United States population, including young children. Our laboratory is screening next-generation probiotics for their ability to modulate gut hormone production in an effort to find microbes that can help individuals maintain a healthy weight.

### Recombineering in lactic acid bacteria

Recombineering technology allows for the precise genetic manipulation of bacterial chromosomes. Using single-stranded DNA (ssDNA) recombineering technology point mutations, small deletions, and small insertions can be recovered without the need for selection. We have now established non-selected recombineering in two lactic acid bacteria strains, Lactobacillus reuteri and Lactococcus lactis. We also have shown that recombineering can function in other Gram-positive bacteria as well. We can achieve average recombineering efficiencies of ~15% in L. lactis, which will now enable directed evolution of multiple chromosomal sites to be achieved simultaneously. Finally, we have also developed an efficient method for inserting genes stably into the chromosome of L. reuteri, which will enable the use of this human-derived organism to be used in the intestinal delivery of biotherapeutics and vaccines.

Email: Robert.Britton@bcm.edu
Our laboratory works on basic and translational projects designed to establish how nutritional support, enteral versus parenteral, affects gut and liver function and susceptibility to disease in early development. We have used the neonatal piglet to establish unique models of parenteral nutrition-associated liver disease (PNALD), necrotizing enterocolitis (NEC) and short-bowel syndrome (SBS) to address clinically-relevant problems in pediatric gastroenterology.

Current projects in the laboratory seek to identify the cellular and molecular mechanism that lead to PNALD and metabolic dysfunction associated with prematurity and neonatal parenteral nutrition (PN) support. Our recent studies in preterm pigs show that new generation lipid emulsions prevent PNALD. We are currently exploring how specific nutrients in commercial lipid emulsions, such as phytosterols, alter the susceptibility to PNALD and shape the gut microbiome and metabolome. We are exploring how parenteral lipid emulsions affect bile acid homeostasis and activity of the farnesoid X receptor–fibroblast growth factor 19 (FGF19) signaling pathway in the liver and gut.

Studies also are aimed at establishing how dietary carbohydrate composition shapes the gut microbiome and the incidence of NEC. Our recent studies suggest that lactose vs. corn syrup solid-based formula protects against NEC in preterm pigs and that this correlates with changes in the gut microbiome and metabolomic profiles. New studies are focusing on how human donor milk and probiotics shape the gut perinatal microbiome and may reduce the risk of NEC. We are also focused on how developmental changes in host citrulline and arginine metabolism measured using in vivo stable isotopic kinetic studies may contribute to intestinal perfusion and ischemia that has been linked to NEC. We are pursuing the molecular basis of this finding using metabolic studies in cultured enteroids.

We take an integrative experimental approach dictated by the research question to address relevant functions at the whole animal, tissue, cellular or molecular level. We use sophisticated metabolic, cell biological and molecular approaches, such as stable isotope metabolomics, 16S rDNA sequencing, RNA-seq transcriptomics, and confocal microscopic imaging to identify the cellular localization of specific signals involved in the metabolism, proliferation and survival of relevant cell types, including gut enteroids and hepatocyte spheroids.

Email: Doug.burrin@ars.usda.gov
The focus of my research is on disorders of esophageal motility in children. Gastroesophageal reflux disease (GERD) is considered one of the most common gastrointestinal motility disorders, affecting an estimated 1.8% to 8.2% of all children and adolescents worldwide. We now understand that the majority of acid reflux occurs as a result of transient relaxations of the lower esophageal sphincter. Despite the prevalence of GERD, there are still many unanswered questions regarding its diagnosis and management.

I am particularly interested in studying extra-intestinal manifestations of GERD in the airways and lungs. Although varied conditions such as asthma, otitis media, sleep apnea and chronic laryngitis have all been linked to GERD, there is still poor understanding regarding the pathogenesis of these complications. A major reason for this is the lack of an accurate and reliable tool for the diagnosis of reflux in the anatomic areas above the esophagus. Investigations have looked at the accuracy of measuring changes in pH in the proximal esophagus and posterior oropharynx, as well as the use of esophageal impedance monitoring to measure both acid and non-acid reflux. Current projects are looking at the role of gastroesophageal reflux in affecting changes to the human oral microbiome and its relationship to dental lesions. In addition, we are studying the use of transmission electron microscopy to look for ultrastructural changes in the esophageal epithelium known as dilated intercellular spaces (DIS) which have been associated with GERD and alterations in epithelial permeability.

My second area of investigation includes evaluating the use of high-resolution manometry techniques for the diagnosis of esophageal motility disorders in general. We have compared the use of this new modality to conventional techniques and are interested in understanding how these new measures of motility can be used to improve diagnosis, management and clinical outcomes.

Email: ehchiou@bcm.edu
Clinical and Translational Research in Childhood Motility and Functional Gastrointestinal Disorders

Associate Professor
Department of Pediatrics
Director, Neurogastroenterology and Motility Program
Texas Children’s Hospital

Our group’s research is focused on childhood gastrointestinal functional and motility disorders. These disorders include irritable bowel syndrome (IBS), functional dyspepsia, gastroparesis, and constipation. We have several areas of investigation relating to diet and IBS, diet and gut microbiome interactions in symptom generation in childhood IBS, and evaluation of diagnostic and therapeutic modalities for childhood gastroparesis, functional dyspepsia, and defecation disorders.

The Role of Diet and the Diet-Gut Microbiome Interaction in Childhood IBS
We seek to elucidate the role of diet in generating symptoms (e.g. abdominal pain) in children with IBS. Our efforts have ranged from focus groups and questionnaires to pilot dietary interventions and randomized clinical trials. Within our randomized controlled trials we have focused on the low fermentable oligosaccharide disaccharide monosaccharide and polyols (FODMAP) diet. In conjunction with the Texas Children’s Microbiome Center we use bacterial metagenomics and metabolomics to characterize the role of diet-microbiome interactions in generating childhood IBS symptoms. New projects include a specific focus on fructans (one of the FODMAP carbohydrates), biopsy studies, guided imagery treatment, human and microbiome carbohydrate enzyme genetics, and expansion of our work to elucidate diet-microbiome interactions in healthy children.

Diagnostic and Therapeutic Modalities for Childhood Gastroparesis and Functional Dyspepsia
Our group investigates the role of diagnostic testing such as endoscopy and gastric emptying scintigraphy in children with functional dyspepsia and gastroparesis. We have evaluated 4 hour gastric emptying scintigraphy studies in children and have evaluated the relationship of gastric retention to dyspepsia symptoms. New projects in this area include a long-term registry of children with these disorders, biopsy studies, evaluation of guided imagery as a therapy, and evaluation of electrotherapy in children with these disorders.

Diagnostic and Therapeutic Modalities for Childhood Defecation Disorders
Our group also investigates the role of diagnostic modalities such as anorectal manometry and stool form scales in children with defecation disorders. Stool form scales in which a child selects what his/her stool appears like is helpful clinically and in the clinical research setting. We are also actively investigating the role of therapies such as BoTox injections and physical therapy for children with these disorders. New projects in this area include head-to-head comparisons of stool form scales to determine the best one for children and evaluation of electrotherapies in children with chronic constipation.

Email: chumpita@bcm.edu
Pathogenesis of Intestinal Viral Infections

Associate Professor
Department of Molecular Virology and Microbiology & Immunology
Baylor College of Medicine

MARGARET E. CONNER

Recent Publications


The Conner laboratory focuses on the response of the host and microbiome to gastrointestinal pathogens. One theme of our research is the role of IgA in gastrointestinal mucosal defense against two enteric pathogens, rotavirus and Clostridium difficile. We use mouse models to identify the immunologic factors and underlying mechanisms of IgA induction and maintenance. We are also examining how rotavirus infection affects the intestinal microbiome. We are also exploring the mechanisms of rotavirus- and bacterial-induced intestinal intussusception.

Rotavirus is the most common cause of severe dehydrating diarrhea in children and results in the death of ~500,000 children yearly worldwide. Despite new efficacious vaccines, immune mechanisms that protect against rotavirus have yet to be well defined. We identified that intestinal IgA is critical for protection from rotavirus infection. Polyclonally activates B cells in Peyer’s patches in the intestine. We are now exploring the signaling pathways that induce IgA class switch recombination and current data support that rotavirus induces IgA by non-canonical signaling. Understanding the mechanisms of rotavirus infection is a key factor in the development and regulation of IgA. This information will be used to develop more effective mucosal vaccines and new methods of therapy. Our studies suggest that novel insights about intestinal immunity will be gained by defining basic pathways through which IgA is induced in the intestine in response to viral pathogens.

The first licensed rotavirus vaccine was withdrawn from the market because of an association with intestinal intussusception (ISS). Post-marketing surveillance data indicate that the currently licensed RotaTeq and RotaRix vaccines also pose an increased risk of ISS. We developed a mouse model to study rotavirus-associated ISS and obtained the first direct proof that rotavirus contributes to development of ISS. Induction of ISS is both virus dose- and replication-dependent. ISS is also associated with bacterial infections and we used a lipopolysaccharide (LPS) model of ISS to begin to define mechanisms of this complex process. LPS-ISS is initiated by innate immune signaling that requires TLR4 and phagocytes but may be independent of TNF-a, IL-6, and NO levels. Furthermore, alteration of intestinal motility, specifically, reduced intestinal contraction rate, is a key factor in the development of ISS. Multiple risk factors are associated with ISS in children that are also risk factors in the mouse models and we are exploring how these factors and rotavirus infection contribute to ISS.

Clostridium difficile (CDI) is a gastrointestinal pathogen that is a major and increasing health care burden costing the United States an estimated 3 billion dollars/year. CDI is the most common healthcare-associated infection. Mortality rates range from 5.7% to 15% with an estimated 7,752-20,000 deaths occurring annually from hospital onset CDI. CDI is a toxin-mediated disease in the large intestine. It has long been recognized clinically that immunosuppressed individuals, whether due to age, therapy with immunosuppressive drugs, or immunosuppressive infection, are at increased risk for CDI and relapsing CDI but the critical immunologic factors are not known. There is much indirect/correlative evidence supporting an important role of adaptive immunity to CDI. Using a mouse model, we are empirically probing the requirement for IgA and gut associated lymphoid tissue in adaptive immunity to CDI. Gaining a greater understanding of and identifying the key immunologic mediators of protection will contribute important insights to ongoing efforts to develop efficacious therapeutics and vaccines for CDI.

Email: mconner@bcm.edu
We are covered with and contain a large number of microorganisms, collectively known as the microbiota. It has become increasingly clear that these microbes are an important contributor to human health. My lab is focused on defining the crosstalk between the intestinal immune system and the microbiota. Using mouse models and human biopsy samples, we previously determined that signals from the microbiota promote intestinal homeostasis in a number of ways.

Within the intestine, we find the microbiota is key to induction of epithelial barrier repair and mucosal healing, thereby limiting pathology in models of inflammatory bowel disease (IBD). Further, we find that the microbiota is key to constraining microbe specific effector T cell responses and inducing regulatory T cell responses against fed proteins, facilitating the balance between pro and anti-inflammatory T cell responses. Both of these effects depend on a subset of intestinal antigen presenting cells known to be dysregulated in IBD. Current work in the lab seeks to identify specific microbes which induce these pathways. We are further working to define both the microbial and host the signaling pathways mediating these responses. Our work will allow selective manipulation of the intestinal immune system to either increase immune responses (in the case of infectious diseases) or limit them (in the case of inflammatory disorders such as IBD).

Email: gretchen.diehl@bcm.edu
Clinical Epidemiology and Outcomes of GI and Liver Disorders

Hashem B. El-Serag

Recent Publications


The group at the Division of Clinical Epidemiology and Outcomes at the Houston Center for Quality of Care and Utilization, headed by Dr. El-Serag, examines several aspects of the epidemiology and outcomes of GI and liver disorders.

Dr. El-Serag’s research agenda focuses on epidemiology and outcomes of digestive (esp. Barrett’s esophagus) and liver diseases (esp. HCV and HCC). Dr. El-Serag is an internationally-recognized expert in the clinical epidemiology and comparative effectiveness of liver, esophageal and digestive disorders and their therapies. His seminal work on HCC published in The New England Journal of Medicine has been cited over 2,400 times. His recently completed NIH RC4 grant focused on patient-centered approaches to understanding the comparative effectiveness of screening and surveillance for Barrett’s esophagus and esophageal adenocarcinoma. He and his collaborators are developing innovative comparative effectiveness research (CER) methods, e.g., improving the validity and reliability of secondary databases for CER, extraction of free-text data from electronic databases using natural language processing methods, and refining analytical methods for CER such as matched propensity score models and directed acyclic graphs. His group has assembled, through multiple R01 and VA funding, a single center based large two cohort: one of approximately 2200 patients (400 Barrett’s cases, 1300 endoscopy non-BE controls, 500 primary care controls); and the second of 1100 patients with HCV infection, both cohort with extensive epidemiological, clinical and genetic information and multi-year follow up outcomes data. These datasets have served as frame work for mentored research projects.

Email: hasheme@bcm.edu
We are using viruses that infect distinct types of cells (enterocytes, crypt cells, M cells) in the GI tract as probes to learn about the biology, host response and gene expression of these cells. Our work on the molecular biology of GI viruses uses two viruses, rotaviruses, the major cause of diarrhea in children and animals worldwide, and noroviruses, the cause of almost all (>96%) outbreaks of epidemic gastroenteritis in all age groups. Most studies are multidisciplinary and involve in vitro and in vivo models of infection including studies in volunteers, animal models and novel ex vivo human intestinal mini-gut enteroid cultures.

Our research program is divided into several areas including molecular analysis of GI viral-host interactions that affect pathogenesis and also include studies to develop strategies for mucosal immunization with non-replicating virus-like particles (VLPs), identification of intestinal glycan receptors for GI viruses, and understanding the stem cell response to infection. Cloning and sequencing the first human calicivirus genome from Norwalk virus (NV) led to development and use of new diagnostic assays that have resulted in changing our understanding of the natural history and epidemiology of infections with these viruses. Notably, NV and related viruses are now recognized as important causes of disease in children and in immunocompromised individuals, including transplant patients. Recombinant NV VLPs are a promising candidate vaccine. Recent identification of a correlate of protection and initial efficacy studies with promising results are stimulating norovirus vaccine development and field trials are being planned.

Finally, the molecular basis of the restricted replication of Norwalk viruses to the GI tract of humans is being dissected by using the first infectious cDNAs of Norwalk virus in mammalian cells. Histo-blood group antigens are host susceptibility factors and the role of the innate immune response in blocking replication is being pursued.

Email: mestes@bcm.edu
Advanced Endoscopic Techniques and Pancreaticobiliary Diseases

DOUGLAS FISHMAN

Associate Professor
Department of Pediatrics
Gastroenterology, Endoscopy and Pancreaticobiliary Program (PBP)
Texas Children’s Hospital
Baylor College of Medicine

Recent Publications


The Fishman research group focuses on the characterization of pediatric pancreaticobiliary disease in children as well as the study of pediatric endoscopic practice.

INSPPIRE International Multi-center Pancreatitis Registry
Baylor College of Medicine and Texas Children’s Hospital were charter members of INSPPIRE in 2009. INSPPIRE: International Study Group of Pediatric Pancreatitis: In search for a cure. Our immediate goal is to develop a database of children with ARP and CP and to understand the epidemiology, etiologies, natural history and outcome in a well-phenotyped cohort of children with ARP and CP. We continue to develop an international multi-center consortium to prospectively study pediatric ARP and CP and determine the feasibility of long-term studies. We plan to determine the epidemiology and potential etiologic factors of ARP and CP in children. Drs. Fishman and Himes lead the local group under the leadership of Dr. Aliye UC at the University of Iowa. Our team also collaborates with Dr. William Fisher in the Elkins Pancreas Center, studying the relationship of diabetes and chronic pancreatitis to pancreatic cancer.

PEDS-CORI Endoscopy
Since 1999, Texas Children’s has been the leader of PEDS-CORI, (Clinical Outcomes Research Initiative (PEDS-CORI)) using a structured, computerized endoscopic reporting system to identify and monitor quality indicators for pediatric endoscopy. We are currently adding new sites with a goal of 14 active PEDS-CORI sites to include more than 100 pediatric gastroenterology providers. This is the most comprehensive pediatric endoscopy database in North America. PEDS-CORI has reported numerous findings related to various diseases in pediatric endoscopy and colonoscopy. We recently reported our findings in quality pediatric colonoscopy and aim to further delineate factors to improve quality. We seek to establish additional parameters that will serve as a tool for educators, clinicians and researchers in pediatric endoscopy.

PEDI (Pediatric ERCP Database Initiative) and Choledocholithiasis Research
Along with Dr. David Troendle at UTSW, we are a collaborator in the Pediatric ERCP Database, charged with evaluating and reporting ERCP quality for pediatric patients. This is a REDCAP based database using patient and physician reported information from biliary and pancreatic endoscopic procedures. A sub-group of the project is centered at Texas Children’s seeking to identify appropriate testing algorithms for patients with possible choledocholithiasis (common bile duct stones) being evaluated for ERCP.

Email: douglas.fishman@bcm.edu
Developmental Etiology and Clinical Studies of Biliary Atresia

SANJIV HARPAVAT
Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

Recent Publications


Biliary atresia, the world’s most common indication for pediatric liver transplant, is a poorly understood disease. One commonly held notion is that BA is acquired some time after birth. Two findings support this explanation: (a) infants often appear healthy at birth, and (b) BA does not follow a genetic pattern (discordant in twins, does not run in families). However, the observation that BA follows the same time course without exception, only affecting very young infants, encouraged us to question the acquired explanation.

To test exactly when BA starts, we asked a simple question: What are the direct/conjugated bilirubin concentrations for newborns later diagnosed with BA? We reasoned that if they were normal, then infants do not have disease at birth and instead acquire it at a later point in time. Alternatively, if they were elevated, then infants have disease at birth contrary to current explanations. To answer our question, we called the birth hospitals for infants with BA cared for at our institution. To our surprise, every infant with newborn measurements had elevated concentrations, which continued to rise with time. These results suggest infants are born with BA, and raise the possibility that BA should be considered a developmental disease.

Our current work builds on the initial observations, and follows two lines of research:

Validating a newborn screening system for BA based on direct/conjugated bilirubin measurements. Infants with BA have better outcomes when identified and treated earlier. Unfortunately, in the United States, the BA diagnosis is often delayed. To address this issue, we have initiated a prospective, multi-center screening study to determine whether newborn direct/conjugated bilirubin measurements can effectively identify infants with BA. In addition, we are analyzing the screen’s cost-effectiveness, and assaying different ways to measure conjugated bilirubin concentrations from the state newborn screening blood spot cards.

Exploring intrahepatic and extrahepatic bile duct development, to understand what causes BA. In these experiments, we examine bile ducts at two levels. First, human liver tissue from BA patients is probed using immunohistochemistry, to identify which signaling pathways are perturbed in disease. Second, mouse models are used to recapitulate a BA-like phenotype. For these experiments, we use lineage tracing and condition knock-out technology.

Email: harpavat@bcm.edu
Infantile Disorders of Biliary Function: Closing Current Knowledge Gaps

Associate Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

PAULA M. HERTEL

Recent Publications


Disorders of bile flow (cholestatic liver diseases) that present during infancy and childhood are diverse and, in many respects, still poorly understood. Collectively, these diseases are not uncommon, but individually, they are rare. Biliary atresia, the most common indication for liver transplantation in children, occurs in only approximately 1:10,000 live births. Many other infantile cholestatic liver diagnoses are even less common.

Often, the etiology of cholestasis during infancy is multifactorial. Bile flow may be impaired by numerous factors such as infection, hemolysis, and parenteral nutrition, and bile flow in the immature liver is particularly vulnerable to becoming impaired following one or more of these insults. Genetic factors may also contribute to vulnerability to cholestasis; variants in genes such as those implicated in alpha-1-antitripsin deficiency and progressive familial intrahepatic cholestasis are known to play roles in cholestasis in early life. The cause(s) of cholestasis may remain undetermined in many young patients, however.

Texas Children’s Hospital and Baylor College of Medicine Division of Pediatrics Gastroenterology and Nutrition participates in an NIH-funded, multi-center consortium known as “ChiLDReN” (Childhood Liver Disease Research Network – childrennetwork.org). The Network consists of fourteen clinical sites in the United States and Canada, each of which enrolls children with cholestatic liver diseases in protocols that include four long-term observational studies as well as therapeutic drug trials. The strength of the Network lies in its prospective, longitudinal (up to 10 years) study of children with liver diseases, as well as its ability to capture substantial numbers of study subjects diagnosed with rare diseases by virtue of involvement of multiple top pediatric tertiary care hospitals.

Dr. Hertel is responsible for the conduct of the ChiLDReN Network observational protocols at the Texas Children’s Hospital site, is Chair of the Idiopathic Neonatal Hepatitis working group, and is an active participant in the PFIC (progressive familial intrahepatic cholestasis) and Biliary Atresia Genomics and Pathophysiology workgroups. A wonderful opportunity exists to access the Network’s data and tissue repository by submission (and approval) of ancillary proposals – please contact Dr. Hertel or one of our other ChiLDReN site Co-Investigators for more information. Dr. Hertel would be pleased to direct those interested to a contact with compatible interests.

Email: phertel@bcm.edu
Cells communicate using a myriad of extracellular molecules that are sensed by receptors that are coupled to intracellular signaling pathways. The integration of these pathways helps define cell specialization and regulates virtually all cellular functions. The long-term goal of the Hyser laboratory is to characterize signaling pathways in the gut and liver that are critical for maintaining normal function, and determine how pathogenic and commensal microbes exploit these signaling pathways to their benefit.

A major focus of our studies involves live microscopy imaging of cellular signaling dynamics using cells, enteroid mini-guts, and animal models expressing fluorescent biosensors for important secondary messengers, including Ca2+, cAMP, nitric oxide and many others. Through these studies we have made new and interesting discoveries about the communication pathways exploited by enteric pathogens. For example, using cell lines and enteroids stably expressing the GCaMP6 Ca2+ sensor, we have found that individual rotavirus-infected cells elicit a potent paracrine signal that activates Ca2+ signals in neighboring uninfected cells. This paracrine signal is mediated by the repeated release of purines, which diffuse to and activate purinergic receptors on the neighboring cells. Rotavirus-induced purinergic signaling is involved in multiple aspects of pathogenesis, including increasing virus replication, activation of Cl- secretion, and triggering serotonin release from enteroendocrine cells. We are currently examining other enteric pathogens for the induction of paracrine purinergic signaling.

Our research program is divided into three broad (and overlapping) themes:
1) Host signaling pathways underlying rotavirus diarrhea.
2) Characterization of signaling pathways exploited by enteric diarrheal pathogens.
3) Engineering enteroids to study gastrointestinal functions.

Email: joseph.hyser@bcm.edu
Due to the limited therapies, 20% of pediatric patients with Inflammatory Bowel Disease (IBD) become refractory to traditional medications, requiring surgery within 5 years of diagnosis. Conventional IBD therapy includes immunosuppressive agents, which carry significant side effects, including infection and malignancy. In order to address this critical need for new therapeutic options, I have concentrated on the role of the gut microbiota in disease pathogenesis.

I have focused my research on bacteriotherapy as a therapeutic modality for IBD, studying both human and murine models of disease. While my initial interest was in using fecal microbiota transplantation (FMT) for the treatment of IBD, I learned that the fecal microbiome is complex, dynamic, and highly variable, complicating the dissection of the key therapeutic attributes. Therefore, I sought to identify stable bacteria that carry the therapeutic effects of FMT. I determined that Bacteroides ovatus monotherapy led to improved outcomes compared to FMT (decreased weight loss and inflammation, enhanced epithelial recovery, increased survival) in a murine colitis model. Taking this further, I now aim to determine the mechanism behind the anti-inflammatory effect of B. ovatus therapy during murine colitis, focusing on its ability to produce short chain fatty acids and thereby enhance epithelial barrier function and modulate the immune system. My long-term goal is to advance the field by identifying next generation probiotics, which will be effective and safe for the treatment of IBD.

Email: Faith.ihekweazu@bcm.edu
Glycosylation is the most common post-translational modification of extracellular proteins and plays major roles in various aspects of cellular and organismal biology. We use Drosophila and mouse genetics and cell culture experiments to understand the contribution of glycosylation and deglycosylation to the regulation of animal development and pathophysiology of human disease. A major focus of our work is on POGlut1 and other glycosyltransferases responsible for the addition of O-glucose glycans to epidermal growth factor-like (EGF) repeats. Specifically, we would like to understand how these glycosyltransferases regulate the activity of the Notch signaling pathway.

We have reported a mouse model for a human developmental disorder called Alagille syndrome (ALGS), which is mostly caused by dominant mutations in the Notch pathway ligand JAG1. Alagille syndrome (ALGS) is an autosomal dominant disorder characterized by a congenital cholangiopathy of variable severity accompanied by cardiac, skeletal, renal and other abnormalities. In 94 percent of cases, ALGS is caused by mutations in JAG1, which encodes one of the ligands for the Notch pathway. Our work suggests that Poglut1 is a dominant genetic suppressor of Jag1[+/-] phenotypes in mice. Part of our efforts is dedicated to understanding the mechanisms underlying Jag1 haploinsufficient phenotypes in mice and their suppression by decreasing Poglut1 levels. Ongoing experiments are aimed at using this model to better understand the pathophysiology of ALGS and to determine the basis for its extreme phenotypic variability, even among patients harboring the same JAG1 mutation. We are also taking advantage of this mouse model as a framework for identifying mechanism-based therapies for ALGS.

Email: hamedj@bcm.edu
Epigenomic and Microbiomic Aspects of Inflammatory Bowel Disease

Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Children’s Nutrition Research Center

RICHARD KELLERMAYER

Recent Publications


Our laboratory approaches inflammatory bowel diseases from the perspective of the developmental origins hypothesis. This hypothesis postulates that at various stages of development critical changes in organismic structures can occur as a result of environmental influences. Such critical changes are then maintained throughout life and influence our susceptibility to common disorders, such as inflammatory bowel diseases (IBD), for example. IBD develops on the basis of an exaggerated immune response against the enteric microflora that is transmitted by the intestinal epithelium. One molecular process that has been recognized to potentially play a major role in the developmental origins of human diseases is DNA methylation. DNA methylation is the most stable epigenetic process and can respond dynamically to microbiota changes in the intestinal mucosa. Therefore, epigenetic and microbiome alterations may be intimately related in the mammalian gut. We are studying how nutritional and genetic changes can modify the intercalating network of the mucosal epigenome and microbiome in association with mammalian colitis. Our recent clinical and basic research focus is complex (fecal microbiota transplantation) and select bacteriotherapy to treat murine models of colitis and IBD. These studies should provide the basis for novel diagnostic, preventative and therapeutic measures for IBD.

Email: kellerma@bcm.edu
Biochemical Genetics of the Urea Cycle and Nitric Oxide Synthesis

Professor
Robert and Janice McNair Endowed Chair and Professor
Chairman, Department of Molecular and Human Genetics
Baylor College of Medicine

BRENDAN LEE

Recent Publications


The overall mission of my research program is to translate the study of structural birth defects and inborn errors of metabolism into a basic understanding of development, disease, and novel therapeutic approaches. My research program ranges from study of basic developmental mechanisms to interventional clinical trials. One longstanding area has been the genetic study of biochemical genetic disorders (specifically urea cycle disorders) as models of complex disease (those involving nitric oxide dysregulation). This area has encompassed generation of mouse models of urea cycle disorders (UCDs), stable isotopic metabolic studies in patients with UCDs, longitudinal observational studies, and both investigator-initiated and industry-sponsored interventional trials. In parallel, I have also attempted to develop cell, protein, and viral gene therapy for these conditions (urea cycle disorders, hyperbilirubinemia, hemophilia), in addition to studying the immune response to these therapies.

My clinical research program began with stable isotopic measurements in humans and UCD patients to better diagnose patients with disorders of urea cycle flux and to evaluate the differential bioavailability of different sources of nitrogen (enteral vs. parenteral) to the urea cycle. These human studies have evolved to measure nitric oxide flux in patients with UCDs and specifically with arginase deficiency and argininosuccinic aciduria. These studies have led us to more broadly ask how enzymes of the urea cycle including those that synthesize and degrade arginine, i.e., argininosuccinate lyase and arginase, respectively, regulate systemic nitric oxide synthesis in a variety of human diseases including liver fibrosis and necrotizing enterocolitis.

Interventional studies include the Phase II and III studies of a novel ammonia scavengers in UCD patients and phenylbutyrate/arginine treatment in patients with argininosuccinic aciduria. Currently, I direct the Baylor College of Medicine/Texas Children’s Hospital site of the Urea Cycle Disorders Rare Disease Clinical Research Network. As part of this site, we perform both investigator initiated and industry sponsored studies on treatment of UCDs.

Email: blee@bcm.tmc.edu
Dr. Leung oversees the Viral Hepatitis Clinic at Texas Children’s Hospital which features a robust clinical program, managing and counseling nearly 200 established patients with hepatitis B and C. 7 clinical trials in the treatment of hepatitis are conducted from the clinic with new protocols studying the safety and efficacy of direct acting antivirals for children infected with HCV. Other research protocols within the hepatitis clinic include the study of shearwave elastography, serum biomarkers, and simple biomarkers.

Dr. Leung’s research spans disciplines within hepatology and gastroenterology such as cystic fibrosis (CF), the intestinal microbiome, and nutritional outcomes. Dr. Leung currently has funding from the NIH, CF Foundation, CF Therapeutics Development Network, and Texas Children’s Hospital Pediatric Pilot Award. His efforts as site PI of the NIH funded CF Liver Disease Network has led to BCM being recognized as the largest enrolling site in the country. For the last 5 years, Dr. Leung has served as Lead Co-Principal Investigator of the Cystic Fibrosis Foundation (CFF) funded Multi-center Infant Nutrition Observational Study in Children identified by Newborn Screening (BONUS) study in tandem with Dr. Drucy Borowitz, a matriarch in the field of pediatric cystic fibrosis. His unique skill set in gastrointestinal and hepatology care within cystic fibrosis was recognized by the CFF and he was awarded a Developing Innovative GastroEnterology Specialty Training (DIGEST) Program grant through 2017 to be further mentored by pioneers within the CF GI and Liver field. He is currently a co-investigator for a NIH R01 funded project in the CF Infant microbiome and sits on the Cystic Fibrosis Foundation and Therapeutic Development Network Clinical Research Award and Grants Committee, which has awarded more than $2 million in annual grant funding.

Email: dhleung@bcm.edu
Metabolic Regulation by Nuclear Receptors

Professor
Department of Molecular and Cellular Biology
Baylor College of Medicine

DAVID D. MOORE

Recent Publications


Nuclear Hormone Receptors Regulate Metabolism and Cancer

The 48 members of the nuclear hormone receptor superfamily function as ligand-dependent or, in some cases, ligand-independent transcription factors. The major goal of this laboratory is to understand the roles of the newer members of this superfamily, particularly their impact on metabolic and oncogenic pathways in the liver. One major focus is on CAR, which functions to regulate the response of the liver to xenobiotics, potentially toxic foreign compounds. Activation of CAR by specific xenobiotic stimuli, and also by toxic endogenous compounds such as bile acids and bilirubin, increases the liver's ability to metabolize and eliminate them. CAR-dependent responses are generally protective, but can be deleterious. Thus, chronic activation of CAR by non-genotoxic carcinogens results in liver tumors, due to direct effects of CAR on both hepatocyte proliferation and apoptosis. We are pursuing both the mechanism of this tumor promotion and therapeutic approaches that block it.

We are also studying the role of nuclear receptors in response to other stresses in the liver. We have found that PPARalpha, which is activated in the fasted state, can induce autophagy to promote nutrient availability. In the opposite direction, FXR is activated in the fed state, and blocks such nutrient recycling when it is not needed. More broadly, we are studying the role of FXR in managing energy balance in the resource rich fed state, and the role of PPARalpha in the resource poor fasted state. Overall, we will continue to use pharmacologic and mouse knockout approaches to explore the diverse metabolic and oncogenic functions of the nuclear hormone receptors.

Email: moore@bcm.edu
Immune Regulation and Infections in Chronic Liver Diseases and Transplantation

Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

KRUPA MYSORE

**Recent Publications**


Mysore KR, Himes RW, Schady D, Munoz F. Human Herpesvirus-6 (HHV-6) infection in pediatric liver transplant recipients at Texas Children's Hospital. Oral presentation at 10th International Conference on HHV-6&7, Berlin, Germany, July 2017

My clinical and research interests are in pediatric liver diseases and transplantation. I actively collaborate with divisions of Immunology and Infectious diseases at Texas Children’s Hospital. There are a large number of infectious complications in patients with chronic liver diseases (CLD) and transplantation. We lack the understanding of the immunological deficits predisposing to these infections. My work focuses on basic and translational projects designed to establish how immune dysregulation in CLD and transplantation alters hosts susceptibility to infection. We have used the human blood samples and tissues in the laboratory, using powerful techniques such as flow cytometry, ELISPOT assays, PCR etc. to analyze immune cells. The laboratory data is correlated with clinical patient data which address clinically-relevant problems in pediatric hepatology and transplantation. My Master’s in Clinical Investigation with CSTP has helped me expand translational research studies in the laboratory and facilitated building a biorepository of specimens from children and adolescents who have received liver transplants; a vital resource to investigate biomarkers in pediatric transplantation.

Current projects in the laboratory seek to identify the cellular and molecular mechanism that lead to T cell and dendritic cell dysfunction associated with pediatric CLD in the immediate pre-transplant phase. Our recent studies in adult CLD show that patients with increased expression of T cell inhibitory markers in circulation in the pre-transplant period have increased susceptibility to infections in the immediate post-transplant phase. We are currently identifying underlying mechanisms in liver diseases which alters the T cell co-signaling pathways while simultaneously establishing role of these inhibitory pathways in pediatric liver diseases. Alterations in T cell–dendritic cell interactions and antigen presentation in CLD are being studied as well.

Studies also are aimed at establishing role of immune cells in vaccine response in transplant patients. We specifically are aiming to identify differences in vaccine response across transplant patients and the underlying immune mechanisms for these variabilities. Other active areas of her clinical research include work on implementing ABO-incompatible liver transplant management protocol and evaluating the incidence of Human Herpes Virus (HHV-6) virus in pediatric liver transplantation at Texas Children’s Hospital. Representative publications from recent work are listed below.

Email: mysore@bcm.edu
Malnutrition and Effects on the Liver, Gastrointestinal Tract, and Gut Microbiome

Assistant Professor
Department of Pediatrics
Gastroenterology, Hepatology and Nutrition
Baylor College of Medicine

Our goal is to define mechanisms through which early life undernutrition alters metabolism and to determine how undernutrition impairs intestinal and liver function. Undernutrition causes acute medical problems, but also long term health problems that may result from permanent epigenetic changes that alter transcription or via changes in the gut microbiome. Current studies focus on how malnutrition alters hepatic secretion, transcriptional programming, gastrointestinal motility, and host-microbiome interactions to impact growth. Our work is pertinent to those suffering from nutritional deficiencies caused by a wide range of medical and psychosocial factors, including preterm and underweight newborns in the neonatal intensive care unit, children with severe acute malnutrition in the developing world, and adolescents with anorexia nervosa.

Liver Function Impairment in Malnutrition - Striking problems occur in the malnourished liver via mechanisms that are not yet elucidated. When macronutrients are scarce, the liver decreases production of its secreted factors – the hepatic secretome – to conserve energy. However, underproduction of coagulation factors, complement proteins, and bile acids promotes coagulopathy, immune deficiency, and fat malabsorption, respectively. Our studies implicate altered nuclear receptor signaling in each of these co-morbidities. Malnutrition also leads to steatosis and predisposes children to life-long increased risks of obesity, type 2 diabetes, and cardiovascular diseases via epigenetic changes. We use molecular approaches to decipher underlying mechanisms and propose novel treatments.

Malnutrition-Associated Gastrointestinal Dysmotility - Malnutrition slows gastric emptying and small bowel motility, which could contribute to growth impairment by promoting bacterial overgrowth, bloating, and decreased appetite. We are pursuing the molecular basis of these clinical findings in mouse models. We measure whole intestinal transit time with carmine red gavage; colonic motility via bead expulsion assay; and gastric emptying, small bowel transit, and intestinal permeability with fluorescent techniques. We also examine enteric nervous system structure with light, deconvolution, and confocal microscopy; intestinal tone and contractility with ex vivo force transduction assays; and propulsive transit with spatiotemporal mapping of ex vivo organ preparations.

The Microbiome of Malnutrition - Malnutrition alters gut microbial communities in a way that further impairs growth. We explore diet-host-microbial interactions in the intestinal lumen and mucus layer using in vivo and in vitro models. With a combination of whole metagenomic DNA sequencing with advanced bioinformatics, microbial metabolite profiling, fluorescent microscopy, and germ-free and gnotobiotic mouse models, we seek to understand how diet influences the structure and function of the developing gut microbiome, and how these microbiome changes ultimately affect growth.

Email: geoffrey.preidis@bcm.edu

Recent Publications


The Pediatric Gastroenterology Research Lab was established in 2007. It is co-directed by Yuying Liu, Ph.D., Med., Assistant Professor, and J. Marc Rhoads, M.D., Professor and Division Head of Gastroenterology.

Since 2007, our basic research has been focusing on mechanisms of neonatal necrotizing enterocolitis (NEC) which is the leading cause of gastrointestinal morbidity in premature infants. We have found the critical roles of Toll-like receptor (TLR) and TLR-signaling regulators and mediators, as well as an imbalance of Foxp3+ regulatory T (Treg) and effort memory T (Tem) cell, which promote the development of NEC. In addition, we have been studying the effects of probiotic Lactobacillus reuteri (LR) strains on the development of NEC. Our studies showed the LR reduced the incidence and severity of NEC in animal models via modulation of TLR4 and NFKB signaling in the intestine. LR also causes aredistribution to the Tcell subsets in the intestinal mucosa.

Recently, we observed the LR markedly prolong the survival of Foxp3-deficient scurfy (sf) mice, which may provide evidence for using probiotic LR to treat patients with IPEX syndrome (immune dysregulation, polyendocrinopathy, enteropathy, X-linked) or patients with other autoimmune diseases. We are investigating changes in the microbiota produced by this disease and severe changes in the fecal and plasma metabolic profile. The changes seen are markedly modified by oral L. reuteri treatment.

Drs. Liu & Rhoads also are actively investigating the mechanisms by which LR regulates intestinal inflammation invitro and animal models. The project is designed to investigate how mucosa dendritic cells and Tcells (TH1, TH17, and Tregs) respond to probiotics, and which cells control gastrointestinal inflammation of the newborn. Moreover, we will show if LR treatment increases fecal microbial richness and diversity and alters their metabolic products, in order to understand local systemic beneficial effects. Ultimately, we hope to provide novel insight into the mechanisms of how probiotics regulate neonatal intestinal inflammation.

In our clinical research on colic, which we showed to be an inflammatory condition in babies who cry excessively, we were first to demonstrate elevated fecal calprotectin in this population, indicating that there is an intestinal inflammation in these babies. We are analyzing the microbiota and fecal calprotectin in babies treated with L. reuteri versus placebo in a “road to discovery” trial.

Email: j.marc.rhoads@uth.tcm.edu
Emerging Concepts in Gut Microbiome - Enteric Nervous System Function and Disease

TOR SAVIDGE
Associate Professor
Texas Children's Microbiome Center
Department Pathology and Immunology
Baylor College of Medicine

Dr. Savidge's laboratory is focused on several emerging research concepts, centering on gut microbiota interactions with the enteric nervous system in the induction of intestinal disease. As principal investigator of an independently NIH funded GI research laboratory focusing on neuroimmune-microbe interactions, research efforts are focused on microbial metabolites and neurotransmitter signals that regulate Clostridium difficile pathogenesis. Recent investigative efforts include the discovery of novel small molecule activators and inhibitors of bacterial toxins, and mechanisms of neurotoxin action (Nature Medicine (2011) 17:1136-41). Dr. Savidge was one of the first to report C. difficile toxin B as the major virulence factor in human intestine and research is now focused on understanding how these toxins interact with the host as a way of identifying new approaches to inhibit the disease (Gastroenterology (2003) 125:413-420). Identification of novel small molecule functions in patient specimens has been facilitated by microbiome and metabolomics studies in the Texas Children's Microbiome Center. Recently, these studies led to the new discovery that protein-ligand interactions with bulk water can influence binding affinity and enzyme catalysis (Science (2015) 349:936-938).

Another emerging research concept that Dr. Savidge has actively pioneered is the involvement of the enteric nervous system in intestinal inflammation, notably a previously unappreciated protective role for glial cells in the gut. Enteric glia represent an extensive but poorly characterized cell lineage in the enteric nervous system. Although previously regarded as passive support cells for enteric neurons, there is now an emerging recognition that enteric glia directly regulate enteric nervous system function and mucosal homeostasis. Dr. Savidge’s research played a central role in establishing these novel glial cell concepts, and was the first to demonstrate fulminant intestinal inflammation resulting from loss of glia in the intestine (Cell (1998) 93:189-201 & PNAS (2001) 98:13306-13311). Since then, he has been actively investigating the functional analogy between glial regulation of barrier function in the gut and blood brain barrier, identifying nitric oxide derivatives known as S-nitrosothiols as glial-derived protective molecules in the intestine (Gastroenterology (2007) 132:1344-1358). To study the biology of these nitric oxide derivatives, new systems biology tools have been developed in the Texas Children’s Microbiome Center and are being applied to identify new microbiota S-nitrosothiol signals.

Email: Tor.Savidge@bcm.edu
Benjamin Shneider is a Pediatric Hepatologist with basic research expertise in intestinal gene regulation, bile acid transport and mechanisms of cholestasis. He is actively involved in clinical and translational investigations of liver diseases in children. Dr. Shneider’s leadership goal is to leverage the wide-ranging clinical and research expertise of an exceptionally talented section to provide compassionate, state-of-the-art, discipline-leading and evidence-based care for children with all types of gastrointestinal, hepatic, pancreatic and nutritional disorders. Rapidly-paced advances in biomedical knowledge provide an unprecedented opportunity to simultaneously advance both clinical care and the science of medicine. As Chief of Pediatric Gastroenterology, Hepatology and Nutrition at Texas Children’s Hospital and Baylor College of Medicine, Dr. Shneider will encourage and lead expanding activities in both education and research in order to optimally capitalize on these rapidly paced biomedical advances.

Dr. Shneider’s primary area of basic investigation focuses upon the complex molecular mechanisms involved in the regulation of intestinal bile acid transport. Intestinal reabsorption of bile acids, mediated by the apical sodium dependent bile acid transporter (ASBT = SLC10A2), plays a critical role as a pivotal control point for not only bile acid homeostasis through its effects on the enterohepatic circulation of bile acids, but also in regulating ileal and colonic metabolic signaling in response to bile acids. Dr. Shneider’s laboratory has explored the regulated responses of ASBT to changes in bile acid homeostasis, signaling by growth factors and inflammatory cytokines and during normal ontogeny. Dr. Shneider is also actively involved in clinical investigation of various pediatric liver diseases (e.g. biliary atresia, familial cholestasis, acute liver failure and sclerosing cholangitis). He has been a principal investigator in the Childhood Liver Disease Research Network since its inception in 2002. Juxtaposition of his basic and clinical research expertise has led to novel translational inquiries into cholestatic liver disease, especially Byler’s Disease. Dr. Shneider has consistently pursued advances in evidence-based approaches to the diagnosis and treatment of pediatric liver disorders with particular interest in issues related to chronic cholestasis, cirrhosis and portal hypertension.

Email: Benjamin.Shneider@bcm.edu
My laboratory is focused on understanding the mechanisms that control intestinal development and homeostasis, and translating this knowledge into novel therapeutic approaches to treat diseases of the intestine such as IBD and colorectal cancer. My laboratory has elucidated roles for epithelial transcription factors such as Atoh1 (Math1), Gfi1, and Spdef in development and differentiation of the intestine. Moreover, my laboratory has translated these findings to human diseases, by showing that Atoh1 and its target Spdef are tumor suppressors that are frequently silenced in colon cancers, and that these genes are essential targets of Notch inhibitory drugs. In addition to these mechanistic studies, we have recently developed novel organ culture methods to direct differentiation of human pluripotent stem cells into intestinal tissue to study intestinal development and disease, and we have used intestinal stem cell-derived organoids in quantitative assays to evaluate intestinal stem cell activity.

Email: noah.shroyer@bcm.edu

Recent Publications


Up to 20% of school-age children from around the world meet the criteria for recurrent abdominal pain. The primary research interests in our laboratory are these functional gastrointestinal disorders in children with a focus on functional abdominal pain and irritable bowel syndrome. Our goals are to understand the factors contributing to the development of these conditions and to develop effective treatments and management strategies. We are addressing these disorders using a multidisciplinary approach involving collaboration between basic scientists, clinical researchers, psychologists, and other healthcare workers.

Studies being carried out include characterizing:

a) The gastrointestinal microbial contribution to symptoms;
b) The contribution of alterations in immune function to the expression of pain;
c) The role of low-grade gastrointestinal inflammation in producing gastrointestinal symptoms;
d) The psychological contributions to pain experience; and
e) The genetic contributions to these conditions.

Trainees are exposed to various general aspects of clinical research (study design, IRB preparation, data analysis) as well as aspects specific to Pediatric Gastroenterology (e.g., gastroenterologic function testing.)

Email: rshulman@bcm.edu

Recent Publications


Chronic infection with hepatitis B virus (HBV) affects over 400 million people worldwide and is a significant risk factor for severe liver disease, including hepatocellular carcinoma (HCC). The role of HBV in mediating carcinogenesis is complex. The Slagle Laboratory studies HBx, a small HBV-encoded protein that is required for virus replication in vivo and is a cofactor for tumorigenesis in transgenic mice. Results from our laboratory and others have shown that the interaction of HBx with cellular damaged DNA binding protein (DDB1) is essential for virus replication. DDB1 is an adaptor protein for the CUL4-DDB1 E3 ligase (CRL4) complex. E3 ligases are multi-unit protein complexes present in all cells, and are responsible for recruiting short-lived proteins for destruction. Many viruses, including HBV, specifically bind to CRL4 in order to alter the spectrum of cellular proteins targeted for degradation. Our goal is to understand how HBx binding to DDB1 alters the normal CRL4 structure and/or function. DDB1 regulates such diverse cellular function as DNA replication, cell cycle, the damaged DNA repair response, and innate immunity. We hypothesize that when HBx interacts with DDB1, it alters some normal DDB1 function that leads to increased virus replication. The identification of such functions may aid in the design of novel antivirals that could halt chronic HBV replication and prevent HCC.

Email: bslagle@bcm.tmc.edu

Recent Publications


Recent Publications

Bile Acid Profiles in Pediatric Patients who Received FMT for Clostridium difficile Infection. Tessier, Mary Elizabeth McConnell1; Ihekweazu, Faith O; Nagy-Szakal, Dorothy; Crews, Jonathan; Ross, Cana; Gezguen, Numan; Koo, Heon-mo; Vinter, Michael; Luna, Ruth Ann; Versalovic, James; Kellermayer, Richard; Savidge, Tor. NASPGHAN Annual Meeting, Washington DC. 2015.

Mary Elizabeth M Tessier, Helen Andersson, Cana Ross, Alex Peniche-trujillo, Sara Dann, Michael Francis, Joseph Sorg, Sundararajah Thevananther, Margaret E Conner, Tor Savidge. Obeticholic acid (INT-747) confers disease protection against Clostridium difficile infection. Poster Presentation at DDW, Washington D.C. 2015. Winner of AGA/AGA-GRG Fellow Abstract Prize.


My laboratory is interested in the enterohepatic circulation and cross-talk between the gut microbiome and hepatic function and health. The farnesoid X receptor (FXR)-fibroblast growth factor 19 (FGF19) signaling pathway is an enterohepatic feedback loop for bile acid homeostasis. Bile acids are reabsorbed in the ileum and activate FXR resulting in FGF19 secretion from intestinal epithelial cells. Portal circulation of FGF19 to hepatocytes inhibits CYP7A1, the rate limiting enzyme in bile acid synthesis from cholesterol. Through the study of C. difficile infection, we have examined the role of microbial dysbiosis on bile acid homeostasis via examination of enterohepatic biomarkers. Our studies show that C. difficile may exploit the FXR-FGF19 pathway to promote its virulence.

An overarching question is: does microbial dysbiosis alter this feedback loop? I hope to expand our knowledge of the gut microbiome and metabolome in regards to hepatic health, especially in pediatric cholestatic diseases. I plan to continue my studies in C. difficile and expand research into dysbiosis and metabolic derangement in hepatic and intestinal disease through collaborations with other Pediatric GI faculty. The ultimate goal is to develop treatments for both adult and pediatric liver and intestinal diseases.

Email: metessie@bcm.edu
The major focus of my laboratory is to understand the cellular and molecular mechanisms responsible for the pathogenesis of non-alcoholic fatty liver disorders (NAFLD) and to gain mechanistic insights into key cellular processes responsible for the temporal progression of hepatic steatosis, steatohepatitis (NASH) and hepatocellular carcinoma (HCC). Previous studies in my laboratory have identified the functional significance of extracellular nucleotides and their cognate P2 purinergic receptor signaling in liver regeneration. Extracellular ATP treatment alone was sufficient to induce cell cycle progression in hepatocytes in vitro, and hepatocyte proliferation in response to 70% partial hepatectomy was attenuated in P2Y2-/- mice.

Transient lipid accumulation within hepatocytes is one of the hallmarks of regenerating livers. Interestingly, P2Y2-/- mice subjected to 70% partial hepatectomy had significant defects in lipid accumulation within hepatocytes. Extracellular ATP treatment alone was sufficient to induce cell cycle progression in hepatocytes and hepatocyte proliferation in response to 70% partial hepatectomy was attenuated in P2Y2-/- mice.

Major goals: 1) To identify and characterize cell-specific P2Y2 purinergic signaling critical for the induction of hepatic inflammation, dysregulation of lipid homeostasis and hepatocellular injury in response to high-fat diet; 2) To evaluate the feasibility of P2Y2 purinergic receptor antagonism (with infusion of small molecules) to prevent and reverse NASH in mice; 3) To identify key cellular and molecular mechanisms responsible for the induction early neoplastic changes associated with NASH. These studies will specifically address the impact of dysregulation of P2 purinergic signaling in the pathogenesis of HCC.

Email: sundarat@bcm.edu
Microbiome and Probiotics

JAMES VERSALOVIC
Professor
Department of Pathology & Immunology
Vice Chair of Molecular Pathology and Omics
Head, Department of Pathology
Pathologist-In-Chief
Director, Texas Children’s
Hospital Microbiome Center
Baylor College of Medicine

Recent Publications


The Versalovic laboratory seeks to understand the nature of the human metagenome, the microbiome and how microbial communities impact human health and disease. The primary topics of interest in terms of physiology and disease are mucosal immunity, inflammation, nutritional genetics, and the enteric nervous system.

Metagenomics and the Human Microbiome

The laboratory is deeply engaged in the development of new strategies to characterize the composition and dynamics of the human microbiome. Refinement of DNA sequencing and molecular approaches are being deployed to understand the nature of mucosal-associated microbial communities. Currently, we are trying to characterize the intestinal microbiome and the nature of the core microbiome in healthy children. In parallel, we are also studying the changes in the metagenome that may be associated with disorders of mucosal inflammation and recurrent abdominal (visceral) pain. The tools for analysis include multi-omics, enteroids, and mouse models to study the metagenome and human-associated microbial communities.

Neuro-Immunology, Pain, and Inflammation - Mammal and Microbes

Many patients suffer from chronic disorders of inflammation and chronic pain disorders. Our laboratory has chosen to study intestinal inflammation and abdominal pain as opportunities to gain deeper insights into how specific microbes and the microbiome affect the pathophysiology of chronic diseases. With respect to inflammation, mouse colitis models and patients with inflammatory bowel disease (IBD, Crohn's disease) are being studied in order to examine how fluctuations in metagenomes and microbial transcriptomes may affect patterns of mucosal immunity and immune signaling pathways.

Cancer Prevention, Nutrition and the Microbiome

New projects are being developed for exploration of changes in the mammalian microbiome and how the metagenome may help us develop new strategies important for cancer prevention and human nutrition. Already, vitamin biosynthesis and other nutrient pathways have been identified in selected commensal microbes that may have implications for human nutrition.

Bacterial-Host Genetics - Systems Biology - Metabolic Modeling

The laboratory has used a model commensal model organism, Lactobacillus reuteri, in order to study how microbes regulate signaling pathways in mammalian cells (mouse and human). Gene expression profiling of commensal bacteria by next generation sequencing has enabled the laboratory to study key genes and pathways in prokaryotes that may provide signals or mediators of microbial:host interactions. Targeted and random mutagenesis strategies are being refined to explore biological pathways in microbial genomes and the metagenome and how these microbial signaling networks may be related to the dynamics of mucosal immunity and neurobiology in mouse models and human patients. New probiotics may be engineered or selected for therapeutic applications.

Email: jamesv@bcm.edu
My laboratory studies nuclear receptor in inflammatory bowel disease (IBD) and develops new drugs for IBD patients. We are working on basic and translational projects designed to establish how nuclear signaling affects bowel inflammation and vice versa. Our goal is to explore new therapeutic molecules to treat IBD patients in the future. We have used transgenic mice to establish murine IBD models to address clinically-relevant problems in pediatric gastroenterology. Investigations involve analyses of biological samples from enteroid cultures in vitro and mice in vivo, using histology, RNAscope, immunohistochemistry, real-time PCR, primeFLOW, ELISA, Western blot, spectrophotometry, and gel electrophoresis.

Our current project seeks to define nuclear receptor liver receptor homolog 1 (LRH-1) activation and its downstream effects in bowel inflammation. Our objectives are to investigate how LRH-1 signaling modulates inflammation and to develop therapeutic strategies that target localized steroidogenesis in the intestinal epithelia of patients with IBD. The nuclear receptor LRH-1 is expressed in intestinal epithelia and can drive local production of glucocorticoids and cellular proliferation in response to inflammatory stress. Our laboratory previously identified dilauroyl phosphatidylcholine (DLPC) as an extrinsic agonist for LRH-1. My preliminary results show that DLPC-driven activation of LRH-1 significantly reduces disease activity in both DSS and T-cell transfer model of IBD. It also induces the expression of the steroidogenic enzymes Cyp11A1 and Cyp11B1, and a new LRH-1 target gene Twist1.

To critically test the function of the human nuclear receptor, we have set up cultures of human enteroids generated from ileal or colonic biopsy samples of patients with IBD and have generated humanized mice that express human LRH-1 instead of the endogenous mouse Lrh-1 gene in the enterocytes. We hypothesize that optimal DLPC treatment in these human enteroids and humanized LRH-1 mice will have beneficial effects in DSS or T-cell transfer-induced IBD murine models through a Twist1 and GR-dependent anti-inflammatory program. To test this hypothesis, we aim to: (1) genetically define the roles of Twist1 and GR in the local anti-inflammatory feed forward network; (2) optimize therapeutic effects of DLPC in hLRH-1 mice with IBD; (3) define the response of DLPC treatment in human enteroids. Expected outcomes are an enhanced understanding of LRH-1 signaling in IBD and a near-term clinical trial of a new class of therapeutics for IBD.

Email: hwang@bcm.edu
The main focus of my lab is the use of genetic and cell biological and biochemical approaches to explore the pathogenesis of polyglutamine neurodegenerative diseases, the function of Math1 in neurodevelopment, and how MECP2 mutations cause postnatal neurodevelopmental disorders have been discovered parallels between neural and intestinal differentiation, which led us to study specification in the developing intestine. In the area of neurodevelopment, we have published work on the molecular pathogenesis of several spinocerebellar ataxias (SCAs) and the role of Math1 in neuronal fate.

My lab currently has three main projects: 1) Studying mouse models of SCAs, to identify common pathogenic mechanisms in these related diseases. 2) Studying mice with engineered mutations in MeCP2 (the gene that causes Rett syndrome). 3) The study of the gene Math1 (Atoh1), which governs the development of multiple components of the proprioceptive pathway as well as cerebellar granule cells and hair cells in the inner ear. Somewhat surprisingly, Math1 also determines the ability of stem cells to differentiate into secretory cells (as opposed to absorptive cells) in the mouse intestine, My group reported that mice lacking Math 1 have no secretory lineages in the intestinal epithelium (Science 2001). Moreover, we started to investigate differentiation events downstream of Math1 in the intestine, discovering that Gfi1 functions after Math1 to specify the different secretory cells (Shroyer et al., 2007). As these mice die at birth, the lab has created a new conditional allele that allows deletion of Math1 only in the gut in order to study the role of Math1 in the postnatal intestine and begin to identify downstream targets of this transcription factor.

We also created mice that have Math1-flag tagged allele that allowed us to identify Math1/Atoh1 targets in cerebellar granule precursors. We are using these mice to identify the targets of Math1 with other cells that require Math1 for genesis and specification.

Email: hzoghbi@bcm.edu
ELIGIBILITY CRITERIA

ELIGIBILITY CRITERIA FOR CERTIFICATION IN PEDIATRIC GASTROENTEROLOGY (12/09)

Please refer to the American Board of Pediatrics website for complete details.

INFORMATION FOR ALL CERTIFYING EXAMINATIONS

An applicant must satisfactorily complete the standard length of training before the first day of the month in which the examination is administered. An applicant whose contracted training period does not expire before the first day of the month of the examination will not be eligible for that examination, even if all formal training has been completed earlier and the remaining time is used only for leave.

GENERAL CRITERIA FOR CERTIFICATION IN THE PEDIATRIC SUBSPECIALTIES

In addition to the training requirements, which are specific to each of the pediatric subspecialties, the following are required of candidates seeking certification in the pediatric subspecialties of adolescent medicine, cardiology, child abuse pediatrics, critical care medicine, developmental-behavioral pediatrics, emergency medicine, endocrinology, gastroenterology, hematologic-oncology, infectious diseases, neonatal-perinatal medicine, nephrology, pulmonology, and rheumatology. Each candidate must be familiar with specific subspecialty training requirements as well as the current rules and regulations in A Guide to Board Certification – Booklet of Information.

A. Certification by the American Board of Pediatrics (ABP)

A candidate for subspecialty certification must have achieved initial certification in general pediatrics and continue to maintain general pediatrics certification in order to take a subspecialty examination. No exceptions to this policy will be granted. The requirements for Maintenance of Certification (MOC) can be found on the ABP website. All candidates are urged to ensure that the requirements for maintenance of certification will be met in sufficient time to allow acceptance to the subspecialty certifying examination. Under certain circumstances, individuals registered for the general pediatrics certifying examination may apply for a pediatric subspecialty certifying examination pending notification of the general pediatrics examination results. Before making application, contact the ABP for information.

B. Licensure

An applicant must hold a valid, unrestricted allopathic and/or osteopathic medical license in at least one jurisdiction in the United States, its territories, or Canada. If licenses are held in more than one jurisdiction, all licenses held by a physician should meet this requirement. Temporary or training licenses are not acceptable. Individuals practicing exclusively abroad, i.e., who are not practicing in the United States or Canada, and who do not hold a United States or Canadian license, must provide proof of licensure in the country in which they practice. Applicants for initial certification who intend to practice abroad exclusively must submit a letter stating this fact. In addition, they must submit proof of licensure in the country in which they intend to practice.

C. Verification of Training

Applicants are required to complete training in programs accredited by the Accreditation Council for Graduate Medical Education (ACGME) in the United States or by the Royal College of Physicians and Surgeons of Canada. Those completing training in the United States must have been formally enrolled in the training program and reported annually as a fellow to ACGME and the ABP. An applicant will be asked to list the program(s) where fellowship training occurred as well as the name(s) of the program director(s). The ABP will provide a Verification of Competence Form to the program director(s) for completion. (Note: For new subspecialties, alternatives to the usual training requirements, such as practice experience, will be acceptable as criteria for admission to the examination. Candidates should refer to the specific subspecialty eligibility criteria for details.) The role of the program director in the certification process is to verify training, evaluate clinical competence including professionalism, and provide evidence of the trainee's scholarly activity/research.

The ABP will provide no credit for a year in which clinical competence has been rated as unsatisfactory and will require a repeat year of training. A marginal evaluation in clinical competence indicates the need for remediation of certain portions of clinical training. A trainee may be advanced to a higher level of training under these circumstances as remediation is provided. It is expected that the next year of training will result in a satisfactory evaluation for clinical competence in order for full credit to be provided for the marginal year of training. Two
consecutive marginal evaluations require a repeat year of training. An applicant must have the verification form(s) on file at the ABP in order to be admitted to the subspecialty examination. If an applicant's training is not verified or if the applicant receives an unsatisfactory evaluation in any of the competencies (with the exception of professionalism alone), the applicant will be required to complete an additional period of subspecialty fellowship training before reapplying. The director of the program where the additional training occurred must complete a separate Verification of Competence Form. If the unsatisfactory evaluation is in professionalism only, the applicant will be required to complete an additional period of fellowship training or, at the program director's recommendation and at the ABP's discretion, a period of observation may be required in lieu of additional training. A plan for remediation must be submitted for review and approval by the ABP.

Applicants who wish to appeal evaluations must proceed through institutional due process mechanisms. The ABP is not in a position to reexamine the facts and circumstances of an individual's performance. An applicant must satisfactorily complete all subspecialty training before the first day of the month in which the examination is administered. An applicant whose contracted training period does not expire before the first day of the month of the examination will not be eligible for that examination, even if all formal training has been completed earlier and the remaining time is used only for leave. No credit will be given for subspecialty training during the core general pediatric residency or a chief residency.

An applicant seeking certification in another pediatric subspecialty or a non-ABP specialty (e.g., allergy/immunology) on the basis of practice and/or training may not apply the same period of time toward fulfillment of these requirements.

D. Scholarly Activity/Research
The ABP requires scholarly activity during fellowship training. The requirement accommodates a wide variety of academic scholarly activities. The scholarly activity training requirements (as outlined in Section E (below) apply to all fellows beginning subspecialty training July 1, 2004, and thereafter. Those fellows who began training prior to this date must meet the requirement for meaningful accomplishment in research, which was in place at the time they entered training. Contact the ABP for more information.

The program director is responsible for notifying all fellows of the scholarly activity requirements necessary for certification upon entry to the subspecialty training program. Furthermore, in the description of the candidate's scholarly activity performance on the Verification of Competence Form, the program director must provide a description of the experiences on which the acceptable evidence of scholarly activity is based.

E. Principles Regarding the Assessment of Scholarly Activity (for those who began training July 1, 2004, and thereafter)
All fellows must participate in a core curriculum in scholarly activities. This curriculum should provide skills that lead to an in-depth understanding of biostatistics, clinical and laboratory research methodology, study design, preparation of applications for funding and/or approval of clinical or research protocols, critical literature review, principles of evidence based medicine, ethical principles involving clinical research, and the achievement of proficiency in teaching. In addition to participating in a core curriculum in scholarly activities, all fellows will be expected to engage in projects in which they develop hypotheses or in projects of substantive scholarly exploration and analysis that require critical thinking. Areas in which scholarly activity may be pursued include, but are not limited to: basic, clinical, or translational biomedicine; health services; quality improvement; bioethics; education; and public policy.

In addition to biomedical research, examples of acceptable activities might include a critical meta-analysis of the literature, a systematic review of clinical practice, a critical analysis of public policy, or a curriculum development project with an assessment component. Involvement in scholarly activities must result in the generation of a specific written "work product."

Examples of "work products" include, but are not limited to:

- A peer-reviewed publication in which a fellow played a substantial role
- An in-depth manuscript describing a completed project
- A thesis or dissertation written in connection with the pursuit of an advanced degree
- An extramural grant application that has either been accepted or favorably reviewed
- A progress report for projects of exceptional complexity, such as a multi-year clinical trial
Review of scholarly activity and the written work product will occur at the local level with each Fellow having a Scholarship Oversight Committee responsible for overseeing and assessing the progress of each Fellow and verifying to the ABP that the requirement has been met. The Scholarship Oversight Committee should consist of three or more individuals, at least one of whom is based outside the subspecialty discipline; the Fellowship program director may serve as a trainee's mentor and participate in the activities of the oversight committee, but should not be a standing (i.e., voting) member.

Upon completion of training, the ABP will require:

- Verification from the training program director that the clinical and scholarly skills requirements have been met
- A comprehensive document (i.e., personal statement), written by the Fellow, describing the scholarly activity that includes a description of his/her role in each aspect of the activity and how the scholarly activity relates to the trainee's own career development plan. The Fellow's personal statement, i.e., a comprehensive document written by the Fellow, is integral to the requirement for scholarly activity. This document should be several pages in length and comment on the Fellow's intended career path upon entering Fellowship and reasons for choosing a specific area of scholarly activity. It should describe the scholarly activity and the Fellow's role in each aspect of the activity, as well as any preparation beyond the core Fellowship curriculum needed to ensure successful completion of the project. The personal statement should describe how the scholarly activity furthers the Fellow's career development plan, and should reflect upon the educational value of the pursuit of the project
- The actual "work product" of the scholarly activity as described above
- Signature of the Fellow, program director, and members of the Scholarship Oversight Committee on both the personal statement and work product of the Fellow as described above.

Details of the scholarly activity requirement have been published by the ABP in a document entitled *Training Requirements for Subspecialty Certification* (January 2004), which is downloadable directly from the ABP's Web site. Fellows completing training in RCPSC accredited programs must meet the ABP's requirements for scholarly activity under the mentorship of a Scholarship Oversight Committee, as defined by the ABP above. Scholarly Activity began in the third year of training will not meet the requirement.

F. Miscellaneous Policies/Issues Related to Certification and Training

Transfer of Fellowship Training

While not encouraged for continuity purposes, if a fellow must transfer, the program directors of the current program and the proposed program must communicate to ensure that the fellow who transfers will meet all requirements if he or she desires to apply for a certifying examination in the subspecialty. A Fellow Transfer Information (FT11) form should be completed by the current program director and submitted to the ABP with a copy to the proposed new program. Fellow evaluations should be submitted to the proposed program as well. Months of credit for clinical experience and scholarly activity/research completed must be clearly communicated to the fellow, the new program director, and the ABP. The ABP must be informed of the plan to ensure continued appropriate mentoring for scholarly activity upon transfer, including the role of the Scholarship Oversight Committee. The ABP will send summary evaluations to a new training program if a fellow transfers.

Interruption of Training

Fellows who interrupt fellowship training for greater than 12 continuous months and who wish to re-enter training fellowship training must petition the ABP to determine whether credit may be awarded for prior training. The request for credit must be submitted by the candidate or the fellowship director before the fellow re-enters fellowship training.

Program Requirements for Residency Education in the Subspecialties of Pediatrics

Program Requirements for Residency Education in the subspecialties of pediatrics are approved by the Accreditation Council for Graduate Medical Education (ACGME) or by the Royal College of Physicians and Surgeons of Canada (RCPSC). Program Requirements and a listing of accredited programs may be found on the ACGME website: www.acgme.org, or the RCPSC website: rcpsc.medical.org.
Training Leading to Dual Pediatric Subspecialty Certification

Sequential Dual Training:
If an individual has completed 3 years of training in one subspecialty and the program director has verified both clinical competence and satisfactory completion of scholarly activity, he or she can become eligible to take an examination in a second subspecialty after 2 years of additional training, of which at least 1 year must be broad-based clinical training. The requirement for scholarly activity in the second subspecialty is waived. Individuals approved for subspecialty fast-tracking in the first subspecialty are also eligible for this pathway. This dual training option does not require preapproval by the ABP.

Integrated Dual Training:
An individual and his or her program director(s) may petition the Credentials Committees of two pediatric subspecialties with a proposal for a 4- or 5-year integrated training program that would meet the eligibility requirements for certification in both subspecialties. Petitions for this option must be approved before subspecialty training begins or early in the first year of subspecialty training. Guidelines for dual subspecialty training may be obtained from the ABP or can be found on the ABP website.

Training Leading to Eligibility for Combined (Internal Medicine-Pediatrics) Subspecialty Certification
An individual who has completed internal medicine-pediatrics training should contact the American Board of Internal Medicine and the American Board of Pediatrics regarding opportunities for combined training (i.e., training in both the adult and pediatric subspecialties). Combined training petitions must be submitted prospectively either before training begins or in the first 3 to 6 months of fellowship training and must be approved by both boards. All training in the internal medicine and pediatric subspecialty must be completed in order for an applicant to take a pediatric subspecialty certifying examination. Guidelines for combined training may be obtained from the ABP or can be found on the ABP website.

Subspecialty "Fast-Tracking"
A subspecialty fellow who is believed to have demonstrated accomplishment in research, either before or during residency, may have a part of the training requirement waived. Evidence of such accomplishment might include a PhD in a discipline relevant to the subspecialty or career path of the fellow, or sustained research achievement relevant to the subspecialty or career path of the fellow. The subspecialty program director may petition the Sub-board to waive the requirement for scholarly activity, and to reduce the length of subspecialty training by as much as 1 year. This petition must be made either before the beginning of training or during the first year of training.
A candidate for this pathway must have satisfactorily completed 3 core years of pediatrics or approved combined pediatrics and other specialty training in an accredited program in the US or Canada. This pathway is also available to candidates who have satisfactorily completed at least 3 years of non-accredited general pediatrics training (eg, overseas) and qualified for a waiver of 1 year of general pediatrics training through the Policy Regarding Individuals with Non-Accredited Training. An individual who enters subspecialty training via the Accelerated Research Pathway would not be eligible for subspecialty fast-tracking.
A subspecialty fellow who receives a waiver by the Sub-board must complete at least 2 years of training in the subspecialty with at least 1 year of broad-based clinical training. In order for an individual to be eligible for subspecialty certification, all requirements for general pediatrics certification must be fulfilled.

Time-limited Eligibility for Initial Certification Examinations
Beginning with the examinations administered in 2014, the American Board of Pediatrics will require that applicants have completed the training required for initial certification in the pediatric subspecialties within the previous 7 years (e.g., 2007 or later for examinations administered in 2014). If the required training was not successfully completed within the previous 7 years, the applicant must complete an additional period of supervised practice in order to apply for certification. The subspecialty examinations are offered every other year. Therefore, please note that the pediatric subspecialty examination may not be offered in the year the acceptance expires. The full policy can be found on the ABP website.

Closure of Practice Pathway for Subspecialty Certification
The ABP has established a policy for a closure date for the practice pathway for all subspecialties in which a certificate is offered. The certifying examinations for 2010 were the last examinations for which an individual could apply for certification using practice experience accrued by the deadline stated in the original eligibility criteria when the subspecialty was established. A candidate qualifying for the child abuse pediatrics examination via the practice pathway had until 2013 to apply for certification.

It should be noted that these criteria and conditions are subject to change without notice. All applicants should be familiar with the current Booklet of Information. Applicants are advised to contact the ABP to ascertain whether the information they have is current.
ELIGIBILITY CRITERIA FOR CERTIFICATION IN PEDIATRIC GASTROENTEROLOGY (11/15)

The American Board of Pediatrics (ABP) has established a procedure for certification in pediatric gastroenterology. In addition to the specific admission requirements listed below, General Eligibility Criteria for all ABP Subspecialties [1] must be fulfilled to be eligible for certification.

ADMISSION REQUIREMENTS

Three years of full-time, broad based fellowship training in pediatric gastroenterology are required to be completed in a program accredited for training in pediatric gastroenterology by the Accreditation Council for Graduate Medical Education in the United States or the Royal College of Physicians and Surgeons of Canada. 

No continuous absence of more than 1 year will be permitted. Combined absences/leaves in excess of 3 months during the 3 years of training, whether for vacation, parental leave, illness, and so forth, must be made up. If the program director believes that combined absences/leaves that exceed 3 months are justified, a letter of explanation should be sent by the director for review by the Credentials Committee. Part-time training may be completed over no more than 6 years.

The following must be accomplished in order to become certified in the subspecialty:

- A Verification of Competence Form must be completed by the program director(s) verifying satisfactory completion of the required training, evaluating clinical competence including professionalism, and providing evidence of scholarly activity/research.
- The fellow must meet the criteria stated in the "Principles Regarding the Assessment of Scholarly Activity."
- The fellow must pass the subspecialty certifying examination.

It should be noted that these criteria and conditions are subject to change without notice. All applicants are advised to contact the ABP to ascertain whether the information they have is current.